BIOMARIN PHARMACEUTICAL INC
Form 424B5
March 24, 2006
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Filed Pursuant to Rule 424(b)(5).

A filing fee of $18,457.50, calculated in accordance with

Rule 457(r), has been transmitted to the SEC in connection

with the securities offered from the registration statement

(File No. 333-132566) by means of this prospectus supplement.

PROSPECTUS SUPPLEMENT

(To Prospectus dated March 20, 2006)

$150,000,000

2.50% Senior Subordinated Convertible Notes due 2013

The Offering:

The notes will bear interest at the rate of 2.50% per year on the principal amount of the notes, payable in cash semiannually in arrears on September 29 and March 29 of each year, beginning September 29, 2006. The notes will mature on March 29, 2013. The notes will be our unsecured senior subordinated obligations and will rank junior in right of payment to our existing and future senior debt, equal in right of payment with our existing and future senior subordinated debt, and senior in right of payment to our existing and future subordinated debt. In addition, the notes will effectively rank junior in right of payment to all of our existing and future secured debt, to the extent of the value of the assets securing such debt, and to the debt and all other liabilities of our subsidiaries.

Convertibility of the Notes:

Holders may convert, at any time prior to maturity, any outstanding notes into shares of our common stock. The notes are convertible at a conversion rate of 60.3318 shares per $1,000 principal amount of notes, which is equal to a conversion price of approximately $16.58 per share, subject to adjustment. If a holder elects to convert notes in connection with a fundamental change, such holder may also be entitled to receive a make-whole premium upon conversion in certain circumstances. Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN . On March 23, 2006, the last sale price for our common stock as reported on the Nasdaq

National Market was $13.13 per share.

Purchase of the Notes at the Option of the Holder:

Upon a fundamental change of our company, each holder may require us to purchase all or a portion of such holder s notes at a price equal to the principal and accrued and unpaid interest, if any.

We are concurrently offering 9,000,000 shares, or 10,350,000 shares if the underwriters exercise their overallotment option in full, of our common stock pursuant to a separate prospectus supplement.

Investing in our notes involves risks, including those described in the Risk Factors section beginning on page S-8 of this prospectus supplement.

	Per Note	Total
Public offering price	$1,000	$150,000,000
Underwriting discount	$30	$4,500,000
Proceeds, before expenses, to us	$970	$145,500,000

We have granted the underwriter a 13-day option to purchase up to an additional $22,500,000 principal amount of notes to cover overallotments, if any.

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

The notes will be ready for delivery in book entry form only through the facilities of the Depositary Trust Company on or about March 29, 2006.

Merrill Lynch & Co.

The date of this prospectus supplement is March 23, 2006.

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Prospectus Supplement

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference therein. We have not, and the underwriter has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriter is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date on those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, when making your investment decision. You should also read and consider the information in the documents we have referred you to in the sections of the prospectus entitled Where You Can Find More Information and Information Incorporated by Reference.

General information about us can be found on our website at http://www.BMRN.com . The information on our website is for information only and should not be relied on for investment purposes. The information on our website is not incorporated by reference into either this prospectus supplement or the accompanying prospectus and should not be considered part of this or any other report filed with the Securities and Exchange Commission.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission (SEC), utilizing a shelf registration process. This prospectus supplement provides you with the specific details regarding this offering, including the principal amount, conversion ratio and ranking of our notes, and the risks of investing in our notes. The accompanying prospectus provides you with more general information, some of which does not apply to the offering of our notes. To the extent information in this prospectus supplement is inconsistent with the accompanying prospectus or any of the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, you should rely on this prospectus supplement. You should read and consider the information in both this prospectus supplement and the accompanying prospectus together with the additional information described under the headings Where You Can Find More Information and Information Incorporated by Reference .

This prospectus supplement and the accompanying prospectus have not been approved by the Financial Services Authority. The notes may not be offered or sold to any person in the United Kingdom except where the offer is exempt from the general prohibition against the offer of securities to the public under section 85 of the Financial Services and Markets Act 2000 (FMSA) by virtue of one or more of the criteria set out in section 86 of FMSA.

This prospectus supplement and the accompanying prospectus is directed only at (i) persons outside the United Kingdom, (ii) persons who have professional experience in matters relating to investments and who are investment professionals within the meaning of Article 19(5) of FMSA (Financial Promotion) Order 2005 of the United Kingdom (the Financial Promotion Order), (iii) persons who fall within Article 49(2)(a) through (d) (high net worth companies, unincorporated associations, etc.) of the Financial Promotion Order, or (iv) any other persons to whom this prospectus supplement and the accompanying prospectus for the purposes of Section 21 of FSMA can otherwise lawfully be made (all such persons together being referred to as Relevant Persons), and must not be acted on or relied upon by persons other than Relevant Persons.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this prospectus, the prospectus supplement or any document incorporated by reference in this prospectus or any prospectus supplement regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management are forward-looking statements.

Forward-looking statements include, but are not limited to, statements about:

- our expectations with respect to regulatory submissions and approvals and our clinical trials;
- our expectations with respect to our collaborations with Serono S.A. (Serono) and Genzyme Corporation (Genzyme); and
- our estimates regarding our capital requirements and our need for additional financing.

The words anticipates , believes , estimates , expects , intends , may , plans , projects , will , would and similar expressions are inte forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. We have identified some of the important factors that could cause future events to materially differ from our current expectations and they are described in this prospectus supplement under the caption Risk Factors as well as in our most recent Annual Report on Form 10-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statement.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement. This summary does not contain all the information that you should consider before investing in our notes. You should read the entire prospectus supplement and the accompanying prospectus carefully, including Risk Factors , the financial statements and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before making an investment decision. This prospectus supplement contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from the results anticipated in these forward-looking statements as a result of factors described under the Risk Factors section and elsewhere in this prospectus supplement. Unless the context otherwise requires, any reference to BioMarin, we, our and us in this prospectus supplement refers to BioMarin Pharmaceutical Inc., and its subsidiaries.

BioMarin Pharmaceutical Inc.

Overview

We develop and commercialize innovative biopharmaceuticals for serious diseases and medical conditions. We select product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market. Our product portfolio is comprised of two approved products and multiple investigational product candidates. Approved products include Aldurazyme® (laronidase) and Naglazyme (galsulfase). Additionally, we have rights to receive payments and royalties related to Orapred® (see Recent Developments Orapred License Agreement).

Marketed Products

Aldurazyme

Aldurazyme has been approved for marketing in the United States (U.S.) by the U.S. Food and Drug Administration (FDA), in the European Union (E.U.) by the European Commission (EC) and in other countries for the treatment of mucopolysaccharidosis I (MPS I), for which no other drug treatment currently exists. MPS I is a progressive and debilitating life-threatening genetic disease, which frequently results in death during childhood or early adulthood. It is caused by the deficiency of alpha-L-iduronidase, an enzyme normally required for the breakdown of certain complex carbohydrates known as glycosaminoglycans (GAGs). Aldurazyme has been granted orphan drug exclusivity in the U.S. and the E.U., which gives Aldurazyme seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS I, expiring in 2010 and 2013, respectively. We developed Aldurazyme through a 50/50 joint venture with Genzyme. Aldurazyme net revenue recorded by our joint venture for 2005 totaled $76.4 million, compared to $42.6 million for 2004.

Naglazyme

In May 2005, the FDA granted marketing approval for Naglazyme for the treatment of mucopolysaccharidosis VI (MPS VI), a debilitating life-threatening genetic disease for which no other drug treatment currently exists. MPS VI is caused by the deficiency of N-acetylgalactosamine 4-sulfatase (arylsulfatase B), an enzyme normally required for the breakdown of GAGs. Naglazyme net product sales recorded for 2005 totaled $6.1 million. In January 2006, the EC granted marketing approval for Naglazyme in the E.U. Naglazyme has been granted orphan drug exclusivity in the U.S. and the E.U., which gives Naglazyme seven years of market exclusivity in the U.S. and 10 years of market exclusivity in the E.U. for the treatment of MPS VI, expiring in 2012 and 2016, respectively. Product launch in the E.U. is underway on a country-by-country basis.

