

ILLUMINA INC
Form 424B2
May 11, 2006

Table of Contents

The information in this prospectus supplement is not complete and may be changed. This prospectus supplement 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(b)(2)
File No. 333-134012

Subject to Completion. Preliminary Prospectus Supplement dated May 11, 2006.

PROSPECTUS SUPPLEMENT TO PROSPECTUS DATED MAY 11, 2006

3,500,000 Shares

Illumina, Inc.

Common Stock

Illumina, Inc. is offering 3,500,000 shares to be sold in the offering.

Our shares are quoted on the Nasdaq National Market under the symbol ILMN. The last reported sale price of our common stock on May 10, 2006 was \$29.50 per share.

See Risk Factors on page S-10 to read about factors you should consider before buying shares of the common stock.

	Per Share	Total
Public offering price	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to Illumina	\$	\$

The underwriters may also purchase up to an additional 525,000 shares from Illumina at the initial price to public less the underwriting discount.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares against payment in New York, NY on _____, 2006.

Goldman, Sachs & Co.

Merrill Lynch & Co.

Cowen and Company

Robert W. Baird & Co.

The date of this prospectus supplement is _____, 2006.

TABLE OF CONTENTS

	<u>Page</u>
<u>Prospectus Supplement</u>	
<u>About this Prospectus</u>	S-1
<u>Prospectus Supplement Summary</u>	S-3
<u>Risk Factors</u>	S-10
<u>Forward-Looking Statements</u>	S-17
<u>Use of Proceeds</u>	S-18
<u>Price Range of Our Common Stock</u>	S-18
<u>Dividend Policy</u>	S-18
<u>Capitalization</u>	S-19
<u>Dilution</u>	S-20
<u>Business</u>	S-21
<u>Management</u>	S-32
<u>Description of Capital Stock</u>	S-34
<u>Underwriting</u>	S-36
<u>Where You Can Find More Information</u>	S-39
<u>Incorporation of Certain Documents by Reference</u>	S-39
<u>Legal Matters</u>	S-40
<u>Experts</u>	S-40
 <u>Prospectus</u>	
<u>About this Prospectus</u>	1
<u>Risk Factors</u>	2
<u>Use of Proceeds</u>	9
<u>Where You Can Find More Information</u>	9
<u>Incorporation of Certain Documents by Reference</u>	9
<u>Legal Matters</u>	10
<u>Experts</u>	10

ABOUT THIS PROSPECTUS

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering. The second part, the accompanying prospectus dated May 11, 2006, gives more general information about our common stock. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any permitted free writing prospectuses we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. Under no circumstances should

the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement or the accompanying prospectus is correct as of any time after the respective dates of such information.

S-1

Table of Contents

Unless the context requires otherwise, the words Illumina, we, company, us and our refer to Illumina, Inc. and its subsidiaries, and the term you refers to a prospective investor.

This prospectus supplement and the documents incorporated by reference into this prospectus supplement include trademarks, service marks and trade names owned by us or others. All trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement are the property of their respective owners. Illumina®, Making Sense Out of Life®, Sentrix®, GoldenGate®, DASL®, Oligator®, BeadArray™, Array of Arrays™, Infinium™, VeraCode™ and BeadXpress™ are trademarks of Illumina and/or one or more of our subsidiaries.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and accompanying prospectus and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include information about the shares we are offering as well as information regarding our business and financial data. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety.

Business Overview

We are a leading developer, manufacturer and marketer of next-generation life science tools and integrated systems for the large scale analysis of genetic variation and biological function. Using our proprietary technologies, we provide a comprehensive line of products and services that currently serve the genotyping and gene expression markets, and we expect to enter the market for molecular diagnostics. Our customers include leading genomic research centers, pharmaceutical companies, academic institutions, clinical research organizations and biotechnology companies. Our tools provide researchers around the world with the performance, throughput, cost effectiveness and flexibility necessary to perform the billions of genetic tests needed to extract valuable medical information from advances in genomics and proteomics. We believe this information will enable researchers to correlate genetic variation and biological function, which will enhance drug discovery and clinical research, allow diseases to be detected earlier and permit better choices of drugs for individual patients.

Our products primarily serve the estimated \$350 million genotyping and \$800 million gene expression markets, which are expected to grow at 40% and 5-10% per year, respectively. We principally focus on the fast-growing genotyping market and are expanding our presence in the gene expression market. Growth in these markets has been primarily driven by technological improvements that have enabled a dramatic reduction in the cost per test, making large scale analysis economically feasible to a broader group of researchers. This has also enabled the ability to perform whole genome genotyping, creating a new market segment and accelerating the growth of the genotyping market. Whole genome genotyping is the ability to examine the genetic variation across the entire genome by interrogating a large number of single base variants, known as single nucleotide polymorphisms (SNPs), in the genetic code. We introduced our first whole genome genotyping products in 2005 and have experienced rapid growth as a result of the differentiated performance of our products. We believe that demand for whole genome genotyping products and services will be driven by continued large association studies by academia, as well as pharmacogenomics research by pharmaceutical and biotechnology companies. Ultimately, we believe genotyping will become the standard of care in clinical practice.

We are able to meet the needs of a wide variety of customers in our target markets by providing flexible and cost effective solutions that are based on our patented and proprietary BeadArray technology. Our BeadArray platform is a modular system which enables researchers to design experiments according to their needs. The platform includes disposable arrays and reagents, instrumentation and software, which is used to control the systems and analyze the results of an experiment.

Our strategy is to make our BeadArray platform the industry standard for products and services utilizing array technologies for genetic analysis. We believe that by continuing to innovate, we can offer customers products with the high throughput, flexibility and customizability that they are seeking, thereby growing both our installed base and corresponding sales of our consumable products. We also believe that the discoveries our technology has enabled will create a significant long-term opportunity for us in molecular diagnostics.

Technology, Products and Services

BeadArray Technology

Our BeadArray technology utilizes microscopic beads that are covered with hundreds of thousands of oligonucleotide (oligo) probes, each a single-stranded length of synthetic nucleic acids. Our Oligator technology enables us to produce the millions of unique oligos that are required to implement our BeadArray technology on a

S-3

Table of Contents

cost-effective basis. Each oligo includes a short address sequence used to identify the individual bead and, in fixed content arrays, also includes another sequence, or probe, that is used to hybridize to the genomic or ribonucleic acid area of interest. To form an array, we randomly draw hundreds of thousands of coated beads into microwells, which contain on average between 15 and 30 copies of each bead type. Because the coated beads assemble randomly into the wells, we identify the position of each individual bead on the array by performing a final procedure called positional decoding, which uses the address portion of the oligo sequence to identify each bead type and location. This proprietary decoding procedure enables us to test the functionality of each bead in every microwell on every array during our manufacturing process which ensures that each array we ship to customers is of the highest quality. In addition, since our arrays contain multiple copies of a given bead type, the reliability and accuracy of the resulting data is significantly improved by allowing statistical processing of the results of identical beads. We believe we are the only microarray company to provide this level of quality control in the industry. In addition, our manufacturing process allows us to create highly customizable arrays in our two array formats, the Sentrix BeadChip and Sentrix Array Matrix.

Sentrix BeadChip and Sentrix Array Matrix

Researchers whose experiments require an examination of a large number of data points across a small number of samples use our Sentrix BeadChips, which provide a high level of multiplexing capability for both SNP genotyping and gene expression studies. Sentrix BeadChips are patterned silicon chips about the size of a microscope slide. Coated microbeads randomly assemble themselves into microwells on the silicon wafer and follow the process described above for positional decoding. The flexibility of the Sentrix BeadChip format has enabled us to develop products that can currently be used to examine up to 16 samples per chip and analyze over 500,000 genetic sequences for a given sample. For example, our latest product, the HumanHap550, allows researchers to investigate more than 550,000 SNPs per array.

For researchers examining fewer data points across many samples, our Sentrix Array Matrix combines high throughput with an extremely cost-effective format. This format contains 96 fiber optic bundles which can interrogate 1,536 unique data points and are arranged in the standard microtiter plate format. This standardized format allows researchers to conduct high throughput experiments for 96 samples simultaneously and can be easily automated using standard robotic equipment, further increasing throughput and productivity.

Infinium, GoldenGate and DASL Proprietary Assays

Our proprietary assay technologies allow users to take advantage of the BeadArray platform. We have three key assays:

Infinium A whole-genome genotyping assay designed to interrogate a large number of SNPs at unlimited levels of loci multiplexing;

GoldenGate A genotyping assay designed for lower level multiplexing; and

DASL A gene expression assay designed for focused gene studies and compatible with degraded RNA samples typical of formalin-fixed paraffin-embedded tissue samples, which are often used in oncology research.

Instrumentation

Our two array formats can be scanned with our BeadArray reader, which is the central component of our BeadStation and BeadLab systems. The BeadArray reader is a confocal laser scanner capable of scanning multiple high-density

array formats. The BeadStation system is designed as a benchtop solution that can be expanded to achieve any required level of throughput. The BeadLab system is a turnkey solution, comprised of our BeadStation system, our automation options, our Laboratory Information Management System (LIMS) and significant additional components to fully equip a laboratory to process millions of assays per day.

S-4

Table of Contents**SNP Genotyping Services**

In conjunction with our sales of products for genotyping, we also provide SNP genotyping services based on our products and technologies to customers across various markets. We have had peak days in which we have generated more than 40 million SNP genotypes. To our knowledge, no other SNP genotyping platform can achieve comparable levels of throughput while delivering such high accuracy and low cost.

VeraCode Technology

The BeadArray technology is most effective in applications which require mid to high levels of multiplexing from low to high levels of throughput. We believe the molecular diagnostics market will require systems which are extremely high throughput and cost effective in the mid- to low-multiplex range. To address this market, we acquired the VeraCode technology through our acquisition of CyVera Corporation in April 2005. Based on digitally encoded microbeads, VeraCode enables low-cost multiplexing from 1 to 384-plex in a single well. We plan to implement the VeraCode technology using our newly designed BeadXpress System and our existing assays. We believe that this system will be the ideal platform for creating lower multiplex genotyping, gene expression and protein-based assays. In the research market, we expect our customers to utilize our BeadArray technology for their higher multiplex projects and then move to our BeadXpress system for their lower multiplex projects utilizing the same assays and informatics infrastructure. Additionally, we believe that the cost and multiplex advantages of the BeadXpress system using our VeraCode technology will be especially appealing in the molecular diagnostics market. We expect to launch the BeadXpress system before the end of 2006 along with several assays for the system.

Selected Current and Future Products

Application	Assay/Method	Array Format	Product Configurations
SNP Genotyping	GoldenGate (96, 384, 768, 1,536 Multiplex)	Array Matrix	Custom Assays Linkage V4 MHC Panel Cancer Panel Mouse Linkage
	Infinium (Unlimited Multiplexing)	BeadChip	Human-1 HumanHap300, HumanHap240S, HumanHap550 Copy Number Polymorphism analysis
Gene Expression	Whole Genome (Direct Hybridization)	BeadChip	Human 6, Human RefSeq 8 Mouse 6, Mouse RefSeq 8
	Focused Sets (High Sample, Moderate Number of Genes)	Array Matrix	96 Samples × 1,400 Genes
	DASL (Paraffin-Embedded)	BeadChip	16 Samples × 1,400 Genes
		Array Matrix	1,536 User-defined genes Universal array

	Samples)		
SNP Genotyping / Gene Expression / Protein Analysis	GoldenGate Custom Assays	VeraCode Technology (2006 launch)	1 384 multiplex custom SNP genotyping Molecular Diagnostic Products Proteomics

S-5

Table of Contents

Key Advantages of Our Technology

We believe that our technology provides distinct advantages, in a variety of applications, by creating cost effective, highly miniaturized arrays and turnkey systems with the following features:

High Throughput. The miniaturization of our BeadArray technology provides very high information content per unit area. To increase sample throughput, we have formatted our array matrix in a pattern arranged to match the wells of standard microtiter plates, allowing throughput levels of up to nearly 150,000 unique assays per microtiter plate, and we use laboratory robotics to speed process time. Similarly, we have patterned our whole-genome expression BeadChips to support up to 48,000 gene expression assays for six samples with each BeadChip. Our Infinium assay is supported by full automation and LIMS to address high throughput laboratories.

Cost Effectiveness. Our array products substantially reduce the cost of our customers' experiments as a result of our proprietary manufacturing process and our ability to capitalize on cost reductions generated by advances in fiber optics, plasma etching processes, digital imaging and bead chemistry. In addition, our products require smaller reagent volumes than other array technologies, thereby reducing reagent costs for our customers. Our Oligator technology further reduces reagent costs, as well as our cost of coating beads.

Flexibility. We are able to offer flexible solutions to our customers based on our ability to attach different kinds of molecules, including DNA, RNA, proteins and other chemicals, to our beads. In addition, we can have BeadChips manufactured in multiple shapes and sizes with wells organized in various arrangements to optimize them for different markets and market segments. In combination, the use of beads and etched wells provides the flexibility and scalability for our BeadArray technology to be tailored to perform many applications in many different market segments, from drug discovery to diagnostics. Our Oligator technology allows us to manufacture a wide diversity of lengths and quantities of oligos.

Quality and Reproducibility. The quality of our products is dependent upon each element in the system, the array, the assay used to perform the experiment and the instrumentation and software used to capture the results. Each array is manufactured with a high density of beads, which enables us to have multiple copies of each individual bead type. We measure the copies simultaneously and combine them into one data point. This allows us to make a comparison of each bead against its own population of identical beads, which permits the statistical calculation of a more reliable and accurate value for each data point. Finally, the manufacture of the array includes a proprietary decoding step that also functions as a quality control test of every bead on every array, improving the overall quality of the data. When we develop the assays used with our products, we focus on performance, cost and ease of use. By developing assays that are easy to use, we can reduce the potential for the introduction of error into the experiment. We believe that this enables researchers to obtain high quality and reproducible data from their experiments. Additionally, we manufacture substantially all of the reagents used in our assays, allowing us to control the quality of the product delivered to the customer.

Our Corporate Information

We were incorporated in California in April 1998 and reincorporated in Delaware in July 2000. Our principal executive offices are located at 9885 Towne Centre Drive, San Diego, California 92121, and our telephone number is (858) 202-4500. We maintain an Internet website at www.illumina.com. We have not incorporated by reference into this prospectus supplement or accompanying prospectus the information in, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus supplement or accompanying prospectus.

Table of Contents

The Offering

Common stock we are offering	3,500,000 shares
Common stock outstanding as of April 2, 2006, as adjusted for this offering	45,196,733 shares
Risk factors	See Risk Factors on page S-10 and the other information included or incorporated by reference in this prospectus supplement or accompanying prospectus for a discussion of the factors you should consider before you make an investment decision.
Nasdaq National Market symbol	ILMN
Use of proceeds	See Use of Proceeds on page S-18 for information on how we expect to use the net proceeds from this offering.

The number of shares of our common stock outstanding as adjusted for this offering is based on 41,696,733 shares outstanding as of April 2, 2006 and excludes:

8,139,647 shares of our common stock issuable upon exercise of options outstanding as of April 2, 2006, at a weighted average exercise price of \$9.91 per share, of which options to purchase 2,792,545 shares were exercisable as of that date; and

6,879,757 shares of our common stock available for future grant under our equity incentive plans as of April 2, 2006.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to 525,000 additional shares of our common stock.

Table of Contents**Summary Consolidated Financial Data**

The following summary consolidated financial data for each of the three fiscal years ended January 1, 2006, January 2, 2005 and December 28, 2003 is derived from our audited consolidated financial statements incorporated by reference into this prospectus supplement. The following summary consolidated financial data as of April 2, 2006 and for the three months ended April 2, 2006 and April 3, 2005 is derived from our unaudited interim condensed consolidated financial statements, which are incorporated by reference into this prospectus supplement.

