

Isis Pharmaceuticals, Inc.

\$125,000,000 5¹/₂% Convertible Subordinated Notes Due 2009 and 7,518,800 Shares of Common Stock Issuable Upon Conversion of the Notes

The notes and the common stock issuable upon conversion of the notes may be offered and sold from time to time pursuant to this prospectus by the holders of those securities. The selling security holders will receive all of the net proceeds from the sale of the securities and will pay any applicable discounts, commission or concessions. The selling security holders and any underwriters, broker-dealers or agents that participate in the sale of the securities may be "underwriters" within the meaning of the Securities Act, and any discounts, commissions, concessions or profit they earn on any resale of the securities may be underwriting discounts or commissions under the Securities Act.

On May 1, 2002, we issued and sold \$125,000,000 of 5¹/₂% convertible subordinated notes due 2009 in a private placement in reliance on an exemption from registration under the Securities Act. The initial purchasers of the notes in that offering resold the notes in offerings in reliance on an exemption from registration under Rule 144A and Regulation S of the Securities Act. The notes are convertible into 60.1504 shares of our common stock, par value \$0.001 per share, per \$1,000 principal amount of notes and subject to adjustment in certain circumstances. This results in an initial conversion price of \$16.625 per share.

We will pay cash interest on the notes semiannually on May 1 and November 1 of each year, with the first payment to be made on November 1, 2002, at the rate of 5¹/₂% per annum. The notes will mature on May 1, 2009.

The notes are junior to all of our existing and future senior indebtedness and we structurally subordinated to all existing and future liabilities of our subsidiaries, including trade payables. As of June 30, 2002, we and our subsidiaries had approximately \$75.8 million of consolidated indebtedness and other liabilities effectively ranking senior to the convertible notes, assuming the repayment of a portion of our debt held by Elan International Services, Ltd. and its related entities which occurred on July 3, 2002.

We may redeem some or all of the notes at any time before May 3, 2005, at a redemption price of \$1,000 per \$1,000 principal amount of notes, if the price of our common stock reaches certain levels and certain other conditions are met. We will make an additional payment in cash or common stock or a combination thereof with respect to the notes called for provisional redemption in an amount equal to the aggregate amount of interest that would have been payable on the notes from the last day through which interest was paid on the notes (or May 1, 2002 if no interest was paid) through May 1, 2005 (or May 2, 2005, if redeemed on that date). On or after May 3, 2005, we may at our option redeem the convertible notes, in whole or in part, at the prices stated in this prospectus, plus any accrued and unpaid interest to the redemption date. Holders of the notes may require us to repurchase all or a portion of their convertible notes upon a change in control, as defined herein, at 100% of their principal amount, plus any accrued and unpaid interest to the repurchase date.

Our common stock is listed on the Nasdaq National Market under the symbol "ISIS." On August 14, 2002, the last reported bid price of our common stock was \$10.88 per share. The notes trade on the Private Offerings, Resales and Trading Through Automated Linkages, or "PORTAL," Market of the National Association of Securities Dealers, Inc.

**Investing in our common stock involves risks.
See "Risk Factors" beginning on page 5**

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 August 14, 2002

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SUMMARY

This summary highlights selected information appearing elsewhere in this prospectus and may not contain all of the information that is important to you. This prospectus includes information about the securities we are offering, as well as information regarding our business and detailed financial data. We encourage you to read this prospectus in its entirety, including the documents incorporated by reference. As used in this prospectus, unless otherwise specified or the context requires otherwise, the terms "Isis," "we," "our" and "us" refer to Isis Pharmaceuticals, Inc.

Our Business

We are a biopharmaceutical company pioneering RNA-based drug discovery technologies to identify and commercialize novel drugs to treat important diseases. RNA, or ribonucleic acid, is a molecule that provides to a cell the information that it needs to produce proteins, including those proteins that are involved in disease. Interference with RNA can keep the body from producing proteins that are involved in disease. We have a strong proprietary position in RNA-based drug discovery technologies. With our primary technology, antisense, we create inhibitors designed to bind with high specificity to their RNA target and modulate protein production. With our Ibis technology, we use our expertise in RNA to design small molecule therapeutics that bind to RNA. We also use our antisense technology in collaborations with pharmaceutical companies to identify and prioritize attractive gene targets for their drug discovery programs. We believe we have established a leadership position in exploiting RNA as a target for drugs.

We used our antisense technology to commercialize our first product, Vitravene. Vitravene demonstrates our ability to meet U.S. Food and Drug Administration, or FDA, regulatory requirements and to manufacture commercial antisense drugs. We have 13 products in our development pipeline with eight in human clinical trials designed to assess safety and efficacy. Our products in development address numerous therapeutic areas with major market potential, including cancer and inflammatory, viral, metabolic and dermatological diseases. We are expanding the therapeutic opportunities for antisense drugs by developing a variety of formulations to enhance patient convenience and compliance. Our second-generation drugs, which represent approximately half of our drugs in development, may be able to be dosed as infrequently as once per month. We are also making progress on oral formulations for our second-generation drugs.

Affinitac, formerly known as LY900003 or ISIS 3521, is our most advanced product in development. In August 2001, we licensed Affinitac to Eli Lilly and Company as part of a broad strategic collaboration. Affinitac is undergoing Phase III clinical trials in combination with traditional cancer chemotherapy drugs to treat non-small cell lung cancer, the most common form of lung cancer. In January 2002, we completed enrollment of a 600 patient Phase III trial that we initiated in late 2000. We initiated this trial based on promising results in a Phase II trial in patients with non-small cell lung cancer. Results from the Phase II study showed a median survival time of 15.9 months in patients using our drug in combination with standard chemotherapy. The typical median survival time of similar cancer patients receiving standard chemotherapy alone is approximately seven or eight months. In April 2002, Lilly launched a global Phase III trial of Affinitac in patients with non-small cell lung cancer. If the data from our Phase III trial are sufficiently positive to support a single study New Drug Application, or NDA, we and Lilly plan to file the NDA in 2003. If two Phase III studies are required, we and Lilly plan to file the NDA in 2004. In November 2000, the FDA granted Affinitac fast track review status. In November 2001, we initiated a Phase III clinical trial for another product, ISIS 2302, in an inflammatory bowel disease known as Crohn's disease. We have six additional products undergoing Phase II clinical trials.

Our GeneTrove division uses our antisense technology as a tool to provide pharmaceutical companies with important information about genes that these companies are interested in targeting for their drug discovery programs. We provide this information rapidly and efficiently, using the same

proprietary methods and systems that we developed to create antisense drugs. We are collaborating with nine major pharmaceutical partners for these services, which are Abbott Laboratories, Inc.; Amgen Inc.; Aventis (Rhone-Poulenc Rorer); Celera Genomics Group; Chiron Corporation; Eli Lilly and Company; Johnson & Johnson Pharmaceutical Research & Development, LLC; Merck & Co., Inc.; and Pharmacia Corporation. We supplemented our GeneTrove services business with the introduction in August 2001 of a subscription database product. This database will contain proprietary information about the function of thousands of genes, which we believe pharmaceutical companies will find valuable in designing and prioritizing their drug discovery programs. Our GeneTrove division is generating near-term revenues while enhancing our own antisense drug discovery efforts and our patent portfolio.

Our Ibis Therapeutics division designs small molecule drugs that work by binding to RNA, in contrast to traditional drugs, which bind to proteins. Our scientists have invented methods of identifying RNA targets and screening for drugs that bind to RNA. Beyond its therapeutic focus, Ibis has expanded the application of its technology to develop a new diagnostic platform to detect infectious agents. Since its inception, Ibis has received significant financial support from various federal government agencies to use its technology for the development of RNA-based countermeasures to biological warfare. In October 2001, Ibis received a two-year contract from the Defense Advanced Research Projects Agency, or DARPA, to develop a device to detect infectious agents used in biological warfare attacks. Under this two-year contract, for the research program Triangulation Identification Genetic Evaluation of biological Risks, or TIGER, we expect to receive up to \$8.9 million in funding. In June 2000, Ibis initiated its first collaboration with a pharmaceutical industry partner, Agouron Pharmaceuticals, Inc., a Pfizer company. In May and October 2001, we received a \$2.5 million milestone payment and a \$1.5 million milestone payment, respectively, under this collaboration. This collaboration is scheduled to end in June 2002 in accordance with its terms.

We have a broad patent portfolio relating to our technologies. We have rights to more than 900 issued patents, which we believe represent the largest antisense and RNA-oriented patent estate in the pharmaceutical industry. In 2001, we continued to fortify our antisense technology portfolio by exclusively licensing Hybridon's antisense chemistry and delivery technology patents. Our intellectual property is a strategic asset that we are exploiting to generate near-term revenue and that we expect will also provide us with revenue in the future. The principal purpose of our intellectual property portfolio is to protect our inventions in RNA-based drug discovery. Our intellectual property estate also enables us to expand our pipeline by granting partners limited access to antisense technology. Licensing partnerships may include antisense and Ibis drug discovery alliances such as those we have with Lilly and Amgen, GeneTrove functional genomics collaborations such as those we have with Chiron, Amgen and Pharmacia or licenses to non-antisense patents for drug discovery such as our license to Eyetech Pharmaceuticals, Inc.

Recent Developments

In August 2002 we entered an agreement with Hybridon which cancelled the remaining financial obligations related to our Collaboration and License Agreement with Hybridon completed in May 2001. Under the original agreement, Hybridon owed us an additional 4 million shares of Hybridon common stock, payable immediately. We owed Hybridon \$4.5 million in cash or stock, due in May 2003. We have agreed with Hybridon to cancel each of these obligations.

Isis was incorporated in California in January 1989 and in April 1991 changed its state of incorporation to Delaware. Our executive offices are located at 2292 Faraday Avenue, Carlsbad, California 92008, and our telephone number is (760) 931-9200.

Isis Pharmaceuticals™, GeneTrove™ and Ibis Therapeutics™ are our trademarks. Vitravene® is a registered trademark of Novartis AG. Affinitac™ is a trademark of Eli Lilly and Company. This prospectus also contains trademarks and servicemarks of other companies.

NOTES AND COMMON STOCK ISSUABLE UPON CONVERSION OF THE NOTES

Issuer	Isis Pharmaceuticals, Inc.
Convertible notes	\$125,000,000 aggregate principal amount of 5 ¹ / ₂ % convertible subordinated notes due 2009.
Maturity	The convertible notes will mature on May 1, 2009.
Interest payment dates	We will pay interest on the convertible notes semi-annually in arrears on May 1 and November 1 of each year, starting on November 1, 2002.
Conversion rights	The convertible notes are convertible into 60.1504 shares of our common stock, par value \$0.001 per share, per \$1,000 principal amount of convertible notes, subject to adjustment in certain circumstances. This rate results in an initial conversion price of \$16.625 per share. See "Description of Notes—Conversion Rights."
Subordination	The convertible notes are: <ul style="list-style-type: none"> • unsecured; • junior to all of our existing and future senior indebtedness; and • structurally subordinated to all existing and future liabilities of our subsidiaries, including trade payables. <p>As of June 30, 2002 we and our subsidiaries had approximately \$75.8 million of consolidated indebtedness and other liabilities effectively ranking senior to the convertible notes, assuming the repayment of a portion of our debt held by Elan International Services, Ltd. and its related entities which occurred on July 3, 2002. The indenture under which the convertible notes were issued does not restrict our or our subsidiaries' ability to incur additional senior or other indebtedness or liabilities. See "Description of Notes—Subordination of Notes."</p>
Sinking fund	None.
Provisional Redemption	We may redeem the convertible notes, in whole or in part, at any time before May 3, 2005, at a redemption price equal to \$1,000 per note to be redeemed if (a) the closing price of our common stock has exceeded 150% of the conversion price then in effect for at least 20 trading days within a period of 30 consecutive trading days ending on the trading day before the date of the mailing of the provisional redemption notice and (b) the registration statement of which this prospectus is a part is effective and available for use and is expected to remain effective and available for use for the 30 days following the provisional redemption date, unless registration is no longer required. Upon any provisional redemption, we will make an additional payment with respect to the convertible notes called for redemption equal to the total value of the aggregate amount of interest that would have been payable on the convertible notes from the last day through which interest was paid on the convertible notes (or May 1, 2002 if no interest has been paid) through May 1, 2005 (or May 2, 2005, if redeemed on that date). We may make these additional payments, at our option, in cash or common stock or a combination thereof. We will be obligated to make this additional payment on all convertible notes called for provisional redemption, including any notes converted after the notice date and before the provisional redemption date. See "Description of Notes—Provisional Redemption."

Redemption of convertible notes at our option	On or after May 3, 2005, we may, at our option, redeem the convertible notes, in whole or in part, at the redemption prices described in this prospectus, plus any accrued and unpaid interest to the redemption date. See "Description of Notes—Redemption of Notes at Our Option."
Change in control	If we experience a change in control, as defined in the indenture, each holder may require us to purchase all or a portion of the holder's convertible notes at 100% of the principal amount, plus any accrued and unpaid interest to the repurchase date. See "Description of Notes—Change in Control Permits Purchase of Convertible Notes by Us at the Option of the Holder."
Events of default	If an event of default on the convertible notes has occurred and is continuing, the principal amount of the convertible notes plus any accrued and unpaid interest may be declared immediately due and payable. These amounts automatically become due and payable upon certain events of default. See "Description Notes—Events of Default."
Use of proceeds	We will not receive any proceeds from the sale of the notes or common stock offered in this prospectus. See "Selling Security Holders."
Listing and trading	The convertible notes trade on The PORTAL Market. Our common stock is listed on the Nasdaq National Market under the symbol "ISIS."
Risk factors	In analyzing an investment in the convertible notes offered by this prospectus, prospective investors should carefully consider, along with other matters referred to in this prospectus, the information set forth under "Risk Factors."