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Products in Development

We are developing several investigational product candidates for the treatment of genetic diseases including: Phenoptin (sapropterin dihydrochloride), a proprietary oral form of tetrahydrobiopterin (6R-BH_4, also commonly referred to as BH_4), for the treatment of phenylketonuria (PKU); and Phenylase (phenylalanine ammonia lyase), an enzyme substitution therapy for the treatment of phenylketonurics who are not 6R-BH_4-responsive.

Phenoptin

In December 2004, we announced that we initiated our Phase 2 clinical trial of Phenoptin for PKU. Patients enrolled in the Phase 2 clinical trial who met certain criteria were eligible to enroll in the Phase 3 clinical trial, which began in April 2005. The Phase 3 clinical trial of Phenoptin was a six-week, multi-center, international, double-blind, placebo-controlled study. On March 15, 2006, we announced positive results from the Phase 3 clinical trial (see Recent Developments Phase 3 Phenoptin Data). We also plan to conduct a supplemental diet study in children between 4 to 12 years of age. We have received orphan drug designation for Phenoptin for the treatment of PKU in both the U.S. and E.U. If Phenoptin is approved for marketing, it will have seven years of market exclusivity in the U.S. and ten years of market exclusivity in the E.U. In January 2006, the FDA designated Phenoptin as a fast-track product for the treatment of PKU.

PKU is an inherited metabolic disease that affects at least 50,000 diagnosed patients under the age of 40 in the developed world. We believe that 30% to 50% of those with PKU could benefit from treatment with Phenoptin, if approved. PKU is caused by a deficiency of an enzyme, phenylalanine hydroxylase (PAH), which is required for the metabolism of Phenylalanine (Phe). Phe is an amino acid found in protein-containing foods. Without sufficient quantity or activity of PAH, Phe accumulates to abnormally high levels in the blood resulting in a variety of serious neurological complications. Currently, the only way to manage PKU is through an extremely restricted diet that patients find very difficult to follow. Phenoptin, our lead product candidate for the treatment of PKU, is a proprietary, synthetic oral form of 6R-BH_4, a small-molecule therapeutic that is a co-factor for PAH. If approved, Phenoptin could become the first drug for the treatment of PKU.

In May 2005, the Company entered into an agreement with Serono for the further development and commercialization of Phenoptin and Phenylase for PKU, and 6R-BH_4, the active ingredient in Phenoptin, for other diseases including those associated with endothelial dysfunction. Through the agreement, Serono acquired exclusive rights to market these products in all territories outside the U.S. and Japan, and BioMarin retained exclusive rights to market these products in the U.S. BioMarin and Serono will generally share equally all development costs following successful completion of Phase 2 clinical trials for each product candidate in each indication. BioMarin and Serono are individually responsible for the costs of commercializing the products within their respective territories. Serono will also pay BioMarin royalties on its net sales of these products and milestone payments for the successful completion of certain development and approval milestones.

Endothelial dysfunction is a condition characterized by the inability of the endothelium (the single cell layer lining that forms the barrier between blood vessel walls and the blood) to respond to physiological changes correctly. In preclinical and investigator-sponsored studies, BH_4 administration has improved vascular endothelial function in animal models and in patients with diabetes and other cardiovascular diseases. BH_4 is a naturally occurring enzyme cofactor required for the production of nitric oxide, a molecule that is key to the regulation of dilation and constriction of blood vessels. We plan to conduct additional preclinical and clinical studies of BH_4 for endothelial dysfunction in 2006.

Other Programs

We are evaluating other therapies for serious medical conditions including Phenylase and Vibrilase (vibriolysin).

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Phenylase is an investigational enzyme substitution therapy currently in preclinical development. It is being developed as a subcutaneous injection and is intended for those who suffer from classic PKU and for those who are not 6R-BH_4 responsive, and do not respond to Phenoptin.

Vibrilase is an investigational topical enzyme therapy for use in the debridement of serious burns. In August 2004, we announced positive data from a Phase 1b clinical trial of Vibrilase. Data from the trial suggest that treatment with Vibrilase is generally safe and well-tolerated. Additionally, we are evaluating preclinical development of several other enzyme product candidates for genetic and other diseases as well as an immune tolerance platform technology designed to overcome limitations associated with the delivery of existing pharmaceuticals.

Recent Developments

Phase 3 Phenoptin Data

On March 15, 2006, Serono and we announced positive results of a Phase 3, double-blind, placebo-controlled clinical study of Phenoptin for the treatment for PKU. Results confirmed that all pre-specified primary and secondary endpoints were met and data from the Phase 3 study demonstrate a statistically significant reduction at six weeks in blood Phe levels in patients receiving Phenoptin, compared with those receiving placebo.

Following the six-week double-blind study, patients were eligible to enroll into an on-going 22 week Phase 3 open-label extension study designed to further evaluate the long-term safety and efficacy of Phenoptin, as well as dose titration. Serono and we expect to file marketing authorization applications for Phenoptin for PKU in the U.S. and E.U. in 2007. We have licensed to Serono exclusive rights for Phenoptin outside of the U.S. and Japan.

The Phase 3 study enrolled 89 patients with elevated blood Phe levels aged eight years and above at 29 sites in the U.S., Europe and Canada. All patients demonstrated a reduction in blood Phe levels (approximately 30% or more) following treatment with Phenoptin in a Phase 2 screening study.

The patients were randomly assigned to receive placebo or 10 mg/kg of Phenoptin daily for six weeks. Patients were evaluated every two weeks for changes in blood Phe levels and adverse events. The primary endpoint of the study was the difference in mean blood Phe levels between the placebo and Phenoptin groups at Week 6, adjusted for baseline levels. A total of 87 patients completed six weeks of treatment.

Results from the Phase 3 double-blind study are summarized below:

Primary Endpoint

Patients treated with Phenoptin for six weeks had a mean decrease in blood Phe level of 236 μM (29%) compared to an increase of 3 μM (3%) in the placebo group ($p<0.0001$). Prior to treatment, patients in the Phenoptin group and placebo group had mean blood Phe levels of 843 μM and 888 μM, respectively.

Secondary Endpoints

At Week 6, the percentage of patients in the Phenoptin group with blood Phe levels less than or equal to 600 μM was 54% compared to 23% in the placebo group ($p=0.004$). At baseline the proportions were 17% and 19% for the Phenoptin and placebo groups, respectively.

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The mean blood Phe level at each visit among patients receiving Phenoptin showed a consistent reduction compared to the blood Phe levels in patients receiving placebo ($p<0.001$) throughout the six-week period.

The type and incidence of adverse events was similar in the Phenoptin and placebo groups. Phenoptin was generally well tolerated and investigators reported no serious adverse events occurred.

Orapred License Agreement

On March 15, 2006, we entered into an agreement with Alliant Pharmaceuticals (Alliant) pursuant to which we licensed to Alliant exclusive North American rights to the Orapred (prednisolone sodium phosphate oral solution) product line, including Orapred ODT (prednisolone sodium phosphate orally disintegrating tablets).

Under the terms of the agreement, Alliant paid us $2.5 million upon signing of the definitive agreement and will make milestone payments of up to $15.5 million contingent primarily on the approval and commercial launch of Orapred ODT in the U.S., both of which are anticipated to occur in the second half of 2006. Upon approval and commercial launch of Orapred ODT in the U.S., we will be required to make milestone payments of $3.2 million to a third party. Alliant will pay us royalties ranging from 25% to 30% on net sales of Orapred ODT, net of royalties owed to a third party, in exchange for the exclusive rights to commercialize Orapred products in North America. We have retained commercial rights outside of North America.

Net sales of Orapred, including the branded and authorized generic products, for the 12 months ended December 31, 2005 were $6.9 million.

Orapred ODT, a new formulation of Orapred currently under review by the FDA, utilizes a proprietary orally disintegrating tablet technology to provide a taste-masked, non-refrigerated and easy-to-administer formulation of prednisolone. In August 2005, we filed a New Drug Application for Orapred ODT with the FDA. Pursuant to the Prescription Drug User Fee Act, we expect that the FDA will take action on the application by June 1, 2006. If approved, Orapred would be the first orally disintegrating tablet corticosteroid dosage form available in the U.S.

