

ILLUMINA INC
Form 424B2
August 04, 2008

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed pursuant to Rule 424(b)(2)
File No. 333-134012

Subject to Completion. Dated August 4, 2008.

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.

The common stock is listed on The NASDAQ Global Select Market under the symbol ILMN. The last reported sale price of the common stock on August 1, 2008 was \$92.74 per share.

See Risk Factors beginning on page S-7 of this prospectus supplement to read about factors you should consider before buying shares of the common stock.

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.

| | Per Share | Total |
|--|-----------|-------|
| Initial price to public | \$ | \$ |
| Underwriting discount | \$ | \$ |
| Proceeds, before expenses, to Illumina, Inc. | \$ | \$ |

To the extent that the underwriter sells more than 3,500,000 shares of common stock, the underwriter has the option to purchase up to an additional 525,000 shares from Illumina, Inc. at the initial price to public less the underwriting discount.

The underwriter expects to deliver the shares against payment in New York, New York on August , 2008.

Goldman, Sachs & Co.

Prospectus Supplement dated August , 2008.

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No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement and the accompanying prospectus. You must not rely on any unauthorized information or representations. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of their respective dates.

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of our common stock. The second part, the accompanying prospectus dated May 11, 2006, gives more general information about us and 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 free writing prospectuses we have authorized for use in connection with this offering. We have not, and the underwriter has not, authorized anyone to give you different or additional information. You should not assume that the information included or incorporated by reference in this prospectus supplement and accompanying prospectus is accurate as of any date after the respective dates of the documents containing the information.

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, the accompanying prospectus and the documents incorporated by reference 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 or the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and the 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 detailed financial data. You should read this prospectus supplement, the accompanying prospectus and any free writing prospectuses we have authorized for use in connection with this offering in their entirety, including the information incorporated by reference.

Business Overview

We are a leading developer, manufacturer and marketer of next-generation life sciences 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 sequencing, genotyping and gene expression markets. In the future, 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.

Recent Developments

On August 1, 2008, we closed our acquisition of Avantome Inc., a development-stage company. The primary purpose of the acquisition was to obtain Avantome's low-cost, long-read sequencing technology. As consideration for the acquisition, we paid \$25.0 million in cash up front and may pay up to an additional \$35.0 million in contingent cash consideration based on the achievement of certain milestones.

On July 22, 2008, we announced that our board of directors approved a two-for-one stock split to be effected in the form of a stock dividend. The stock split is subject to stockholder approval of a proposed amendment to our certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 500 million. We intend to seek approval of this amendment to our certificate of incorporation at a special meeting of our stockholders, which we expect to hold on September 9, 2008. If the amendment is approved, we anticipate that the record date for the stock split will be September 10, 2008 and that the payment date for the stock split will be September 22, 2008. Our board of directors retains the right to change the amount of the stock dividend or not to effect the dividend at all.

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 <http://www.illumina.com>. We have not incorporated by reference into this prospectus supplement or the 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 the accompanying prospectus.

The Offering

| | |
|--|--|
| Common stock we are offering | 3,500,000 shares |
| Common stock to be outstanding as of June 29, 2008, as adjusted for this offering | 68,053,019 shares |
| Risk factors | See Risk Factors beginning on page S-7 and the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of the factors you should consider before you make an investment decision. |
| The NASDAQ Global Select Market symbol | ILMN |
| Use of proceeds | See Use of Proceeds on page S-17 for information on how we expect to use the net proceeds from this offering. |

The number of shares of our common stock outstanding as of June 29, 2008, as adjusted for this offering, is based on 64,553,019 shares outstanding as of June 29, 2008, including 7,409,545 shares held in treasury, and excludes:

9,662,777 shares of our common stock issuable upon exercise of options outstanding as of June 29, 2008, at a weighted average exercise price of \$30.45 per share;

10,748,961 shares of our common stock issuable upon exercise of warrants outstanding as of June 29, 2008, at a weighted average exercise price of \$56.54 per share;

3,730,108 shares of our common stock available for future grant under our equity incentive plans as of June 29, 2008; and

up to 9,161,160 shares of our common stock, subject to adjustment, issuable upon conversion of our outstanding convertible notes.