For a more complete description of the terms of the convertible notes, see "Description of Notes." For a more complete description of the terms of our common stock, see "Description of Capital Stock," including the documents incorporated by reference in this prospectus that are referred to therein.

RISK FACTORS

Investing in our securities involves a high degree of risk. In addition to the other information in this prospectus, you should carefully consider the risks described below before purchasing our securities. If any of the following risks actually occur, our business could be materially harmed, and our financial condition and results of operations could be materially and adversely affected. As a result, the trading price of our securities could decline, and you might lose all or part of your investment.

RISKS RELATED TO OUR BUSINESS

If we or our partners fail to obtain regulatory approval for our products, we will not be able to sell them.

We and our partners must conduct time-consuming, extensive and costly clinical trials to show the safety and efficacy of each of our drug candidates, before a drug candidate can be approved for sale. We must conduct these trials in compliance with U.S. Food and Drug Administration regulations and with comparable regulations in other countries. If the FDA or another regulatory agency believes that we or our partners have not sufficiently demonstrated the safety or efficacy of our drug candidates, it will not approve them or will require additional studies, which can be time consuming and expensive and which will delay commercialization of a drug candidate. We and our partners may not be able to obtain necessary regulatory approvals on a timely basis, if at all, for any of our drug candidates. Failure to receive these approvals or delays in such receipt could prevent or delay commercial introduction of a product and, as a result, could negatively impact our ability to generate revenue from product sales. In addition, following approval of a drug candidate, we and our partners must comply with comprehensive government regulations regarding how we manufacture, market and distribute products. If we fail to comply with these regulations, regulators could force us to withdraw a drug candidate from the market or impose other penalties or requirements that could have a similar negative impact.

We have only introduced one commercial product, Vitravene. We cannot guarantee that any of our other drug candidates will be safe and effective, will be approved for commercialization or will be successfully commercialized by us or our partners.

If the results of clinical testing indicate that any of our drugs under development are not suitable for commercial use, or if additional testing is required to demonstrate such suitability, we may need to abandon one or more of our drug development programs.

Drug discovery and development has inherent risks, including the risk that molecular targets prove not to be important in a particular disease, the risk that compounds that demonstrate attractive activity in preclinical studies do not demonstrate similar activity in human beings, and the risk that a compound is not safe or effective for use in humans. Antisense technology in particular is relatively new and unproven. Most of our resources are being applied to create safe and effective drugs for human use. Any of the risks described above could prevent us from meeting this goal. In the past, we have invested in clinical studies of drug candidates, including some that remain in our pipeline, that have not resulted in proof of efficacy against targeted indications.

If our products are not accepted by the market, we are not likely to generate significant revenues or become profitable.

Our success will depend upon the medical community, patients and third-party payors accepting our products as medically useful, cost-effective and safe. We cannot guarantee that any of our products in development, if approved for commercialization, will be used by doctors to treat patients. We currently have one commercially available product, Vitravene, a treatment for cytomegalovirus, or CMV, retinitis in AIDS patients, which addresses a small market. We and our partners may not be successful in commercializing additional products.

The degree of market acceptance for any of our products depends upon a number of factors, including:

- the receipt and scope of regulatory approvals;
- the establishment and demonstration in the medical and patient community of the efficacy and safety of our drug candidates and their potential advantages over competing products;
- the cost of our drug candidates compared to other available therapies;
- the patient convenience of the dosing regimen for our drug candidates; and
- reimbursement policies of government and third-party payors.

Based on the profile of our drug candidates, physicians, patients, patient advocates, payors or the medical community in general may not accept and use any products that we may develop.

If any of our collaborative partners fail to fund our collaborative programs or develop or sell any of our products under development, or if we are unable to obtain additional partners, progress on our drug development programs could be delayed or stop.

We have entered into collaborative arrangements with third parties to develop certain product candidates. We enter into these collaborations in order to:

- fund our research and development activities;
- access manufacturing by third parties;
- seek and obtain regulatory approvals; and
- successfully commercialize existing and future product candidates.

If any of our partners fails to develop or sell any drug in which we have retained a financial interest, our business may be negatively affected. These collaborations may not continue or result in commercialized drugs. Our collaborators can terminate their relationships with us under certain circumstances, some of which are outside of our control. Our most advanced drug candidate, Affinitac, is being developed collaboratively with Lilly, with the development funded by Lilly. Additional drug candidates in our development pipeline are being developed and/or funded by corporate partners, including Antisense Therapeutics Limited, Elan Corporation, plc, Merck & Co., Inc. and OncoGenex Technologies Inc. Failure by any of these pharmaceutical company partners to continue to fund and/or develop these drug candidates would have a material adverse effect on our business.

Certain of our partners are pursuing other technologies or developing other drug candidates either on their own or in collaboration with others, including our competitors, to develop treatments for the same diseases targeted by our own collaborative programs. Such competition may negatively impact the partners' focus on and commitment to our drug candidate and, as a result, could delay or otherwise negatively affect the commercialization of such drug candidate.

Historically, corporate partnering has played a key role in our strategy to fund our development programs and to add key development resources. We plan to continue to rely on additional collaborative arrangements to develop and commercialize our products. However, we may not be able to negotiate additional attractive collaborative arrangements, and, even if negotiated, the collaborative arrangements may not be successful.

If our GeneTrove business is unable to market its products and services as planned, we could lose our investment in this technology.

Our business could suffer if pharmaceutical companies do not use our GeneTrove target validation or gene functionalization services. We have invested in the development of a gene target validation and gene functionalization service business for validation and functionalization of gene targets for drug

discovery. If pharmaceutical companies fail to use these services due to competition or other factors, our GeneTrove business could fail to make the planned contribution to our financial performance.

In addition, if customers do not subscribe to the database at the level we have planned, our GeneTrove business could fail to make the planned contribution to our financial performance.

We have incurred losses, and our business will suffer if we fail to achieve profitability in the future.

Because drug discovery and development and the development of database products and research services require substantial lead time and money prior to commercialization, our expenses have exceeded our revenues since we were founded in January 1989. As of June 30, 2002, our accumulated losses were approximately \$426 million. Most of the losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Most of our revenue has come from collaborative arrangements, with additional revenue from interest income and research grants and the sale or licensing of patents. Our current product revenues are derived solely from sales of Vitravene. This product has limited sales potential. We expect to incur additional operating losses over the next several years, and these losses may increase if we cannot increase or sustain revenue. We may not successfully develop any additional products or services, or achieve or sustain future profitability.

If we fail to obtain timely funding, we may need to curtail or abandon some of our programs.

Most of our product candidates are still undergoing clinical trials or are in the early stages of research and development. All of our products under development will require significant additional research, development, preclinical and/or clinical testing, regulatory approval and a commitment of significant additional resources prior to their commercialization. Based on our current operating plan, we believe that our available cash, cash equivalents and short-term investments at June 30, 2002 combined with investment income and committed contractual cash payments, will be sufficient to meet our anticipated requirements

for at least the next 36 months. If we fail to meet our goals regarding commercialization of our drug products, gene function database product and research services and licensing of our proprietary technologies, we may need additional funding in the future. Our future capital requirements will depend on many factors, such as the following:

- the profile and launch timing of our drugs;
- continued scientific progress in our research, drug discovery and development programs;
- the size of these programs and progress with preclinical and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- competing technological and market developments, including the introduction by others of new therapies that address our markets;
- success in the marketing of our gene function database and research service products; and
- changes in existing collaborative relationships and our ability to establish and maintain additional collaborative arrangements.

If we need additional funds, we may need to raise them through public or private financing. Additional financing may not be available at all or on acceptable terms. If additional funds are raised by issuing equity securities, the shares of existing stockholders will be diluted and their price, as well as the price of our other securities, may decline. If adequate funds are not available, we may be required to cut back on one or more of our research, drug discovery or development programs or obtain funds through arrangements with collaborative partners or others. These arrangements may require us to give up rights to certain of our technologies, product candidates or products.

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If we cannot manufacture our products or contract with a third party to manufacture our products at costs that allow us to charge competitive prices to buyers, we will not be able to market products profitably.

If we successfully commercialize any of our drug candidates, we may be required to establish large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. Pharmaceutical products of the chemical class represented by our drug candidates, called oligonucleotides, have never been manufactured on a large scale, and to our knowledge there is no commercial scale oligonucleotide manufacturer in business today. We have a limited number of suppliers for certain capital equipment and raw materials that we use to manufacture our drugs, and some of these suppliers will need to increase their scale of production to meet our projected needs for commercial manufacturing. Further, we must continue to improve our manufacturing processes to allow us to reduce our product costs. We may not be able to manufacture at a cost or in quantities necessary to make commercially successful products.

Also, manufacturers, including us, must adhere to the FDA's current Good Manufacturing Practices regulations, which are enforced by the FDA through its facilities inspection program. We and our contract manufacturers may not be able to comply or maintain compliance with Good Manufacturing Practices regulations. Non-compliance could significantly delay our receipt of marketing approval for potential products or result in FDA enforcement action.

If we fail to compete effectively, our products will not contribute significant revenues.

Our competitors are engaged in all areas of drug discovery throughout the world, are numerous, and include, among others, major pharmaceutical companies and specialized biopharmaceutical firms. Other companies are engaged in developing antisense technology. Our competitors may succeed in developing drug candidates that are more effective than any drug candidates that we are developing. These competitive developments could make our products obsolete or non-competitive.

Our GeneTrove division competes with others in the use of antisense technology for gene target validation and gene functionalization, as well as with other technologies useful for target validation and gene functionalization. Our competition may provide services having more value to potential customers or may market their services more effectively to potential customers. In either case, our gene functionalization and target validation businesses may not contribute to our financial performance as planned.

Many of our competitors have substantially greater financial, technical and human resources than we do. In addition, many of these competitors have significantly greater experience than we do in conducting preclinical testing and human clinical trials of new pharmaceutical products and in obtaining FDA and other regulatory approvals of products for use in health care. Accordingly, our competitors may succeed in obtaining regulatory approval for products earlier than we do. We will also compete with respect to marketing and sales capabilities, areas in which we have limited or no experience.

If we are unable to protect our patents or our proprietary rights, others may be able to compete more directly against us.

Our success depends to a significant degree upon our ability to develop and secure intellectual property rights to proprietary products and services. However, patents may not be granted on any of our pending patent applications in the United States or in other countries. In addition, the scope of any of our issued patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, our issued patents or patents licensed to us may be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier.

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Intellectual property litigation could be expensive and prevent us from pursuing our programs.

It is possible that in the future we may have to defend our intellectual property rights. In the event of an intellectual property dispute, we may be forced to litigate to defend our rights or assert them against others. Disputes could involve litigation or proceedings declared by the U.S. Patent and Trademark Office or the International Trade Commission. Intellectual property litigation can be extremely expensive, and this expense, as well as the consequences should we not prevail, could seriously harm our business.

On July 9, 2001, we initiated litigation against Sequitur, Inc. alleging patent infringement. On December 12, 2001, we initiated a second action against Sequitur, Inc. alleging patent infringement. On May 2, 2002 we initiated a third action against Sequitur, Inc. alleging patent infringement. If we do not prevail in the defense of these patents, it could impact our ability to realize future licensing revenues.

If a third party claims that our products or technology infringe their patents or other intellectual property rights, we might be forced to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to such intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or applications held by others that relate to our business. This is especially true since patent applications in the United States are filed confidentially. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain unresolved.

If we do not progress in our programs as anticipated, the price of our securities could decrease.

For planning purposes, we estimate the timing of a variety of clinical, regulatory and other milestones, such as when a certain product candidate will enter the clinic, when a clinical trial will be completed or when an application for marketing approval will be filed. Some of our estimates are included in this prospectus. Our estimates are based on present facts and a variety of assumptions. Many of the underlying assumptions are outside of our control. If milestones are not achieved when we expect them to be, investors could be disappointed and the price of our securities would likely decrease.

The loss of key personnel, or the inability to attract and retain highly skilled personnel, could make it more difficult to run our business and reduce our likelihood of success.

We are dependent on the principal members of our management and scientific staff. We do not have employment agreements with any of our management. The loss of our management and key scientific employees might slow the achievement of important research and development goals. It is also critical to our success that we recruit and retain qualified scientific personnel to perform research and development work. We may not be able to attract and retain skilled and experienced scientific personnel on acceptable terms because of intense competition for experienced scientists among many pharmaceutical and health care companies, universities and non-profit research institutions. Our collaboration with Lilly requires us to add a significant number of skilled scientific personnel. Our inability to add these employees may impact the success of our Lilly collaboration.

If the price of our securities continues to be highly volatile, this could make it harder for you to liquidate your investment and could increase your risk of suffering a loss.