Company Information

Our principal executive offices are located at 105 Digital Drive, Novato, California 94949 and our telephone number is (415) 506-6700. BioMarin, Naglazyme, Phenoptin, Vibrilase, and Phenylase are our trademarks. Aldurazyme is a registered trademark of BioMarin/Genzy LLC. Orapred is a registered trademark of Medicis Pediatrics, Inc., and is used under license. All other service marks and all brand names or trademarks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective holders.

Concurrent Common Stock Offering

Concurrently with this offering of notes, we are offering 9,000,000 shares, or 10,350,000 shares if the underwriters exercise their overallotment option in full, of common stock to the public, which we refer to herein as the common stock offering. The common stock offering is being conducted as a separate public offering by means of a separate prospectus supplement. This offering is not contingent upon the common stock

offering, and the common stock offering is not contingent upon this offering.

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THE OFFERING

The following is a brief summary of the terms of this offering. For a complete description of the terms of the notes, see Description of the Notes in this prospectus supplement.

Issuer	BioMarin Pharmaceutical Inc.
Notes to be offered	$150,000,000 aggregate principal amount, or $172,500,000 if the underwriter exercises its option to purchase additional notes in full, of senior subordinated convertible notes due 2013.
Maturity date	March 29, 2013.
Interest and payment dates	2.50% per year on the principal amount, payable semiannually in arrears in cash on September 29 and March 29 of each year, beginning September 29, 2006.
Conversion rights	The notes are convertible, at the option of the holder, at any time on or prior to maturity, into shares of our common stock at a conversion rate of 60.3318 shares per $1,000 principal amount of notes per share, which is equal to a conversion price of approximately $16.58 per share. The conversion rate is subject to adjustment.
Make-whole premium upon a fundamental change	If a fundamental change (as described in this prospectus supplement) occurs, other than a fundamental change described under the third bullet point under the definition of a change in control described below under Description of the Notes Repurchase at Option of Holders Upon a Fundamental Change, we will pay a make-whole premium on notes converted in connection with a fundamental change by increasing the conversion rate on such notes. The amount of the make-whole premium, if any, will be based on our common stock price and the effective date of the fundamental change. A description of how the make-whole premium will be determined and a table showing the make-whole premium that would apply at various common stock prices and fundamental change effective dates is set forth under Description of the Notes Make-Whole Premium Upon a Fundamental Change.
Repurchase of notes by us at the option of the holders upon a fundamental change	If we undergo a fundamental change, except in certain circumstances, each holder will have the option to require us to repurchase all or any portion of such holder s notes. The fundamental change repurchase price will be 100% of the principal amount of the notes to be repurchased plus accrued and unpaid interest, if any.
Ranking	The notes will be unsecured and rank subordinated to our existing and future senior debt, equally with our existing and future senior

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	subordinated debt, and senior to our existing and future subordinated debt, including without limitation, our 3.50% convertible subordinated notes due 2008. As of March 14, 2006, we had $113.0 million in senior debt outstanding and $125.0 million 3.50% convertible subordinated notes due 2008, which will rank junior to the notes. Because the notes will be subordinated to our existing and future senior debt, in the event of bankruptcy, liquidation, dissolution or acceleration of payment on the senior debt, holders of the notes will not receive any payment until holders of the senior debt have been paid in full. The indenture under which the notes will be issued will not prevent us or our subsidiaries from incurring additional senior debt or other obligations.
Use of proceeds	We intend to apply the net proceeds of this offering and of the concurrent offering of common stock described above towards the commercialization of our products; additional clinical trials of Phenoptin, BH_4 for other indications, Phenylase and Vibrilase; preclinical studies and clinical trials for our other product candidates; potential licenses and acquisitions of complementary technologies, products and companies; general corporate purposes, including acquisition costs related to the purchase of our facility located at 46 Galli Drive for which we are currently under contract; and working capital. We may also use a portion of proceeds of these offerings to purchase some or all of our 3.50% convertible subordinated notes due 2008 pursuant to the redemption provisions of the indenture governing such notes whereby we have the right to call the notes beginning June 20, 2006, or in one or more privately negotiated transactions from time to time. This offering is not contingent on the concurrent common stock offering. See Use of Proceeds.
Form and denomination	The notes will be issued in minimum denominations of $1,000 and any integral multiple of $1,000.
Trading	The notes will not be listed on any securities exchange or included in any automated quotation system. The notes will be new securities for which there is currently no public market.
Nasdaq symbol for common stock	Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN .
Material U.S. federal income tax considerations	The notes and the shares of our common stock issuable upon conversion of the notes will be subject to special and complex U.S. federal income tax rules. Holders are encouraged to consult their tax advisors as to the U.S. federal, state, local or other tax consequences of acquiring, owning and disposing of the notes.
Risk factors	See Risk Factors and other information included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our notes.

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RISK FACTORS

An investment in our notes involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. You should carefully consider the following risk factors, together with all of the other information contained in this prospectus supplement and the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our notes to decline, and you may lose all or part of your investment.

Risks Related to Our Business

If we continue to incur operating losses for a period longer than anticipated, we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

Since we began operations in March 1997, we have been engaged primarily in research and development and have operated at a net loss for the entire time. Our first product, Aldurazyme, was approved for commercial sale in the U.S. and the E.U. and has generated approximately $130.5 million in net sales revenue to our joint venture from the product s launch in May 2003 through December 31, 2005. We acquired exclusive rights to Orapred in May 2004 and reported $25.5 million in Orapred net product sales following the acquisition through December 31, 2005. On June 1, 2005 we announced that the FDA granted marketing approval for Naglazyme for the treatment of MPS VI. We reported $6.1 million in Naglazyme net product sales during 2005. We have no revenues from sales of our product candidates. As of December 31, 2005, we had an accumulated deficit of $563.1 million. We expect to continue to operate at a net loss for the foreseeable future. Our future profitability depends on our marketing and selling of Naglazyme, the successful commercialization of Aldurazyme by our joint venture partner, Genzyme, the amount of royalties we receive from our license of Orapred, the receipt of regulatory approval of our product candidates and our ability to successfully manufacture and market any approved drugs, either by ourselves or jointly with others. The extent of our future losses and the timing of profitability are highly uncertain. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or discontinue operations.

If we fail to obtain the capital necessary to fund our operations, our financial results and financial condition will be adversely affected and we will have to delay or terminate some or all of our product development programs.

We will require additional financing to fund our future operations, including the commercialization of our approved drugs and drug product candidates currently under development, preclinical studies and clinical trials, and potential licenses and acquisitions. We may be unable to raise additional financing when needed due to a variety of factors, including our financial condition, the status of our product programs, and the general condition of the financial markets. If we fail to raise additional financing as we need such funds, we will have to delay or terminate some or all of our product development programs and our financial condition and operating results will be adversely affected.

We expect to continue to spend substantial amounts of capital for our operations for the foreseeable future. The amount of capital we will need depends on many factors, including:

our ability to successfully market and sell Naglazyme;

our joint venture partner s ability to successfully commercialize Aldurazyme;

the progress, timing and scope of our preclinical studies and clinical trials;

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- the amount of royalties we receive from our license of Orapred;
- the time and cost necessary to obtain regulatory approvals and the costs of post-marketing studies which may be required by regulatory authorities;
- the time and cost necessary to develop commercial manufacturing processes, including quality systems, and to build or acquire manufacturing capabilities;
- our ability to maintain compliance with our debt covenants;
- the time and cost necessary to respond to technological and market developments;
- any changes made or new developments in our existing collaborative, licensing and other commercial relationships or any new collaborative, licensing and other commercial relationships that we may establish; and
- whether our convertible debt is converted to common stock in the future.

Moreover, our fixed expenses such as rent, license payments, interest expense and other contractual commitments are substantial and will increase in the future. These fixed expenses will increase because we expect to enter into:

- additional licenses and collaborative agreements;
- additional contracts for consulting, maintenance and administrative services;
- additional contracts for product manufacturing; and
- additional financing facilities.

We believe that our cash, cash equivalents, short-term investment securities and cash balances related to long-term debt at December 31, 2005, plus funds contractually committed to us will be sufficient to meet our operating and capital requirements into the first quarter of 2007. These estimates are based on assumptions and estimates, including the availability of a $25.0 million loan from Medicis. These assumptions and estimates may prove to be wrong. Additionally, we are required to maintain a total unrestricted cash balance of at least $25.0 million under our credit facility with Comerica. We will need to sell equity or debt securities to raise additional funds if we are unable to satisfy our liquidity requirements. The sale of additional securities may result in additional dilution to our stockholders. Furthermore, additional financing may not be available in amounts or on terms satisfactory to us or at all. This could result in the delay, reduction or termination of our research, which could harm our business.