Unless we specifically state otherwise, the information in this prospectus supplement:

does not give effect to our proposed two-for-one stock split; and

assumes that the underwriter does not exercise its option to purchase up to 525,000 additional shares of our common stock.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following summary consolidated financial data for the years ended December 30, 2007, December 31, 2006 and January 1, 2006 are derived from our audited consolidated financial statements that are incorporated by reference into this prospectus supplement. The following summary consolidated financial data for the six months ended June 29, 2008 and July 1, 2007, and as of June 29, 2008, are derived from our unaudited interim condensed consolidated financial statements that 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 the 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](#).

| Statement of Operations Data | December 30, 2007 | Year Ended December 31, 2006 | January 1, 2006 | Six Months Ended June 29, 2008 | July 1, 2007 |
|--|------------------------------|---|----------------------------|---|-------------------------|
| (in thousands, except per share data) | | | | | |
| Revenue: | | | | | |
| Product revenue | \$ 326,699 | \$ 155,811 | \$ 57,752 | \$ 239,235 | \$ 135,562 |
| Service and other revenue | 40,100 | 28,775 | 15,749 | 22,803 | 21,123 |
| Total revenue | 366,799 | 184,586 | 73,501 | 262,038 | 156,685 |
| Costs and expenses: | | | | | |
| Cost of product revenue (including non-cash stock compensation expense of \$4,045, \$1,289, \$0, \$2,642 and \$1,839, respectively, excluding impairment of manufacturing equipment and amortization of intangible assets) | 119,991 | 51,271 | 19,920 | 89,673 | 48,850 |
| Cost of service and other revenue (including non-cash stock compensation expense of \$279, \$235, \$0, \$179 and \$140, respectively) | 12,445 | 8,073 | 3,261 | 6,867 | 6,412 |
| Research and development (including non-cash stock compensation expense of \$10,016, \$3,891, \$84, \$6,754 and \$4,428, respectively) | 73,943 | 33,373 | 27,809 | 44,057 | 34,140 |
| Selling, general and administrative (including non-cash stock compensation expense of \$19,406, \$8,889, \$186, \$13,556 and \$9,056, respectively) | 101,256 | 54,057 | 28,158 | 69,443 4,069 | 46,930 |

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| | | | | | |
|--|--------------|-----------|-------------|-----------|--------------|
| Impairment of manufacturing equipment | | | | | |
| Amortization of intangible assets | 2,429 | | | 5,084 | 1,104 |
| Acquired in-process research and development | 303,400 | | 15,800 | | 303,400 |
| Litigation settlements (judgment), net | 54,536 | | | | |
| Total costs and expenses | 668,000 | 146,774 | 94,948 | 219,193 | 440,836 |
| Income (loss) from operations | (301,201) | 37,812 | (21,447) | 42,845 | (284,151) |
| Interest and other income, net | 12,416 | 4,808 | 736 | 4,410 | 5,066 |
| Income (loss) before income taxes | (288,785) | 42,620 | (20,711) | 47,255 | (279,085) |
| Provision (benefit) for income taxes | (10,426) | 2,652 | 163 | 18,429 | 9,727 |
| Net income (loss) | \$ (278,359) | \$ 39,968 | \$ (20,874) | \$ 28,826 | \$ (288,812) |
| Net income (loss) per basic share | \$ (5.14) | \$ 0.90 | \$ (0.52) | \$ 0.51 | \$ (5.39) |
| Net income (loss) per diluted share | \$ (5.14) | \$ 0.82 | \$ (0.52) | \$ 0.44 | \$ (5.39) |
| Shares used in calculating basic net income (loss) per share | 54,154 | 44,501 | 40,147 | 56,310 | 53,604 |
| Shares used in calculating diluted net income (loss) per share | 54,154 | 48,754 | 40,147 | 65,231 | 53,604 |