This information is only a summary and should be read together with the consolidated financial statements, the related notes and other financial information incorporated by reference into this prospectus supplement and on file with the SEC. For more details on how you can obtain our SEC reports incorporated by reference into this prospectus supplement, see [Where You Can Find More Information](#).

	(Unaudited)				
	Year Ended	Three Months Ended			
	January 1, 2006	January 2, 2005	December 28, 2003	April 2, 2006	April 3, 2005
	(in thousands, except per share data)				
Statement of Operations Data					
Revenue:					
Product revenue	\$ 57,752	\$ 40,497	\$ 18,378	\$ 23,261	\$ 12,165
Service and other revenue	13,935	8,075	6,496	5,267	2,691
Research revenue	1,814	2,011	3,161	574	292
Total revenue	73,501	50,583	28,035	29,102	15,148
Costs and expenses:					
Cost of product revenue	19,920	11,572	7,437	7,676	3,937
Cost of service and other revenue	3,261	1,687	2,600	1,617	662
Research and development	27,809	21,462	23,800	8,216	5,893
Selling, general and administrative	28,158	25,576	20,064	12,134	6,035
Acquired in-process research and development	15,800				
Litigation judgment (settlement), net		(4,201)	756		
Total costs and expenses	94,948	56,096	54,657	29,643	16,527
Loss from operations	(21,447)	(5,513)	(26,622)	(541)	(1,379)
Interest and other income (loss), net	573	(712)	(441)	568	195
Income (loss) before income taxes	(20,874)	(6,225)	(27,063)	27	(1,184)
Provision for income taxes				131	51
Net loss	\$ (20,874)	\$ (6,225)	\$ (27,063)	\$ (104)	\$ (1,235)
Net loss per share, basic and diluted	\$ (0.52)	\$ (0.17)	\$ (0.85)	\$ 0.00	\$ (0.03)
Shares used in calculating net loss per share, basic and diluted	40,147	35,845	31,925	41,475	38,347

On January 1, 2006, we adopted Statement of Financial Accounting Standards (SFAS) No. 123R (revised 2004), *Share-Based Payment*. We have elected to use the modified prospective transition method as permitted by SFAS No. 123R and, accordingly, prior periods have not been restated to reflect the impact of SFAS No. 123R. We recorded \$3.1 million of non-cash stock-based compensation expense during the three months ended April 2, 2006 as a result of the adoption of SFAS No. 123R. This non-cash stock-based compensation expense reduced our net income per share by \$0.07 on a basic and diluted basis for the three months ended April 2, 2006. Excluding the impact of non-cash stock-based compensation expense, net income would have been approximately \$3.0 million, or \$0.07 per share on a basic and diluted per share basis, for the three months ended April 2, 2006. As a result of our

S-8

Table of Contents

adoption of SFAS No. 123R, certain prior period amounts have been reclassified to conform with current period presentation.

We believe that the presentation of results excluding items such as non-cash stock compensation expense provides meaningful supplemental information to both management and investors that is indicative of our core operating results and facilitates the comparison of operating results across reporting periods. We use these non-GAAP measures when evaluating our financial results, as well as for internal planning and forecasting purposes. In addition, management's bonus compensation is based on our performance against these non-GAAP measures. These non-GAAP measures should not be viewed as a substitute for our GAAP results.

	As of April 2, 2006	
	Actual	As adjusted⁽¹⁾
	(Unaudited)	
	(in thousands)	
Balance sheet data		
Cash and cash equivalents	\$ 49,044	\$ 145,774
Working capital	59,892	156,622
Total assets	112,526	209,256
Long-term debt, less current portion	25	25
Stockholders' equity	78,722	175,452

(1) As adjusted to give effect to the sale of 3,500,000 shares of common stock we are offering pursuant to this prospectus supplement at an assumed public offering price of \$29.50 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses to be paid by us.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. In addition to the other information included and incorporated by reference in this prospectus or accompanying prospectus supplement or in any free writing prospectus we have authorized for use in connection with this offering, you should carefully consider the risks described below before purchasing our common stock. If any of the following risks actually occurs, our business, results of operations and financial condition will likely suffer, the trading price of our common stock may decline, and you might lose part or all of your investment.

Risks Related to Our Business

Litigation or other proceedings or third party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products or services or impact our stock price.

Our commercial success depends in part on our non-infringement of the patents or proprietary rights of third parties and the ability to protect our own intellectual property. As described in this prospectus supplement under Business Legal Proceedings, Affymetrix, Inc. filed a complaint against us in July 2004, alleging infringement of six of its patents.

On April 20, 2006, a claims construction hearing was held as part of this proceeding. We expect a ruling related to the claims construction within the next several weeks, but there is no fixed time for such a ruling. At issue is the meaning of 15 terms, and depending on the court's ruling on each of the 15 terms, or a mix of rulings across all the terms, an advantage (or at least the perception of an advantage) may be obtained by one party or the other as to one or more issues. We are not able to predict the timing or the substance of the court's rulings. Any adverse ruling or perception of an adverse ruling may have an adverse impact on our stock price, and such impact may be disproportionate to the actual import of the ruling itself.

Including Affymetrix, third parties have asserted or may assert that we are employing their proprietary technology without authorization. As we enter new markets, we expect that competitors will likely assert that our products infringe their intellectual property rights as part of a business strategy to impede our successful entry into those markets. In addition, third parties may have obtained and may in the future obtain patents and claim that use of our technologies infringes these patents. We could incur substantial costs and divert the attention of our management and technical personnel in defending ourselves against any of these claims. Furthermore, parties making claims against us may be able to obtain injunctive or other relief, which effectively could block our ability to further develop, commercialize and sell products, and could result in the award of substantial damages against us. In the event of a successful claim of infringement against us, we may be required to pay damages and obtain one or more licenses from third parties, or be prohibited from selling certain products. We may not be able to obtain these licenses at a reasonable cost, or at all. We could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins. In that event, we could encounter delays in product introductions while we attempt to develop alternative methods or products. Defense of any lawsuit or failure to obtain any of these licenses on favorable terms could prevent us from commercializing products, and the prohibition of sale of any of our products could materially affect our ability to grow and to attain profitability.

We expect intense competition in our target markets, which could render our products obsolete, result in significant price reductions or substantially limit the volume of products that we sell. This would limit our ability to compete and achieve and maintain profitability. If we cannot continuously develop and commercialize

new products, our revenue may not grow as intended.

We compete with life sciences companies that design, manufacture and market instruments for analysis of genetic variation and biological function and other applications using technologies such as two-dimensional electrophoresis, capillary electrophoresis, mass spectrometry, flow cytometry, microfluidics, next-generation DNA sequencing and mechanically deposited, inkjet and photolithographic arrays. We anticipate that we will face increased competition in the future as existing companies develop new or improved products and as new companies enter the market with new technologies. The markets for our products are characterized by rapidly changing

S-10

Table of Contents

technology, evolving industry standards, changes in customer needs, emerging competition, new product introductions and strong price competition. For example, prices per data point for genotyping have fallen significantly over the last two years and we anticipate that prices will continue to fall. One or more of our competitors may render our technology obsolete or uneconomical. Some of our competitors have greater financial and personnel resources, broader product lines, a more established customer base and more experience in research and development than we do. Furthermore, the life sciences and pharmaceutical companies, which are our potential customers and strategic partners, could develop competing products. If we are unable to develop enhancements to our technology and rapidly deploy new product offerings, our business, financial condition and results of operations will suffer.

Our manufacturing capacity may limit our ability to sell our products.

We are currently ramping up our capacity to meet our anticipated demand for our products. Although we have significantly increased our manufacturing capacity and we believe that we have sufficient plans in place to ensure we have adequate capacity to meet our business plan in 2006, there are uncertainties inherent in expanding our manufacturing capabilities and we may not be able to increase our capacity in a timely manner. For example, manufacturing and product quality issues may arise as we increase production rates at our manufacturing facility and launch new products. As a result, we may experience difficulties in meeting customer, collaborator and internal demand, in which case we could lose customers or be required to delay new product introductions, and demand for our products could decline. Additionally, in the past, we have experienced variations in manufacturing conditions that have temporarily reduced production yields. Due to the intricate nature of manufacturing products that contain DNA, we may encounter similar or previously unknown manufacturing difficulties in the future that could significantly reduce production yields, impact our ability to launch or sell these products, or to produce them economically, prevent us from achieving expected performance levels or cause us to set prices that hinder wide adoption by customers.

We have not yet achieved annual operating profitability and may not be able to do so.

We have incurred net losses each year since our inception. As of April 2, 2006, our accumulated deficit was \$144.7 million and we incurred a net loss of \$0.1 million for the three months ended April 2, 2006. We may not be profitable in 2006, due in part to the impact of SFAS No. 123R, which is expected to add additional expense of \$12.0 million to \$15.0 million in 2006. Our ability to achieve annual profitability will depend, in part, on the rate of growth, if any, of our revenue and on the level of our expenses. We expect to continue incurring significant expenses related to research and development, sales and marketing efforts to commercialize our products and the continued development of our manufacturing capabilities. In addition, we expect that our selling and marketing expenses will increase at a higher rate in the future as a result of the launch of new products. As a result, we expect that our operating expenses will increase significantly as we grow and, consequently, we will need to generate significant additional revenue to achieve and maintain profitability. Even if we maintain profitability, we may not be able to increase profitability on a quarterly basis.

The growth and profitability of our oligo business depends on a third party.

In December 2004, we entered into a collaboration agreement with Invitrogen to sell and market our oligos worldwide. Under the terms of the collaboration, Invitrogen is responsible for sales, marketing and technical support, while we are responsible for the manufacture of the collaboration products. As Invitrogen is solely responsible for the sales and marketing support of the collaboration, our continued growth and profitability related to these products depends on the extent to which Invitrogen is successful in penetrating the oligo market and selling the collaboration products. If Invitrogen is not successful in selling the collaboration products, our business, financial condition and results of operations may suffer.

We have a limited history of commercial sales of systems and consumable products, and our success depends on our ability to develop commercially successful products and on market acceptance of our new and relatively unproven technologies.

We may not possess all of the resources, capability and intellectual property necessary to develop and commercialize all the products or services that may result from our technologies. Sales of our genotyping and gene

S-11

Table of Contents

expression systems only began in 2003, and some of our other technologies are in the early stages of commercialization or are still in development. You should evaluate us in light of the uncertainties and complexities affecting similarly situated companies developing tools for the life sciences and pharmaceutical industries. We must conduct a substantial amount of additional research and development before some of our products will be ready for sale, and we currently have fewer resources available for research and development activities than many of our competitors. We may not be able to develop or launch new products in a timely manner, or at all, or they may not meet customer requirements or be of sufficient quality or at a price that enables us to compete effectively in the marketplace. Problems frequently encountered in connection with the development or early commercialization of products and services using new and relatively unproven technologies might limit our ability to develop and successfully commercialize these products and services. In addition, we may need to enter into agreements to obtain intellectual property necessary to commercialize some of our products or services, which may not be available on favorable terms, or at all.

Historically, life sciences and pharmaceutical companies have analyzed genetic variation and biological function using a variety of technologies. In order to be successful, our products must meet the commercial requirements of the life sciences and pharmaceutical industries as tools for the large-scale analysis of genetic variation and biological function.

Market acceptance will depend on many factors, including:

- our ability to demonstrate to potential customers the benefits and cost effectiveness of our products and services relative to others available in the market;

- the extent and effectiveness of our efforts to market, sell and distribute our products;

- our ability to manufacture products in sufficient quantities with acceptable quality and reliability and at an acceptable cost;

- the willingness and ability of customers to adopt new technologies requiring capital investments; and

- the extended time lag and sales expenses involved between the time a potential customer is contacted on a possible sale of our products and services and the time the sale is consummated or rejected by the customer.

Any inability to adequately protect our proprietary technologies could harm our competitive position.

Our success will depend in part on our ability to obtain patents and maintain adequate protection of our intellectual property in the United States and other countries. If we do not protect our intellectual property adequately, competitors may be able to use our technologies and thereby erode our competitive advantage. The laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting their proprietary rights abroad. These problems can be caused by the absence of rules and methods for defending intellectual property rights.

The patent positions of companies developing tools for the life sciences and pharmaceutical industries, including our patent position, generally are uncertain and involve complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We intend to apply for patents covering our technologies and products, as we deem appropriate. However, our patent applications may be challenged and may not result in issued patents or may be invalidated or narrowed in scope after they are issued. Questions as to inventorship may also arise. For example, a former employee recently filed a complaint against us, claiming he is

entitled to be named as joint inventor of certain of our U.S. patents and pending U.S. and foreign patents and seeking a judgment that the related patents and applications are unenforceable. Any finding that our patents and applications are unenforceable could harm our ability to prevent others from practicing the related technology, and a finding that others have inventorship rights to our patents and applications could require us to obtain licenses to practice the technology, which may not be available on favorable terms, if at all.

In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. There also is risk that others may independently develop similar or alternative technologies or design around our patented technologies. Also, our

Table of Contents

patents may fail to provide us with any competitive advantage. We may need to initiate additional lawsuits to protect or enforce our patents, or litigate against third party claims, which would be expensive and, if we lose, may cause us to lose some of our intellectual property rights and reduce our ability to compete in the marketplace. Furthermore, these lawsuits may divert the attention of our management and technical personnel.

We also rely upon trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information. These measures, however, may not provide adequate protection for our trade secrets or other proprietary information. We seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants. Nevertheless, employees, collaborators or consultants may still disclose our proprietary information, and we may not be able to meaningfully protect our trade secrets. In addition, others may independently develop substantially equivalent proprietary information or techniques or otherwise gain access to our trade secrets.

Our sales, marketing and technical support organization may limit our ability to sell our products.

We currently have fewer resources available for sales and marketing and technical support services as compared to some of our primary competitors. In order to effectively commercialize our genotyping and gene expression systems and other products to follow, we will need to expand our sales, marketing and technical support staff both domestically and internationally. We may not be successful in establishing or maintaining either a direct sales force or distribution arrangements to market our products and services. In addition, we compete primarily with much larger companies that have larger sales and distribution staffs and a significant installed base of products in place, and the efforts from a limited sales and marketing force may not be sufficient to build the market acceptance of our products required to support continued growth of our business.

If we are unable to develop and maintain operation of our manufacturing capability, we may not be able to launch or support our products in a timely manner, or at all.

We currently possess only one facility capable of manufacturing our products and services for both sale to our customers and internal use. If a natural disaster were to significantly damage our facility or if other events were to cause our operations to fail, these events could prevent us from developing and manufacturing our products and services. Also, many of our manufacturing processes are automated and are controlled by our custom-designed Laboratory Information Management System (LIMS). Additionally, as part of the decoding step in our array manufacturing process, we record several images of each array to identify what bead is in each location on the array and to validate each bead in the array. This requires significant network and storage infrastructure. If either our LIMS system or our networks or storage infrastructure were to fail for an extended period of time, it would adversely impact our ability to manufacture our products on a timely basis and may prevent us from achieving our expected shipments in any given period.

If we are unable to find third-party manufacturers to manufacture components of our products, we may not be able to launch or support our products in a timely manner, or at all.

The nature of our products requires customized components that currently are available from a limited number of sources. For example, we currently obtain the fiber optic bundles and BeadChip slides included in our products from single vendors. If we are unable to secure a sufficient supply of those or other product components, we will be unable to meet demand for our products. We may need to enter into contractual relationships with manufacturers for commercial-scale production of some of our products, or develop these capabilities internally, and we cannot assure you that we will be able to do this on a timely basis, for sufficient quantities or on commercially reasonable terms. Accordingly, we may not be able to establish or maintain reliable, high-volume manufacturing at commercially reasonable costs.

We may encounter difficulties in integrating recently completed or future acquisitions that could adversely affect our business.