The market price of our common stock, like that of the securities of many other biopharmaceutical companies, has been and is likely to continue to be highly volatile. These fluctuations in our common stock price may significantly affect the trading price of the convertible notes. During the 12 months preceding June 30, 2002, the market price of our common stock has ranged from \$6.76 to \$27.15 per share. The market price of our securities can be affected by many factors, including, for example, fluctuations in our operating results, announcements of collaborations, clinical trial results,

technological innovations or new drug products being developed by us or our competitors, governmental regulation, regulatory approval, developments in patent or other proprietary rights, public concern regarding the safety of our drugs and general market conditions.

Provisions in our certificate of incorporation, other agreements and Delaware law may prevent stockholders from receiving a premium for their shares.

Our certificate of incorporation provides for classified terms for the members of our board of directors. Our certificate also includes a provision that requires at least 66²/₃% of our voting stockholders to approve a merger or certain other business transactions with, or proposed by, any holder of 15% or more of our voting stock, except in cases where certain directors approve the transaction or certain minimum price criteria and other procedural requirements are met.

Our certificate of incorporation also requires that any action required or permitted to be taken by our stockholders must be taken at a duly called annual or special meeting of stockholders and may not be taken by written consent. In addition, special meetings of our stockholders may be called only by the board of directors, the chairman of the board or the chief executive officer. We also have implemented a stockholders' rights plan, also called a poison pill, which could make it uneconomical for a third party to acquire our company on a hostile basis. These provisions, as well as Delaware law and other of our agreements, may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices, and may limit the ability of our stockholders to approve transactions that they think may be in their best interests. In addition, our board of directors has the authority to fix the rights and preferences of and issue shares of preferred stock, which may have the effect of delaying or preventing a change in control of our company without action by our stockholders.

If registration rights that we have previously granted are exercised, then the price of our securities may be negatively affected.

We have granted registration rights in connection with the issuance of our securities to Elan International Services, Ltd., Eli Lilly and Company and Reliance Insurance Company. In the aggregate, these registration rights cover approximately 4,166,667 shares of our common stock which are currently outstanding and additional shares of our common stock which may become outstanding upon the conversion of outstanding convertible securities. If these registration rights are exercised by the holders, it will bring additional shares of our common stock into the market, which may have an adverse effect on the price of our securities.

RISKS RELATED TO THE CONVERTIBLE NOTES

The convertible notes are subordinated to our senior indebtedness and are structurally subordinated to all liabilities of our subsidiaries.

The convertible notes are junior in right of payment to all of our existing and future senior indebtedness and are structurally subordinated to all liabilities of our subsidiaries, including trade payables. As of June 30, 2002, we and our subsidiaries had approximately \$75.8 million of consolidated liabilities effectively

ranking senior to the convertible notes, assuming the repayment of a portion of our debt held by Elan International Services, Ltd. and its related entities which occurred on July 3, 2002. The indenture governing the convertible notes does not restrict the incurrence of additional senior indebtedness or other debt or liabilities by us or our subsidiaries. By reason of such subordination, in the event of the insolvency, bankruptcy, liquidation, reorganization, dissolution or winding up of our business, our assets will be available to pay the amounts due on the convertible notes only after all of our senior indebtedness has been paid in full, and, therefore, there may not be sufficient assets remaining to pay amounts due on any or all of the convertible notes then outstanding. See "Description of Notes—Subordination of Convertible Notes."

We may not have the ability to raise the funds necessary to finance the change in control offer required by the indenture.

If we undergo a change in control, as defined in the indenture, each holder of the convertible notes may require us to repurchase all or a portion of the holder's convertible notes. We cannot assure you that there will be sufficient funds available for any required repurchases of these securities if a change in control occurs. In addition, the terms of any agreements related to borrowing which we may enter from time to time may prohibit or limit our repurchase of the convertible notes or make our repurchase of convertible notes an event of default under those agreements. If we fail to repurchase the convertible notes in that circumstance, we will be in default under the indenture governing the convertible notes. See "Description Notes—Change in Control Permits Purchase of Convertible Notes by Us at the Option of the Holder."

Absence of a public market for the convertible notes could cause purchasers of the convertible notes to be unable to resell them for an extended period of time.

Although the notes trade on The PORTAL Market, there is not an established trading market for the notes and we cannot assure you that an active public market for the notes will develop, or if such a market develops, how liquid it will be. At the time of the initial offering and sale of the notes, the initial purchasers of the notes informed us that they intended to make a market in the notes. The initial purchasers may cease their market-making activities, if any, at any time without notice.

If a trading market does not develop or is not maintained, holders of the convertible notes may experience difficulty in reselling, or an inability to sell, the convertible notes. If a market for the convertible notes develops, it may be discontinued at any time. If a public trading market develops for the convertible notes, future trading prices of the convertible notes will depend on many factors, including, among other things, the price of our common stock into which the convertible notes are convertible, prevailing interest rates, our operating results and the market for similar securities. Depending on the price of our common stock into which the convertible notes are convertible, prevailing interest rates, the market for similar securities and other factors, including our financial condition, the convertible notes may trade at a discount from their principal amount.

If the private placement of the notes prior to this registration statement violated securities laws, purchasers in the private offering would have the right to seek refunds or damages.

On May 1, 2002, we issued and sold the notes in a private placement transaction. The initial purchasers of the notes in that offering resold the notes to persons reasonably believed to be qualified institutional buyers (as defined in Rule 144A under the Securities Act) and non-U.S. persons (as defined in Regulation S under the Securities Act). On April 24, 2002, an article appeared in a San Diego newspaper regarding this offering in which one of our officers was interviewed. The newspaper article could form the basis for a claim that, in connection with our private placement of the convertible notes, we engaged in an unregistered public offering of the convertible notes in violation of the securities laws. We would dispute any such claim. However, if such a claim were made and it prevailed, the initial purchasers of the notes and persons who purchased the convertible notes from the initial purchasers would have the right, for a period of one year, to obtain recovery of the consideration paid in connection with their purchase of the convertible notes or, if they have already sold the convertible notes, to recover any losses resulting from their purchase of the convertible notes.

**RATIO OF EARNINGS TO FIXED CHARGES
(in thousands, except ratio of earnings to fixed charges)**

The following table sets forth our ratio of earnings to fixed charges for the years ended December 31, 1997, 1998, 1999, 2000, 2001, for the six months ended June 30, 2002, for the pro forma year ended December 31, 2001, and the pro forma six months ended June 30, 2002. As earnings were inadequate to cover the combined fixed charges, we have provided the average deficiency amounts. For purposes of this computation, earnings are defined as net loss excluding the preferred stock dividend requirement on our Series A and Series B preferred stock. Fixed charges are the sum of (i) interest costs including the amortization of deferred financing costs; and (ii) the portion of operating lease rental expense that is representative of the interest factor of 15%. On a pro forma basis, we have assumed as of January 1, 2001, the early extinguishment of our 14% senior subordinated debt, which occurred on May 1, 2002, assumed the receipt of \$125 million in proceeds from the private placement of our 5¹/₂% convertible subordinated notes due 2009, which occurred on May 1, 2002, and the prepayment of a portion of our 12% convertible debt with Elan, on July 3, 2002. The pro forma results for 2001 and for the six months ended June 30, 2002, are representative of the reduction in interest expense for the payment of our 14% senior subordinated debt, prepayment of our 12% convertible notes and the additional interest expense associated with the issuance of our 5¹/₂% convertible subordinated notes.

	Year ended December 31,					Six months ended June 30, 2002	Pro Forma Year ended December 31, 2001	Pro Forma Six months ended June 30, 2002
	1997	1998	1999	2000	2001			
Ratio of earnings to fixed charges	—	—	—	—	—	—	—	—
Coverage deficiency	\$ (31,066)	\$ (42,983)	\$ (59,225)	\$ (53,485)	\$ (73,832)	\$ (38,837)	\$ (73,832)	\$ (38,837)

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements regarding our business and the therapeutic and commercial potential of our technologies and products in development. Such statements are subject to certain risks and uncertainties, particularly those inherent in discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in the process of conducting gene functionalization and target validation services and in launching new products and services for or with collaborators, and the endeavor of building a business around such potential products. Actual results could differ materially from those discussed in this prospectus. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled "Risk factors" in this prospectus. As a result, you are cautioned not to rely on these forward-looking statements.

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USE OF PROCEEDS

We will receive no proceeds from the resale by the selling security holders of the notes or the common stock issuable upon conversion of the notes. The selling security holders will receive all of the net proceeds from the resales.

SELLING SECURITY HOLDERS

We initially issued the notes to the initial purchasers of the notes who then resold the notes in transactions exempt from the registration requirements of the Securities Act to persons reasonably believed to be "qualified institutional buyers" (as defined in Rule 144A under the Securities Act) and non-U.S. persons outside the U.S. pursuant to Regulation S under the Securities Act. The selling security holders (which term includes their transferees, pledgees, donees or their successors) may from time to time offer and sell pursuant to this prospectus or any applicable prospectus supplement any or all of the notes and common stock issuable upon conversion of the notes.

No offer or sale under this prospectus may be made by a selling security holder unless that holder is listed in the table in this prospectus or until that holder has notified us and a supplement to this prospectus has been filed or an amendment to the registration statement of which this prospectus is a part has become effective. We will supplement or amend this prospectus to include additional selling security holders upon request and upon provision of all required information to us. Information concerning the selling security holders may change from time to time and any changed information will be set forth in supplements to this prospectus if and when necessary.

The following table sets forth information about each selling security holder, including the name, the number and percentage of the notes beneficially owned and being offered by the selling security holder and the number and percentage of common stock beneficially owned and being offered by the selling security holder. The percentages of common stock beneficially owned and being offered are based on the number of shares of our common stock that were outstanding as of June 30, 2002. Unless otherwise indicated below, none of the selling security holders nor any of their affiliates, officers, directors or principal equity holders has held any position or office or has had any material relationship with us within the past three years.

Name	Principal Amount of Notes Beneficially Owned and Offered Hereby (1)	Percentage of Notes Outstanding	Shares of Common Stock Beneficially Owned and Offered Hereby	Percentage of Common Stock Outstanding
Akela Capital Master Fund	3,000,000	2.4%	180,451	*
Allstate Insurance Company	600,000	*	36,090	*
Allstate Life Insurance Company	400,000	*	24,060	*
Alpine Associates	7,950,000	6.4%	478,195	*
Alpine Partners	1,050,000	*	63,157	*
American Investors Life Ins	100,000	*	6,015	*
American Samoa Government	18,000	*	1,082	*
Aristeia International	5,197,000	4.2%	312,601	*
Aristeia Trading LLC	1,553,000	1.2%	93,413	*
Ascend Managed Account Ltd	19,767	*	1,188	*
Ascend Offshore Fund Ltd	129,203	*	7,771	*
Ascend Partners LP	20,720	*	1,246	*
Ascend Partners Sapient LP	30,280	*	1,821	*
ATSF Transamerica Convertible Securities	30,000	*	1,804	*
Baird, Patrick & Co	1,500,000	1.2%	90,225	*

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BP Amoco PLC Master Trust	571,000	*	34,345	*
Canyon Capital Arbitrage Master Fund, Ltd.	3,300,000	2.6%	198,496	*
Canyon Mac 18, Ltd. (RMF)	550,000	*	33,082	*
Canyon Value Realization Fund (Cayman) Ltd.	4,950,000	4.0%	297,744	*
Cheyne Capital Management Limited	2,000,000	1.6%	120,300	*
Context Convertible Arbitrage Fund	300,000	*	18,045	*
Deutsche Bank Securities Inc.	3,500,000	2.8%	210,526	*

DKR Fixed Income Holding Fund Ltd.	1,000,000	*	60,150	*
Dodeca Fund, LP	600,000	*	36,090	*
Estate of James Campbell	146,000	*	8,781	*
Fidelity Financial Trust: Fidelity				
Convertible Securities Fund	1,500,000	1.2%	90,225	*
First Union Securities Inc.	13,500,000	10.8%	812,030	1.5%
Grace Brothers Management, LLC	750,000	*	45,112	*
Highbridge International LLC	20,000,000	16.0%	1,203,008	2.2%
Hotel Union & Hotel Industry of Hawaii				
Pension Plan	193,000	*	11,609	*
IDEX Transamerica Convertible				
Securities Fund	75,000	*	4,511	*
JC Penney Insurance Co Group	500,000	*	30,075	*
Jefferies & Co.	750,000	*	45,112	*
Jefferies & Company Inc.	4,000	*	240	*
K D Convertible Arbitrage Fund LP	1,000,000	*	60,150	*
KBC Financial Products (Caymen				
Islands) Limited	3,500,000	2.8%	210,526	*
KBC Financial Products USA Inc.	2,650,000	2.1%	159,398	*
Lincoln Nat'l Global Asset Allocation				
Fund, Inc.	90,000	*	5,413	*
Liongate Capital	2,000,000	1.6%	120,300	*
McMahan Securities Co. Ltd.	1,550,000	1.2%	93,233	*
Morgan Stanley & Co, Incorporated	2,000,000	1.6%	120,300	*
Pacific Life Insurance Company	500,000	*	30,075	*
Putnam Asset Allocation Funds-Balanced				
Portfolio	720,000	*	43,308	*
Putnam Asset Allocation Funds-				
Conservative Portfolio	560,000	*	33,684	*
Putnam Convertible Opportunity &				
Income Trust	180,000	*	10,827	*

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Putnam Convertible Income-Growth				
Trust	4,780,000	3.8%	287,518	*
Putnam Variable Trust — Putnam VT				
Global Asset Allocation Fund	170,000	*	10,225	*
S.A.C. Capital Associates, LLC	1,000,000	*	60,150	*
Sterling Investment Co.	500,000	*	30,075	*
The James Campbell Corporation	121,000	*	7,278	*
TQA Master Fund Ltd.	1,000,000	*	60,150	*
Transamerica Life Insurance & Annuity				
Co.	4,450,000	3.6%	267,669	*
Tribeca Investments LLC	5,000,000	4.0%	300,752	*
UBS Warburg LLC	5,745,000	4.6%	345,564	*
Viacom Inc. Pension Plan	19,000	*	1,142	*
Victory Capital Management as agent for				
Victory Convertible Securities Fund	250,000	*	15,037	*
Victus Capital LP	1,500,000	1.2%	90,225	*
Wachovia Securities International Ltd	7,500,000	6.0%	451,128	*
WPG Convertible Arbitrage Overseas				
Master Fund LP	1,500,000	1.2%	90,225	*
Zurich Institutional Benchmarks Master				
Fund, Ltd.	928,000	*	55,819	*

* Less than one percent

(1) We prepared this table based on the information supplied to us by the selling security holders named in the table and we have not sought to verify such information. This table only reflects information regarding selling security holders who have provided us with such information. We expect that we will update this table as we receive more information from holders of the notes who have not yet provided us with their information.