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| Balance Sheet Data | As of June 29, 2008 | |
|---|---------------------|----------------------------|
| | Actual | As Adjusted ⁽¹⁾ |
| (in thousands) | | |
| Cash, cash equivalents and short-term investments | \$ 303,275 | \$ 618,995 |
| Working capital | 20,608 | 336,328 |
| Total assets | 992,685 | 1,308,405 |
| Current portion of long-term debt | 400,000 | 400,000 |
| Long-term obligations, less current portion | 14,885 | 14,885 |
| Stockholders' equity | 491,752 | 807,472 |

(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 \$92.74 per share, after deducting underwriting discounts and commissions and estimated offering expenses to be paid by us. Each \$1.00 increase (decrease) in the initial public offering price per share would increase (decrease) each of pro forma as adjusted cash, cash equivalents and short-term investments, working capital, total assets and stockholders' equity by approximately \$3.4 million, assuming that the number of shares we are offering, as set forth on the cover page of this prospectus supplement, remains the same and that the underwriter does not exercise its option to purchase additional shares. Depending on market conditions and other considerations at the time we price this offering, we may sell a greater or lesser number of shares than the number set forth on the cover page of this prospectus supplement. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) each of pro forma as adjusted cash, cash equivalents and short-term investments, working capital, total assets and stockholders' equity by approximately \$90.3 million, assuming the initial public offering price per share remains the same. This pro forma as adjusted information is illustrative only, and following the pricing of this offering, we will adjust this information based on the actual initial public offering price and other terms of this offering.

RISK FACTORS

Investing in our common stock involves a high degree of risk. In addition to the other information included or incorporated by reference in this prospectus supplement or accompanying prospectus, or any free writing prospectus we have authorized 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. 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

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 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, nanotechnology, 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, 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, life sciences and pharmaceutical companies, which are our potential customers and strategic partners, could develop competing products. For example, during the third quarter of fiscal 2007, Applied Biosystems, Inc., launched the SOLiD™ System, its next generation sequencing technology. 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.

We may encounter difficulties in managing our growth. These difficulties could impair our profitability.

We have experienced and expect to continue 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 profitability could suffer. 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.

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. 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 and San Francisco area, is intense, and the turnover rate can be high. Failure to attract 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.

If we are unable to increase our manufacturing capacity and 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 continue to ramp up our capacity to meet the anticipated demand for our products. Although we have significantly increased our manufacturing capacity and we believe we have plans in place sufficient to ensure we have adequate capacity to meet our business plan for the remainder of 2008 and in 2009, 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 facilities 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.

Additionally, we currently manufacture in a limited number of locations. Our manufacturing facilities are located in San Diego and Hayward, California and Little Chesterford, United Kingdom. We are in the process of expanding our manufacturing operations into Singapore, a country in which we have no past manufacturing experience. These areas are subject to natural disasters such as earthquakes or floods. If a natural disaster were to significantly damage one of our facilities or if other events were to cause our operations to fail, these events could prevent us from manufacturing our products, providing our services and developing new products.

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 may adversely impact our ability to manufacture our products on a timely basis and would 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 use multiple components in our products that are single-sourced. 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.

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 compared to some of our primary competitors. In order to effectively commercialize our sequencing, 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.

Any inability to protect effectively 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. In addition, 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 challenges in protecting their proprietary rights abroad. These challenges can be caused by the absence of rules and methods for the establishment and enforcement of intellectual property rights abroad.

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. 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 certain rights to practice related technologies, 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. Accordingly, our patents may fail to provide us with any competitive advantage. We may also need to initiate 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. These lawsuits may be costly and divert the attention of our management and technical personnel.