In April 2005, we acquired CyVera Corporation and may in the future acquire technology, products or businesses related to our current or future business. We have limited experience in acquisition activities and may

S-13

Table of Contents

have to devote substantial time and resources in order to complete acquisitions. Further, these potential acquisitions entail risks, uncertainties and potential disruptions to our business. For example, we may not be able to successfully integrate a company's operations, technologies, products and services, information systems and personnel into our business. An acquisition may further strain our existing financial and managerial resources, and divert management's attention away from our other business concerns. In connection with the CyVera acquisition, we assumed certain liabilities and hired certain employees of CyVera, which is expected to continue to result in an increase in our research and development expenses and capital expenditures. There may also be unanticipated costs and liabilities associated with an acquisition that could adversely affect our operating results.

We may encounter difficulties in managing our growth. These difficulties could increase our losses.

We expect to experience rapid and substantial growth in order to achieve our operating plans, which will place a strain on our human and capital resources. If we are unable to manage this growth effectively, our losses could increase. Our ability to manage our operations and growth effectively requires us to continue to expend funds to enhance our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. If we are unable to scale up and implement improvements to our manufacturing process and control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, then we will not be able to make available the products required to successfully commercialize our technology. Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth.

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

Our future capital requirements will be substantial and will depend on many factors including our ability to successfully market our genetic analysis systems and services, the need for capital expenditures to support and expand our business, the progress and scope of our research and development projects, the filing, prosecution and enforcement of patent claims, the outcome of our legal proceedings with Affymetrix, the defense of any future litigation involving us and the need to enter into collaborations with other companies or acquire other companies or technologies to enhance or complement our product and service offerings. We anticipate that our current cash and cash equivalents, revenue from sales and funding from grants will be sufficient to fund our anticipated operating needs, barring unforeseen developments. However, this expectation is based upon our current operating plan, which may change as a result of many factors. Consequently, we may need additional funding in the future. Our inability to raise capital would seriously harm our business and product development efforts. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, such as an acquisition, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity, the issuance of these securities could result in dilution to our stockholders.

We have no credit facility or committed sources of capital available as of April 2, 2006. To the extent operating and capital resources are insufficient to meet future requirements, we will have to raise additional funds to continue the development and commercialization of our technologies. These funds may not be available on favorable terms, or at all. If adequate funds are not available on attractive terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to achieve our goals.

We are highly dependent on our management and scientific personnel, including Jay Flatley, our president and chief executive officer, and John Stuelpnagel, our senior vice president and chief operating officer. The loss of their services

could adversely impact our ability to achieve our business objectives. We will need to hire additional qualified personnel with expertise in molecular biology, chemistry, biological information processing, sales, marketing and technical support. We compete for qualified management and scientific personnel with other life science companies, universities and research institutions, particularly those focusing on genomics. Competition for these individuals, particularly in the San Diego area, is intense, and the turnover rate can be high. Failure to attract

S-14

Table of Contents

and retain management and scientific personnel would prevent us from pursuing collaborations or developing our products or technologies.

Our planned activities will require additional expertise in specific industries and areas applicable to the products developed through our technologies, including the life sciences and healthcare industries. Thus, we will need to add new personnel, including management, and develop the expertise of existing management. The failure to do so could impair the growth of our business.

A significant portion of our sales are to international customers.

Approximately 47% and 42% of our revenue for the three months ended April 2, 2006 and April 3, 2005, respectively, was derived from customers outside the United States. During fiscal 2005, 38% of our revenue came from customers outside the United States, as compared to 52% in fiscal 2004. We intend to continue to expand our international presence and export sales to international customers and we expect the total amount of non-U.S. sales to continue to grow. Export sales entail a variety of risks, including:

currency exchange fluctuations;

unexpected changes in legislative or regulatory requirements of foreign countries into which we import our products;

difficulties in obtaining export licenses or other trade barriers and restrictions resulting in delivery delays; and

significant taxes or other burdens of complying with a variety of foreign laws.

In addition, sales to international customers typically result in longer payment cycles and greater difficulty in accounts receivable collection. We are also subject to general geopolitical risks, such as political, social and economic instability and changes in diplomatic and trade relations. One or more of these factors could have a material adverse effect on our business, financial condition and operating results.

Our success depends upon the continued emergence and growth of markets for analysis of genetic variation and biological function.

We design our products primarily for applications in the life sciences and pharmaceutical industries. The usefulness of our technology depends in part upon the availability of genetic data and its usefulness in identifying or treating disease. We are initially focusing on markets for analysis of genetic variation and biological function, namely SNP genotyping and gene expression profiling. Both of these markets are new and emerging, and they may not develop as quickly as we anticipate, or reach their full potential. Other methods of analysis of genetic variation and biological function may emerge and displace the methods we are developing. Also, researchers may not seek or be able to convert raw genetic data into medically valuable information through the analysis of genetic variation and biological function. In addition, factors affecting research and development spending generally, such as changes in the regulatory environment affecting life sciences and pharmaceutical companies, and changes in government programs that provide funding to companies and research institutions, could harm our business. If useful genetic data is not available or if our target markets do not develop in a timely manner, demand for our products may grow at a slower rate than we expect, and we may not be able to achieve or sustain profitability.

We expect that our results of operations will fluctuate. This fluctuation could cause our stock price to decline.

Our revenue is subject to fluctuations due to the timing of sales of high-value products and services projects, the impact of seasonal spending patterns, the timing and size of research projects our customers perform, changes in overall spending levels in the life sciences industry, the timing and amount of government grant funding programs and other unpredictable factors that may affect customer ordering patterns. Given the difficulty in predicting the timing and magnitude of sales for our products and services, we may experience quarter-to-quarter fluctuations in revenue resulting in the potential for a sequential decline in quarterly revenue. A large portion of our expenses are relatively fixed, including expenses for facilities, equipment and personnel. In addition, we expect operating expenses to continue to increase significantly. Accordingly, if revenue does not grow as anticipated, we may not be

S-15

Table of Contents

able to achieve and maintain profitability. Any significant delays in the commercial launch of our products, unfavorable sales trends in our existing product lines, or impacts from the other factors mentioned above, could adversely affect our revenue growth in 2006 or cause a sequential decline in quarterly revenues. Due to the possibility of fluctuations in our revenue and expenses, we believe that quarterly comparisons of our operating results are not a good indication of our future performance. If our operating results fluctuate or do not meet the expectations of stock market analysts and investors, our stock price probably would decline.

Risks Related to Owning Our Common Stock

Our poison pill, provisions of our charter documents and Delaware General Corporation Law may deter or prevent a business combination that may be favorable to you.

Provisions of our charter documents could deter or prevent a third party from acquiring us, even if doing so would be beneficial to our stockholders. These provisions include:

establishing a classified board of directors, so that only a portion of our total board can be elected at each annual meeting;

setting limitations on the removal of our directors;

granting our board of directors the authority to issue blank check preferred stock without stockholder approval;

prohibiting cumulative voting in the election of our directors, which would permit less than a majority of stockholders to elect directors;

limiting our stockholders' ability to call special meetings; and

prohibiting stockholder action by written consent.

We have also established a rights agreement, also called a poison pill. Generally, our rights agreement permits our existing stockholders to purchase a large number of our shares at a substantial discount to the market price if a third party attempts to gain control of a sufficient equity position in us. Our rights agreement could have the effect of deterring or preventing a third party from acquiring us in a transaction that might be favorable to you.

In addition, Section 203 of the Delaware General Corporation Law generally prohibits us from engaging in any business combination with certain persons who own 15% or more of our outstanding voting stock or any of our associates or affiliates who at any time in the past three years have owned 15% or more of our outstanding voting stock. These provisions could adversely affect the price that investors are willing to pay for shares of our common stock and could prevent you from realizing any premium that stockholders may otherwise receive in connection with a corporate takeover.

We may invest or spend the proceeds of this offering in ways with which you may not agree and that may not earn a return for our stockholders.

We will retain broad discretion over the use of the proceeds from any offering we make pursuant to this prospectus supplement. You may not agree with the way we decide to use those proceeds, and our use of the proceeds may not yield a significant return or any return at all for our stockholders.

We do not intend to pay cash dividends on our common stock in the foreseeable future.

We have not declared or paid any cash dividends on our common stock or other securities, and we currently do not anticipate paying any cash dividends in the foreseeable future. Accordingly, our stockholders will not realize a return on their investment unless the trading price of our common stock appreciates. We cannot assure you that our common stock will appreciate in value after the offering or even maintain the price at which you purchased your shares.

Market volatility may affect our stock price, and the value of your investment in our common stock may experience sudden decreases.

There has been, and will likely continue to be, significant volatility in the market price of securities of life sciences and biotechnology companies, including us. These fluctuations can be unrelated to the operating

Table of Contents

performance of these companies. During the period from January 1, 2004 to May 10, 2006, the lowest and highest reported trading prices of our common stock on the Nasdaq National Market were \$4.23 and \$32.00, respectively. Factors such as the following could cause the market price of our common stock to fluctuate substantially:

- announcements of new products or services by us or our competitors;
- litigation involving or affecting us;
- quarterly fluctuations in our or other companies' financial results;
- shortfalls in our actual financial results compared to our guidance or the forecasts of stock market analysts;
- acquisitions or strategic alliances by us or our competitors;
- the gain or loss of a significant customer; and
- general conditions in our industry and in the financial markets.

A decline in the market price of our common stock could cause you to lose some or all of your investment and may adversely impact our ability to attract and retain employees, acquire other companies or businesses and raise capital. In addition, stockholders may initiate securities class action lawsuits if the market price of our stock drops significantly, which may cause us to incur substantial costs and could divert the time and attention of our management.

New investors in our common stock will experience immediate and substantial dilution.

The offering price of our common stock will be substantially higher than the net tangible book value of our common stock immediately after the offering. As a result, purchasers of our common stock in this offering will incur immediate and substantial dilution of approximately \$25.67 per share, based on the assumed public offering price of \$29.50 per share. Purchasers could experience additional dilution upon the exercise of outstanding stock options. See "Dilution" for a more detailed discussion of the dilution new investors will incur in this offering.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the information incorporated by reference into them, contain forward-looking statements. Forward-looking statements provide our current expectations or forecasts of future events. Forward-looking statements include statements about our expectations, beliefs, plans, objectives, intentions, assumptions and other statements that are not historical facts. Words or phrases such as "anticipate," "believe," "continue," "ongoing," "estimate," "expect," "intend," "may," "plan," "potential," "predict," or phrases, or the negatives of those words or phrases, may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. Examples of forward-looking statements include, among others, statements regarding the integration of CyVera's technology with our existing technology, the commercial launch of new products, including products based on CyVera's technology, and the duration for which our existing cash and other resources is expected to fund our operating activities.

Forward-looking statements are subject to known and unknown risks and uncertainties and are based on potentially inaccurate assumptions that could cause actual results to differ materially from those expected or implied by the forward-looking statements. Our actual results could differ materially from those anticipated in our forward-looking statements for many reasons, including the factors described in the section entitled "Risk Factors" in this prospectus

supplement. Accordingly, you should not unduly rely on these forward-looking statements, which speak only as of the date of the document containing them or as otherwise indicated. We undertake no obligation to publicly revise any forward-looking statement to reflect circumstances or events after the date of the forward-looking statement or to reflect the occurrence of unanticipated events. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus supplement.

S-17

Table of Contents**USE OF PROCEEDS**

We estimate that the net proceeds from the sale of the 3,500,000 shares of common stock we are offering will be approximately \$96.7 million, assuming a public offering price of \$29.50 per share and after deducting estimated underwriting discounts and commissions and the estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate the net proceeds to us will be approximately \$111.3 million.

We intend to use the net proceeds from this offering to fund research and development, to continue expanding our manufacturing capacity as required and to provide for working capital needs. We may also use a portion of the net proceeds to acquire, license or invest in complementary businesses, technologies or products. While we evaluate acquisition, licensing, investment and similar opportunities and engage in related discussions from time to time, we currently have no material agreements or commitments with respect to any such acquisition, license or investment.

Although we have identified some of the potential uses of the proceeds from this offering, we have and reserve broad discretion in the application of these proceeds. Pending any ultimate use of any portion of the proceeds from this offering, we intend to invest the proceeds in a variety of capital preservation investments.

PRICE RANGE OF OUR COMMON STOCK

Our common stock is traded publicly through The Nasdaq National Market under the symbol ILMN. The following table presents quarterly information on the price range of our common stock. This information indicates the high and low sales prices reported by The Nasdaq National Market. These prices do not include retail markups, markdowns or commissions.

	High	Low
Fiscal year ended January 2, 2005		
First quarter	\$ 10.24	\$ 6.50
Second quarter	8.88	6.07
Third quarter	7.22	4.23
Fourth quarter	9.65	6.16
Fiscal year ended January 1, 2006		
First quarter	\$ 11.35	\$ 6.72
Second quarter	12.95	7.90
Third quarter	14.83	10.82
Fourth quarter	16.80	12.76
Fiscal year ending December 31, 2006		
First quarter	\$ 27.98	\$ 13.75
Second quarter (through May 10, 2006)	32.00	21.60

As of April 20, 2006, there were approximately 212 holders of record of our common stock. On May 10, 2006, the last sale price reported on The Nasdaq National Market for our common stock was \$29.50 per share.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance operations, and we do not anticipate paying cash dividends in the foreseeable future.

S-18

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of April 2, 2006:

on an actual basis; and

on an adjusted basis to give effect to the sale of 3,500,000 shares of our common stock we are offering at an assumed public offering price of \$29.50 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses to be paid by us.

	As of April 2, 2006	
	Actual	As adjusted
	(Unaudited)	
	(in thousands, except share and per share data)	
Cash and cash equivalents	\$ 49,044	\$ 145,774
Long-term debt, less current portion	25	25
Stockholders' equity:		
Preferred stock, \$0.01 par value per share; 10,000,000 shares authorized; no shares issued and outstanding, actual and as adjusted		
Common stock, \$0.01 par value per share; 120,000,000 shares authorized; 41,696,733 shares issued and outstanding, actual; 45,196,733 shares issued and outstanding, as adjusted	416	452
Additional paid-in capital	222,753	319,447
Accumulated other comprehensive income	243	243
Accumulated deficit	(144,690)	(144,690)
Total stockholders' equity	78,722	175,452
Total capitalization	\$ 78,747	\$ 175,477

The table above should be read in conjunction with our consolidated financial statements and related notes incorporated by reference in this prospectus supplement. This table excludes:

8,139,647 shares of our common stock issuable upon exercise of options outstanding as of April 2, 2006, at a weighted average exercise price of \$9.91 per share, of which options to purchase 2,792,545 shares were exercisable as of that date; and

6,879,757 shares of our common stock available for future grant under our equity incentive plans as of April 2, 2006.

Table of Contents**DILUTION**

If you invest in our common stock, you will experience dilution to the extent of the difference between the public offering price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of April 2, 2006 was approximately \$76.5 million, or \$1.84 per share of common stock. Net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of common stock outstanding as of April 2, 2006. After giving effect to the sale of the 3,500,000 shares of common stock we are offering at an assumed public offering price of \$29.50 per share, and after deducting estimated underwriting discounts and commissions and our estimated offering expenses, our as-adjusted net tangible book value as of April 2, 2006 would have been approximately \$173.3 million, or approximately \$3.83 per share of common stock. This represents an immediate increase in net tangible book value of approximately \$1.99 per share to existing stockholders and an immediate dilution of approximately \$25.67 per share to new investors. The following table illustrates this calculation on a per-share basis:

Assumed initial public offering price per share		\$ 29.50
Net tangible book value per share as of April 2, 2006	\$ 1.84	
Increase per share attributable to the offering	1.99	
As-adjusted net tangible book value per share after this offering		3.83
Dilution per share to new investors		\$ 25.67

If the underwriters exercise in full their option to purchase additional shares, our as-adjusted net tangible book value as of April 2, 2006 would increase to approximately \$4.11 per share, representing an increase to existing stockholders of approximately \$2.27 per share, and there would be an immediate dilution of approximately \$25.39 per share to new investors.