The selling security holders listed in the above table may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act, some or all of their notes since the date on which the information in the above table was provided to us. Information about the selling security holders may change over time.

Because the selling security holders may offer all or some of the notes or the shares of common stock issuable upon conversion of the notes from time to time, we cannot estimate the amount of the notes or shares of common stock that will be held by the selling security holders upon the termination of any particular offering by a selling security holder. See "Plan of Distribution."

PLAN OF DISTRIBUTION

The selling security holders, which term includes their transferees, pledgees or donees or their successors, may from time to time sell the notes and the underlying common stock covered by this prospectus directly to purchasers or offer the notes and underlying common stock through underwriters, broker-dealers

securities for whom they may act as agent, which discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved.

The notes and the underlying common stock may be sold in one or more transactions.

- at fixed prices;
- at prevailing market prices at the time of sale;
- at varying prices determined at the time of sale; or
- at negotiated prices.

These sales may be effected in transactions, which may involve block transactions, in the following manner:

- on any national securities exchange or quotation service on which the notes or the common stock may be listed or quoted at the time of sale;
- in the over-the-counter-market;
- in transactions otherwise than on these exchanges or services or in the over-the-counter market; or
- through the writing and exercise of options, whether these options are listed on an options exchange or otherwise.

In connection with the sale of the notes and common stock, the selling security holders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging positions they assume. The selling security holders may sell the notes or common stock and deliver notes or common stock to close out short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities.

The aggregate proceeds to the selling security holders from the sale of the securities offered by them hereby will be the purchase price of such securities less discounts and commissions, if any. The selling security holder reserves the right to accept and, together with its agent from time to time, to reject, in whole or in part, any proposed purchase of securities to be made directly or through agents. We will not receive any of the proceeds from the resale by the selling security holders of the notes or the common stock issuable upon conversion of the notes.

The notes are traded on The PORTAL Market. Our common stock is listed for trading on the Nasdaq National Market under the symbol "ISIS."

In order to comply with the securities laws of some states, if applicable, the securities may be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from registration or qualification requirements is available and is complied with.

The selling security holders, and any underwriters, broker-dealers or agents that participate in the sale of the securities, may be "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the securities may be underwriting discounts and commissions under the Securities Act. The selling security holders have acknowledged that they understand their obligations to comply with the provisions of the Securities Exchange Act of 1934 and the rules thereunder relating to stock manipulation, particularly Regulation M.

At the time of a particular offering of securities by a selling security holder, a supplement to this prospectus, if required, will be circulated setting forth the aggregate amount and type of securities being offered and the terms of the offering, including the name or names of any underwriters, broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling security holders and any discounts, commissions or concessions allowed or reallocated or paid to broker-dealers.

We entered into a registration rights agreement for the benefit of holders of the notes to register their notes and the underlying common stock under applicable federal and state securities laws under specific circumstances and at specific times. The registration rights agreements provides for cross indemnification of the selling security holders and us and their and our respective directors, officers and controlling person against specific liabilities in connection with the offer and sale of the notes and the underlying common stock, including liabilities under the Securities Act.

DESCRIPTION OF NOTES

On May 1, 2002, we issued and sold the notes in a private placement transaction. The initial purchasers of the notes in that offering resold the notes to persons reasonably believed to be qualified institutional buyers (as defined in Rule 144A under the Securities Act) and non-U.S. persons (as defined in Regulation S under the Securities Act). The convertible notes were issued under the indenture dated May 1, 2002 between us and Wells Fargo Bank Minnesota, National Association, as trustee. The following statements are subject to the detailed provisions of the indenture and are qualified in their entirety by reference to the indenture. The indenture has been filed as an exhibit to the registration statement of which this prospectus is a part. Particular provisions of the indenture which are referred to in this prospectus are incorporated by reference as a part of the statements made, and the statements are qualified in their entirety by the reference. For purposes of this summary, the terms "Isis," "we," "us" and "our" refer only to Isis Pharmaceuticals, Inc. and not to any of our subsidiaries. References to "interest" shall be deemed to include "liquidated damages" unless the context otherwise requires.

GENERAL

The convertible notes represent our unsecured general obligations, subordinate in right of payment to our obligations as described under "—Subordination of Convertible Notes," and convertible into our common stock as described under "—Conversion Rights." The convertible notes are limited to \$125,000,000 aggregate principal amount. Interest on the convertible notes will be payable semi-annually on May 1 and November 1 of each year, with the first interest payment to be made on November 1, 2002, at the rate of 5¹/₂% per annum, to the persons who are registered holders of the convertible notes at the close of

business on the preceding April 15 and October 15, respectively. Unless previously redeemed, repurchased or converted, the convertible notes will mature on May 1, 2009. The convertible notes will be payable at the office of the paying agent, which initially will be an office or agency of the trustee, or an office or agency maintained by us for such purpose, in the Borough of Manhattan, the City of New York. Payments in respect of the convertible notes may, at our option, be made by check and mailed to the holders of record as shown on the register for the convertible notes.

We issued the convertible notes without coupons in denominations of \$1,000 and integral multiples thereof.

Holders may present for conversion any convertible notes that are eligible for conversion at the office of the conversion agent, and may present convertible notes for registration of transfer at the office of the registrar for the convertible notes, which initially will be the trustee.

The indenture does not contain any financial covenants or any restrictions on the payment of dividends or on the repurchase of our securities. The indenture does not require us to maintain any sinking fund or other reserves for repayment of the convertible notes.

CONVERSION RIGHTS

Before the close of business on the date of maturity of the convertible notes, subject to prior redemption or repurchase, holders of convertible notes may convert the convertible notes, or portions thereof (if the portions are \$1,000 or whole multiples thereof) into 60.1504 shares of common stock per \$1,000 of principal amount of convertible notes. This rate results in an initial conversion price of approximately \$16.625 per share. Except as described below, the number of shares into which a convertible note is convertible will not be adjusted for dividends on any common stock issued on conversion. We will not issue fractional shares of common stock upon conversion of convertible notes and instead will pay a cash adjustment based on the market price of the common stock on the last trading day prior to the conversion date. In the case of convertible notes called for redemption,

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conversion rights will expire at the close of business on the date one business day prior to the redemption date.

We are not obligated to pay accrued interest on convertible notes submitted for conversion. Accordingly, if a convertible note is converted between a record date for the payment of interest and the next succeeding interest payment date, convertible notes submitted for conversion must be accompanied by funds equal to the interest payable to the registered holder on the interest payment date on the principal amount of such notes submitted for conversion. We will then make the interest payment due on the interest payment date to the registered holder of the convertible note on the record date. Notwithstanding anything to the contrary in this paragraph, any convertible note submitted for conversion need not be accompanied by any payment if either (1) the convertible note has been called for redemption or (2) the convertible note is converted on an interest payment date.

As soon as practicable following the conversion date, we will deliver through the conversion agent a certificate for the full number of full shares of common stock into which any convertible note is converted, together with any cash payment for fractional shares. For a discussion of the tax treatment of a holder receiving common shares upon surrendering convertible notes for conversion, see "Certain United States Federal Income Tax Considerations—U.S. Holders—Conversion of the notes."

We will adjust the conversion rate for:

- dividends or distributions on shares of our common stock payable in common stock;
- subdivisions, combinations or certain reclassifications of our common stock;
- distributions to all holders of common stock of certain rights or warrants entitling them for a period of 60 days or less to purchase common stock at less than the current market price at the time;
- distributions to all holders of our common stock of our assets, debt securities, shares of our capital stock other than our common stock, or certain rights to purchase our securities, but excluding cash dividends from current or retained earnings;
- all-cash distributions to all or substantially all holders of our common stock in an aggregate amount that, together with
 - any cash and the fair market value of any other consideration payable in respect of any tender offer (within the meaning of the U.S. federal securities laws) by us or any of our subsidiaries for our common stock consummated within the preceding 12 months not triggering a conversion rate adjustment, and
 - all other all-cash distributions to all or substantially all holders of our common stock made within the preceding 12 months not triggering a conversion rate adjustment,

exceeds an amount equal to 10% of the market capitalization of our common stock on the business day immediately preceding the day on which we declare the distribution;

- the purchase of our common stock pursuant to a tender offer made by us or any of our subsidiaries to the extent that the same involves aggregate consideration that, together with
 - any cash and the fair market value of any other consideration payable in respect of any tender offer by us or any of our subsidiaries for our common stock consummated within the preceding 12 months not triggering a conversion rate adjustment, and
 - all-cash distributions to all or substantially all holders of our common stock made within the preceding 12 months not triggering a conversion rate adjustment,

exceeds an amount equal to 10% of the market capitalization of our common stock on the expiration date of the tender offer.

Each adjustment referred to above will be made upon conclusion of the applicable event. We will not adjust the conversion rate, however, if holders of convertible notes are to participate in the transaction without conversion, or in certain other cases.

To the extent that our stockholders rights plan is still in effect, upon conversion of the notes into common stock, the holders will receive, in addition to the common stock, the rights described in our stockholders rights plan, whether or not the rights have separated from the common stock at the time of conversion, subject to certain limited exceptions. If we implement a new stockholders rights plan, we will be required under the indenture to provide that the holders of notes will receive the rights upon conversion of the notes, whether or not these rights were separated from the common stock prior to conversion, subject to certain limited exceptions.

Except as stated above, the number of shares issuable on conversion will not be adjusted for the issuance of common stock or any securities convertible into or exchangeable for common stock, or carrying the right to purchase any of the foregoing. The terms of the convertible notes do not require any adjustment for rights to purchase common stock pursuant to our present or any future stockholder rights plan or pursuant to any plans we have for reinvestment of dividends or interest, or for a change in the par value of the common stock. To the extent that convertible notes become convertible into cash, no adjustment will be required thereafter as to cash.

No adjustment in the conversion rate will be required unless the adjustment would require a change of at least 1% in the conversion rate then in effect; provided that any adjustment that would otherwise be required to be made will be carried forward and taken into account in any subsequent adjustment. We reserve the right to make such increases in the conversion rate in addition to those required in the foregoing provisions as we in our discretion shall determine to be advisable in order that stock-related distributions hereafter made by us to our stockholders shall not be taxable or for any other appropriate reason.

If we are party to a consolidation, merger or binding share exchange pursuant to which the common stock is converted into cash, securities or other property, at the effective time of the transaction, the right to convert a convertible note into common stock will be changed into a right to convert it into the kind and amount of cash, securities or other property which the holder would have received if the holder had converted its convertible note immediately prior to the transaction.

In the event of:

- a taxable distribution to holders of shares of common stock which results in an adjustment of the conversion rate; or
- an increase in the conversion rate at our discretion,

the holders of the convertible notes may, in certain circumstances, be deemed to have received a distribution subject to federal income tax as a dividend. See "Certain United States Federal Income Tax Considerations—U.S. Holders—Constructive dividends on the notes."

PROVISIONAL REDEMPTION

We may redeem in cash any portion of the notes at any time prior to May 3, 2005 upon at least 30 and not more than 60 days notice by mail to the holders of the notes, at a redemption price equal to \$1,000 per note plus the "make whole" payment described below, if (1) the closing price of our common stock on the Nasdaq National Market (or other primary exchange where our common stock is traded) has exceeded 150% of the conversion price for at least 20 trading days in any consecutive 30-day trading period ending on the trading day prior to the mailing of the notice of redemption and

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(2) the shelf registration statement covering resales of the notes and the common stock issuable upon conversion of the notes is effective and available for use and is expected to remain effective and available for use for the 30 days following the redemption date, unless registration is no longer required. Notes will be redeemed only in integral multiples of \$1,000 principal amount.