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

Negative conditions in the global credit markets may impair the liquidity of a portion of our investment portfolio.

Our investment securities consist of marketable debt securities, including treasury bills and commercial paper with strong credit ratings, corporate bonds and short maturity mutual funds providing similar financial returns. Additionally, as of June 29, 2008, we had \$55.9 million of auction rate securities issued primarily by municipalities and universities. These securities are debt instruments with a long-term maturity and with an interest rate that is reset in short intervals through auctions. The recent negative conditions in the global credit markets have prevented some investors from liquidating their holdings of auction rate securities because the amount of securities submitted for sale has exceeded the amount of purchase orders for such securities. If there is insufficient demand at the time of an auction for the securities we hold, the auction may not be completed and the interest rates may be reset to predetermined lower rates. When auctions for these securities fail, the investments may not be readily convertible to cash until a future auction of these investments is successful or they are redeemed or mature.

All of our auction rate securities are currently rated AAA, the highest rating, by a rating agency. Although their credit ratings have not deteriorated, there has been insufficient demand at auction for all of our high-grade auction rate securities during the second quarter of 2008. As a result, these securities are currently not liquid. In the event we need to access the funds that are in an illiquid state, we will not be able to do so without a loss of principal, until a future auction on these investments is successful, the securities are redeemed by the issuer or they mature. As a result, we have recorded an unrealized loss of \$3.1 million for the six months ended June 29, 2008, resulting in a reduction to the fair value of our auction rate securities to \$52.8 million as of June 29, 2008. Due to the lack of actively traded market data, the value of these securities and resulting unrealized loss was determined using management's assumptions of pricing by market participants, including assumptions about risk, which requires the exercise of significant judgment. Although it could take until the final maturity of the underlying notes (ranging from 23 years to 39 years) to realize the recorded value of these investments, we currently believe these securities are not permanently impaired, primarily due to the government guarantee of the underlying securities and our ability to hold these securities for the foreseeable future. Due to our intent to hold these securities until they recover in value, we have classified them as long-term investments on our balance sheet. Our cash and cash equivalents and short-term investments totaled \$303.3 million as of June 29, 2008. Based on the liquidity of these funds and our projected cash flows from operations, we believe the illiquidity of these auction rate securities will not materially affect our ability to execute our current business plan.

We may encounter difficulties in integrating acquisitions that could adversely affect our business, specifically the effective launch and customer acceptance of new technology platforms.

We acquired Solexa in January 2007, CyVera in April 2005, and Avantome in August 2008, and we 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 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 these acquisitions, we assumed certain liabilities and hired certain employees, 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. To finance any acquisitions, we may choose to issue shares of our common stock as consideration, which could result in dilution to our stockholders. Additionally, an acquisition may have a substantial negative impact on near-term expected financial results.

Changes in our effective income tax rate could impact our profitability.

We are subject to income taxes in both the United States and numerous foreign jurisdictions. Significant judgments based on interpretations of existing tax laws or regulations are required in determining the provision for income taxes. Our effective income tax rate could be adversely affected by various factors including, but not limited to, changes in the mix of earnings in tax jurisdictions with different statutory tax rates, changes in the valuation of deferred tax assets and liabilities, changes in existing tax laws or tax rates, changes in the level of non-deductible expenses including share-based compensation, changes in our future levels of research and development spending, mergers and acquisitions, and the result of examinations by various tax authorities.

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 on our ability to protect our own intellectual property. Third parties have asserted and may in the future 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 allowing them to claim that the 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. Any adverse ruling or perception of an adverse ruling in defending ourselves against these claims could have a material adverse impact on our stock price, which may be disproportionate to the actual import of the ruling itself. Furthermore, parties making claims against us may be able to obtain injunctive or other relief, which effectively could block our ability to develop further, 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. In addition, we may be unable to obtain these licenses at a reasonable cost, if at all. We could therefore incur substantial costs related to royalty payments for licenses obtained from third parties, which could negatively affect our gross margins. In addition, 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 maintain profitability.