The number of shares of common stock outstanding used for existing stockholders in the table and calculations above is based on shares outstanding as of April 2, 2006 and excludes:

8,139,647 shares of our common stock issuable upon exercise of options outstanding as of April 2, 2006, at a weighted average exercise price of \$9.91 per share, of which options to purchase 2,792,545 shares were exercisable as of that date; and

6,879,757 shares of our common stock available for future grant under our equity incentive plans as of April 2, 2006.

The exercise of outstanding options having an exercise price less than the public offering price will increase dilution to new investors.

Table of Contents

BUSINESS

Introduction

We develop, manufacture and market next-generation tools for the large-scale analysis of genetic variation and biological function. Understanding genetic variation and biological function is critical to the development of personalized medicine, a key goal of genomics. Using our technologies, we have developed a comprehensive line of products that are designed to provide the performance, throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to extract medically valuable information from advances in genomics and proteomics. This information is expected to correlate genetic variation and biological function with particular disease states, enhancing drug discovery and clinical research, allowing diseases to be detected earlier and permitting better choices of drugs for individual patients.

In 2001, we began commercial sale of short pieces of DNA called oligonucleotides, which we refer to as oligos, manufactured using our proprietary Oligator technology. We believe our Oligator technology is more cost effective than competing technologies, and this advantage enabled us to market our oligos under a price leadership strategy while still achieving attractive gross margins.

In 2001, we commercialized the first implementation of our BeadArray technology, the Sentrix Array Matrix. This is a disposable matrix of 96 fiber optic bundles arranged in a pattern that matches the standard 96-well microtiter plate. Each fiber optic bundle performs more than 1,500 unique assays, which enables researchers to perform focused genotyping experiments in a high-throughput format. This format was also used to initiate our single nucleotide polymorphism (SNP) genotyping services product line. As a result of the increasing market acceptance of our high throughput, low cost BeadArray technology, we have entered into genotyping service contracts with many leading genotyping centers.

Our production-scale BeadLab is a turn-key platform that includes all hardware and software necessary to enable researchers to perform genetic analysis research on what we believe is an unprecedented scale. This system is being marketed to a small number of high throughput genotyping users. As of April 2, 2006, we have installed and recorded revenue for 11 BeadLabs.

In 2003, we announced the launch of several new products, including 1) a new array format, the Sentrix BeadChip, which significantly expands market opportunities for our BeadArray technology and provides increased experimental flexibility for life science researchers; 2) a gene expression product line on both the Sentrix Array Matrix and the Sentrix BeadChip that allows researchers to analyze a focused set of genes across eight to 96 samples on a single array; and 3) a benchtop SNP genotyping and gene expression system, the BeadStation, for performing moderate-scale genotyping and gene expression using our technology. The BeadStation includes our BeadArray Reader, analysis software and assay reagents and is designed to match the throughput requirements and variable automation needs of individual research groups and core labs. Sales of these products began in the first quarter of 2004 and, as of April 2, 2006, we have shipped 139 BeadStations.

In late 2004, we announced a strategic collaboration with Invitrogen Corporation (Invitrogen) to synthesize and distribute oligos. In the third quarter of 2005, we began shipping oligo products in connection with this agreement. As part of the agreement, we have developed the next generation of our Oligator DNA synthesis technology, which we have designed to support both plate- and the larger tube-based oligo markets. Invitrogen is responsible for sales, marketing and technical support and we are responsible for manufacturing. Profits from sales of collaboration products are divided equally between the two companies.

In 2005, we began shipments of Sentrix BeadChips for whole-genome gene expression and whole-genome genotyping. The whole-genome gene expression BeadChips are designed to enable high-performance, cost-effective, whole-genome expression profiling of multiple samples on a single chip, resulting in a dramatic reduction in cost of whole-genome expression analysis. Our whole-genome expression product line includes multi-sample products for both the Human and Mouse Genomes. The whole-genome genotyping BeadChip is designed to scale to high levels of multiplexing without compromising data quality and to provide scientists the ability to query hundreds of thousands of SNPs in parallel. In the second quarter of 2005, we commenced shipment

S-21

Table of Contents

of our first whole-genome genotyping BeadChip, the HumanHap-1, which interrogates more than 100,000 SNPs in parallel.

In April 2005, we completed the acquisition of CyVera Corporation, a privately-held Connecticut-based company, pursuant to which CyVera became a wholly-owned subsidiary of Illumina. We believe that CyVera's digital-microbead technology, renamed the VeraCode technology, is highly complementary to our portfolio of products and services. The acquisition is expected to provide us with a comprehensive approach to bead-based assays for biomarker research and development and in-vitro and molecular diagnostic opportunities, including those that require low-complexity as well as high-complexity testing. We expect the first products based on the VeraCode technology to be available before the end of 2006. The purchase price associated with this transaction was approximately \$17.8 million. We allocated \$15.8 million of this purchase price to acquired in-process research and development and charged such amount against earnings in the second quarter of 2005.

In December 2005, we began shipping the new Sentrix HumanHap300 Genotyping BeadChip to customers around the world. Using the Infinium assay, which enables us to select virtually any SNP in the genome, the HumanHap300 BeadChip allows analysis of more than 317,000 SNPs. We selected the SNPs for inclusion on the chip in collaboration with a consortium of scientists that are leaders in the genotyping field. We believe this product has quality and performance features that support our expectation that it will become an important discovery tool for researchers seeking to understand the genetic basis of common, yet complex diseases.

In the first quarter of 2006, we introduced the Sentrix HumanHap240S BeadChip for genome-wide disease association studies. This product is a companion to our Sentrix HumanHap300 BeadChip and enables researchers to interrogate an additional 240,000 SNPs utilizing our Infinium assay. We also introduced the Sentrix HumanHap550 BeadChip in the first quarter of 2006. The Sentrix HumanHap550 BeadChip contains over 550,000 SNPs on a single microarray, and we believe it provides the most comprehensive genomic coverage of any product currently available. The HumanHap550 BeadChip is currently available for commercial shipment.

We are seeking to continue to expand our customer base for our BeadArray technology; however, we can give no assurance that our sales efforts will continue to be successful.

We were incorporated in California in April 1998. We reincorporated in Delaware in July 2000. Our principal executive offices are located at 9885 Towne Centre Drive, San Diego, California 92121. Our telephone number is (858) 202-4500.

Industry Background

Genetic Variation and Biological Function

Every person inherits two copies of each gene, one from each parent. The two copies of each gene may be identical, or they may be different. These differences are referred to as genetic variation. Examples of the physical consequences of genetic variation include differences in eye and hair color. Genetic variation can also have important medical consequences, including predisposition to disease and differential response to drugs. Genetic variation affects disease susceptibility, including predisposition to cancer, diabetes, cardiovascular disease and Alzheimer's disease. In addition, genetic variation may cause people to respond differently to the same drug treatment. Some people may respond well, others may not respond at all, and still others may experience adverse side effects. A common form of genetic variation is a SNP. A SNP is a variation in a single position in a DNA sequence. It is estimated that the human genome contains over nine million SNPs.

While in some cases a single SNP will be responsible for medically important effects, it is now believed that combinations of SNPs may contribute to the development of most major diseases. Since there are millions of SNPs, it is important to investigate many representative, well-chosen SNPs simultaneously in order to discover medically valuable information.

Another contributor to disease and dysfunction is the over- or under-expression of genes within an organism's cells. A very complex network of genes interacts to maintain health in complex organisms. The challenge for scientists is to delineate the associated genes' expression patterns and their relationship to disease. Until recently, this problem was addressed by investigating effects on a gene-by-gene basis. This is time consuming, and

Table of Contents

difficulties exist when several pathways can not be observed or controlled at the same time. With the advent of microarray technology, thousands of genes can now be tested at the same time.

SNP Genotyping

SNP genotyping is the process of determining which base (A, C, G or T) is present at a particular site in the genome within an individual or other organism. The use of SNP genotyping to obtain meaningful statistics on the effect of an individual SNP or a collection of SNPs, and to apply that information to clinical trials and diagnostic testing, requires the analysis of millions of SNP genotypes and the testing of large populations for each disease. For example, a single large clinical trial could involve genotyping 300,000 SNPs per patient in 1,000 patients, thus requiring 300 million assays. Using previously available technologies, this scale of SNP genotyping was both impractical and prohibitively expensive.

Large-scale SNP genotyping can be used in a variety of ways, including studies designed to understand the genetic contributions to disease (disease association studies), genomics-based drug development, clinical trial analysis, disease predisposition testing, and disease diagnosis. SNP genotyping can also be used outside of healthcare, for example in the development of plants and animals with desirable commercial characteristics. These markets will require billions of SNP genotyping assays annually.

Gene Expression Profiling

Gene expression profiling is the process of determining which genes are active in a specific cell or group of cells and is accomplished by measuring mRNA, the intermediary messenger between genes (DNA) and proteins. Variation in gene expression can cause disease, or act as an important indicator of disease or predisposition to disease. By comparing gene expression patterns between cells from different environments, such as normal tissue compared to diseased tissue or in the presence or absence of a drug, specific genes or groups of genes that play a role in these processes can be identified. Studies of this type, often used in drug discovery, require monitoring thousands, and preferably tens of thousands, of mRNAs in large numbers of samples. Once a smaller set of genes of interest has been identified, researchers can then examine how these genes are expressed or suppressed across numerous samples, for example, within a clinical trial.

As gene expression patterns are correlated to specific diseases, gene expression profiling is becoming an increasingly important diagnostic tool. Diagnostic use of expression profiling tools is anticipated to grow rapidly with the combination of the sequencing of various genomes and the availability of more cost-effective technologies.

Our Technologies

BeadArray Technology

We have developed a proprietary array technology that enables the large-scale analysis of genetic variation and biological function. Our BeadArray technology combines microscopic beads and a substrate in a simple proprietary manufacturing process to produce arrays that can perform many assays simultaneously. Our BeadArray technology provides a unique combination of high throughput, cost effectiveness, and flexibility. We achieve high throughput with a high density of test sites per array and we are able to format arrays either in a pattern arranged to match the wells of standard microtiter plates or in various configurations in the format of standard microscope slides. We seek to maximize cost effectiveness by reducing consumption of expensive reagents and valuable samples, and through the low manufacturing costs associated with our technologies. Our ability to vary the size, shape and format of the well patterns and to create specific bead pools, or sensors, for different applications provides the flexibility to address multiple markets and market segments. We believe that these features have enabled our BeadArray technology to

become a leading platform for the emerging high-growth market of SNP genotyping and expect they will enable us to become a key player in the gene expression market.

Our proprietary BeadArray technology combines microwells etched into a substrate and specially prepared beads that self-assemble into an array. We have deployed our BeadArray technology in two different Sentrix array formats, the Array Matrix and the BeadChip. Our first bead-based product was the Array Matrix which incorporates fiber optic bundles. The fiber optic bundles, which we cut into lengths of less than one inch, are manufactured to our

S-23

Table of Contents

specifications. Each bundle is comprised of approximately 50,000 individual fibers and 96 of these bundles are placed into an aluminum plate, which forms an Array Matrix. BeadChips are fabricated in microscope slide-shaped sizes with varying numbers of sample sites per slide. Both formats are chemically etched to create tens to hundreds of thousands of wells for each sample site.

In a separate process, we create sensors by affixing a specific type of molecule to each of the billions of microscopic beads in a batch. We make different batches of beads, with the beads in a given batch coated with one particular type of molecule. The particular molecules on a bead define that bead's function as a sensor. For example, we create a batch of SNP sensors by attaching a particular DNA sequence, or oligo, to each bead in the batch. We combine batches of coated beads to form a pool specific to the type of array we intend to create. A bead pool one milliliter in volume contains sufficient beads to produce thousands of arrays. One of the advantages of this technology is that it allows us to create universal arrays for SNP genotyping, and by varying the reagent kit, we are able to use the array to test for any combination of SNPs.

To form an array, a pool of coated beads is brought into contact with the array surface where they are randomly drawn into the wells, one bead per well. The tens of thousands of beads in the wells comprise our individual arrays. Because the beads assemble randomly into the wells, we perform a final procedure called "decoding" in order to determine which bead type occupies which well in the array. We employ several proprietary methods for decoding, a process that requires only a few steps to identify all the beads in the array. One beneficial by-product of the decoding process is a validation of each bead in the array. This quality control test characterizes the performance of each bead and can identify and eliminate use of any empty wells. We ensure that each bead type on the array is sufficiently represented by including multiple copies of each bead type. Multiple bead type copies improve the reliability and accuracy of the resulting data by allowing statistical processing of the results of identical beads. We believe we are the only microarray company to provide this level of quality control in the industry.

An experiment is performed by preparing a sample, such as DNA from a patient, and introducing it to the array. The design features of our Array Matrix allow it to be simply dipped into a solution containing the sample, whereas our BeadChip allows processing of samples on a slide-sized platform. The molecules in the sample bind to their matching molecules on the coated bead. The BeadArray Reader detects the matched molecules by shining a laser on the fiber optic bundle or on the BeadChip. Since the molecules in the sample have a structure that causes them to emit light in response to a laser, detection of a binding event is possible. This allows the measurement of the number of molecules bound to each coated bead, resulting in a quantitative analysis of the sample.

VeraCode Technology

The BeadArray technology is most effective in applications which require mid- to high levels of multiplexing from low to high levels of throughput. We believe the molecular diagnostics market will require systems which are extremely high throughput and cost effective in the mid- to low-multiplex range. To address this market, we acquired the VeraCode technology through our acquisition of CyVera Corporation in April 2005. Based on digitally encoded microbeads, VeraCode enables low-cost multiplexing from 1 to 384-plex in a single well. We plan to implement the VeraCode technology using our newly designed BeadXpress System and our existing assays. We believe that this system will be the ideal platform for creating lower multiplex genotyping, gene expression and protein based assays. In the research market, we expect our customers to utilize our BeadArray technology for their higher multiplex projects and then move to our BeadXpress system for their lower multiplex projects utilizing the same assays. Additionally, we believe that the cost and multiplex advantages of the BeadXpress system using our VeraCode technology will be especially appealing in the molecular diagnostics market. We expect to launch the BeadXpress system before the end of 2006 along with several assays for the system.

Oligator Technology

Genomic applications require many different short pieces of DNA that can be made synthetically, called oligos. We have developed our proprietary Oligator technology for the parallel synthesis of many different oligos to meet the requirements of large-scale genomics applications. We believe that our Oligator technology is substantially more cost effective and provides significantly higher throughput than available commercial alternatives. Our synthesis machines are computer controlled and utilize many robotic processes to minimize the amount of labor used in the manufacturing

S-24

Table of Contents

process. In 2005, we implemented our fourth-generation Oligator technology, which is capable of manufacturing over 13,000 different oligos per run. This is an improvement over prior generations of technology where we could only manufacture approximately 3,000 oligos per run. This increase in scale was necessary to enable us to support the manufacture of oligos under our collaboration with Invitrogen as well as to support our increased internal need for oligos, a critical component of our BeadArray technology, for product sales and new product development.

Key Advantages of Our Technology

We believe that our technology provides distinct advantages, in a variety of applications, over competing technologies, by creating cost-effective, highly miniaturized arrays with the following advantages:

High Throughput. The miniaturization of our BeadArray technology provides very high information content per unit area. To increase sample throughput, we have formatted our array matrix in a pattern arranged to match the wells of standard microtiter plates, allowing throughput levels of up to nearly 150,000 unique assays per microtiter plate, and we use laboratory robotics to speed process time. Similarly, we have patterned our whole-genome expression BeadChips to support up to 48,000 gene expression assays for six samples with each BeadChip. Our Infinium assay is supported by full automation and LIMS to address high throughput laboratories.