If we redeem notes under these circumstances, we will make a "make whole" payment on the redeemed notes equal to the total value of the aggregate amount of interest that would have been payable on the notes from the last day through which interest was paid on the notes (or May 1, 2002 if no interest has been paid) through May 1, 2005 (or May 2, 2005, if redeemed on that date). We must make these "make whole" payments on all notes called for redemption prior to May 3, 2005, including notes converted after the date we mailed the notice. The "make whole" payment for notes converted shall not be reduced by accrued and unpaid interest. We may make these "make whole" payments, at our option, either in cash or in our common stock or a combination thereof. We will specify the type of consideration for the "make whole" payment in the redemption notice. Payments made in our common stock will be valued at 95% of the average of the closing sales prices of our common stock on the Nasdaq National Market (or other U.S. national securities exchange where our common stock is then traded) for the five trading days ending on the day prior to the redemption date.

Because the sale price of the common stock will be determined before the redemption date, if we specify that we will make payment of the redemption price in our common stock, holders of notes bear the market risk that our common stock will decline in value between the date the sale price is calculated and the redemption date.

REDEMPTION OF CONVERTIBLE NOTES AT OUR OPTION

No sinking fund is provided for the convertible notes. The convertible notes are redeemable at our option, in whole or in part, at any time on or after May 3, 2005, on any date not less than 30 nor more than 60 days after the mailing of a redemption notice to each holder of convertible notes to be redeemed at the address of the holder appearing in the security register. The redemption price for the convertible notes, expressed as a percentage of principal amount, is as follows for the periods set forth below:

Period	Redemption Price
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May 3, 2005 to April 30, 2006	103.143%
May 1, 2006 to April 30, 2007	102.357%
May 1, 2007 to April 30, 2008	101.571%
May 1, 2008 to April 30, 2009	100.786%

Accrued and unpaid interest will also be paid to the redemption date.

If we will redeem less than all of the outstanding convertible notes, the trustee will select the convertible notes to be redeemed on a pro rata basis in principal amounts of \$1,000 or integral multiples of \$1,000. If a portion of a holder's convertible notes is selected for partial redemption and the holder converts a portion of the convertible notes, the converted portion shall be deemed to be the portion selected for redemption.

CHANGE IN CONTROL PERMITS PURCHASE OF CONVERTIBLE NOTES BY US AT THE OPTION OF THE HOLDER

In the event of a change in control, as defined below, with respect to us, each holder will have the right, at its option, subject to the terms and conditions of the indenture, to require us to purchase for cash all or any portion of the holder's convertible notes in integral multiples of \$1,000 principal amount, at a price for each \$1,000 principal amount of such convertible notes equal to 100% of the principal amount of such convertible notes tendered, plus any accrued and unpaid interest to the

purchase date. We will be required to purchase the convertible notes no later than 30 business days after notice of a change in control has been mailed as described below. We refer to this date in this prospectus as the "change in control purchase date."

Within 30 business days after the occurrence of a change in control, we must mail to the trustee and to all holders of convertible notes at their addresses shown in the register of the registrar and to beneficial owners as required by applicable law a notice regarding the change in control, which notice must state, among other things:

- the events causing a change in control;
- the date of such change in control;
- the last date on which a holder may exercise the purchase right;
- the change in control purchase price;
- the change in control purchase date;
- the name and address of the paying agent and the conversion agent;
- the conversion price, the conversion rate and any adjustments to the conversion rate;
- that convertible notes with respect to which a change in control purchase notice is given by the holder may be converted, if otherwise convertible, only if the change in control purchase notice has been withdrawn in accordance with the terms of the indenture; and
- the procedures that holders must follow to exercise these rights.

To exercise this right, the holder must deliver a written notice so as to be received by the paying agent no later than the close of business on the third business day prior to the change in control purchase date. The required purchase notice upon a change in control must state:

- the certificate numbers of the convertible notes to be delivered by the holder, if applicable;
- the portion of the principal amount of convertible notes to be purchased, which portion must be \$1,000 or an integral multiple of \$1,000; and
- that we are to purchase such convertible notes pursuant to the applicable provisions of the convertible notes.

A holder may withdraw any change in control purchase notice by delivering to the paying agent a written notice of withdrawal prior to the close of business on the second business day prior to the change in control purchase date. The notice of withdrawal must state:

- the principal amount of the convertible notes being withdrawn;
- the certificate numbers of the convertible notes being withdrawn, if applicable; and
- the principal amount, if any, of the convertible notes that remain subject to a change in control purchase notice.

Our obligation to pay the change in control purchase price for a convertible note for which a change in control purchase notice has been delivered and not validly withdrawn is conditioned upon delivery of the convertible note, together with necessary endorsements, to the paying agent at any time after the delivery of such change in control purchase notice. We will cause the change in control purchase price for such convertible note to be paid promptly following the later of the change in control purchase date or the time of delivery of such convertible note.

If the paying agent holds money sufficient to pay the change in control purchase price of the convertible note on the change in control purchase date in accordance with the terms of the indenture,

then, immediately after the change in control purchase date, interest on such convertible note will cease to accrue, whether or not the convertible note is delivered to the paying agent. Thereafter, all other rights of the holder shall terminate, other than the right to receive the change in control purchase price upon delivery of the convertible note.

Under the indenture, a "change in control" is deemed to have occurred at such time as:

- any "person" or "group" (as such terms are used for purposes of Sections 13(d) and 14(d) of the Exchange Act), other than us, our subsidiaries or their employee benefit plans, is or becomes the "beneficial owner" (as such term is used in Rule 13d-3 under the Exchange Act), directly or indirectly, of 50% or more of the voting power of our common stock or other capital stock into which our common stock is reclassified or changed;
- at any time the following persons cease for any reason to constitute a majority of our board of directors:
 - individuals who on the issue date of the convertible notes constituted our board of directors, and
 - any new directors whose election by our board of directors or whose nomination for election by our stockholders was approved by at least a majority of the directors then still in office who were either directors on the issue date of the convertible notes or whose election or nomination for election was previously so approved; or
- the sale, lease or transfer of all or substantially all of our assets and property to any "person" or "group" (as such terms are used in Sections 13(d) and 14(d) of the Exchange Act), including any group acting for the purpose of acquiring, holding or disposing of securities within the meaning of Rule 13d-5(b)(1) under the Exchange Act.

However, a change in control will be deemed not to have occurred if either:

- the last sale price of our common stock for any five trading days during the ten trading days immediately preceding the change in control is at least equal to 105% of the conversion price in effect on such trading day; or
- in the case of a merger or consolidation, all or substantially all of the consideration for our outstanding common stock (excluding cash payments for fractional shares and cash payments pursuant to dissenters' appraisal rights) in the merger or consolidation constituting the change in control consists of common stock traded on a U.S. national securities exchange or quoted on the Nasdaq National Market (or which will be so traded or quoted when issued or exchanged in connection with such change in control) and as a result of such transaction or transactions the convertible notes become convertible solely into such common stock.

In connection with any purchase offer in the event of a change in control, we will to the extent applicable:

- comply with the provisions of Rule 13e-4, Rule 14e-1 and any other tender offer rules under the Exchange Act which may then be applicable; and
- file Schedule TO or any other required schedule under the Exchange Act.

The phrase "all or substantially all" of our assets will likely be interpreted under applicable law and will be dependent upon particular facts and circumstances. As a result, there may be a degree of uncertainty in ascertaining whether a sale, lease or transfer of "all or substantially all" of our assets has occurred, in which case a holder's ability to require us to purchase the holder's convertible notes upon a change in control may be impaired. In addition, we can give no assurance that we will be able to acquire the convertible notes tendered upon a change in control.

The change in control purchase feature of the convertible notes may in certain circumstances make more difficult or discourage a takeover of our company.

We could, in the future, enter into certain transactions, including certain recapitalizations, that would not constitute a change in control with respect to the change in control purchase feature of the convertible notes but that would increase the amount of our, or our subsidiaries', indebtedness.

We may not purchase convertible notes at the option of holders upon a change in control if there has occurred and is continuing an event of default with respect to the convertible notes, other than a default in the payment of the change in control purchase price with respect to the convertible notes.

SUBORDINATION OF CONVERTIBLE NOTES

Upon any distribution to our creditors in our liquidation, winding up or dissolution or in a bankruptcy, reorganization, insolvency, receivership or similar proceeding relating to us or our property, the payment of all amounts due on the convertible notes (other than cash payments due upon conversion in lieu of fractional shares) will be subordinated, to the extent provided in the indenture, in right of payment to the prior payment in full of all senior indebtedness and all indebtedness of our subsidiaries.

We will not pay, directly or indirectly, any amount due on the convertible notes (including any repurchase price pursuant to the exercise of the repurchase right), or acquire any of the convertible notes, in the following circumstances:

- if any default in payment of principal, premium, if any, or interest on senior indebtedness (as defined below) exists, unless and until the default has been cured or waived or has ceased to exist;
- if any default, other than a default in payment of principal, premium, if any, or interest, has occurred with respect to senior indebtedness, and that default permits the holders of the senior indebtedness to accelerate its maturity, until the expiration of the "payment blockage period" described below unless and until the default has been cured or waived or has ceased to exist; or
- if the maturity of senior indebtedness has been accelerated, until the senior indebtedness has been paid or the acceleration has been cured or waived.

A "payment blockage period" is a period that begins on the date that we receive a written notice from any holder of senior indebtedness or a holder's representative, or from a trustee under an indenture under which senior indebtedness has been issued, that an event of default with respect to and as defined under any senior indebtedness (other than default in payment of the principal of, or premium, if any, or interest on any senior indebtedness), which event of default permits the holders of senior indebtedness to accelerate its maturity, has occurred and is continuing and ends on the earlier of (1) the date on which such event of default has been cured or waived or (2) 180 days from the date notice is received. Notwithstanding the foregoing, only one payment blockage notice with respect to the same event of default may be given during any period of 360 consecutive days unless such event of default has been cured or waived for a period of not less than 90 consecutive days; provided that in no event shall more than one interest payment be blocked during any such 360-day period. No new payment blockage notice may be commenced by the holders of senior indebtedness during any period of 360 consecutive days unless all events of default which triggered the preceding payment blockage period have been cured or waived. However, if the maturity of such senior indebtedness is accelerated, no payment may be made on the convertible notes until such senior indebtedness that has matured has been paid or such acceleration has been cured or waived.

Senior indebtedness is defined in the indenture as all indebtedness (as defined below) of ours outstanding at any time except indebtedness that by its terms is subordinate in right of payment to the

convertible notes or indebtedness that is not otherwise senior in right of payment to the convertible notes. Senior indebtedness does not include our indebtedness to any of our subsidiaries.

Indebtedness is defined with respect to any person as the principal of, and premium, if any, and interest on (a) all indebtedness of such person for borrowed money (including all indebtedness evidenced by notes, bonds, debentures or other securities sold by such person for money), (b) all obligations incurred by such person in the acquisition (whether by way of purchase, merger, consolidation or otherwise and whether by such person or another person) of any business, real property or other assets (except inventory and related items acquired in the ordinary course of the conduct of the acquiror's usual business), (c) direct or indirect guarantees or similar agreements by such person of indebtedness described in clause (a), (b), (e), (f), (g) or (h) of another person, (d) all renewals, extensions, refundings, deferrals, restructurings, amendments, supplements and modifications of any indebtedness, obligation or guarantee, (e) all reimbursement obligations and other liabilities, contingent or otherwise, of such person with respect to letters of credit, bankers' acceptances or similar facilities issued for the account of such person, (f) all capital lease obligations of such person, (g) all net obligations of such person under interest rate swap, currency exchange or similar agreements of such person and (h) all obligations and other liabilities, contingent or otherwise, under any lease or related document, including a purchase agreement, conditional sale or other title retention agreement, in connection with the lease of real property or improvements thereon (or any personal property included as part of any such lease) which provides that such person is contractually obligated to purchase or cause a third party to purchase the leased property or pay an agreed upon residual value of the leased property, including such person's obligations under such lease or related document to purchase or cause a third party to purchase such leased property or pay an agreed upon residual value of the leased property to the lessor.

By reason of the subordination provisions described above, in the event of insolvency, funds which would otherwise be payable to noteholders will be paid to the holders of senior indebtedness to the extent necessary to pay senior indebtedness in full. As a result of these payments, our general creditors may recover less, ratably, than holders of senior indebtedness and such general creditors may recover more, ratably, than holders of convertible notes or other subordinated indebtedness of ours.

We have subsidiaries which are separate and distinct legal entities and which have no obligation, contingent or otherwise, to pay any amounts due on the convertible notes or to make any funds available therefor, whether by dividends, loans or other payments. The payment of dividends and loans and advances to us by our subsidiaries may be subject to statutory or contractual restrictions, are contingent upon the earnings of our subsidiaries and are subject to various business considerations.

The convertible notes are effectively subordinated to all indebtedness and other liabilities and commitments (including trade payables) of our subsidiaries. Any right that we have to receive assets of any of our subsidiaries upon its liquidation or reorganization (and the consequent right of the holders of the convertible notes to participate in those assets) will be effectively subordinated to the claims of that subsidiary's creditors (including trade creditors), except to the extent that we ourselves are recognized as a creditor of that subsidiary, in which case our claims would still be subordinate to any security interests in the assets of that subsidiary and any indebtedness of that subsidiary senior to that held by us.

There are no restrictions in the indenture upon the creation of additional senior indebtedness by us, or on the creation of any indebtedness by us or any of our subsidiaries. As of June 30, 2002, we had approximately \$75.8 million of consolidated indebtedness and other obligations effectively ranking senior to the convertible notes, assuming the repayment of a portion of our debt held by Elan International Services, Ltd. and its related entities which occurred on July 3, 2002.