We have a significant amount of indebtedness. We may not be able to make payments on our indebtedness, and we may incur additional indebtedness in the future, which could adversely affect our operation and profitability.

In February 2007, we issued \$400.0 million of 0.625% convertible senior notes due February 2014. The notes bear interest semi-annually, mature on February 15, 2014 and obligate us to repurchase the notes at the option of the holders if a designated event (as defined in the indenture for the notes), such as certain merger transactions involving us, occurs. In addition, upon conversion of the notes, we must pay in cash the principal portion of the notes being converted. Our ability to make payments on the notes will depend on our future operating performance and our ability to generate cash and may also depend on our ability to obtain additional debt or equity financing. We may need to use our cash to pay principal and interest on our debt, which will reduce the funds available to fund our research and development programs, strategic initiatives and working capital requirements. Our ability to generate sufficient operating cash flow to service the notes and fund our operating requirements will depend on our continued ability to commercialize new products and expand our manufacturing capabilities. Our debt service obligations increase our vulnerabilities to competitive pressures, because our competitors may be less leveraged than we are. If we are unable to generate sufficient operating cash flow to service our indebtedness and fund our operating requirements, we may be forced to reduce our development programs or seek additional debt or equity financing, which may not be available to us on satisfactory terms, or at all, or may dilute the interests of our existing stockholders. Our level of indebtedness may make us more vulnerable to economic or industry downturns. If we incur new indebtedness, the risks relating to our business and our ability to service our indebtedness will intensify.

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, 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 is relatively fixed, including expenses for facilities, equipment and personnel. In addition, we expect operating expenses to continue to increase significantly in absolute dollars. Accordingly, if revenue does not grow as anticipated, we may not be able to maintain annual 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 future revenue growth or cause a sequential decline in quarterly revenue. 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 could decline.

We may not be able to sustain operating profitability.

Prior to 2006, we had incurred net losses each year since our inception, and in 2007 we reported a net loss of \$278.4 million, reflecting significant charges associated with our acquisition of Solexa in January 2007 and the settlement of our litigation with Affymetrix. As of June 29, 2008, our accumulated deficit was \$354.2 million. Our ability to sustain profitability will depend, in part, on the rate of growth, if any, of our revenue and on the level of our expenses. Non-cash stock-based compensation expense and expenses related to our acquisition of Solexa are also likely to continue to adversely affect our future profitability. 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 research and

development and selling and marketing expenses will increase at a higher rate in the future as a result of the development and launch of new products. Although we have regained profitability, we may not be able to sustain profitability on a quarterly basis.

A significant portion of our sales is to international customers.

Approximately 48% of our revenue for the three months ended June 29, 2008 and July 1, 2007 was derived from shipments to customers outside the United States. Approximately 48% and 35% of our revenue for the six months ended June 29, 2008 and July 1, 2007, respectively, was derived from shipments to customers outside the United States. We intend to continue to expand our international presence by selling to customers located outside of the U.S. 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 in overcoming other trade barriers and restrictions resulting in delivery delays;

challenges in obtaining and enforcing patents abroad; 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 focusing on markets for analysis of genetic variation and biological function, namely sequencing, SNP genotyping and gene expression profiling. 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 sustain profitability.

We may not have the ability to pay the cash payments due upon conversion of our outstanding convertible notes.

In February 2007, we issued \$400.0 million of 0.625% convertible senior notes due February 2014. The notes are convertible into cash and, if applicable, shares of our common stock only if specified conditions are satisfied. During the first quarter of 2008, we determined that one of these conditions was satisfied, and, accordingly, the notes were convertible from and including April 1, 2008 through and including June 30, 2008. The requirements of the same condition were again satisfied in the

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second quarter of 2008, and, accordingly, the notes will continue to be convertible through and including September 30, 2008.