If we fail to maintain regulatory approval to commercially market or sell our drugs, or if approval is delayed, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.

We must obtain regulatory approval before marketing or selling our drug products in the U.S. and in foreign jurisdictions. In the U.S., we must obtain FDA approval for each drug that we intend to commercialize. The FDA approval process is typically lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. Aldurazyme, Naglazyme and Orapred have received regulatory approval to be commercially marketed and sold in the U.S., and Aldurazyme and Naglazyme have received regulatory approval to be commercially marketed and sold in the E.U. and other countries. If we fail to obtain regulatory approval for our other product candidates, we will be unable to market and sell those drug products. Because of the risks and uncertainties in pharmaceutical development, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval.

From time to time during the regulatory approval process for our products and our product candidates, we engage in discussions with the FDA and foreign regulatory authorities regarding the regulatory requirements

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of our development programs. To the extent appropriate, we accommodate the requests of the regulatory authorities and, to date, we have generally been able to reach reasonable accommodations and resolutions regarding the underlying issues. However, we are often unable to determine the outcome of such deliberations until they are final. If we are unable to effectively and efficiently resolve and comply with the inquiries and requests of the FDA and foreign regulatory authorities, the approval of our product candidates may be delayed and their value may be reduced.

After any of our products receive regulatory approval, they remain subject to ongoing FDA regulation, including, for example, changes to the product labeling, new or revised regulatory requirements for manufacturing practices and reporting adverse reactions and other information. If we do not comply with the FDA s regulations, the range of possible sanctions includes FDA issuance of adverse publicity, product recalls or seizures, fines, total or partial suspensions of production and/or distribution, suspension of FDA s review of marketing applications, enforcement actions, including injunctions and civil or criminal prosecution. The FDA can withdraw a product s approval under some circumstances, such as the failure to comply with existing or future regulatory requirements or unexpected safety issues. Further, the FDA may condition approval of our product candidates on the completion of additional post-marketing clinical studies. These post-marketing studies may suggest that a product causes undesirable side effects or may present a risk to safety. If data we collect from post-marketing studies suggest that one of our approved products may present a risk to safety, the FDA could withdraw our product approval, suspend production or place other marketing restrictions on our products. If regulatory sanctions are applied or if regulatory approval is delayed or withdrawn, our management s credibility, the value of our company and our operating results will be adversely affected. Additionally, we will be unable to generate revenue from the sale of these products, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased.

To obtain regulatory approval to market our products, preclinical studies and costly and lengthy preclinical and clinical trials are required and the results of the studies and trials are highly uncertain.

As part of the regulatory approval process, we must conduct, at our own expense, preclinical studies in the laboratory on animals and clinical trials on humans for each product candidate. We expect the number of preclinical studies and clinical trials that the regulatory authorities will require will vary depending on the product candidate, the disease or condition the drug is being developed to address and regulations applicable to the particular drug. We may need to perform multiple preclinical studies using various doses and formulations before we can begin clinical trials, which could result in delays in our ability to market any of our product candidates. Furthermore, even if we obtain favorable results in preclinical studies on animals, the results in humans may be significantly different. After we have conducted preclinical studies in animals, we must demonstrate that our drug products are safe and efficacious for use in the targeted human patients in order to receive regulatory approval for commercial sale.

Adverse or inconclusive clinical results would stop us from filing for regulatory approval of our product candidates. Additional factors that can cause delay or termination of our clinical trials include:

- slow or insufficient patient enrollment;
- slow recruitment of, and completion of necessary institutional approvals at, clinical sites;
- longer treatment time required to demonstrate efficacy;
- lack of sufficient supplies of the product candidate;

adverse medical events or side effects in treated patients;

lack of effectiveness of the product candidate being tested; and

regulatory requests for additional clinical trials.

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Typically, if a drug product is intended to treat a chronic disease, as is the case with some of our product candidates, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more.

The fast-track designation for our product candidates, if obtained, may not actually lead to a faster review process and a delay in the review process or in the approval of our products will delay revenue from the sale of the products and will increase the capital necessary to fund these programs.

Our product candidates may not receive fast-track designation or a six-month review timeframe. Even with fast-track designation, it is not guaranteed that the total review process will be faster or that approval will be obtained, if at all, earlier than would be the case if the product had not received fast-track designation.

If we fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before we can begin commercial manufacture of our products, we must obtain regulatory approval of our manufacturing facilities, processes and quality systems; and the manufacture of our drugs must comply with GMP regulations. The GMP regulations govern facility compliance, quality control and documentation policies and procedures. In addition, our manufacturing facilities are continuously subject to inspection by the FDA, the State of California and foreign regulatory authorities, before and after product approval. Our manufacturing facility in Novato, California (Galli Drive) and GMP warehouse facilities have been inspected and licensed by the State of California for clinical pharmaceutical manufacture and have been approved by the FDA, the EC and health agencies in other countries for the commercial manufacture of Aldurazyme and by the FDA and EC for the commercial manufacture of Naglazyme. We have entered into contracts with third-party manufacturers to produce Orapred and Phenoptin.

Due to the complexity of the processes used to manufacture Aldurazyme, Naglazyme and our product candidates, we may be unable to continue to pass or initially pass federal or international regulatory inspections in a cost effective manner. For the same reason, any potential third-party manufacturer of Aldurazyme, Naglazyme or our product candidates may be unable to comply with GMP regulations in a cost effective manner. As anticipated by GMP requirements, manufacturing deviations and deviations from GMP can and do occur from time to time. When a deviation occurs, we take corrective actions, which may not always be successful. Continued or extensive deviations can cause a manufacturing facility to be out of compliance with GMP. If we, or our third-party manufacturers with whom we contract, are unable to comply with manufacturing regulations, we may be subject to fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

If we fail to obtain or maintain orphan drug exclusivity for some of our products, our competitors may sell products to treat the same conditions and our revenues will be reduced.

As part of our business strategy, we intend to develop some drugs that may be eligible for FDA and E.U. orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, defined as a patient population of less than 200,000 in the U.S. The company that first obtains FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. Similar regulations are available in the E.U. with a 10-year period of market exclusivity.

Because the extent and scope of patent protection for some of our drug products is particularly limited, orphan drug designation is especially important for our products that are eligible for orphan drug designation. For

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eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products that do not have patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced.

Even though we have obtained orphan drug designation for certain of our product candidates and even if we obtain orphan drug designation for our future product candidates, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any orphan indication. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

Because the target patient populations for some of our products are small, we must achieve significant market share and obtain high per-patient prices for our products to achieve profitability.

Aldurazyme and Naglazyme both target diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development costs and achieve profitability. Aldurazyme targets patients with MPS I and Naglazyme targets patients with MPS VI. We believe that we will need to market worldwide to achieve significant market penetration of each product. In addition, we are developing other drug candidates to treat conditions, such as other genetic diseases, with small patient populations. Due to the expected costs of treatment for Aldurazyme and Naglazyme, we may be unable to maintain or obtain sufficient market share for Aldurazyme or Naglazyme at a price high enough to justify our product development efforts.

If we are found in violation of federal or state fraud and abuse laws, we may be required to pay a penalty or be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operation.

We are subject to various federal and state health care fraud and abuse laws, including antikickback laws, false claims laws and laws related to ensuring compliance. The federal health care program antikickback statute makes it illegal for any person, including a pharmaceutical company, to knowingly and willfully offer, solicit, pay or receive any remuneration, directly or indirectly, in exchange for or to induce the referral of business, including the purchase, order or prescription of a particular drug, for which payment may be made under federal health care programs, such as Medicare and Medicaid. Under federal government regulations, certain arrangements (safe harbors) are deemed not to violate the federal antikickback statute. We seek to comply with these safe harbors. False claims laws prohibit anyone from knowingly and willfully presenting or causing to be presented for payment to third party payers (including government payers) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Other cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products has resulted in the submission of false claims to government health care programs. Under the Health Insurance Portability and Accountability Act of 1996, we also are prohibited from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payers, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines and/or exclusion or suspension from federal and state health care programs such as Medicare and Medicaid.