MERGER OR CONSOLIDATION, OR CONVEYANCE, TRANSFER OR LEASE OF PROPERTIES AND ASSETS

The indenture provides that we may not consolidate with or merge with or into any other person or convey, transfer or lease our properties and assets substantially as an entirety to another person, unless:

- the resulting, surviving or transferee person is a corporation, limited liability company or other limited liability entity organized and existing under the laws of the United States, any state thereof or the District of Columbia; provided that this condition will not apply if independent tax counsel experienced in such matters delivers an opinion to us stating that, under then existing laws, there would be no adverse tax consequences to the holders of the convertible notes in the event this condition were not satisfied;
- such person assumes all our obligations under the convertible notes and the indenture; and
- we or such successor person shall not immediately thereafter be in default under the indenture.

Upon the assumption of our obligations by such a person in such circumstances, subject to certain exceptions, we shall be discharged from all obligations under the convertible notes and the indenture.

Although such transactions are permitted under the indenture, certain of the foregoing transactions could constitute a change in control permitting each holder to require us to purchase the convertible notes of such holder as described in "—Change in Control Permits Purchase of Convertible Notes by Us at the Option of the Holder."

EVENTS OF DEFAULT

The following will be events of default for the convertible notes:

- default in the payment of the principal amount, redemption price or change in control purchase price with respect to any convertible note when such amount becomes due and payable;
- default in the payment of accrued and unpaid interest, if any (including liquidated damages), on the convertible notes for 30 days;
- failure by us to comply with any of our other covenants in the convertible notes or the indenture upon receipt by us of notice of such default by the trustee or by holders of not less than 25% in aggregate principal amount of the convertible notes then outstanding and our failure to cure (or obtain a waiver of) such default within 60 days after receipt of such notice; or
- certain events of bankruptcy, insolvency or reorganization affecting us.

If an event of default shall have occurred and be continuing, either the trustee or the holders of not less than 25% in aggregate principal amount of convertible notes then outstanding may declare the principal amount of the convertible notes plus accrued and unpaid interest, if any, on the convertible notes accrued through the date of such declaration to be immediately due and payable. In the case of certain events of our bankruptcy, insolvency or reorganization, the principal amount of the convertible notes plus accrued and unpaid interest, if any, accrued thereon through the occurrence of such event shall automatically become and be immediately due and payable.

MODIFICATIONS OF THE INDENTURE

We and the trustee may enter into supplemental indentures that add, change or eliminate provisions of the indenture or modify the rights of the holders of the convertible notes with the consent

of the holders of at least a majority in principal amount of the convertible notes then outstanding. However, without the consent of each holder, no supplemental indenture may:

- reduce the rate or change the time of payment of interest (including any liquidated damages) on any convertible note;
- make any convertible note payable in money or securities other than that stated in the convertible note;
- change the stated maturity of any convertible note;
- reduce the principal amount, redemption price or change in control purchase price with respect to any convertible note;
- make any change that adversely affects the right of a holder to require us to purchase a convertible note;
- change the right to convert, or receive payment with respect to, a convertible note, or the right to institute suit for the enforcement of any payment with respect to, or conversion of, the convertible notes; or
- change the provisions in the indenture that relate to modifying or amending the indenture.

Without the consent of any holder of convertible notes, we and the trustee may enter into supplemental indentures for any of the following purposes:

- to evidence a successor to us and the assumption by that successor of our obligations under the indenture and the convertible notes;
- to add to our covenants for the benefit of the holders of the convertible notes or to surrender any right or power conferred upon us;
- to secure our obligations in respect of the convertible notes;
- to make any changes or modifications to the indenture necessary in connection with the registration of the convertible notes under the Securities Act and the qualification of the indenture under the Trust Indenture Act;

- to cure any ambiguity, defect, omission or inconsistency in the indenture in a manner that does not adversely affect the rights of any holder;
- to provide for uncertificated convertible notes; or
- to make any change that does not adversely affect the rights of any holder.

The holders of a majority in principal amount of the outstanding convertible notes may, on behalf of the holders of all convertible notes:

- waive compliance by us with restrictive provisions of the indenture, as detailed in the indenture; and
- waive any past default under the indenture and its consequences, except a default in the payment of the principal amount, accrued and unpaid interest, if any (including liquidated damages), redemption price or change in control purchase price or obligation to deliver common shares upon conversion with respect to any convertible note or in respect of any provision which under the indenture cannot be modified or amended without the consent of the holder of each outstanding convertible note affected.

NO PERSONAL LIABILITY OF DIRECTORS, OFFICERS, EMPLOYEES, INCORPORATORS AND SHAREHOLDERS

No director, officer, employee, incorporator or shareholder of ours, as such, shall have any liability for any of our obligations under the convertible notes or the indenture or for any claim based on, in respect of, or by reason of, such obligations or their creation. Each holder of convertible notes by accepting a convertible note waives and releases all such liability. The waiver and release are part of the consideration for issuance of the convertible notes. The waiver may not be effective to waive liabilities under the federal securities laws, and it is the view of the SEC that a waiver of such liabilities is against public policy.

SATISFACTION AND DISCHARGE

We may discharge our obligations under the indenture while notes remain outstanding if (1) all outstanding notes have or will become due and payable at their scheduled maturity within one year or (2) all outstanding notes are scheduled for redemption within one year, and in either case, we have deposited with the trustee an amount sufficient to pay and discharge all outstanding notes on the date of their scheduled maturity or the scheduled date of redemption.

UNCLAIMED MONEY; PRESCRIPTION

If money deposited with the trustee or paying agent for the payment of principal or interest or for redemption of the convertible notes remains unclaimed for two years or such shorter period under applicable state escheat laws, the trustee and paying agent shall notify us and shall pay the money back to us at our written request. Thereafter, holders of convertible notes entitled to the money must look to us for payment, subject to applicable law, and all liability of the trustee and the paying agent shall cease. Other than as described in this paragraph, the indenture does not provide for any prescription period for the payment of interest and principal on the convertible notes.

REPORTS TO TRUSTEE

We will regularly furnish to the trustee copies of our annual report to stockholders, containing audited financial statements, and any other financial reports which we furnish to our stockholders.

RULE 144A INFORMATION REQUIREMENTS

We agreed in the indenture to furnish to the holders or beneficial holders of the convertible notes and prospective purchasers of the convertible notes designated by the holders of the convertible notes, upon their request, the information required to be delivered pursuant to Rule 144A(d)(4) under the Securities Act at any time while the convertible notes or the common stock issuable upon conversion of the convertible notes are restricted securities within the meaning of the Securities Act, if we are not subject to the informational requirements of the Exchange Act.

TRUSTEE AND TRANSFER AGENT

The trustee for the convertible notes is Wells Fargo Bank Minnesota, N.A. The holders of a majority in principal amount of the then outstanding convertible notes will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, subject to certain exceptions. If an uncured event of default occurs, the trustee must exercise its rights and powers under the indenture using the same degree of care and skill as a prudent person would use under the circumstances in the conduct of his or her own affairs. The trustee may refuse to perform any duty or exercise any right or power unless it receives indemnity reasonably satisfactory to the trustee against any loss, liability or expense.

The transfer agent for our common stock is American Stock Transfer and Trust.

LISTING AND TRADING

The convertible notes trade on The PORTAL Market. Our common stock is listed on the Nasdaq National Market under the symbol "ISIS."

BOOK ENTRY, DELIVERY AND FORM

Notes resold under the registration statement of which this prospectus forms a part will be represented by one or more permanent global securities in definitive, fully registered form, which will be deposited with the trustee as custodian for DTC and registered in the name of DTC or a nominee of DTC in New York, New York for the accounts of participants in DTC. We initially issued the notes in the form of two global securities, bearing a legend relating to restrictions on transfer, which was deposited with the trustee as custodian for DTC and registered in the name of a nominee of DTC. Except as set forth below, the global securities may be transferred, in whole and not in part, only to DTC or another nominee of DTC. You may hold your beneficial interests in the global securities

directly through DTC if you have an account with DTC or indirectly through organizations that have accounts with DTC. Notes in definitive certificated form (referred to as certificated securities) will be issued only in certain limited circumstances described below.

DTC has advised us that it is:

- a limited purpose trust company organized under the laws of the State of New York;
- a member of the Federal Reserve System;
- a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and
- a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC was created to hold securities of institutions that have accounts with DTC (referred to as participants) and to facilitate the clearance and settlement of securities transactions among its participants in such securities through electronic book-entry changes in accounts of the participants, thereby eliminating the need for physical movement of securities certificates. DTC's participants include securities brokers and dealers, which may include the initial purchasers, banks, trust companies, clearing corporations and certain other organizations. Access to DTC's book-entry system is also available to others such as banks, brokers, dealers and trust companies (referred to as indirect participants) that clear through or maintain a custodial relationship with a participant, whether directly or indirectly.

Pursuant to procedures established by DTC, upon the deposit of the global securities with DTC, DTC credited, on its book-entry registration and transfer system, the principal amount of notes represented by such global securities to the accounts of participants. The accounts to be credited were designated by the initial purchasers. Ownership of beneficial interests in the global securities will be limited to participants or persons that may hold interests through participants. Ownership of beneficial interests in the global securities will be shown on, and the transfer of those beneficial interests will be effected only through, records maintained by DTC (with respect to participants' interests), the participants and the indirect participants. The laws of some jurisdictions may require that certain purchasers of securities take physical delivery of such securities in definitive form. These limits and laws may impair the ability to transfer or pledge beneficial interests in the global securities.

Owners of beneficial interests in global securities who desire to convert their interests into common stock should contact their brokers or other participants or indirect participants through whom they hold such beneficial interests to obtain information on procedures, including proper forms and cut-off times, for submitting requests for conversion.

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So long as DTC, or its nominee, is the registered owner or holder of a global security, DTC or its nominee, as the case may be, will be considered the sole owner or holder of the notes represented by the global security for all purposes under the indenture and the notes. In addition, no owner of a beneficial interest in a global security will be able to transfer that interest except in accordance with the applicable procedures of DTC. Except as set forth below, as an owner of a beneficial interest in the global security, you will not be entitled to have the notes represented by the global security registered in your name, will not receive or be entitled to receive physical delivery of certificated securities, except as described below, and will not be considered to be the owner or holder of any notes under the global securities. We understand that under existing industry practice, if an owner of a beneficial interest in the global securities desires to take any action that DTC, as the holder of the global securities, is entitled to take, DTC would authorize the participants to take such action, and the participants would authorize beneficial owners owning through such participants to take such action or would otherwise act upon the instructions of beneficial owners owning through them.

We will make payments of principal of, premium, if any, and interest (including any additional interest) on the notes represented by the global securities registered in the name of and held by DTC or its nominee to DTC or its nominee, as the case may be, as the registered owner and holder of the global securities. Neither the trustee, any paying agent nor we will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial interests in the global securities or for maintaining, supervising or reviewing any records relating to such beneficial interests.

We expect that DTC or its nominee, upon receipt of any payment of principal of, premium, if any, or interest (including liquidated damages) on the global securities, will credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the principal amount of the global securities, as shown on the records of DTC or its nominee. We also expect that payments by participants or indirect participants to owners of beneficial interests in the global securities held through such participants or indirect participants will be governed by standing instructions and customary practices and will be the responsibility of such participants or indirect participants. We will not have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial interests in the global securities for any note or for maintaining, supervising or reviewing any records relating to such beneficial interests or for any other aspect of the relationship between DTC and its participants or indirect participants or the relationship between such participants or indirect participants and the owners of beneficial interests in the global securities owning through such participants.

Transfers between participants in DTC will be effected in the ordinary way in accordance with DTC rules and will be settled in same-day funds.

DTC has advised us that it will take any action permitted to be taken by a holder of notes only at the direction of one or more participants to whose account DTC's interests in the global securities is credited and only in respect of that portion of the aggregate principal amount of notes as to which the participant or participants have given such direction. However, if DTC notifies us that it is unwilling to be a depository for the global securities or ceases to be a clearing agency or there is a continuing event of default under the notes, DTC will exchange the global securities for certificated securities which it will distribute to its participants and which will be appropriately legended, if required.

Although DTC is expected to follow the foregoing procedures in order to facilitate transfers of interests in the global securities among participants of DTC, it is under no obligation to perform or continue to perform these procedures, and these procedures may be discontinued at any time. Neither the trustee nor we will have any responsibility or liability for the performance by DTC or the participants or indirect participants of their respective obligations under the rules and procedures governing their respective operations.

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PAYMENTS OF PRINCIPAL AND INTEREST

The indenture requires that payments in respect of the notes held of record by DTC or its nominee (including notes evidenced by the global securities) be made in same day funds. Payments in respect of the notes held of record by holders other than DTC may, at our option, be made by check and mailed to such holders of record as shown on the register for the notes.

REGISTRATION RIGHTS; LIQUIDATED DAMAGES

We and the initial purchasers of the notes entered into a registration rights agreement dated May 1, 2002. Under the registration rights agreement, we agreed with the initial purchasers of the notes to file a shelf registration statement, of which this prospectus is a part, covering the resales of the notes and the common stock issuable upon the conversion of the notes in accordance with Rule 415 under the Securities Act.