Generally, upon conversion of a note, we must pay the conversion value of the note in cash, up to the principal amount of the note. Any excess of the conversion value over the principal amount is payable in shares of our common stock. We currently do not have sufficient cash to pay the cash amounts that would be due, based on current stock prices, if all the notes were converted. However, as was the case during the second calendar quarter of 2008, the notes currently continue to trade above their conversion value. As a result, we do not currently expect any notes to be converted during the third calendar quarter of 2008. Holders of the notes may nonetheless convert their notes during this period.

If a significant amount of the notes are tendered for conversion, we may have to seek additional financing to satisfy our conversion obligation. We may be unable to obtain any needed additional financing on favorable terms, if at all. In addition, if we raise funds by issuing additional equity securities, our existing stockholders may experience dilution. Additional debt financing, if available, may subject us to restrictive covenants and will increase our interest expense. If we fail to deliver the consideration that is due upon conversion when required, we will be in default under the indenture for the notes, which may permit the noteholders to cause the notes to be immediately payable in full.

We could lose the tax deduction on our outstanding convertible notes.

We could lose some or all of the tax deduction for interest expense associated with our \$400.0 million 0.625% convertible senior notes due February 2014 if the foregoing notes are not subject to the special Treasury Regulations governing integration of certain debt instruments, which we do not expect to be the case, the notes are converted, or we invest in non-taxable investments.

Risks Related to 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 our 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, for a period of three years, from engaging in any business combination with certain persons who own 15%

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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 this offering. 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. Our common stock may not appreciate in value after this offering or and may not 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 performance of these companies. During the period from January 1, 2006 to August 1, 2008, the lowest and highest reported trading prices of our common stock on The NASDAQ Global Select Market were \$13.75 and \$95.75, 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.

Investors in this offering will pay a much higher price than the book value of our common stock.

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. Those purchasers could experience additional dilution upon the exercise of outstanding stock options and warrants.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, that are subject to the safe harbor created by those sections. 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, pre words 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, the commercial launch of new products and the duration 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 forward-looking statements for many reasons, including the factors described in the section titled 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 in which they are contained. Except as required by law, we undertake no obligation to publicly revise any forward-looking statement to reflect circumstances or events after the date of this prospectus supplement or to reflect the occurrence of unanticipated events. You should, however, review the factors and risks we describe in the reports we file from time to time with the SEC. See Where You Can Find More Information.

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 \$315.7 million, assuming an public offering price of \$92.74 per share and after deducting underwriting discounts and commissions and the estimated offering expenses payable by us. If the underwriter exercises its option to purchase additional shares in full, we estimate the net proceeds to us will be approximately \$363.1 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.

Each \$1.00 increase (decrease) in the initial public offering price per share would increase (decrease) the net proceeds to us from this offering, after deducting underwriting discounts and commissions and our estimated offering expenses, by approximately \$3.4 million, assuming that the number of shares we are offering, as set forth on the cover page of this prospectus supplement, remains the same and that the underwriter does not exercise its option to purchase additional shares. Depending on market conditions and other considerations at the time we price this offering, we may sell a greater or lesser number of shares than the number set forth on the cover page of this prospectus supplement. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting underwriting discounts and commissions and our estimated offering expenses, by approximately \$90.3 million, assuming the initial public offering price per share remains the same.

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. Accordingly, we reserve the right to use these proceeds for different purposes or uses which we have not listed above.

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, which may include short-term, interest-bearing instruments.