Cost Effectiveness. Our array products substantially reduce the cost of our customers' experiments as a result of our proprietary manufacturing process and our ability to capitalize on cost reductions generated by advances in fiber optics, plasma etching processes, digital imaging and bead chemistry. In addition, our products require smaller reagent volumes than other array technologies, thereby reducing reagent costs for our customers. Our Oligator technology further reduces reagent costs, as well as our cost of coating beads.

Flexibility. We are able to offer flexible solutions to our customers based on our ability to attach different kinds of molecules, including DNA, RNA, proteins and other chemicals, to our beads. In addition, we can have BeadChips manufactured in multiple shapes and sizes with wells organized in various arrangements to optimize them for different markets and market segments. In combination, the use of beads and etched wells provides the flexibility and scalability for our BeadArray technology to be tailored to perform many applications in many different market segments, from drug discovery to diagnostics. Our Oligator technology allows us to manufacture a wide diversity of lengths and quantities of oligos.

Quality and Reproducibility. The quality of our products is dependent upon each element in the system, the array, the assay used to perform the experiment and the instrumentation and software used to capture the results. Each array is manufactured with a high density of beads, which enables us to have multiple copies of each individual bead type. We measure the copies simultaneously and combine them into one data point. This allows us to make a comparison of each bead against its own population of identical beads, which permits the statistical calculation of a more reliable and accurate value for each data point. Finally, the manufacture of the array includes a proprietary decoding step that also functions as a quality control test of every bead on every array, improving the overall quality of the data. When we develop the assays used with our products, we focus on performance, cost and ease of use. By developing assays that are easy to use, we can reduce the potential for the introduction of error into the experiment. We believe that this enables researchers to obtain high quality and reproducible data from their experiments. Additionally, we manufacture substantially all of the reagents used in our assays, allowing us to control the quality of the product delivered to the customer.

Our Strategy

Our goal is to make our BeadArray and BeadXpress platforms the industry standard for products and services serving the genetic analysis markets. We plan to achieve this by:

focusing on emerging high-growth markets;

rapidly commercializing our BeadLab, BeadStation, BeadXpress, Sentrix Array Matrix and BeadChip products;

expanding our technologies into multiple product lines, applications and market segments; and

strengthening our technological leadership.

S-25

Table of Contents

Products and Services

The first implementation of our BeadArray technology, the Sentrix Array Matrix, is a disposable matrix with 96 fiber optic bundles arranged in a pattern that matches the standard 96-well microtiter plate. Each fiber optic bundle performs more than 1,500 unique assays. The BeadChip, introduced in 2003, is fabricated in multiple configurations to support multiple applications and scanning technologies.

We have provided genotyping services using our proprietary BeadArray technology since 2001. In addition, we have developed our first genotyping and gene expression products based on this technology. These products include disposable Sentrix Array Matrices and BeadChips, GoldenGate and Infinium reagent kits for SNP genotyping, BeadArray Reader scanning instruments and an evolving portfolio of custom and standard gene expression products.

SNP Genotyping

In 2001, we introduced the first commercial application of our BeadArray technology by launching our SNP genotyping services product line. Since this launch, we have had peak days in which we operated at over 40 million genotypes per day based on individual samples. To our knowledge, no other genotyping platform can achieve comparable levels of throughput while delivering such high accuracy and low cost.

We designed our first consumable BeadArray product, the Sentrix Array Matrix, for SNP genotyping. The Sentrix Array Matrix uses a universal format that allows it to analyze any set of SNPs. We have also developed reagent kits based on GoldenGate assay protocols and the BeadArray Reader, a laser scanner, which is used to read our array products.

Depending on throughput and automation requirements, our customers can select the system configuration to best meet their needs. For production-scale throughput, our BeadLab would be appropriate, and for moderate-scale throughput, our BeadStation would be selected. Our BeadLab includes our BeadArray Reader, combined with LIMS, standard operating procedures and analytical software and fluid handling robotics. This production-scale system was commercialized in late 2002 and when installed, this system can routinely produce millions of genotypes per day.

The BeadStation, a system for performing moderate-scale genotyping designed to match the throughput requirements of individual research groups and core labs, was commercialized in late 2003. The BeadStation includes our BeadArray Reader and genotyping and/or gene expression analysis software. Multiple BeadStations can be configured to achieve any level of desired throughput and are fully upgradeable to a full BeadLab through various steps that add automation, sample preparation equipment and LIMS capability. For use in custom SNP genotyping, both the BeadLab and BeadStation utilize GoldenGate assay reagents and our Array Matrix.

In 2003, we announced the availability of an assay set for genetic linkage analysis. This standard product has been deployed in our genotyping services operation and is also sold to customers who use our SNP genotyping systems. Genetic linkage analysis can help identify chromosomal regions with potential disease associations across a related set of samples.

In 2005, we announced the MHC Panel Set, which allows the interrogation of a difficult-to-assay area of the genome, often associated with autoimmune diseases. In addition, we announced the Mouse-6 and MouseRef-8 Gene Expression BeadChip allowing the study of the levels of gene expression in mouse model.

In 2005, we commenced shipping the Sentrix Human-1 Genotyping BeadChip for whole-genome genotyping. This BeadChip provides to scientists the ability to interrogate over 100,000 SNPs located in high-value genetic regions of

the human genome. Also, in December 2005, we began shipping the new Sentrix HumanHap300 Genotyping BeadChip to customers around the world. Using the Infinium assay, which enables us to select virtually any SNP in the genome, the HumanHap300 BeadChip allows analysis of more than 317,000 SNPs. We selected the SNPs for inclusion on the chip in collaboration with a consortium of scientists that are leaders in the genotyping

Table of Contents

field. We believe this product's quality and performance support our expectation that it will become an important discovery tool for researchers seeking to understand the genetic basis of common yet complex diseases.

In the first quarter of 2006, we introduced the Sentrix HumanHap240S BeadChip for genome-wide disease association studies. This product is a companion to our Sentrix HumanHap300 BeadChip and enables researchers to interrogate an additional 240,000 SNPs utilizing our Infinium assay. We also introduced the Sentrix HumanHap550 BeadChip in the first quarter of 2006. The Sentrix HumanHap550 BeadChip contains over 550,000 SNPs on a single microarray, and we believe it provides the most comprehensive genomic coverage of any product currently available. Through an application called Copy Number Polymorphisms, the HumanHap family of BeadChips also provides high-resolution information on amplifications, deletions and loss of heterozygosity throughout the genome, abnormalities common in cancers and congenital diseases. In addition, we announced additional standard panels in the first quarter of 2006, including mouse linkage and cancer panels.

Gene Expression Profiling

With the addition of application specific accessory kits, our production-scale BeadLabs and BeadStations are capable of performing a growing number of applications, including gene expression profiling.

In 2003, we introduced our focused set gene expression products on both the Sentrix Array Matrix and Sentrix BeadChip platforms. Our system includes a BeadArray Reader for imaging Sentrix Array Matrices and BeadChips, a hybridization chamber and software for data extraction. In addition, we have developed standard gene expression products for each of the human, mouse and arabidopsis genomes with an additional panel that focuses on human toxicology.

In 2005, we began shipment of the Sentrix Human-6 and HumanRef-8 Expression BeadChip products. Both products allow large-scale expression profiling of multiple samples on a single chip and are imaged using our BeadArray Reader. The Human-6 BeadChip is designed to analyze six discrete whole-human-genome samples on one chip, interrogating in each sample approximately 48,000 transcripts from the estimated 30,000 genes in the human genome. The HumanRef-8 BeadChip product analyzes eight samples in parallel against 24,000 transcripts from the roughly 22,000 genes represented in the consensus RefSeq database, a well-characterized whole-genome subset used broadly in genetic analysis. We expect that these gene expression BeadChips will dramatically reduce the cost of whole-genome expression analysis, allowing researchers to expand the scale and reproducibility of large-scale biological experimentation.

Scanning Instrumentation

The BeadArray Reader, an instrument we developed, is a key component of both our production-scale BeadLab and our benchtop BeadStation. This scanning equipment uses a laser to read the results of experiments that are captured on our arrays and was designed to be used in all areas of genetic analysis that use our Sentrix Array Matrices and Sentrix BeadChips.

High-Throughput Oligo Synthesis

We have put in place a state of the art oligo manufacturing facility. This facility serves both the commercial needs under our collaboration with Invitrogen and our internal needs. In addition to their use to coat beads, these oligos are components of the reagent kits for our BeadArray products and are used for assay development. We manufacture oligos in a wide range of lengths and in several scales, with the ability to add many types of modifications. We offer a range of quality control options and have implemented a laboratory information management system to control much of the manufacturing process. In 2003, we introduced the first standard product offerings in our Oligator product line,

a whole-genome oligo reference set designed and optimized for spotted gene expression microarrays, and in 2004, we introduced a mouse genome oligo set, also for use on spotted gene expression arrays. In 2005, we stopped selling oligos directly into the market and began shipping oligos under our collaboration with Invitrogen.

S-27

Table of Contents

Collaboration with Invitrogen Corporation

In December 2004, we entered into a strategic collaboration with Invitrogen. The goal of the collaboration is to combine our expertise in oligo manufacturing with the sales, marketing and distribution capabilities of Invitrogen. In connection with the collaboration, we have developed the next generation Oligator DNA synthesis technology. This technology includes both plate-and tube-based capabilities. Under the terms of the agreement, Invitrogen paid us an upfront non-refundable collaboration payment of \$2.3 million in the first quarter of 2005. Additionally, upon the achievement of a certain milestone, Invitrogen was obligated to make a milestone payment of \$1.1 million to us. As of January 1, 2006, this milestone has been achieved and the milestone payment was received. We have used these funds to invest in our San Diego facility to enable the development and implementation of fourth-generation Oligator technology and to extend the technology into the larger market for tube-based oligo products. We began manufacturing and shipping the plate-based and certain tube-based oligo products under the collaboration in the third quarter of 2005. In addition, the agreement provides for the transfer of our Oligator technology into two Invitrogen facilities outside North America. Collaboration profit from the sale of collaboration products will be divided equally between the two companies.

Intellectual Property

We have an extensive patent portfolio, including, as of May 1, 2006, ownership of, or exclusive licenses to, 42 issued U.S. patents and 95 pending U.S. patent applications, including three allowed applications that have not yet issued as patents, some of which derive from a common parent application. Our issued patents, which cover various aspects of our array, assay, oligo synthesis, instrument and chemical detection technologies, expire between 2011 and 2024. We are seeking to extend this patent protection on our BeadArray, DASL, GoldenGate, Infinium, CyVera, Oligator, Sentrix, Array of Arrays and related technologies. We have received or filed counterparts for many of these patents and applications in one or more foreign countries.

We also rely upon trade secrets, know-how, copyright and trademark protection, as well as continuing technological innovation and licensing opportunities to develop and maintain our competitive position. Our success will depend in part on our ability to obtain patent protection for our products and processes, to preserve our copyrights and trade secrets, to operate without infringing the proprietary rights of third parties and to acquire licenses related to enabling technology or products used with our BeadArray, DASL, GoldenGate, Infinium, Sentrix, Array of Arrays, CyVera and Oligator technologies.

We are party to various exclusive and non-exclusive license agreements with third parties, which grant us rights to use key aspects of our array technology, assay methods, chemical detection methods, reagent kits and scanning equipment. We have exclusive licenses from Tufts University to patents that cover our use of BeadArray technology. These patents were filed by Dr. David Walt, a member of our board of directors, the Chairman of our Scientific Advisory Board and one of our founders. Our exclusive licenses expire with the termination of the underlying patents, which will occur between 2010 and 2019. In 2001, we entered into a non-exclusive license agreement with Amersham Biosciences that covers certain technology contained in our BeadArray Reader. In 2002, we obtained a non-exclusive license from Dade Behring Marburg GmbH that relates to certain components of our GoldenGate assay. We also have additional nonexclusive licenses from various third parties for other components of our products. In all cases, the agreements remain in effect over the term of the underlying patents, may be terminated at our request without further obligation and require that we pay customary royalties while the agreement is in effect.

Research and Development

We have made substantial investments in research and development since our inception. We have assembled a team of skilled engineers and scientists who are specialists in biology, chemistry, informatics, instrumentation, optical

systems, software, manufacturing and other related areas required to complete the development of our products. Our research and development efforts have focused primarily on the tasks required to optimize our BeadArray and Oligator technologies and to support commercialization of the products and services derived from these technologies. As of April 2, 2006, we had a total of 132 employees engaged in research and development activities.

S-28

Table of Contents

Marketing and Distribution

Our current products address the genetic analysis portion of the life sciences market, in particular, experiments involving SNP genotyping and gene expression profiling. These experiments may be involved in many areas of biologic research, including basic human disease research, pharmaceutical drug discovery and development, pharmacogenomics, toxicogenomics and agricultural research. Our potential customers include pharmaceutical, biotechnology, agrichemical, diagnostics and consumer products companies, as well as academic or private research centers. The genetic analysis market is relatively new and emerging and its size and speed of development will be ultimately driven by, among other items:

the ability of the research community to extract medically valuable information from genomics and to apply that knowledge to multiple areas of disease-related research and treatment;

the availability of sufficiently low cost, high-throughput research tools to enable the large amount of experimentation required to study genetic variation and biological function; and

the availability of government and private industry funding to perform the research required to extract medically relevant information from genomic analysis.

We market and distribute our products directly to customers in North America, major European markets, Japan and Singapore. In each of these areas, we have dedicated sales, service and application support personnel responsible for expanding and managing their respective customer bases. In smaller markets in the Pacific Rim countries and Europe, we sell our products and provide services to customers through distributors that specialize in life science products. We expect to significantly increase our sales and distribution resources during 2006 and beyond as we launch a number of new products and expand the number of customers that can use our products.

In 2004, we entered into a strategic collaboration with Invitrogen with a goal of leveraging our strength in oligo synthesis with Invitrogen's extensive sales, marketing and distribution channels. We transitioned all responsibility for oligo sales, marketing and technical support to Invitrogen in the beginning of the third quarter of 2005.

Manufacturing

We manufacture our array platforms, reagent kits, scanning equipment and oligos in-house. In early 2006, we completed an expansion program to triple our BeadChip manufacturing capacity from the levels in the second quarter of 2005. We believe that we currently have the ability to manufacture our products in sufficient quantity to meet our business plan for 2006. We are focused on continuing to enhance the quality and manufacturing yield of our Sentrix Array Matrices and BeadChips and are exploring ways to continue increasing the level of automation in the manufacturing process. We intend to add capacity to manufacture Sentrix Array Matrices and BeadChips throughout 2006. We currently depend upon outside suppliers for materials used in the manufacture of our products. We intend to continue, and may extend, the outsourcing of portions of our manufacturing process to subcontractors where we determine it is in our best commercial interests.

During 2001, we moved into a new facility which allowed us to design the manufacturing areas to fit our specific processes, and optimize material flow and personnel movement. In addition, we have implemented information management systems for many of our manufacturing and services operations to manage all aspects of material and sample use. We adhere to access and safety standards required by federal, state and local health ordinances, such as standards for the use, handling and disposal of hazardous substances.

We introduced a number of initiatives in 2002 and 2003 to improve the yield and quality of our oligos while reducing the manufacturing cost substantially. By refining our understanding of the design and operation of our Oligator technology, we have been able to make numerous changes in our process, which we believe provides us a more cost effective system than competing technologies. In 2005, we expanded our Oligator technology under the collaboration agreement with Invitrogen discussed above. In addition, we expanded our oligo manufacturing facility to support high-volume shipments.