We will use our commercially reasonable best efforts to cause a shelf registration statement to be declared effective and, subject to certain rights to suspend use of the shelf registration statement, to keep it effective until the earliest of (i) the date on which the notes or underlying shares of common stock have been effectively registered under the Securities Act and disposed of, whether or not in accordance with the shelf registration statement, and (ii) the date which is two years after the later of the date of original issue of the notes and the last date that we or any of our affiliates was the owner of such notes (or any predecessor thereto) or such shorter period of time as permitted by Rule 144(k) under the Securities Act or any successor provision thereunder. There can be no assurance that we will be able to maintain an effective and current registration statement as required. The absence of such a registration statement may limit a holder's ability to sell the securities offered hereby or adversely affect the price at which the securities can be sold.

We have agreed to pay predetermined liquidated damages as described herein to holders of the notes and the holders of common stock issued upon conversion of the notes if the shelf registration statement is not filed with the SEC by July 30, 2002 (90 days from the date the notes were originally issued), the shelf registration statement is not declared effective by October 28, 2002 (180 days from the date on which the notes were originally issued) or the shelf registration statement ceases to be effective (without being succeeded immediately by an additional registration statement filed and declared effective) or usable for the sale of the notes or the common stock underlying the notes for a period of time (including any period of time where we suspend use of the shelf registration statement) which shall exceed 30 days in the aggregate in any 3-month period or 60 days in the aggregate in any 12-month period. The liquidated damages shall accrue at a rate of 0.25% per year per \$1,000 principal amount of the notes and, if applicable, on an equivalent basis per share of common stock (valued on the basis of the conversion price then in effect and subject to adjustment in the event of stock splits, stock recombinations, stock dividends and the like) for each 90-day period until the shelf registration statement is declared effective or again becomes effective or usable, as the case may be, up to a maximum amount of liquidated damages of 0.75% per year per \$1,000 principal amount of the notes and, if applicable, on an equivalent basis per share of common stock (subject to adjustment as set forth above).

The foregoing summary does not purport to be complete and is subject to, and is qualified in its entirety by references to, the provisions of the registration rights agreement. A copy of the registration rights agreement has been filed as an exhibit to the registration statement of which this prospectus is a part.

GOVERNING LAW

The indenture and the convertible notes are governed by and construed in accordance with the laws of the State of New York, without giving effect to such state's conflicts of laws principles.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of

- Series A Convertible Exchangeable 5% Preferred Stock, 120,150 shares of which were authorized, issued and outstanding at June 30, 2002;
- Series B Convertible Exchangeable 5% Preferred Stock, 16,620 shares of which were authorized and 12,015 shares of which were issued and outstanding at June 30, 2002;
- Series C Junior Participating Preferred Stock, 1,000,000 shares of which were authorized and none of which was issued and outstanding at June 30, 2002; and
- common stock, 100,000,000 shares of which are authorized and 54,191,776 shares of which were outstanding as of June 30, 2002.

The description of our common stock is incorporated by reference to filings with the SEC. See "Incorporation by Reference."

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain any future earnings to support operations and to finance the growth and development of our business and we do not anticipate paying cash dividends for the foreseeable future.

CERTAIN UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

The following discusses the material U.S. federal income tax consequences to holders of the notes or our common stock into which the notes may be converted. This discussion is for general information only and does not address all aspects of U.S. federal income taxation that may be relevant to you in light of your personal circumstances. This summary is based on the provisions of the Internal Revenue Code of 1986, as amended, applicable existing and proposed U.S. Treasury regulations, and judicial authority and current administrative rulings and practice, all of which are subject to change, possibly on a retroactive basis, or to differing interpretation. Except as otherwise noted, this summary applies only to holders, as defined below, that hold the notes and our common stock into which

the notes may be converted as capital assets within the meaning of Section 1221 of the Internal Revenue Code (generally, for investment). It does not address tax consequences applicable to those U.S. holders that may be subject to special tax rules, such as:

- financial institutions;
- regulated investment companies;
- tax-exempt organizations;
- expatriates;
- persons subject to the alternative minimum tax provisions of the Internal Revenue Code;
- pension funds;
- insurance companies;
- dealers in securities or foreign currencies;
- persons that will hold notes as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction for tax purposes;
- persons deemed to sell notes or common stock under the constructive sale provisions of the Internal Revenue Code;

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- persons who hold notes through a partnership or other pass through entity; or
 - persons that have a primary form of currency other than the U.S. dollar (except as disclosed below under "—Non-U.S. Holders").

We have not sought any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with our statements and conclusions. Moreover, this discussion does not address the effect of any applicable state, local or foreign tax laws. INVESTORS CONSIDERING THE PURCHASE OF NOTES SHOULD CONSULT THEIR OWN TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME, GIFT AND ESTATE TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES ARISING UNDER THE LAWS OF ANY STATE, LOCAL OR FOREIGN TAXING JURISDICTION OR UNDER ANY APPLICABLE TAX TREATY.

For purposes of this discussion, the term U.S. holder means a beneficial owner of a note or common stock that is for U.S. federal income tax purposes, (i) a citizen or resident of the United States, (ii) a corporation created or organized in or under the laws of the United States, (iii) an estate, the income of which is subject to U.S. federal income taxation regardless of its source, or (iv) a trust if (a) its administration is subject to the primary supervision of a court within the United States and one or more U.S. persons have authority to control all of its substantial decisions, or (b) it was in existence on August 20, 1996, and has elected to continue to be treated as a U.S. trust. For U.S. federal income tax purposes, income earned through a foreign or domestic partnership or similar entity is generally attributed to its owners. A non-U.S. holder means a holder of a note or common stock that is not a U.S. holder for U.S. federal income tax purposes.

U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences resulting from the ownership and disposition of the notes and common stock by U.S. holders.

Payment of interest

Stated interest

Any interest we pay on a note generally will be includable in the income of a U.S. holder as ordinary income at the time the interest is received or accrued, in accordance with each U.S. holder's method of accounting for U.S. federal income tax purposes.

Make whole payments

If we call the notes for provisional redemption, holders would be entitled to a "make whole" payment in excess of stated principal and interest, either upon the redemption or upon a conversion of the notes after they are called for redemption but before they are actually redeemed. We intend to treat the possibility that we will pay such make whole payments as subject to a remote and incidental contingency, within the meaning of applicable Treasury Regulations and, therefore, we believe that any make whole payments will not affect the yield to maturity on the notes and thus will be taxable to U.S. holders at the time make whole payments accrue or are received in accordance with each such holder's method of accounting. However, because of the lack of authority on point, the tax consequences of these additional payments are uncertain. In general, a redemption premium payment paid in cash on a note called for provisional redemption would likely be treated as capital gain in accordance with the rules described in the following paragraph. However, since any make whole payment would be calculated by reference to foregone interest, a U.S. holder could be required to recognize interest income on the receipt of such payment. Our determination that there is a remote likelihood of paying

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make whole payments upon provisional redemption of the notes is binding on each U.S. holder unless the holder explicitly discloses in the manner required by applicable Treasury Regulations that its determination is different from ours. Our determination is not, however, binding on the IRS.

Sale, exchange or redemption of the notes

Except as set forth below under "—U.S. Holders—Conversion of the notes" and "—U.S. Holders—Market discount," upon the sale, exchange or redemption of a note (including the repurchase of a note for cash pursuant to the exercise of a repurchase right in the event of a change in control), a U.S. holder generally will recognize capital gain or loss equal to the difference between the amount realized on the sale, exchange or redemption and the U.S. holder's adjusted tax basis in that note. For these purposes, the amount realized on the sale, exchange or redemption of a note does not include any amount attributable to accrued but unpaid interest, which will be taxable as such unless previously taken into account. A U.S. holder's adjusted tax basis in a note generally will be the U.S. dollar value of the purchase price of that note on the date of purchase increased by any market discount previously included in income by the holder and reduced by any amortized premium. Gain or loss so recognized will generally be capital gain or loss and will be long-term capital gain or loss if, at the time of the sale, exchange or redemption, the note was held for more than one year. In general, the maximum federal tax rate for noncorporate taxpayers on long-term capital gain is 20% with respect to capital assets including the notes and common stock (18% if such capital assets are held for more than five years). Capital gain on assets having a holding period of one year or less at the time of their disposition is taxed as short-term capital gain at a current maximum federal rate of 38.6% in the hands of noncorporate taxpayers. For individual taxpayers, the deductibility of capital losses is subject to limitations. For corporate taxpayers, both capital gains and ordinary income are subject to a maximum regular federal tax rate of 35%.

Constructive dividends on the notes

The conversion price of the notes may adjust under certain circumstances. Section 305 of the Internal Revenue Code treats as a distribution taxable as a dividend (to the extent of our current or accumulated earnings and profits) certain actual or constructive distributions of stock with respect to stock or convertible securities. Under applicable Treasury Regulations, an adjustment of conversion price may, under certain circumstances, be treated as a constructive dividend to the extent it increases the proportional interest of a U.S. holder of a note in our fully diluted common stock, whether or not the holder ever converts the note into our common stock. Generally, a holder's tax basis in a note will be increased by the amount of any constructive dividend. Similarly, a failure to adjust the conversion price of the notes to reflect a stock dividend or similar event could in some circumstances give rise to constructive dividend income to U.S. holders of common stock.

Conversion of the notes

A U.S. holder generally will not recognize any income, gain or loss upon conversion of a note into our common stock, other than with respect to cash received in lieu of a fractional share of common stock, except to the extent that the common stock issued upon conversion is treated as attributable to accrued interest on the note (which will be treated as interest for federal income tax purposes) and except with respect to market discount, as described below under "—U.S. Holders—Market discount." A U.S. holder's tax basis in the common stock received on conversion or repurchase of a note will be the same as that U.S. holder's adjusted tax basis in the note at the time of conversion or repurchase reduced by any basis allocable to a fractional share. The holding period for the common stock received on conversion or repurchase will generally include the holding period of the note converted or repurchased. However, a holder's tax basis in shares of common stock attributable to accrued interest

generally will equal the amount of accrued interest included in income and the holding period will begin on the day following the date of conversion or repurchase.

You should treat cash received in lieu of a fractional share of common stock upon conversion or repurchase as a payment in exchange for a fractional share of common stock. The receipt of cash in lieu of a fractional share of common stock generally will result in capital gain or loss (measured by the difference between the cash you received for the fractional share and your adjusted tax basis in the fractional share). The fair market value of the shares of common stock received which is attributable to accrued interest will be taxable as ordinary income.

Dividends on common stock

If we make distributions on our common stock, those distributions will generally be treated as a dividend, subject to tax as ordinary income, to the extent of our current or accumulated earnings and profits as of the year of distribution, then as a tax-free return of capital to the extent of the U.S. holder's adjusted tax basis in the common stock and thereafter as gain from the sale or exchange of that stock.

In general, a dividend distribution to a corporate U.S. holder may qualify for the 70% dividends received deduction if the U.S. holder owns less than 20% of the voting power and value of our stock (other than any non-voting, non-convertible, non-participating preferred stock). A corporate U.S. holder that owns 20% or more of the voting power and value of our stock (other than any non-voting, non-convertible, non-participating preferred stock) generally will qualify for an 80% dividends received deduction.

Sale of common stock

Upon the sale or exchange of our common stock, a U.S. holder generally will recognize capital gain or loss equal to the difference between (i) the amount of cash and the fair market value of any property received upon the sale or exchange and (ii) the U.S. holder's adjusted tax basis in the common stock. That capital gain or loss will be long-term if the U.S. holder's holding period is more than one year and will be short-term if the holding period is equal to or less than one year. In the case of certain noncorporate taxpayers, including individuals, long-term capital gains are taxed at a maximum federal rate of 20% (18% if such capital assets are held for more than five years), and short-term capital gains are taxed at a current maximum federal rate of 38.6%. A U.S. holder's basis and holding period in our common stock received upon conversion of a note are determined as discussed above under "—U.S. Holders—Conversion of the notes." Corporate taxpayers are subject to a maximum regular federal tax rate of 35% on all capital gains and ordinary income.

Market discount

The resale of notes may be affected by the impact on a purchaser of the market discount provisions of the Internal Revenue Code. For this purpose, the market discount on a note generally will equal the amount, if any, by which the stated redemption price at maturity of the note immediately after its acquisition

exceeds the U.S. holder's adjusted tax basis in the note. Subject to a limited exception, these provisions generally require a U.S. holder who acquires a note at a market discount to treat as ordinary income any gain recognized on the disposition of that note to the extent of the accrued market discount on that note at the time of maturity or disposition, unless the U.S. holder elects to include accrued market discount in income over the life of the note.

This election to include market discount in income over the life of the note, once made, applies to all market discount obligations acquired on or after the first taxable year to which the election applies and may not be revoked without the consent of the IRS. In general, market discount will be treated as accruing on a straight-line basis over the remaining term of the note at the time of acquisition, or, at

the election of the U.S. holder, under a constant yield method. If an election is made, it will apply only to the note with respect to which it is made, and may not be revoked. A U.S. holder who acquires a note at a market discount and who does not elect to include accrued market discount in income over the life of the note may be required to defer the deduction of a portion of the interest on any indebtedness incurred or maintained to purchase or carry the note until maturity or until the note is disposed of in a taxable transaction. If a U.S. holder acquires a note with market discount and receives common stock upon conversion of the note, the amount of accrued market discount not previously included in income with respect to the converted note through the date of conversion will be treated as ordinary income when the holder disposes of the common stock.