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Many states have adopted laws similar to the federal antikickback statute, some of which apply to referral of patients for health care services reimbursed by any source, not just governmental payers. In addition, California passed a law that requires pharmaceutical companies to comply with both the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the July 2002 PhRMA Code on Interactions with Healthcare Professionals.

Neither the government nor the courts have provided definitive guidance on the application of these laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, are required to pay a penalty or are suspended or excluded from participation in federal or state health care programs, our business, financial condition and results of operation may be adversely affected.

If we fail to obtain an adequate level of reimbursement for our drug products by third-party payers, the sales of our drugs would be adversely affected or there may be no commercially viable markets for our products.

The course of treatment for patients using Aldurazyme and Naglazyme is expensive. We expect patients to need treatment throughout their lifetimes. We expect that most families of patients will not be capable of paying for this treatment themselves. There will be no commercially viable market for Aldurazyme or Naglazyme without reimbursement from third-party payers. Additionally, even if there is a commercially viable market, if the level of reimbursement is below our expectations, our revenue and gross margins will be adversely affected.

Third-party payers, such as government or private health care insurers, carefully review and increasingly challenge the prices charged for drugs. Reimbursement rates from private companies vary depending on the third-party payer, the insurance plan and other factors. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis.

We currently have limited expertise in obtaining reimbursement. We rely on the expertise of our joint venture partner, Genzyme, to obtain reimbursement for the costs of Aldurazyme. We are developing our own reimbursement capabilities for Naglazyme and have initiated the process for obtaining reimbursement in the E.U. Reimbursement in the E.U. must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The negotiation process in some countries can exceed 12 months. For our future products and for Naglazyme outside the U.S., we will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates for our products, they may not be commercially viable or our future revenues and gross margins may be adversely affected.

In the future, government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

We expect that, in the future, reimbursement will be increasingly restricted both in the U.S. and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. Governmental and private third-party payers have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments, have been made in the U.S. In some foreign markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect reimbursement for medical treatment by third-party payers, which may render our products not commercially viable or may adversely affect our future revenues and gross margins.

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In the U.S., we expect branded pharmaceutical products to be subject to increasing pricing pressures. Implementation of the Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA), providing an out-patient prescription drug benefit under the Medicare program, became effective on January 1, 2006. While it is difficult to predict the final business impact of this legislation, there is additional risk associated with increased pricing pressures. While the MMA prohibits the Secretary of Health and Human Services (HHS) from directly negotiating prescription drug prices with manufacturers, we expect continued challenges to that prohibition over the next several years. Also, the MMA retains the authority of the HHS to prohibit the importation of prescription drugs, but we expect Congress to consider several measures that could remove that authority and allow for importation of products into the U.S. regardless of their safety or cost. If adopted, such legislation would likely have a negative effect on our U.S. sales.

As a result of the passage of the MMA, aged and disabled patients jointly eligible for Medicare and Medicaid will receive certain prescription drug benefits through Medicare, instead of Medicaid, as of January 1, 2006. This may relieve some state budget pressures but is unlikely to result in reduced pricing pressures. Additionally, in the U.S., we are required to provide rebates to state governments on their purchases of certain of our products under state Medicaid programs. Many states have begun to implement supplemental rebates and restricted formularies in their Medicaid programs, and these programs are expected to continue in the post-MMA environment. Other cost containment measures have been adopted or proposed by federal, state, and local government entities that provide or pay for health care. In most international markets, we operate in an environment of government-mandated cost containment programs, which may include price controls, reference pricing, discounts and rebates, restrictions on physician prescription levels, restrictions on reimbursement, compulsory licenses, health economic assessments, and generic substitution. Several states are also attempting to extend discounted Medicaid prices to non-Medicaid patients. Additionally, notwithstanding the federal law prohibiting pharmaceutical importation, several states have implemented importation schemes for their citizens, usually involving a website that links patients to selected Canadian pharmacies. At least one state has such a program for its state employees. In the absence of federal action to curtail state activities, we expect other states to launch importation efforts. As a result, we expect pressures on pharmaceutical pricing to continue.

International operations are also generally subject to extensive price and market regulations, and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or reduce the value of our intellectual property portfolio.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenue and results of operations.

If we are unable to protect our proprietary technology, we may not be able to compete as effectively.

Where appropriate, we seek patent protection for certain aspects of our technology. Patent protection may not be available for some of the products we are developing. If we must spend significant time and money protecting our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biopharmaceutical products are complex and uncertain. The scope and extent of patent protection for some of our products and product candidates are particularly uncertain because key information on some of our product candidates has existed in the public domain for many years. Other parties have published the structure of the enzymes and compounds, the methods for purifying or producing the enzymes and compounds or the methods of treatment. The composition and genetic sequences of animal and/or human versions of Aldurazyme, Naglazyme and many of our product candidates, including BH_4, have been published and are believed to be in the public domain. Publication of this information may prevent us from obtaining composition-of-matter patents, which are generally believed to offer the strongest patent protection.

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For enzymes or compounds with no prospect of broad composition-of-matter patents, other forms of patent protection or orphan drug status may provide us with a competitive advantage. As a result of these uncertainties, investors should not rely on patents as a means of protecting our products or product candidates, including Aldurazyme, Naglazyme, Orapred or BH_4.

We own or license patents and patent applications related to Aldurazyme, Naglazyme, Orapred, and certain of our product candidates. However, these patents and patent applications do not ensure the protection of our intellectual property for a number of reasons, including the following:

- We do not know whether our patent applications will result in issued patents. For example, we may not have developed a method for treating a disease before others developed similar methods.

- Competitors may interfere with our patent process in a variety of ways. Competitors may claim that they invented the claimed invention prior to us. Competitors may also claim that we are infringing on their patents and therefore cannot practice our technology as claimed under our patent. Competitors may also contest our patents by showing the patent examiner that the invention was not original, was not novel or was obvious. In litigation, a competitor could claim that our issued patents are not valid for a number of reasons. If a court agrees, we would lose that patent. As a company, we have no meaningful experience with competitors interfering with our patents or patent applications.

- Enforcing patents is expensive and may absorb significant time of our management. Management would spend less time and resources on developing products, which could increase our operating expenses and delay product programs.

- Receipt of a patent may not provide much practical protection. If we receive a patent with a narrow scope, then it will be easier for competitors to design products that do not infringe on our patent.

In addition, competitors also seek patent protection for their technology. Due to the number of patents in our field of technology, we cannot be certain that we do not infringe on those patents or that we will not infringe on patents granted in the future. If a patent holder believes our product infringes on their patent, the patent holder may sue us even if we have received patent protection for our technology. If someone else claims we infringe on their technology, we would face a number of issues, including the following:

- Defending a lawsuit takes significant time and can be very expensive.

- If the court decides that our product infringes on the competitor s patent, we may have to pay substantial damages for past infringement.

- The court may prohibit us from selling or licensing the product unless the patent holder licenses the patent to us. The patent holder is not required to grant us a license. If a license is available, we may have to pay substantial royalties or grant cross licenses to our patents.

- Redesigning our product so it does not infringe may not be possible or could require substantial funds and time.

It is also unclear whether our trade secrets are adequately protected. While we use reasonable efforts to protect our trade secrets, our employees or consultants may unintentionally or willfully disclose our information to competitors. Enforcing a claim that someone else illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts

outside the U.S. are sometimes less willing to protect trade secrets. Our competitors may independently develop equivalent knowledge, methods and know-how.

We may also support and collaborate in research conducted by government organizations, hospitals, universities or other educational institutions. These research partners may be unwilling to grant us any exclusive rights to technology or products derived from these collaborations prior to entering into the relationship.

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If we do not obtain required licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or even be prohibited from developing, manufacturing or selling products requiring these licenses. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties.

The U.S. Patent and Trademark Office (USPTO) has issued three patents to a third-party that relate to alpha-L-iduronidase. If we are not able to successfully challenge these patents, we may be prevented from producing Aldurazyme in the U.S. unless and until we obtain a license.