PRICE RANGE OF OUR COMMON STOCK

Our common stock is traded publicly on The NASDAQ Global Select 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 Global Select Market. These prices do not include retail markups, markdowns or commissions.

| | High | Low |
|---|-------------|------------|
| Calendar Year Ended December 31, 2006 | | |
| First Calendar Quarter | \$ 27.98 | \$ 13.75 |
| Second Calendar Quarter | 32.00 | 21.60 |
| Third Calendar Quarter | 40.00 | 27.02 |
| Fourth Calendar Quarter | 45.87 | 32.20 |
| Calendar Year Ended December 31, 2007 | | |
| First Calendar Quarter | \$ 42.19 | \$ 28.11 |
| Second Calendar Quarter | 42.08 | 28.94 |
| Third Calendar Quarter | 53.88 | 40.04 |
| Fourth Calendar Quarter | 63.38 | 50.34 |
| Calendar Year Ended December 31, 2008 | | |
| First Calendar Quarter | \$ 77.30 | \$ 55.77 |
| Second Calendar Quarter | 90.38 | 69.80 |
| Third Calendar Quarter (through August 1, 2008) | 95.75 | 82.66 |

As of July 28, 2008, there were approximately 574 holders of record of our common stock. On August 1, 2008, the last sale price reported on The NASDAQ Global Select Market for our common stock was \$92.74 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.

CAPITALIZATION

The following table sets forth our cash, cash equivalents, short-term investments and capitalization as of June 29, 2008:

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 \$92.74, after deducting underwriting discounts and commissions and estimated offering expenses to be paid by us.

| | As of June 29, 2008 | |
|--|----------------------------|--------------------|
| | Actual | As adjusted |
| (in thousands, except share and per share data) | (unaudited) | |
| Cash, cash equivalents and short-term investments ⁽¹⁾ | \$ 303,275 | \$ 618,995 |
| 0.625% Convertible Senior Notes due 2014 ⁽²⁾ | \$ 400,000 | \$ 400,000 |
| Long-term obligations, less current portion | \$ 14,885 | \$ 14,885 |
| 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; 64,553,019 shares issued and outstanding (including treasury shares), actual; 68,053,019 shares issued and outstanding (including treasury shares), as adjusted | 646 | 681 |
| Additional paid in capital ⁽¹⁾ | 1,097,619 | 1,413,304 |
| Accumulated other comprehensive loss | (739) | (739) |
| Accumulated deficit | (354,152) | (354,152) |
| Treasury stock, at cost; 7,409,545 shares | (251,622) | (251,622) |
| Total stockholders' equity ⁽¹⁾ | 491,752 | 807,472 |
| Total capitalization ⁽¹⁾ | \$ 506,637 | \$ 822,357 |

(1) Each \$1.00 increase (decrease) in the initial public offering price per share would increase (decrease) each of as adjusted cash, cash equivalents and short-term investments, additional paid in capital, total stockholders' equity and total capitalization by approximately \$3.4 million, assuming that the number of shares we are offering, as set forth on the cover page of this prospectus supplement, remains the same and that the underwriter does not exercise its option to purchase additional shares. Depending on market conditions and other considerations at the time we price this offering, we may sell a greater or lesser number of shares than the number set forth on the cover page of this prospectus supplement. An increase (decrease) of 1,000,000 in the number of shares we are

offering would increase (decrease) each of as adjusted cash, cash equivalents and short-term investments, additional paid in capital, total stockholders' equity and total capitalization by approximately \$90.3 million, assuming the initial public offering price per share remains the same. This as adjusted information is illustrative only, and following the pricing of this offering, we will adjust this information based on the actual initial public offering price and other terms of this offering.

(2) Our convertible notes were classified as a current liability as of June 29, 2008.

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 is based on 64,553,019 shares of our common stock outstanding as of June 29, 2008, including 7,409,545 shares held in treasury, and excludes:

9,662,777 shares of our common stock issuable upon exercise of options outstanding as of June 29, 2008, at a weighted average exercise price of 30.45 per share;

10,748,961 shares of our common stock issuable upon exercise of warrants outstanding as of June 29, 2008, at a weighted average exercise price of 56.54 per share;

3,730,108 shares of our common stock available for future grant under our equity incentive plans as of June 29, 2008; and

up to 9,161,160 shares of our common stock, subject to adjustment, issuable upon conversion of our outstanding convertible notes.