S-29

Table of Contents

Competition

Although we expect that our BeadArray products and services will provide significant advantages over currently available products and services, we expect to encounter intense competition from other companies that offer products and services for the SNP genotyping and gene expression markets. These include companies such as Affymetrix, Agilent, Amersham Biosciences (acquired by GE Corp. and now named GE Healthcare), Applied Biosystems, Beckman Coulter, Caliper Technologies, Luminex, Monogram Biosciences, Perlegen Sciences, NimbleGen, Sequenom and Third Wave Technologies. Some of these companies have or will have substantially greater financial, technical, research, and other resources and larger, more established marketing, sales, distribution and service organizations than we do. In addition, they may have greater name recognition than we do in the markets we need to address and in some cases a large installed base of systems. Each of these markets is very competitive and we expect new competitors to emerge and the intensity of competition to increase in the future. In order to effectively compete with these companies, we will need to demonstrate that our products have superior throughput, cost and accuracy advantages over the existing products. Rapid technological development may result in our products or technologies becoming obsolete. Products offered by us could be made obsolete either by less expensive or more effective products based on similar or other technologies. Although we believe that our technology and products will offer advantages that will enable us to compete effectively with these companies, we cannot assure you that we will be successful.

Segment and Geographic Information

We operate in one business segment, for the development, manufacture and commercialization of tools for genetic analysis. Our operations are treated as one segment as we only report operating results on an aggregate basis to chief operating decision makers of Illumina.

During 2005, \$28.0 million, or 38%, of our total revenue came from customers outside the United States, as compared to \$26.4 million, or 52%, in 2004. Sales to territories outside of the United States are generally denominated in U.S. dollars. We expect that sales to international customers will be an important and growing source of revenue. We have sales support resources in Western Europe and direct sales offices in Japan, Singapore and China. In addition, we have distributor relationships in various countries in the Pacific Rim region and Europe.

Seasonality

Historically, customer purchasing patterns have not shown significant seasonal variation, although demand for our products is usually lowest in the first quarter of the calendar year and highest in the third quarter of the calendar year as academic customers spend unused budget allocations before the end of the government's fiscal year.

Environmental Matters

We are dedicated to the protection of our employees and the environment. Our operations require the use of hazardous materials which subject us to a variety of federal, state and local environmental and safety laws and regulations. We believe we are in material compliance with current applicable laws and regulations; however, we could be held liable for damages and fines should contamination of the environment or individual exposures to hazardous substances occur. In addition, we cannot predict how changes in these laws and regulations, or the development of new laws and regulations, will affect our business operations or the cost of compliance.

Employees

As of April 2, 2006, we had a total of 414 employees, of which 74 hold Ph.D. degrees. None of our employees are represented by a labor union. We consider our employee relations to be positive.

Legal Proceedings

We have incurred substantial costs in defending ourselves against patent infringement claims, and expect to devote substantial financial and managerial resources to protect our intellectual property and to defend against the claims described below as well as any future claims asserted against us.

S-30

Table of Contents

Affymetrix Litigation

On July 26, 2004, Affymetrix, Inc. (Affymetrix) filed a complaint in the U.S. District Court for the District of Delaware alleging that the use, manufacture and sale of our BeadArray products and services, including our Array Matrix and BeadChip products, infringe six Affymetrix patents. Affymetrix seeks an injunction against the sale of products, if any, that are determined to be infringing these patents, unspecified monetary damages, interest and attorneys' fees. On September 15, 2004, we filed our answer to Affymetrix' complaint, seeking declaratory judgments from the court that we do not infringe the Affymetrix patents and that such patents are invalid, and we filed counterclaims against Affymetrix for unfair competition and interference with actual and prospective economic advantage.

On February 15, 2006, the court allowed us to file our first amended answer and counterclaims, adding allegations of inequitable conduct with respect to all six asserted Affymetrix patents, violation of Section 2 of the Sherman Act, and unclean hands. In March 2006, Affymetrix notified us of its decision to drop one of the six patents from the suit and of its intention to assert infringement of certain additional claims of the remaining five patents. We have filed a motion to preclude Affymetrix from asserting infringement of those additional claims. On April 20, 2006, a claims construction hearing was held. While rulings on our motion and on the claims construction issues could be issued at any time, we expect a ruling on the claims construction issues in the next several weeks. Trial is scheduled for October 16, 2006. We believe we have meritorious defenses against each of the infringement claims alleged by Affymetrix and intend to vigorously defend against this suit. However, we cannot be sure that we will prevail in this matter. Any unfavorable determination, and in particular, any significant cash amounts required to be paid by us or prohibition of the sale of our products and services, could result in a material adverse effect on our business, financial condition and results of operations.

Dr. Anthony W. Czarnik v. Illumina, Inc.

On June 15, 2005, Dr. Anthony Czarnik, a former employee, filed suit against us in the U.S. District Court for the District of Delaware seeking correction of inventorship of certain of our patents and patent applications and alleging that we committed inequitable conduct and fraud in not naming him as an inventor. Dr. Czarnik seeks an order requiring us and the U.S. Patent and Trademark Office to correct the inventorship of certain of our patents and patent applications by adding Dr. Czarnik as an inventor, a judgment declaring certain of our patents and patent applications unenforceable, unspecified monetary damages and attorney's fees. On August 4, 2005, we filed a motion to dismiss the complaint for lack of standing and failure to state a claim. While this motion was pending, Dr. Czarnik filed an amended complaint on September 23, 2005. On October 7, 2005, we filed a motion to dismiss the amended complaint for lack of standing and failure to state a claim, and this motion is still pending. There has been no trial date set for this case. We believe we have meritorious defenses against this claim.

Table of Contents**MANAGEMENT**

Our executive officers and directors and their respective ages, as of May 1, 2006, are:

Name	Age	Position(s)
Jay T. Flatley	53	President, Chief Executive Officer and Director
Christian O. Henry	38	Vice President, Chief Financial Officer
Tristan B. Orpin	40	Vice President of Worldwide Sales
John R. Stuelpnagel, D.V.M.	48	Co-Founder, Senior Vice President, Chief Operating Officer and Director
Arthur L. Holden	52	Senior Vice President, Corporate and Market Development
William H. Rastetter	58	Chairman of the Board of Directors
Daniel M. Bradbury	45	Director
Karin Eastham	56	Director
Paul Grint	48	Director
David R. Walt	53	Director

Jay T. Flatley has served as our President, Chief Executive Officer and a director since October 1999. Prior to joining Illumina, Mr. Flatley was co-founder, President, Chief Executive Officer and a director of Molecular Dynamics, a life sciences company, from May 1994 to September 1999. He served in various other positions with that company from 1987 to 1994. From 1985 to 1987, Mr. Flatley was Vice President of Engineering and Vice President of Strategic Planning at Plexus Computers, a UNIX computer company. Mr. Flatley also serves as a director at GenVault. Mr. Flatley holds a B.A. in Economics from Claremont McKenna College and a B.S. and M.S. in Industrial Engineering from Stanford University.

Christian O. Henry joined Illumina in June 2005 as Vice President and Chief Financial Officer. He is responsible for worldwide financial operations, controllership functions and facilities management. Mr. Henry served previously as the Chief Financial Officer for Tickets.com, a publicly traded, online ticket provider that was recently acquired by Major League Baseball Advanced Media, LP. Prior to that, Mr. Henry was Vice President, Finance and Corporate Controller of Affymetrix, Inc., a publicly traded life sciences company. He previously held a similar position at Nektar Therapeutics (formerly Inhale Therapeutic Systems, Inc.). Mr. Henry received a BA in biochemistry and cell biology from the University of California, San Diego, and an M.B.A. from the University of California, Irvine. Mr. Henry is a certified public accountant.

Tristan B. Orpin has served as our Vice President of Worldwide Sales since December 2002. Prior to joining us, Mr. Orpin was the Vice President of Sales and Marketing at Sequenom, a genomics company, from August 2001 to November 2002, and was Director of Sales and Marketing at Sequenom from September 1999 to August 2001. From December 1988 to September 1999, Mr. Orpin served in several senior sales and marketing positions at Bio-Rad Laboratories, a life sciences company. Mr. Orpin received his BSc. in Biochemistry from the University of Melbourne.

John R. Stuelpnagel, D.V.M., one of our founders, has been our Senior Vice President since April 2002, our Chief Operating Officer since January 2005 and a director since April 1998. From April 2002 to October 2004, he served as Senior Vice President of Operations. From October 1999 to April 2002, he served as our Vice President of Business Development. From April 1998 to October 1999, he served as our acting President and Chief Executive Officer and

was acting Chief Financial Officer through April 2000. While founding Illumina, Dr. Stuelpnagel was an associate with CW Group, a venture capital firm, from June 1997 to September 1998, and with Catalyst Partners, a venture capital firm, from August 1996 to June 1997. Dr. Stuelpnagel received his B.S. in Biochemistry and his Doctorate in Veterinary Medicine from the University of California, Davis and his M.B.A. from the University of California, Los Angeles.

Arthur L. Holden joined Illumina in April 2006 as Senior Vice President, Corporate and Market Development. From 1999 to 2006, Mr. Holden served as the Chairman, Chief Executive Officer and principal founder of First Genetic Trust, Inc., a provider of secure information technology applications and related services to support both the development and adoption of personalized medicine. From 1999 to 2006, Mr. Holden also served as Chairman

Table of Contents

of the Pharmaceutical Biomedical Research Consortium and the DMD Translational Research Consortium. From 1998 to 2006, Mr. Holden also served as Chief Executive Officer of the SNP Consortium, Ltd. From 1994 to 1998, Mr. Holden served as Chief Executive Officer and a director of Celsis International, PLC, an industrial biotechnology company. Prior to Celsis, Mr. Holden spent the majority of his career as an executive at Baxter International. Mr. Holden serves on a number of commercial and non-profit boards. He earned his M.B.A. from Northwestern University's Kellogg School of Management and a B.S. from Union College.

William H. Rastetter, Ph.D. has been a director since November 1998 and chairman of the board since January 2005. Dr. Rastetter retired as the Executive Chairman of Biogen Idec Inc., a biopharmaceutical company, at the end of 2005, and had served in this position since the merger of Biogen, Inc. and IDEC Pharmaceuticals Corporation in November 2003. He served as Chief Executive Officer of IDEC Pharmaceuticals, a biotechnology company, from December 1986 through November 2003 and as chairman of the board of directors from May 1996 to November 2003. Additionally, he served as President of IDEC Pharmaceuticals from 1986 to 2002, and as Chief Financial Officer from 1988 to 1993. From 1982 to 1986, Dr. Rastetter served in various positions at Genentech, Inc., a biotechnology company, and previously he was an associate professor at the Massachusetts Institute of Technology. Dr. Rastetter holds a S.B. in Chemistry from the Massachusetts Institute of Technology and received his M.A. and Ph.D. in Chemistry from Harvard University.

Daniel M. Bradbury has been a director since January 2004. Since June 2003, Mr. Bradbury has served as Chief Operating Officer of Amylin Pharmaceuticals, a biopharmaceutical company. He served in various other positions with that company from 1994 to 2003. From 1984 to 1994, Mr. Bradbury held a number of positions at SmithKline Beecham Pharmaceuticals, a drug manufacturer. Mr. Bradbury is a director of Cerexa, Inc., a biopharmaceutical company, and Novacea, Inc., a biopharmaceutical company, and serves on the Advisory Council of the Keck Graduate Institute. Mr. Bradbury holds a B.Pharm. (Hons.) from Nottingham University and a Diploma in Management Studies from Harrow and Ealing Colleges of Higher Education, is a member of the Royal Pharmaceutical Society of Great Britain and is a Certified Director.

Karin Eastham has served as a director since August 2004. Ms. Eastham has over 25 years experience in financial and operations management, primarily in life sciences companies. Since May 2004, she has been serving as Executive Vice President and Chief Operating Officer, and as a member of the Board of Trustees, of the Burnham Institute for Medical Research, a non-profit corporation engaged in basic biomedical research and the home to three research centers—a Cancer Center, the Del E. Webb Center for Neuroscience and Aging and a Center for Research on Infectious and Inflammatory Diseases. From April 1999 to May 2004, Ms. Eastham served as Senior Vice President, Finance, Chief Financial Officer, and Secretary of Diversa Corporation, a biotechnology company. She previously held similar positions with CombiChem, Inc., a computational chemistry company, and Cytel Corporation, a biopharmaceutical company. Ms. Eastham also held several positions, including Vice President, Finance, at Boehringer Mannheim Corporation, from 1976 to 1988. Ms. Eastham also serves as a director for the biopharmaceutical companies Tercica, Inc., Amylin Pharmaceuticals, Inc., and SGX Pharmaceuticals, Inc. Ms. Eastham received a B.S. and an M.B.A. from Indiana University and is a Certified Public Accountant and a Certified Director.

Paul Grint M.D. has been a director since April 2005. Dr. Grint is currently Chief Medical Officer and Head of Development at Kalypsys Inc., a biotechnology company. Prior to joining Kalypsys, Dr. Grint was Senior Vice President and Chief Medical Officer of Zephyr Sciences, Inc., a biopharmaceutical company. He held similar positions at Pfizer, a drug manufacturer, in La Jolla, California, IDEC Pharmaceuticals, a biotechnology company, and Schering-Plough, a drug manufacturer. He has more than 15 years of experience in biologics and small molecule drug development, marked by the successful development of numerous commercial products in the fields of infectious disease, immunology and oncology. Dr. Grint began his pharmaceutical career at the Wellcome Research Laboratories in the UK and received his medical degree from the University of London, St. Bartholomew's Hospital Medical College in London. He is a Fellow of the Royal College of Pathologists, a member of numerous professional and

medical societies and the author or co-author of over 50 publications.

David R. Walt, Ph.D., one of our founders, has been a director and Chairman of our Scientific Advisory Board since June 1998. Dr. Walt has been the Robinson Professor of Chemistry at Tufts University since September 1995. Dr. Walt has published over 175 papers and holds over 40 patents. Dr. Walt holds a B.S. in Chemistry from the University of Michigan and received his Ph.D. in Chemical Biology for SUNY at Stony Brook.

S-33

Table of Contents

DESCRIPTION OF CAPITAL STOCK

General

We are authorized to issue 120,000,000 shares of common stock, \$0.01 par value per share, and 10,000,000 shares of undesignated preferred stock, \$0.01 par value per share.

Common Stock

As of April 2, 2006, we had 41,696,733 shares of common stock outstanding.

The holders of common stock are entitled to one vote per share on all matters to be voted upon by the stockholders, and they are not permitted to cumulate their votes for the election of directors or any other matter submitted to a vote of the stockholders. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of common stock are entitled to receive ratably any dividends that may be declared from time to time by the board of directors out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, the holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock then outstanding. The common stock has no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without action by our stockholders, to designate and issue up to 10,000,000 shares of preferred stock in one or more series. The board of directors may also designate the rights, preferences and privileges of each series of preferred stock, any or all of which may be greater than the rights of the common stock.

Preferred Share Rights

We have authorized and reserved 120,000 shares of series A junior participating preferred stock for issuance in connection with our stockholder rights plan set forth in our rights agreement, dated as of May 3, 2001, by and between us and Equiserve Trust Company, N.A., as rights agent. One preferred share purchase right attaches to each share of our common stock. The rights will expire in May 2011, unless extended or unless we earlier redeem or exchange the rights.

Generally, in certain circumstances where a person or group acquires 15% or more of our common stock, the rights holders will be entitled to receive, upon exercise of a preferred stock purchase right, a number or fraction of shares of our series A junior participating preferred stock whose market value is designed to approximate twice the exercise price of the right.

The series A preferred stock purchasable upon exercise of the rights will not be redeemable. Each share of series A preferred stock will be entitled to an aggregate dividend of 1,000 times the dividend declared per share of our common stock. In the event of liquidation, the holders of our series A preferred stock generally will be entitled to the greater of \$1,000 per share or an aggregate payment of 1,000 times the payment made per share of our common stock. Each share of series A preferred stock will have 1,000 votes, voting together with the common stock. In the event of any merger, consolidation or other transaction in which shares of common stock are exchanged, each share of series A

preferred stock will be entitled to receive 1,000 times the amount received per share of common stock. These rights are protected by customary anti-dilution provisions.

In addition, in certain circumstances where we are acquired in a business combination, the rights holders will be entitled to receive, upon exercise of a preferred stock purchase right, shares of common stock of the acquiring corporation with a market value equal to twice the exercise price of the right.