The USPTO has issued three patents to a third-party that include composition-of-matter, isolated genomic nucleotide sequences, vectors including the sequences, host cells containing the vectors, and method of use claims for human, recombinant alpha-L-iduronidase. Aldurazyme is based on human, recombinant alpha-L-iduronidase. We believe that these patents are invalid or not infringed on a number of grounds. A corresponding patent application was filed by a third party in the European Patent Office claiming composition-of-matter for human, recombinant alpha-L-iduronidase, and it was rejected over prior art and withdrawn and cannot be re-filed. However, corresponding applications are still pending in Canada and Japan, and these applications are being prosecuted by the applicants. We do not know whether any of these applications will issue as patents or the scope of the claims that would issue from these applications. In addition, under U.S. law, issued patents are entitled to a presumption of validity, and our challenges to the U.S. patents may be unsuccessful. Even if we are successful, challenging the U.S. patents may be expensive, require our management to devote significant time to this effort and may adversely impact commercialization of Aldurazyme in the U.S.

The holder of the patents described above has granted an exclusive license for products relating to these patents to one of our competitors, Transkaryotic Therapies Inc. (TKT), which was acquired by Shire PLC in 2005. If we are unable to successfully challenge the patents, we may be unable to produce Aldurazyme in the U.S. (or in Canada or Japan, should patents issue in these countries) unless we can reach an accommodation with the patent holder and licensee. Neither the current licensee nor the patent holder is required to grant us a license or other accommodation and even if a license or other accommodation is available, we may have to pay substantial license fees, which could adversely affect our business and operating results.

On October 8, 2003, Genzyme, our joint venture partner, and TKT announced their collaboration to develop and commercialize an unrelated drug product. In connection with the collaboration agreement, Genzyme and TKT signed a global legal settlement involving an exchange of non-suits between the companies. As part of this exchange, TKT has agreed not to initiate any patent litigation against Genzyme or our joint venture relating to Aldurazyme. If any or all of the TKT-licensed patents are deemed (or ruled) to cover Aldurazyme, our joint venture may be required to reach additional accommodations with the holder of the patents, who is not party to the TKT-Genzyme settlement discussed above.

If our joint venture with Genzyme were terminated, we could be barred from commercializing Aldurazyme or our ability to successfully commercialize Aldurazyme would be delayed or diminished.

We rely on Genzyme to apply the expertise it has developed through the launch and sale of other enzyme-based products to the marketing of Aldurazyme. We have very limited experience selling, marketing or obtaining reimbursement for orphan pharmaceutical products. In addition, without Genzyme we would be required to pursue foreign regulatory approvals. We have limited experience in seeking foreign regulatory approvals.

Either Genzyme or we may terminate the joint venture for specified reasons, including if the other party is in material breach of the agreement, has experienced a change of control, or has declared bankruptcy and also is in breach of the agreement. Although we are not currently in breach

of the joint venture agreement and we believe that Genzyme is not currently in breach of the joint venture agreement, there is a risk that either party could breach the agreement in the future. Either party may also terminate the agreement upon one year prior written notice for any reason.

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If the joint venture is terminated for breach, the non-breaching party would be granted, exclusively, all of the rights to Aldurazyme and any related intellectual property and regulatory approvals and would be obligated to buy out the breaching party s interest in the joint venture. If we are the breaching party, we would lose our rights to Aldurazyme and the related intellectual property and regulatory approvals. If the joint venture is terminated without cause, the non-terminating party would have the option, exercisable for one year, to buy out the terminating party s interest in the joint venture and obtain all rights to Aldurazyme exclusively. In the event of termination of the buy out option without exercise by the non-terminating party as described above, all right and title to Aldurazyme is to be sold to the highest bidder, with the proceeds to be split equally between Genzyme and us.

If the joint venture is terminated by either party because the other declared bankruptcy and is also in breach of the agreement, the terminating party would be obligated to buy out the other and would obtain all rights to Aldurazyme exclusively. If the joint venture is terminated by a party because the other party experienced a change of control, the terminating party shall notify the other party, the offeree, of its intent to buy out the offeree s interest in the joint venture for a stated amount set by the terminating party at its discretion. The offeree must then either accept this offer or agree to buy the terminating party s interest in the joint venture on those same terms. The party who buys out the other would then have exclusive rights to Aldurazyme.

If we were obligated, or given the option, to buy out Genzyme s interest in the joint venture, and gain exclusive rights to Aldurazyme, we may not have sufficient funds to do so and we may not be able to obtain the financing to do so. If we fail to buy out Genzyme s interest we may be held in breach of the agreement and may lose any claim to the rights to Aldurazyme and the related intellectual property and regulatory approvals. We would then effectively be prohibited from developing and commercializing Aldurazyme.

If our license agreement with Ascent Pediatrics is terminated or becomes non-exclusive, our royalty revenues from Orapred would be reduced or eliminated.

The license agreement with Ascent Pediatrics is terminable upon specified material breaches by Ascent Pediatrics or us. If the license agreement were terminated, we would no longer have the ability to manufacture or sublicense Orapred.

Ascent Pediatrics has the right under the license agreement to cause the license to become non-exclusive in the event of certain specified breaches by us. If the license becomes non-exclusive, Ascent Pediatrics would be able to commercialize Orapred itself or license it to others, which would reduce our competitive advantage and which could reduce our revenue significantly.

Our strategic alliance with Serono may be terminated at any time by Serono, and if it is terminated, our expenses could increase and our operating performance could be adversely affected.

Serono may terminate the agreement forming our strategic alliance with them at any time by giving 90 days prior written notice if such termination occurs prior to the commercialization of any of the products licensed under our agreement, or by giving 180 days prior written notice if such termination occurs after the commercialization of such a product. Either Serono or we may terminate our strategic alliance under certain circumstances, including if the other party is in material breach of the agreement and does not remedy the breach within a specified period of time, or has suffered certain financial difficulties, including filing for bankruptcy or making an assignment for the benefit of creditors. Although we are not currently in breach of the agreement and we believe that Serono is not currently in breach of the agreement, there is a risk that either party could breach the agreement in the future. Upon a termination of the agreement by Serono by giving notice or by us for a material breach by Serono, all rights licensed to us under the agreement become irrevocable and fully-paid except in those countries where restricted by applicable law or for all intellectual property that Serono does not own. Upon a termination of the agreement by Serono for a

material breach by us or based on our financial difficulty, or upon the expiration of the royalty term of the products licensed under the agreement, all rights

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licensed to Serono under the agreement become irrevocable and fully-paid upon the payment of amounts due by Serono to us which accrued prior to the expiration of the royalty term, except in those countries where restricted by applicable law or for all intellectual property that we do not own and for which we do not have a royalty-free license. Upon a termination of the agreement for a material breach by us or for our financial difficulty, all rights and licenses granted by Serono to us under or pursuant to the agreement will automatically terminate. Under the terms of our agreement with Serono, Serono is responsible to pay for a portion of the development costs of products developed pursuant to such agreement. However, at any time upon 90 days notice, Serono can opt out of this responsibility. If Serono opts out, or if the agreement is terminated by either Serono or us, and we continue the development of products related to that agreement, we would be responsible for 100% of future development costs, and our expenses could increase and our operating performance could be adversely affected.

If the option under the securities purchase agreement with Medicis to purchase all of the issued and outstanding capital stock of Ascent Pediatrics is accelerated by Medicis, we may not have sufficient funds to exercise the option, which could result in a termination of the license agreement and our revenue could decrease significantly.

Pursuant to our agreement with Alliant, we are obligated to exercise the option under our securities purchase agreement with Medicis to purchase all issued and outstanding capital stock of Ascent Pediatrics in approximately three years. The exercise of the option is subject to acceleration on specified material breaches of our license agreement with Ascent Pediatrics or a bankruptcy or insolvency proceeding involving Medicis or Ascent Pediatrics, and if such acceleration is due to a specified breach of the license by us, then the option exercise price together with an amount equal to all license payments remaining under our license agreement with Ascent Pediatrics will become due on the accelerated closing date for the purchase of shares under the option.

If the option were accelerated, we may not have sufficient funds at that time to exercise the option and/or to make the license payments, and may not be able to obtain the financing to do so, in which case we would not be able to consummate the transaction to acquire such shares and would be in breach of the license agreement and the securities purchase agreement. If we are in breach of the license agreement, Ascent Pediatrics may terminate the license and we would no longer have the ability to manufacture, market, sell, or distribute Orapred and our revenue could decrease significantly.