UNDERWRITING

The company and Goldman, Sachs & Co. have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, the underwriter has agreed to purchase the number of shares indicated on the cover of this prospectus supplement.

The underwriter is 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 underwriter sells more shares than the total number set forth on the cover of this prospectus supplement, it has an option to buy up to an additional 525,000 shares from the company. It may exercise that option for 30 days.

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

| | Paid by the Company | No Exercise | Full Exercise |
|-----------|---------------------|-------------|---------------|
| Per share | | \$ | \$ |
| Total | | \$ | \$ |

Shares sold by the underwriter 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 underwriter to securities dealers may be sold 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 underwriter may change the offering price and the other selling terms. The offering of the shares by the underwriter is subject to receipt and acceptance and subject to the underwriter's right to reject any order in whole or in part.

The company and certain of its directors and officers have agreed with the underwriter, 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 underwriter. This agreement does not apply to shares issuable upon conversion, exchange or exercise of convertible, exchangeable or exercisable securities outstanding as of the date of this prospectus supplement or under any existing employee benefit plans or to shares subject to certain Rule 10b5-1 plans.

In connection with the offering, the underwriter 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 underwriter of a greater number of shares than it is required to purchase in the offering. Covered short sales are short sales made in an amount not greater than the underwriter's option to purchase additional shares from the company in the offering. The underwriter may close out any covered short position by either exercising its 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 underwriter will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase additional shares pursuant to the option granted to it. Naked short sales are any short sales in excess of such option. The underwriter must close out any naked short position by purchasing shares in the open market. A naked short

position is more likely to be created if the underwriter is 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 underwriter in the open market prior to the completion of the offering.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriter for its own account, may have the effect of preventing or retarding a decline in the market price of the company's stock, and may stabilize, maintain or otherwise affect the market price of the

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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 The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), the 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 authorized or regulated to operate in the financial markets or, if not so authorized 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;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the underwriter for any such offer; or
- (d) in any other circumstances which do not require the publication by the Issuer 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 the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for 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 underwriter has represented and agreed that:

- (a) 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 the FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to the Issuer; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement,

invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case 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 laws of Hong Kong) other than with respect to shares which are or are intended to be

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disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus 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 Financial Instruments and Exchange Law of Japan (the Securities and Exchange Law) and the 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 Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

The company estimates that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$350,000.

In compliance with FINRA 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 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 underwriter against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriter and its 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.

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 <http://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 <http://www.illumina.com>. We have not incorporated by reference into this prospectus supplement or the 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 the accompanying prospectus.

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 have filed with the SEC prior to the date of this prospectus supplement or the accompanying prospectus and which is incorporated by reference into this prospectus supplement or the accompanying prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus supplement, the accompanying prospectus 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 or accompanying prospectus, as applicable, 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 supplement:

our annual report on Form 10-K for the fiscal year ended December 30, 2007, filed with the SEC on February 26, 2008 (file no. 000-30361);

our quarterly reports filed on Form 10-Q for the fiscal quarters ended March 30, 2008 and June 29, 2008, filed with the SEC on April 28, 2008 and July 25, 2008, respectively (file no. 000-30361);

our current reports on Form 8-K, excluding the portions that were furnished in accordance with SEC rules, as filed with the SEC on January 4, 2008, January 15, 2008, March 17, 2008, March 25, 2008, March 26, 2008, April 17, 2008, May 19, 2008 and June 17, 2008 (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

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

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LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Dewey & LeBoeuf LLP, New York, NY, and for the underwriter 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 December 30, 2007, and the effectiveness of our internal control over financial reporting as of December 30, 2007, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements and schedule are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

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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.

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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.

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,

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

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

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

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

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

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.

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.

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.

3,500,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Goldman, Sachs & Co.