Amortizable premium

A U.S. holder who purchases a note at a premium over its stated principal amount, plus accrued interest, generally may elect to amortize that premium (referred to as Section 171 premium) from the purchase date to the note's maturity date under a constant-yield method that reflects semiannual compounding based on the note's payment period. Amortizable premium, however, will not include any premium attributable to a note's conversion feature. The premium attributable to the conversion feature is the excess, if any, of the note's purchase price over what the note's fair market value would be if there were no conversion feature. Amortized Section 171 premium is treated as an offset to interest income on a note and not as a separate deduction. The election to amortize premium on a constant yield method, once made, applies to all debt obligations held or subsequently acquired by the electing U.S. holder on or after the first day of the first taxable year to which the election applies and may not be revoked without the consent of the IRS.

Backup withholding and information reporting

A U.S. holder of notes or common stock may be subject to backup withholding at a rate of 30% with respect to certain reportable payments, including interest payments, dividend payments and, under certain circumstances, principal payments on the notes. These backup withholding rules apply if the U.S. holder, among other things, (i) fails to furnish a social security number or other taxpayer identification number certified under penalties of perjury within a reasonable time after the request therefor, (ii) furnishes an incorrect taxpayer identification number, (iii) fails to report properly interest or dividends or (iv) under certain circumstances, fails to provide a certified statement, signed under penalties of perjury, that the taxpayer identification number furnished is the correct number and that the U.S. holder is not subject to backup withholding. A U.S. holder who does not provide us with its correct taxpayer identification number may also be subject to penalties imposed by the IRS. Any amount withheld from a payment to a holder under the backup withholding rules is creditable against the holder's federal income tax liability. Backup withholding will not apply, however, with respect to payments made to certain U.S. holders, including corporations and tax-exempt organizations, provided their exemption from backup withholding is properly established. We will report to U.S. holders of notes and common stock and to the IRS the amount of any reportable payments for each calendar year and the amount of tax withheld, if any, with respect to those payments.

NON-U.S. HOLDERS

The following discussion is a summary of the principal U.S. federal income and estate tax consequences resulting from the ownership of the notes or our common stock by non-U.S. holders.

Payment of interest

Generally, interest income of a non-U.S. holder that is not effectively connected with a U.S. trade or business will be subject to a withholding tax at a 30% rate (or lower rate specified by an applicable income tax treaty). However, interest income earned on the notes by a non-U.S. holder may qualify for

an exemption, referred to as the portfolio interest exemption, and as a result should not be subject to U.S. federal income tax or withholding (subject to the discussion below of backup withholding). Interest we pay on the notes to a non-U.S. holder generally should qualify for the portfolio interest exemption if:

- (1) the interest is not effectively connected with the conduct of a trade or business within the United States by the non-U.S. holder;
- (2) the non-U.S. holder does not actually or constructively own 10% or more of the total voting power of all classes of our stock entitled to vote;
- (3) the non-U.S. holder is not a controlled foreign corporation that is related to us through stock ownership (for this purpose, the holder of notes would be deemed to own constructively the common stock into which it could be converted);
- (4) the non-U.S. holder, under penalty or perjury, certifies to us or our agent that it is not a U.S. person and provides its name and address (or otherwise satisfies the applicable identification requirements); and
- (5) the non-U.S. holder is not a bank receiving interest pursuant to a loan agreement entered into in the ordinary course of its trade or business.

If a non-U.S. holder satisfies certain requirements, the certification described above may be provided by a securities clearing organization, a bank, or other financial institution that holds customers' securities in the ordinary course of its trade or business.

Recently revised Treasury regulations have modified the certification and identification requirements. These regulations now require foreign partnerships and certain foreign trusts to provide additional documentation which (i) certifies that the individual partners, beneficiaries, or owners of the partnership or trust are not U.S. holders, and (ii) provides the individual partners', beneficiaries' or owners' names and addresses.

A non-U.S. holder that is not exempt from tax under these rules will be subject to U.S. federal income tax withholding at a rate of 30% on payments of interest, unless the interest is effectively connected with the conduct of a U.S. trade or business of the holder or a lower treaty rate applies and, in either case, the non-U.S. holder provides us with proper certification as to the holder's exemption from withholding. If the interest is effectively connected to the conduct of a U.S. trade or business, it will be subject to the U.S. federal income tax on net income that applies to U.S. persons generally (and, with respect to corporate holders and under certain circumstances, the branch profits tax, which is generally imposed at a 30% rate). Non-U.S. holders should consult applicable income tax treaties, which may provide different rules. Even though effectively connected interest is subject to income tax, and may be subject to the branch profits tax, it is not subject to withholding tax if the holder delivers a properly executed IRS Form W-8ECI to us or to our agent. It is not clear whether the above discussion would be applicable to make whole payments, if any, received by non-U.S. holders.

Conversion of the notes

A non-U.S. holder generally will not be subject to U.S. federal income tax on the conversion of a note into shares of our common stock. To the extent a non-U.S. holder receives cash in lieu of a fractional share of common stock on conversion, that cash may give rise to gain that would be subject to the rules described below with respect to the sale or exchange of a note or common stock.

Constructive dividends on notes

The conversion price of the notes may adjust in certain circumstances. An adjustment could potentially give rise to a deemed distribution to non-U.S. holders of the notes. See "—U.S. Holders—

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Constructive dividends on the notes" above. In that case, the deemed distribution would be subject to the rules below regarding withholding of U.S. federal tax on dividends in respect of common stock. See "—Non-U.S. Holders—Dividends" below.

Dividends

Subject to the discussion below of backup withholding, dividends, if any, paid on our common stock to a non-U.S. holder generally will be subject to a 30% U.S. federal withholding tax, subject to reduction for non-U.S. holders eligible for the benefits of certain income tax treaties. Dividends for this purpose may include stock distributions treated as deemed dividends as discussed in "—U.S. Holders—Constructive dividends on the notes" above. Under recently revised Treasury regulations holders will be required to satisfy certain certification requirements to claim treaty benefits.

Except to the extent otherwise provided under an applicable tax treaty, a non-U.S. holder generally will be taxed in the same manner as a U.S. holder on dividends paid (or deemed paid) that are effectively connected with the conduct of a trade or business in the United States by the non-U.S. holder (and, if required by a tax treaty, are attributable to a permanent establishment maintained in the United States).

If that non-U.S. holder is a foreign corporation, it may also be subject to a U.S. branch profits tax on that effectively connected income at a 30% rate or a lower rate as may be specified by an applicable income tax treaty.

Gain on disposition of the notes and common stock

A non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on gain realized on the sale, exchange or redemption of a note, or the sale or exchange of common stock, unless:

- (i) in the case of an individual non-U.S. holder, that holder is present in the United States for 183 days or more in the year of the sale, exchange or redemption and certain other requirements are met; or
- (ii) the gain is effectively connected with the conduct of a U.S. trade or business of the non-U.S. holder.

However, if we were to become a U.S. real property holding corporation, or USRPHC, a non-U.S. holder could be subject to federal income tax withholding with respect to gain realized on the disposition of notes or shares of common stock. In that case, any withholding tax withheld pursuant to the rules applicable to dispositions of U.S. real property interests would be creditable against that non-U.S. holder's U.S. federal income tax liability and could entitle that non-U.S. holder to a refund upon furnishing required information to the IRS. We do not believe that we are a USRPHC or will become a USRPHC in the future.

If we call the notes for provisional redemption, non-U.S. holders could also be subject to U.S. federal income tax and withholding on any make whole payments received either upon redemption or upon conversion of the notes after they are called for redemption but before they are actually redeemed. If these payments were later determined not to be subject to U.S. federal income tax, a non-U.S. holder would be entitled to a refund of the tax withheld.

U.S. federal estate tax

A note held by an individual who at the time of death is not a citizen or resident of the United States, as specially defined for U.S. federal estate tax purposes, will not be subject to U.S. federal estate tax if the individual did not actually or constructively own 10% or more of the total combined

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voting power of all classes of our stock and, at the time of the individual's death, payments with respect to that note would not have been effectively connected with the conduct by that individual of a trade or business in the United States. Common stock held by an individual who at the time of death is not a citizen or

resident of the United States, as specially defined for U.S. federal estate tax purposes, will be included in that individual's estate for U.S. federal estate tax purposes, and the applicable rate of tax may be reduced or eliminated if an estate tax treaty otherwise applies. Estates of non-resident aliens are generally allowed a statutory credit which has the effect of offsetting the U. S. federal estate tax imposed on the first \$60,000 of the taxable estate.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the amount of any interest or dividends paid to that non-U.S. holder, and tax withheld, if any, with respect to those payments. Copies of these information returns may also be made available under the provisions of a specific treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is incorporated.

U.S. backup withholding and information reporting will not apply to payments of interest or principal on the notes by us or our agent to a non-U.S. holder if the non-U.S. holder satisfies the certification or identification requirements described in "—Non-U.S. Holders—Payment of interest," above, unless the payor knows or has reason to know that the holder is not entitled to an exemption from information reporting or backup withholding tax. The payment of the proceeds on the disposition of notes or shares of common stock to or through the U.S. office of a U.S. or foreign broker will be subject to information reporting and backup withholding unless the owner provides the certification described above or otherwise establishes an exemption. The proceeds of the disposition by a non-U.S. holder of notes or shares of common stock effected outside the United States to or through a foreign office of a broker generally will not be subject to backup withholding or information reporting. However, if the broker is a U.S. person or has certain connections to the United States, information reporting requirements, but not backup withholding, will apply unless the broker has documentary evidence in its files of the holder's non-U.S. status and has no actual knowledge (or reason to know) to the contrary or unless the holder otherwise establishes an exemption.

THE COMPANY

Deductibility of interest

Generally, under Section 279 of the Internal Revenue Code, an interest deduction in excess of \$5.0 million is not permitted with respect to certain corporate acquisition indebtedness. Corporate acquisition indebtedness includes any indebtedness that is:

- issued to provide consideration for the direct or indirect acquisition of stock or assets of another corporation;
- subordinated;
- convertible directly or indirectly into the stock of the issuing corporation; and
- issued by a corporation that has a debt to equity ratio that exceeds 2 to 1.

Our ability to deduct all of the interest payable on the notes will depend on the application of the foregoing tests to us. The availability of an interest deduction with respect to the notes was not determinative in our issuance of the notes in the initial private placement of the notes.

Under Section 163(l) of the Internal Revenue Code, no deduction is permitted for interest paid or accrued on any indebtedness of a corporation that is payable in equity of the issuer or a related party. Debt is treated as debt payable in equity of the issuer if the debt is part of an arrangement designed to result in payment of the instrument with or by reference to the equity. These arrangements could

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include debt instruments that are convertible at the holder's option if it is substantially certain that the option will be exercised. The legislative history indicates that it is not expected the provision will affect debt with a conversion feature where the conversion price is significantly higher than the market price of the stock on the date of the debt issuance. Accordingly, we do not believe that our interest deduction with respect to interest payments on the notes will be adversely affected by these rules.

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LEGAL MATTERS

The validity of the issuance of the notes and the common stock issuable upon conversion of the notes offered hereby will be passed upon for us by Grantland E. Bryce, our Vice President, Legal and General Counsel.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2001, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given upon their authority as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are a public company and file proxy statements and

annual, quarterly and special reports and other information with the SEC. You can inspect and copy the registration statement as well as the reports, proxy statements and other information we have filed with the SEC at the public reference room maintained by the SEC at 450 Fifth Street, N.W., Washington, D.C. 20549, and at the SEC Regional Offices located at 175 West Jackson Blvd., Ste. 900, Chicago, Illinois 60604 and 233 Broadway, New York, New York 10279. You can call the SEC at 1-800-732-0330 for further information about the public reference rooms. We are also required to file electronic versions of these documents with the SEC, which may be accessed from the SEC's World Wide Web site at <http://www.sec.gov>.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" certain of our publicly-filed documents into this prospectus, which means that information included in those documents is considered part of this prospectus. Information that we file with the SEC after the effective date of the registration statement of which this prospectus is a part will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until the offering is completed.

The following documents filed with the SEC are incorporated by reference in this prospectus:

- our Annual Report on Form 10-K for the year ended December 31, 2001;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2002;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2002;
- our Current Report on Form 8-K, filed with the SEC on January 4, 2002;
- our Current Report on Form 8-K, filed with the SEC on January 7, 2002;
- our Current Report on Form 8-K, filed with the SEC on April 23, 2002;
- our Current Report on Form 8-K, filed with the SEC on April 24, 2002;
- our Current Report on Form 8-K, filed with the SEC on April 24, 2002; and
- the description of our common stock in our Registration Statement on Form 8-A filed with the SEC on April 12, 1991, as updated by our Certificate of Amendment of our Restated Certificate of Incorporation filed with our Quarterly Report on Form 10-Q for the period ended June 30, 2001.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, other than exhibits to those documents. You should direct any requests for documents to Vice President of Finance at our principal executive offices at 2292 Faraday Avenue, Carlsbad, California 92008, telephone number (760) 931-9200.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus shall be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus or in any subsequently filed document that also is or is deemed to be incorporated by reference in this prospectus modifies, supersedes or replaces such statement. Any statement so modified, superseded or replaced, shall not be deemed, except as so modified, superseded or replaced, to constitute a part of this prospectus.

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