Table of Contents

Our board of directors may in certain circumstances redeem the rights in whole, but not in part, at a price of \$0.01 per right.

The rights plan is designed to protect our stockholders in the event of unsolicited offers to acquire us and other coercive takeover tactics, which, in the board's opinion, would impair the board's ability to represent our stockholders interests. The rights plan may make an unsolicited takeover more difficult or less likely to occur or may prevent a takeover, even though a takeover may offer our stockholders the opportunity to sell their stock at a price above the prevailing market rate and may be favored by a majority of our stockholders.

The above description of the rights and the series A preferred stock is qualified in its entirety by reference to the rights agreement, which is filed as exhibit to our Annual Report on Form 10-K for the fiscal year ended January 1, 2006, which is incorporated by reference into the accompanying prospectus.

S-35

Table of Contents**UNDERWRITING**

The company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co., Merrill Lynch, Pierce, Fenner & Smith Incorporated, Cowen and Company, LLC and Robert W. Baird & Co. Incorporated are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman, Sachs & Co.	
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Cowen and Company, LLC	
Robert W. Baird & Co. Incorporated	
Total	3,500,000

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to an additional 525,000 shares from the company to cover such sales. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by the company. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 525,000 additional shares.

Paid by the Company	No Exercise	Full Exercise
Per Share	\$	\$
Total	\$	\$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$ per share from the initial public offering price. Any such securities dealers may resell any shares purchased from the underwriters to certain other brokers or dealers at a discount of up to \$ per share from the initial public offering price. If all the shares are not sold at the initial public offering price, the representatives may change the offering price and the other selling terms.

The company and other parties have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representatives. This agreement does not apply to any existing employee benefit plans or certain Rule 10b5-1 plans.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from the company in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them. Naked short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A

Table of Contents

naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short-covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on NASDAQ, in the over-the-counter market or otherwise.

Each of the underwriters has represented and agreed that:

- (a) it has not made or will not make an offer of shares to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (FSMA) except to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by the company of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);
- (b) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to the company; and
- (c) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

- (a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts; or

(c) in any other circumstances which do not require the publication by the Company of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on

S-37

Table of Contents

the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The shares may not be offered or sold by means of any document other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent, or in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong, and no advertisement, invitation or document relating to the shares may be issued, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made thereunder.

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

The securities have not been and will not be registered under the Securities and Exchange Law of Japan (the Securities and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Securities and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

The company estimates that its share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$325,000.

In compliance with NASD guidelines, the maximum compensation to any underwriters or agents in connection with the sale of any securities pursuant to this prospectus supplement and the accompanying prospectus will not exceed 8% of the aggregate total offering price to the public of such securities as set forth on the cover page of this prospectus supplement; however, it is anticipated that the maximum compensation paid will be significantly less than 8%.

The company has agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933.

Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for the company, for which they received or will receive customary fees and expenses.

S-38

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at *www.sec.gov*. The SEC's website contains reports, proxy and information statements and other information regarding issuers, such as us, that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room. We maintain a website at *www.illumina.com*. We have not incorporated by reference into this prospectus supplement the information in, or that can be accessed through, our or the SEC's websites, and you should not consider such information to be a part of this prospectus supplement.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement the information we have filed with the SEC. The information we incorporate by reference into this prospectus supplement is an important part of this prospectus supplement. Any statement in a document we filed with the SEC prior to the date of this prospectus supplement and which is incorporated by reference into this prospectus supplement will be considered to be modified or superseded to the extent a statement contained in this prospectus supplement or any other subsequently filed document that is incorporated by reference into this prospectus supplement modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus supplement, except as modified or superseded.

We incorporate by reference into this prospectus supplement the information contained in the documents listed below, which is considered to be a part of this prospectus:

our annual report on Form 10-K for the fiscal year ended January 1, 2006, filed with the SEC on March 6, 2006 (file no. 000-30361);

our quarterly report on Form 10-Q for the fiscal quarter ended April 2, 2006, filed with the SEC on May 8, 2006 (file no. 000-30361);

our current report on Form 8-K, filed with the SEC on March 29, 2006 (file no. 000-30361);

the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on April 14, 2000, including any amendments or reports filed for the purpose of updating such description (file no. 000-30361);

the description of our preferred stock purchase rights contained in our registration statement on Form 8-A, filed with the SEC on May 14, 2001, including any amendments or reports filed for the purpose of updating such description (file no. 000-30361); and

all filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 after the date of this prospectus supplement but prior to the termination of the offering of the securities covered by this prospectus supplement.

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

Illumina, Inc.
9885 Towne Centre Drive
San Diego, California 92121
(858) 202-4500

S-39

Table of Contents

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Dewey Ballantine LLP, New York, NY, and for the underwriters by Sullivan & Cromwell LLP, Los Angeles, CA.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule included in our Annual Report on Form 10-K for the year ended January 1, 2006, and management's assessment of the effectiveness of our internal control over financial reporting as of January 1, 2006, as set forth in their reports, which are incorporated by reference into this prospectus supplement and elsewhere in the registration statement. Our financial statements and schedule and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

S-40

Table of Contents

PROSPECTUS

—

Common Stock

We may offer to sell shares of our common stock from time to time in one or more offerings. This prospectus describes some of the general terms that may apply to an offering of our common stock. We will describe the details of each offering, including the number of shares offered and the offering price, in a post-effective amendment to the registration statement of which this prospectus is a part, in one or more supplements to this prospectus or in one or more documents incorporated by reference into this prospectus.

We may offer and sell common stock to or through one or more underwriters, dealers or agents, directly to purchasers or otherwise.

Our common stock is quoted on the Nasdaq National Market under the symbol ILMN.

Investing in our common stock involves a high degree of risk. Before buying any shares you should read the discussion of material risks of investing in our common stock in Risk Factors beginning on page 2.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 11, 2006.

Table of Contents

TABLE OF CONTENTS

<u>About this Prospectus</u>	1
<u>Risk Factors</u>	2
<u>Use of Proceeds</u>	9
<u>Where You Can Find More Information</u>	9
<u>Incorporation of Certain Documents by Reference</u>	9
<u>Legal Matters</u>	10
<u>Experts</u>	10

Table of Contents

About this Prospectus

This prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission using the shelf registration process. By using a shelf registration statement, we may offer and sell our common stock from time to time in one or more offerings. There is no limit on the number of shares of common stock we may sell pursuant to the registration statement.

You should rely only on the information contained in or incorporated by reference into this prospectus and any applicable prospectus supplement and the information contained in any permitted free writing prospectuses we have authorized for use with respect to the applicable offering. We have not authorized anyone to provide you with different or additional information. This document may only be used where it is legal to sell our common stock. You should not assume that the information contained in this prospectus, any prospectus supplement or any related permitted free writing prospectus we have authorized is accurate as of any date other than its date, regardless of when you receive those documents or when any particular sale of our common stock occurs.

This prospectus and the information incorporated by reference into this prospectus includes trademarks, service marks and trade names owned by us or others. All trademarks, service marks and trade names included or incorporated by reference in this prospectus are the property of their respective owners.

Unless the context requires otherwise, the words Illumina, we, company, us and our refer to Illumina, Inc. and its subsidiaries, and the term you refers to a prospective investor. Our principal executive offices are located at 9885 Towne Centre Drive, San Diego, California 92121. Our phone number is (858) 202-4500.

Table of Contents

Risk Factors

Investing in our common stock involves a high degree of risk. In addition to the other information included and incorporated by reference in this prospectus or accompanying prospectus supplement or in any free writing prospectus we have authorized, you should carefully consider the risks described below before purchasing our common stock. If any of the following risks actually occurs, our business, results of operations and financial condition will likely suffer. As a result, the trading price of our common stock may decline, and you might lose part or all of your investment.

RISKS RELATED TO OUR BUSINESS

Litigation or other proceedings or third party claims of intellectual property infringement could require us to spend significant time and money and could prevent us from selling our products or services or impact our stock price.

Our commercial success depends in part on our non-infringement of the patents or proprietary rights of third parties and the ability to protect our own intellectual property. As described in our Quarterly Report on Form 10-Q for the quarter period ended April 2, 2006, filed with the SEC on May 8, 2006, under the caption Part II. Other Information. Item 1. Legal Proceedings, Affymetrix, Inc. filed a complaint against us in July 2004, alleging infringement of six of its patents.

On April 20, 2006, a claims construction hearing was held as part of this proceeding. We expect a ruling related to the claims construction within the next several weeks, but there is no fixed time for such a ruling. At issue is the meaning of 15 terms, and depending on the court's ruling on each of the 15 terms, or a mix of rulings across all the terms, an advantage (or at least the perception of an advantage) may be obtained by one party or the other as to one or more issues. We are not able to predict the timing or the substance of the court's rulings. Any adverse ruling or perception of an adverse ruling may have an adverse impact on our stock price, and such impact may be disproportionate to the actual import of the ruling itself.

Including Affymetrix, third parties have asserted or may assert that we are employing their proprietary technology without authorization. As we enter new markets, we expect that competitors will likely assert that our products infringe their intellectual property rights as part of a business strategy to impede our successful entry into those markets. In addition, third parties may have obtained and may in the future obtain patents and claim that use of our technologies infringes these patents. We could incur substantial costs and divert the attention of our management and technical personnel in defending ourselves against any of these claims. Furthermore, parties making claims against us may be able to obtain injunctive or other relief, which effectively could block our ability to further develop, commercialize and sell products, and could result in the award of substantial damages against us. In the event of a successful claim of infringement against us, we may be required to pay damages and obtain one or more licenses from third parties, or be prohibited from selling certain products. We may not be able to obtain these licenses at a reasonable cost, or at all. We could incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins. In that event, we could encounter delays in product introductions while we attempt to develop alternative methods or products. Defense of any lawsuit or failure to obtain any of these licenses on favorable terms could prevent us from commercializing products, and the prohibition of sale of any of our products could materially affect our ability to grow and to attain profitability.

We expect intense competition in our target markets, which could render our products obsolete, result in significant price reductions or substantially limit the volume of products that we sell. This would limit our ability to compete and achieve and maintain profitability. If we cannot continuously develop and commercialize new products, our revenue may not grow as intended.

We compete with life sciences companies that design, manufacture and market instruments for analysis of genetic variation and biological function and other applications using technologies such as two-dimensional electrophoresis, capillary electrophoresis, mass spectrometry, flow cytometry, microfluidics, next-generation DNA sequencing and mechanically deposited, inkjet and photolithographic arrays. We anticipate that we will face increased competition in the future as existing companies develop new or improved products and as new companies enter the market with new technologies. The markets for our products are characterized by rapidly changing technology,

Table of Contents

evolving industry standards, changes in customer needs, emerging competition, new product introductions and strong price competition. For example, prices per data point for genotyping have fallen significantly over the last two years and we anticipate that prices will continue to fall. One or more of our competitors may render our technology obsolete or uneconomical. Some of our competitors have greater financial and personnel resources, broader product lines, a more established customer base and more experience in research and development than we do. Furthermore, the life sciences and pharmaceutical companies, which are our potential customers and strategic partners, could develop competing products. If we are unable to develop enhancements to our technology and rapidly deploy new product offerings, our business, financial condition and results of operations will suffer.

Our manufacturing capacity may limit our ability to sell our products.

We are currently ramping up our capacity to meet our anticipated demand for our products. Although we have significantly increased our manufacturing capacity and we believe that we have sufficient plans in place to ensure we have adequate capacity to meet our business plan in 2006, there are uncertainties inherent in expanding our manufacturing capabilities and we may not be able to increase our capacity in a timely manner. For example, manufacturing and product quality issues may arise as we increase production rates at our manufacturing facility and launch new products. As a result, we may experience difficulties in meeting customer, collaborator and internal demand, in which case we could lose customers or be required to delay new product introductions, and demand for our products could decline. Additionally, in the past, we have experienced variations in manufacturing conditions that have temporarily reduced production yields. Due to the intricate nature of manufacturing products that contain DNA, we may encounter similar or previously unknown manufacturing difficulties in the future that could significantly reduce production yields, impact our ability to launch or sell these products, or to produce them economically, prevent us from achieving expected performance levels or cause us to set prices that hinder wide adoption by customers.

We have not yet achieved annual operating profitability and may not be able to do so.

We have incurred net losses each year since our inception. As of April 2, 2006, our accumulated deficit was \$144.7 million and we incurred a net loss of \$0.1 million for the three months ended April 2, 2006. We may not be profitable in 2006, due in part to the impact of SFAS No. 123R, which is expected to add additional expense of \$12.0 million to \$15.0 million in 2006. Our ability to achieve annual profitability will depend, in part, on the rate of growth, if any, of our revenue and on the level of our expenses. We expect to continue incurring significant expenses related to research and development, sales and marketing efforts to commercialize our products and the continued development of our manufacturing capabilities. In addition, we expect that our selling and marketing expenses will increase at a higher rate in the future as a result of the launch of new products. As a result, we expect that our operating expenses will increase significantly as we grow and, consequently, we will need to generate significant additional revenue to achieve and maintain profitability. Even if we maintain profitability, we may not be able to increase profitability on a quarterly basis.

The growth and profitability of our oligo business depends on a third party.

In December 2004, we entered into a collaboration agreement with Invitrogen to sell and market our oligos worldwide. Under the terms of the collaboration, Invitrogen is responsible for sales, marketing and technical support, while we are responsible for the manufacture of the collaboration products. As Invitrogen is solely responsible for the sales and marketing support of the collaboration, our continued growth and profitability related to these products depends on the extent to which Invitrogen is successful in penetrating the oligo market and selling the collaboration products. If Invitrogen is not successful in selling the collaboration products, our business, financial condition and results of operations may suffer.

We have a limited history of commercial sales of systems and consumable products, and our success depends on our ability to develop commercially successful products and on market acceptance of our new and relatively unproven technologies.

We may not possess all of the resources, capability and intellectual property necessary to develop and commercialize all the products or services that may result from our technologies. Sales of our genotyping and gene

Table of Contents

expression systems only began in 2003, and some of our other technologies are in the early stages of commercialization or are still in development. You should evaluate us in light of the uncertainties and complexities affecting similarly situated companies developing tools for the life sciences and pharmaceutical industries. We must conduct a substantial amount of additional research and development before some of our products will be ready for sale, and we currently have fewer resources available for research and development activities than many of our competitors. We may not be able to develop or launch new products in a timely manner, or at all, or they may not meet customer requirements or be of sufficient quality or at a price that enables us to compete effectively in the marketplace. Problems frequently encountered in connection with the development or early commercialization of products and services using new and relatively unproven technologies might limit our ability to develop and successfully commercialize these products and services. In addition, we may need to enter into agreements to obtain intellectual property necessary to commercialize some of our products or services, which may not be available on favorable terms, or at all.

Historically, life sciences and pharmaceutical companies have analyzed genetic variation and biological function using a variety of technologies. In order to be successful, our products must meet the commercial requirements of the life sciences and pharmaceutical industries as tools for the large-scale analysis of genetic variation and biological function.

Market acceptance will depend on many factors, including:

- our ability to demonstrate to potential customers the benefits and cost effectiveness of our products and services relative to others available in the market;

- the extent and effectiveness of our efforts to market, sell and distribute our products;

- our ability to manufacture products in sufficient quantities with acceptable quality and reliability and at an acceptable cost;

- the willingness and ability of customers to adopt new technologies requiring capital investments; and

- the extended time lag and sales expenses involved between the time a potential customer is contacted on a possible sale of our products and services and the time the sale is consummated or rejected by the customer.

Any inability to adequately protect our proprietary technologies could harm our competitive position.

Our success will depend in part on our ability to obtain patents and maintain adequate protection of our intellectual property in the United States and other countries. If we do not protect our intellectual property adequately, competitors may be able to use our technologies and thereby erode our competitive advantage. The laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting their proprietary rights abroad. These problems can be caused by the absence of rules and methods for defending intellectual property rights.