If we are unable to successfully develop manufacturing processes for our drug products to produce sufficient quantities and at acceptable costs, we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program.

Although we manufacture Aldurazyme and Naglazyme at commercial scale and within our cost parameters, due to the complexity of manufacturing our products we may not be able to manufacture any other drug product successfully with a commercially viable process or at a scale large enough to support their respective commercial markets or at acceptable margins.

Our manufacturing processes may not meet initial expectations and we may encounter problems with any of the following if we attempt to increase the scale or size, or improve the commercial viability of our manufacturing processes:

- design, construction and qualification of manufacturing facilities that meet regulatory requirements;
- schedule;

reproducibility;

production yields;

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purity;

costs;

quality control and assurance systems;

raw material suppliers;

shortages of qualified personnel; and

compliance with regulatory requirements.

Improvements in manufacturing processes typically are very difficult to achieve and are often very expensive and may require extended periods of time to develop. If we contract for manufacturing services with an unproven process, our contractor is subject to the same uncertainties, high standards and regulatory controls, and may therefore experience difficulty if further process development is necessary. Even a developed manufacturing process can encounter difficulties due to changing regulatory requirements, human error, mechanical breakdowns, and other events that cannot always be prevented or anticipated.

The availability of suitable contract manufacturing capacity at scheduled or optimum times is not certain. The cost of contract manufacturing is generally greater than internal manufacturing and therefore our manufacturing processes must be of higher productivity to result in equivalent margins.

Although we have entered into contractual relationships with third-party manufacturers to produce Orapred and Phenoptin, if those manufacturers are unwilling or unable to fulfill their contractual obligations, we may be unable to meet demand for that product or sell that product at all, regulatory approval for Phenoptin or Orapred ODT could be significantly delayed and we may lose potential revenue.

We have built-out approximately 60,000 square feet at our Galli Drive facility for manufacturing capability for Aldurazyme and Naglazyme, including related quality control laboratories, materials capabilities, and support areas. We expect to add additional capabilities in stages over time, which could create additional operational complexity and challenges. We expect that developing manufacturing processes for all of our product candidates will require significant time and resources before we can begin to manufacture them (or have them manufactured by third parties) in commercial quantity at an acceptable cost.

In order to achieve our product cost targets, we must develop efficient manufacturing processes either by:

improving the product yield from our current cell lines, which are populations of cells that have a common genetic makeup;

improving the manufacturing processes licensed from others; or

developing more efficient, lower cost recombinant cell lines and production processes.

A recombinant cell line is a cell line with foreign DNA inserted that is used to produce an enzyme or other protein that it would not otherwise produce. The development of a stable, high production cell line for any given enzyme or other protein is difficult, expensive and unpredictable and may not result in adequate yields. In addition, the development of protein purification processes is difficult and may not produce the high purity required with acceptable yield and costs or may not result in adequate shelf-lives of the final products. If we are not able to develop efficient manufacturing processes, the investment in manufacturing capacity sufficient to satisfy market demand will be much greater and will place heavy financial demands upon us. If we do not achieve our manufacturing cost targets we may be unable to meet demand for our products and lose potential revenue, have reduced margins or be forced to terminate a program.

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In addition, our manufacturing processes subject us to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of hazardous materials and wastes resulting from their use. We may incur significant costs in complying with these laws and regulations.

If our manufacturing processes have a higher than expected failure rate, we may be unable to meet demand for our products and lose potential revenue, have reduced margins, or be forced to terminate a program.

The processes we use to manufacture our product and product candidates are extremely complex. Many of the processes include biological systems, which add significant complexity, as compared to chemical synthesis. We expect that, from time to time, consistent with biotechnology industry expectations, certain production lots will fail to produce product that meets our quality control release acceptance criteria. To date, our historical failure rates for all of our product programs, including Aldurazyme and Naglazyme, have been within our expectations, which are based on industry norms.

In order to produce product within our time and cost parameters, we must continue to produce product within expected failure parameters. Because of the complexity of our manufacturing processes, it may be difficult or impossible for us to determine the cause of any particular lot failure and we must effectively and timely take corrective action in response to any failure.

If we are unable to effectively address manufacturing issues, we may be unable to meet demand for our products and lose potential revenue, have reduced margins, or be forced to terminate a program.

Our sole manufacturing facility for Aldurazyme and Naglazyme is located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facility and equipment, or that of our third-party manufacturers or single-source suppliers, which could materially impair our ability to manufacture Aldurazyme and Naglazyme or our third-party manufacturer s ability to manufacture Orapred or Phenoptin.

Our Galli Drive facility is our only manufacturing facility for Aldurazyme and Naglazyme. It is located in the San Francisco Bay Area near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We, and the third-party manufacturers with whom we contract and our single-source suppliers of raw materials, are also vulnerable to damage from other types of disasters, including fires, floods, power loss and similar events. If any disaster were to occur, our ability to manufacture Aldurazyme and Naglazyme, or to have Orapred manufactured, could be seriously, or potentially completely impaired, and our Aldurazyme and Naglazyme commercialization efforts, revenue from the sale of Aldurazyme and Naglazyme, royalties from the sales of Orapred and our development efforts with respect to Phenoptin could be seriously impaired. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions.

Supply interruptions may disrupt our inventory levels and the availability of our products and cause delays in obtaining regulatory approval for our product candidates, or cause a loss of our market share and reduce our revenues.

Numerous factors could cause interruptions in the supply of our finished products, including:

timing, scheduling and prioritization of production by our contract manufacturers or a breach of our agreements by our contract manufacturers;

labor interruptions;

changes in our sources for manufacturing;

the timing and delivery of shipments;

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our failure to locate and obtain replacement manufacturers as needed on a timely basis; and

conditions affecting the cost and availability of raw materials.

We try to maintain inventory levels that are no greater than necessary to meet our current projections. Any interruption in the supply of finished products could hinder our ability to timely distribute finished products.

With respect to our product candidates, production of product is necessary to perform clinical trials and successful registration batches are necessary to file for approval to commercially market and sell product candidates. Delays in obtaining clinical material or registration batches could delay regulatory approval for our product candidates.

Actions by wholesalers relating to the purchase of Orapred could affect the timing of royalty revenues.

Orapred is sold to major wholesalers and retail pharmacy chains. Consistent with pharmaceutical industry patterns, most Orapred sales are to three major drug wholesale concerns. Distribution allocation is determined by wholesale and drug chain customers. There can be no assurance that these customers will adequately manage their local and regional inventories to avoid spot outages.

It is difficult to control or influence greatly the purchasing patterns of wholesale and retail drug chain customers. These are highly sophisticated customers that purchase our products in a manner consistent with their industry practices and, presumably based upon their projected demand levels. The buying practices of the wholesalers include occasional speculative purchases of product in excess of the current market demand, at their discretion, in anticipation of future price increases. Purchases by any given customer, during any given period, may be above or below actual prescription volumes of Orapred during the same period, resulting in fluctuations in product inventory in the distribution channel. In addition, if wholesaler inventories substantially exceed retail demand, we could experience reduced royalty revenue from sales of Orapred by our licensee in subsequent periods due to overstocking or low end-user demand.

Our recent reduction in our sales force could adversely affect our ability to market our current and future products and could adversely affect our revenues.

During the third quarter of 2005, we reduced our sales force by 52 employees, or approximately 83% of the sales force. We believe that the current size of the sales force is appropriate based on the nature of our products being sold, the expected revenues and the competitive marketplace. We also believe that, to the extent necessary, we could increase the size of our sales force in the future to accommodate demands required by future products. However, if our assessments are incorrect, our ability to market our current and future products could be adversely affected. If this were to happen, the revenues generated by our current and future products would be adversely affected.

If we fail to compete successfully with respect to product sales, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product and our revenue could be adversely affected.

Our competitors may develop, manufacture and market products that are more effective or less expensive than ours. They may also obtain regulatory approvals for their products faster than we can obtain them (including those products with orphan drug designation) or commercialize their products before we do. If we do not compete successfully, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product.