The patent positions of companies developing tools for the life sciences and pharmaceutical industries, including our patent position, generally are uncertain and involve complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We intend to apply for patents covering our technologies and products, as we deem appropriate. However, our patent applications may be challenged and may not result in issued patents or may be invalidated or narrowed in scope after they are issued. Questions as to inventorship may also arise. For example, a former employee recently filed a complaint against us, claiming he is

entitled to be named as joint inventor of certain of our U.S. patents and pending U.S. and foreign patents and seeking a judgment that the related patents and applications are unenforceable. Any finding that our patents and applications are unenforceable could harm our ability to prevent others from practicing the related technology, and a finding that others have inventorship rights to our patents and applications could require us to obtain licenses to practice the technology, which may not be available on favorable terms, if at all.

In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. There also is risk that others may independently develop similar or alternative technologies or design around our patented technologies. Also, our

Table of Contents

patents may fail to provide us with any competitive advantage. We may need to initiate additional lawsuits to protect or enforce our patents, or litigate against third party claims, which would be expensive and, if we lose, may cause us to lose some of our intellectual property rights and reduce our ability to compete in the marketplace. Furthermore, these lawsuits may divert the attention of our management and technical personnel.

We also rely upon trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information. These measures, however, may not provide adequate protection for our trade secrets or other proprietary information. We seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants. Nevertheless, employees, collaborators or consultants may still disclose our proprietary information, and we may not be able to meaningfully protect our trade secrets. In addition, others may independently develop substantially equivalent proprietary information or techniques or otherwise gain access to our trade secrets.

Our sales, marketing and technical support organization may limit our ability to sell our products.

We currently have fewer resources available for sales and marketing and technical support services as compared to some of our primary competitors. In order to effectively commercialize our genotyping and gene expression systems and other products to follow, we will need to expand our sales, marketing and technical support staff both domestically and internationally. We may not be successful in establishing or maintaining either a direct sales force or distribution arrangements to market our products and services. In addition, we compete primarily with much larger companies that have larger sales and distribution staffs and a significant installed base of products in place, and the efforts from a limited sales and marketing force may not be sufficient to build the market acceptance of our products required to support continued growth of our business.

If we are unable to develop and maintain operation of our manufacturing capability, we may not be able to launch or support our products in a timely manner, or at all.

We currently possess only one facility capable of manufacturing our products and services for both sale to our customers and internal use. If a natural disaster were to significantly damage our facility or if other events were to cause our operations to fail, these events could prevent us from developing and manufacturing our products and services. Also, many of our manufacturing processes are automated and are controlled by our custom-designed Laboratory Information Management System (LIMS). Additionally, as part of the decoding step in our array manufacturing process, we record several images of each array to identify what bead is in each location on the array and to validate each bead in the array. This requires significant network and storage infrastructure. If either our LIMS system or our networks or storage infrastructure were to fail for an extended period of time, it would adversely impact our ability to manufacture our products on a timely basis and may prevent us from achieving our expected shipments in any given period.

If we are unable to find third-party manufacturers to manufacture components of our products, we may not be able to launch or support our products in a timely manner, or at all.

The nature of our products requires customized components that currently are available from a limited number of sources. For example, we currently obtain the fiber optic bundles and BeadChip slides included in our products from single vendors. If we are unable to secure a sufficient supply of those or other product components, we will be unable to meet demand for our products. We may need to enter into contractual relationships with manufacturers for commercial-scale production of some of our products, or develop these capabilities internally, and we cannot assure you that we will be able to do this on a timely basis, for sufficient quantities or on commercially reasonable terms. Accordingly, we may not be able to establish or maintain reliable, high-volume manufacturing at commercially reasonable costs.

We may encounter difficulties in integrating recently completed or future acquisitions that could adversely affect our business.

In April 2005, we acquired CyVera Corporation and may in the future acquire technology, products or businesses related to our current or future business. We have limited experience in acquisition activities and may have to devote

Table of Contents

substantial time and resources in order to complete acquisitions. Further, these potential acquisitions entail risks, uncertainties and potential disruptions to our business. For example, we may not be able to successfully integrate a company's operations, technologies, products and services, information systems and personnel into our business. An acquisition may further strain our existing financial and managerial resources, and divert management's attention away from our other business concerns. In connection with the CyVera acquisition, we assumed certain liabilities and hired certain employees of CyVera, which is expected to continue to result in an increase in our research and development expenses and capital expenditures. There may also be unanticipated costs and liabilities associated with an acquisition that could adversely affect our operating results.

We may encounter difficulties in managing our growth. These difficulties could increase our losses.

We expect to experience rapid and substantial growth in order to achieve our operating plans, which will place a strain on our human and capital resources. If we are unable to manage this growth effectively, our losses could increase. Our ability to manage our operations and growth effectively requires us to continue to expend funds to enhance our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. If we are unable to scale up and implement improvements to our manufacturing process and control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, then we will not be able to make available the products required to successfully commercialize our technology. Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth.

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

Our future capital requirements will be substantial and will depend on many factors including our ability to successfully market our genetic analysis systems and services, the need for capital expenditures to support and expand our business, the progress and scope of our research and development projects, the filing, prosecution and enforcement of patent claims, the outcome of our legal proceedings with Affymetrix, the defense of any future litigation involving us and the need to enter into collaborations with other companies or acquire other companies or technologies to enhance or complement our product and service offerings. We anticipate that our current cash and cash equivalents, revenue from sales and funding from grants will be sufficient to fund our anticipated operating needs, barring unforeseen developments. However, this expectation is based upon our current operating plan, which may change as a result of many factors. Consequently, we may need additional funding in the future. Our inability to raise capital would seriously harm our business and product development efforts. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, such as an acquisition, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity, the issuance of these securities could result in dilution to our stockholders.

We have no credit facility or committed sources of capital available as of April 2, 2006. To the extent operating and capital resources are insufficient to meet future requirements, we will have to raise additional funds to continue the development and commercialization of our technologies. These funds may not be available on favorable terms, or at all. If adequate funds are not available on attractive terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to achieve our goals.

We are highly dependent on our management and scientific personnel, including Jay Flatley, our president and chief executive officer, and John Stuelpnagel, our senior vice president and chief operating officer. The loss of their services

could adversely impact our ability to achieve our business objectives. We will need to hire additional qualified personnel with expertise in molecular biology, chemistry, biological information processing, sales, marketing and technical support. We compete for qualified management and scientific personnel with other life science companies, universities and research institutions, particularly those focusing on genomics. Competition for these individuals, particularly in the San Diego area, is intense, and the turnover rate can be high. Failure to attract

Table of Contents

and retain management and scientific personnel would prevent us from pursuing collaborations or developing our products or technologies.

Our planned activities will require additional expertise in specific industries and areas applicable to the products developed through our technologies, including the life sciences and healthcare industries. Thus, we will need to add new personnel, including management, and develop the expertise of existing management. The failure to do so could impair the growth of our business.

A significant portion of our sales are to international customers.

Approximately 47% and 42% of our revenue for the three months ended April 2, 2006 and April 3, 2005, respectively, was derived from customers outside the United States. During fiscal 2005, 38% of our revenue came from customers outside the United States, as compared to 52% in fiscal 2004. We intend to continue to expand our international presence and export sales to international customers and we expect the total amount of non-U.S. sales to continue to grow. Export sales entail a variety of risks, including:

currency exchange fluctuations;

unexpected changes in legislative or regulatory requirements of foreign countries into which we import our products;

difficulties in obtaining export licenses or other trade barriers and restrictions resulting in delivery delays; and

significant taxes or other burdens of complying with a variety of foreign laws.

In addition, sales to international customers typically result in longer payment cycles and greater difficulty in accounts receivable collection. We are also subject to general geopolitical risks, such as political, social and economic instability and changes in diplomatic and trade relations. One or more of these factors could have a material adverse effect on our business, financial condition and operating results.

Our success depends upon the continued emergence and growth of markets for analysis of genetic variation and biological function.

We design our products primarily for applications in the life sciences and pharmaceutical industries. The usefulness of our technology depends in part upon the availability of genetic data and its usefulness in identifying or treating disease. We are initially focusing on markets for analysis of genetic variation and biological function, namely SNP genotyping and gene expression profiling. Both of these markets are new and emerging, and they may not develop as quickly as we anticipate, or reach their full potential. Other methods of analysis of genetic variation and biological function may emerge and displace the methods we are developing. Also, researchers may not seek or be able to convert raw genetic data into medically valuable information through the analysis of genetic variation and biological function. In addition, factors affecting research and development spending generally, such as changes in the regulatory environment affecting life sciences and pharmaceutical companies, and changes in government programs that provide funding to companies and research institutions, could harm our business. If useful genetic data is not available or if our target markets do not develop in a timely manner, demand for our products may grow at a slower rate than we expect, and we may not be able to achieve or sustain profitability.

We expect that our results of operations will fluctuate. This fluctuation could cause our stock price to decline.

Our revenue is subject to fluctuations due to the timing of sales of high-value products and services projects, the impact of seasonal spending patterns, the timing and size of research projects our customers perform, changes in overall spending levels in the life sciences industry, the timing and amount of government grant funding programs and other unpredictable factors that may affect customer ordering patterns. Given the difficulty in predicting the timing and magnitude of sales for our products and services, we may experience quarter-to-quarter fluctuations in revenue resulting in the potential for a sequential decline in quarterly revenue. A large portion of our expenses are relatively fixed, including expenses for facilities, equipment and personnel. In addition, we expect operating expenses to continue to increase significantly. Accordingly, if revenue does not grow as anticipated, we may not be

Table of Contents

able to achieve and maintain profitability. Any significant delays in the commercial launch of our products, unfavorable sales trends in our existing product lines, or impacts from the other factors mentioned above, could adversely affect our revenue growth in 2006 or cause a sequential decline in quarterly revenues. Due to the possibility of fluctuations in our revenue and expenses, we believe that quarterly comparisons of our operating results are not a good indication of our future performance. If our operating results fluctuate or do not meet the expectations of stock market analysts and investors, our stock price probably would decline.

RISKS RELATED TO OWNING OUR COMMON STOCK

Our poison pill, provisions of our charter documents and Delaware General Corporation Law may deter or prevent a business combination that may be favorable to you.

Provisions of our charter documents could deter or prevent a third party from acquiring us, even if doing so would be beneficial to our stockholders. These provisions include:

- establishing a classified board of directors, so that only a portion of our total board can be elected at each annual meeting;
- setting limitations on the removal of our directors;
- granting our board of directors the authority to issue blank check preferred stock without stockholder approval;
- prohibiting cumulative voting in the election of our directors, which would permit less than a majority of stockholders to elect directors;
- limiting our stockholders ability to call special meetings; and
- prohibiting stockholder action by written consent.

We have also established a rights agreement, also called a poison pill. Generally, our rights agreement permits our existing stockholders to purchase a large number of our shares at a substantial discount to the market price if a third party attempts to gain control of a sufficient equity position in us. Our rights agreement could have the effect of deterring or preventing a third party from acquiring us in a transaction that might be favorable to you.

In addition, Section 203 of the Delaware General Corporation Law generally prohibits us from engaging in any business combination with certain persons who own 15% or more of our outstanding voting stock or any of our associates or affiliates who at any time in the past three years have owned 15% or more of our outstanding voting stock. These provisions could adversely affect the price that investors are willing to pay for shares of our common stock and could prevent you from realizing any premium that stockholders may otherwise receive in connection with a corporate takeover.

We may invest or spend the proceeds of this offering in ways with which you may not agree and that may not earn a return for our stockholders.

We will retain broad discretion over the use of the proceeds from any offering we make pursuant to this prospectus. You may not agree with the way we decide to use those proceeds, and our use of the proceeds may not yield a significant return or any return at all for our stockholders.

We do not intend to pay cash dividends on our common stock in the foreseeable future.

We have not declared or paid any cash dividends on our common stock or other securities, and we currently do not anticipate paying any cash dividends in the foreseeable future. Accordingly, our stockholders will not realize a return on their investment unless the trading price of our common stock appreciates. We cannot assure you that our common stock will appreciate in value after the offering or even maintain the price at which you purchased your shares.

Table of Contents

Market volatility may affect our stock price, and the value of your investment in our common stock may experience sudden decreases.

There has been, and will likely continue to be, significant volatility in the market price of securities of life sciences and biotechnology companies, including us. These fluctuations can be unrelated to the operating performance of these companies. During the period from January 1, 2004 to May 10, 2006, the lowest and highest reported trading prices of our common stock on the Nasdaq National Market were \$4.23 and \$32.00, respectively. Factors such as the following could cause the market price of our common stock to fluctuate substantially:

- announcements of new products or services by us or our competitors;
- litigation involving or affecting us;
- quarterly fluctuations in our or other companies' financial results;
- shortfalls in our actual financial results compared to our guidance or the forecasts of stock market analysts;
- acquisitions or strategic alliances by us or our competitors;
- the gain or loss of a significant customer; and
- general conditions in our industry and in the financial markets.

A decline in the market price of our common stock could cause you to lose some or all of your investment and may adversely impact our ability to attract and retain employees, acquire other companies or businesses and raise capital. In addition, stockholders may initiate securities class action lawsuits if the market price of our stock drops significantly, which may cause us to incur substantial costs and could divert the time and attention of our management.

Use of Proceeds

We will specify, in a post-effective amendment to the registration statement of which this prospectus is a part, in an accompanying prospectus supplement or in a document incorporated by reference into this prospectus, how we intend to use the net proceeds received by us from any offerings we make pursuant to this prospectus.

Where You Can Find More Information

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. The SEC's website contains reports, proxy and information statements and other information regarding issuers, such as us, that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room. We maintain a website at www.illumina.com. We have not incorporated by reference into this prospectus the information in, or that can be accessed through, our or the SEC's website, and you should not consider it to be a part of this prospectus.

Incorporation of Certain Documents by Reference

The SEC allows us to incorporate by reference into this prospectus the information we have filed with the SEC. The information we incorporate by reference into this prospectus is an important part of this prospectus. Any statement in a document the we filed with the SEC prior to the date of this prospectus and which is incorporated by reference into this prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus or any other subsequently filed document that is incorporated by reference into this prospectus modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus, except as modified or superseded.

Table of Contents

We incorporate by reference into this prospectus the information contained in the documents listed below, which is considered to be a part of this prospectus:

our annual report on Form 10-K for the fiscal year ended January 1, 2006, filed with the SEC on March 6, 2006 (file no. 000-30361);

our quarterly report on Form 10-Q for the fiscal quarter ended April 2, 2006, filed with the SEC on May 8, 2006 (file no. 000-30361);

our current report on Form 8-K, filed with the SEC on March 29, 2006 (file no. 000-30361);

the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on April 14, 2000, including any amendments or reports filed for the purpose of updating such description (file no. 000-30361);

The description of our preferred stock purchase rights contained in our registration statement on Form 8-A, filed with the SEC on May 14, 2001, including any amendments or reports filed for the purpose of updating such description (file no. 000-30361); and

all filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 after the date of this prospectus but prior to the termination of the offering of the securities covered by this prospectus.

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

ILLUMINA, INC.
9885 Towne Centre Drive
San Diego, California 92121
(858) 202-4500

Legal Matters

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Dewey Ballantine LLP, New York, NY.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule included in our Annual Report on Form 10-K for the year ended January 1, 2006, and management's assessment of the effectiveness of our internal control over financial reporting as of January 1, 2006, as set forth in their reports, which are incorporated by reference into this prospectus and elsewhere in the registration statement. Our financial statements and schedule and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Table of Contents

3,500,000 Shares

Illumina, Inc.

Common Stock

**PROSPECTUS
SUPPLEMENT**

Goldman, Sachs & Co.

Merrill Lynch & Co.

Cowen and Company

Robert W. Baird & Co.

, 2006