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If we fail to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

Our competitors compete with us to attract organizations for acquisitions, joint ventures, licensing arrangements or other collaborations. To date, several of our product programs have been acquired through acquisitions, such as Phenylase, and several of our product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme, Naglazyme, Phenoptin and Vibrilase. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Since each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of enzyme therapeutics, including Genzyme, our joint venture partner. These companies have already begun many drug development programs, some of which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions also compete with us. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patents that we may need for the development of our product candidates. We will attempt to license this proprietary technology, if available. These licenses may not be available to us on acceptable terms, if at all. If we are unable to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

We have limited experience commercializing drug products in the E.U., and if we are unable to successfully market and sell Naglazyme in the E.U., our revenues and profitability will be adversely affected.

As an organization, we have limited experience commercializing drug products outside of the U.S. We have established operations in the E.U. and are in the process of initiating commercialization of Naglazyme ourselves. However, establishing and maintaining a complete and effective commercial structure is a complicated and difficult process. This includes establishing sales, marketing, regulatory, distribution, and reimbursement functions. In order to successfully commercialize Naglazyme, we will need to effectively maintain or contract for all of these functions.

Commercialization in the E.U. is significantly different from commercialization in the U.S. Each country in the E.U. has a different healthcare system and different policies and procedures for funding and reimbursing expensive orphan products, such as Naglazyme, and for treating rare and complicated diseases such

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as MPS VI. Obtaining reimbursement for these types of drugs can be particularly difficult and requires direct and effective negotiations with the government organizations and private third-party organizations.

If we are not successful with these activities, our revenues from sales of Naglazyme in the E.U. will be adversely affected. Further, establishing and maintaining an effective commercial organization requires significant attention of senior management. An adverse affect on revenue from the E.U. or the attention required by senior management to correct an ineffective organization could reduce our overall revenues and profitability.

We depend upon our key personnel and our ability to attract, train and retain employees.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. The loss of the services of any member of our senior management or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of one or more of our senior executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. While certain of our senior executive officers are parties to employment agreements with us, these agreements do not guarantee that they will remain employed with us in the future. In addition, in many cases, these agreements do not restrict their ability to compete with us after their employment is terminated. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

Our success depends on our ability to manage our growth.

Our rapid growth has strained our managerial, operational, financial and other resources. We expect this growth to continue. Based on the FDA and EC approval of Naglazyme for the treatment of MPS VI, we expect to devote additional resources in the immediate future to support the commercialization of Naglazyme.

To manage expansion effectively, we need to continue to develop and improve our research and development capabilities, manufacturing and quality capacities, sales and marketing capabilities and financial and administrative systems. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

Growth in our business may also contribute to fluctuations in our operating results, which may cause the price of our securities to decline. Our revenue may fluctuate due to many factors, including changes in:

- wholesaler buying patterns;

reimbursement rates;

physician prescribing habits; and

the availability or pricing of competitive products.

We may also experience fluctuations in our quarterly results due to price changes and sales incentives. For example, purchasers of our products, particularly wholesalers, may increase purchase orders in anticipation of a price increase and reduce order levels following a price increase. We occasionally offer sales incentives, such as price discounts and extended payment terms, in the ordinary course of business, that could have a similar impact. In addition, some of our products are subject to seasonal fluctuation in demand.

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Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.

Even if our drug products are approved, doctors must use treatments that require using those products. If doctors elect a different course of treatment from that which includes our drug products, this decision would reduce demand for our drug products and adversely affect revenues. For example, if in the future gene therapy becomes widely used as a treatment of genetic diseases, the use of enzyme replacement therapy, like Aldurazyme and Naglazyme in MPS diseases could be greatly reduced. Changes in treatment method can be caused by the introduction of other companies products or the development of new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities.

We are exposed to the potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceuticals. BioMarin/Genzyme LLC maintains product liability insurance for Aldurazyme with aggregate loss limits of $5.0 million. We have also obtained insurance against product liability lawsuits for commercial sale of our products and for the clinical trials of our product candidates with aggregate loss limits of $15.0 million plus additional clinical liability coverage with lower loss limits in other countries where clinical studies are conducted. Pharmaceutical companies must balance the cost of insurance with the level of coverage based on estimates of potential liability. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with the commercial use of Orapred, our clinical trials and commercial use of Aldurazyme and Naglazyme, our clinical trials for Phenoptin and Vibrilase, or our clinical trials for our terminated program for Neutralase, for which our insurance coverage may not be adequate.

The product liability insurance we will need to obtain in connection with the commercial sales of our product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. In addition, while we take, and continue to take what we believe are appropriate precautions, we may be unable to avoid significant liability if any product liability lawsuit is brought against us. If we are the subject of a successful product liability claim that exceeds the limits of any insurance coverage we obtain, we may incur substantial liabilities that would adversely affect our earnings and require the commitment of capital resources that might otherwise be available for the development and commercialization of our product programs.

We will incur increased costs as a result of recently enacted and proposed changes in laws and regulations.

We face burdens relating to the recent trend toward stricter corporate governance and financial reporting standards. New legislation or regulations that follow the trend of imposing stricter corporate governance and financial reporting standards, including compliance with Section 404 of the Sarbanes-Oxley Act of 2002, have led to an increase in our costs of compliance. The new rules could make it more difficult or more costly for us to obtain certain types of insurance, including directors and officers liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our Board committees or as executive officers. A failure to comply with these new laws and regulations may impact market perception of our financial condition and could materially harm our business. Additionally, it is unclear what additional laws or regulations may develop, and we cannot predict the ultimate impact of any future changes in law.

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Risks Related to the Notes and Our Common Stock

The notes will be unsecured and subordinated to our existing and future senior debt, which makes the claims of holders of senior debt senior to the claims of holders of the notes.

The notes will be unsecured and subordinated in right of payment to our existing and future senior debt. In the event of bankruptcy, liquidation or reorganization or upon acceleration of the notes due to an event of default and in specific other events, our assets will be available to pay obligations on the notes only after all senior debt and any secured debt has been paid in full in cash or other payment satisfactory to the holders of such indebtedness has been made. There may not be sufficient assets remaining to pay amounts due on any or all of the notes then outstanding. As a result of these payments, our general creditors may recover less, ratably, than the holders of our senior or secured debt and such general creditors may recover more, ratably, than the holders of our notes or our other subordinated debt. The indenture will not limit the creation of additional senior debt, secured debt or any other indebtedness. Any significant additional senior or secured debt incurred may also materially adversely impact our ability to service our debt, including the notes. In addition, the holders of our senior debt may, under certain circumstances, restrict or prohibit us from making payments on the notes. As of March 14, 2006, we had $113.0 million in senior debt outstanding, including $20.3 million secured senior debt. We anticipate that from time to time we may incur additional indebtedness, including senior debt.

The notes contain no financial covenants; therefore, the note holders will not have protection against adverse changes in our business.

The indenture does not contain any financial covenants, restrict our ability to repurchase our securities, pay dividends or make restricted payments or contain covenants or other provisions to afford holders protection in the event of a transaction that substantially increases the level of our indebtedness. Furthermore, the indenture contains only limited protections in the event of a fundamental change. We could engage in many types of transactions, such as acquisitions, refinancings or recapitalizations, that could substantially affect our capital structure and the value of the notes and our common stock but would not constitute a fundamental change permitting holders to required us to repurchase their notes under the indenture.

The notes are effectively subordinated to the liabilities of our subsidiaries, which may reduce our ability to use the assets of our subsidiaries to make payments on the notes.

The notes are not guaranteed by our subsidiaries and therefore the notes will be effectively subordinated to all existing and future indebtedness and other liabilities of our subsidiaries. In the event of a bankruptcy, liquidation or dissolution of a subsidiary, following payment by the subsidiary of its liabilities, the subsidiary may not have sufficient assets to make payments to us. As of March 14, 2006, our subsidiaries had no indebtedness outstanding (excluding intercompany debt and liabilities and accounts payable incurred in the ordinary course of business).

We may not have the ability to repurchase notes for cash pursuant to their terms.

In certain circumstances, you may require us to repurchase all or a portion of your notes in cash. If you were to require us to repurchase your notes, including following certain fundamental changes, we cannot assure you that we will be able to pay the amount required in cash. Our ability to repurchase the notes is subject to our liquidity position at the time, and may be limited by law, by the indenture, and by indebtedness and agreements that we may enter into in the future which may replace, supplement or amend our existing or future debt. In addition, if we did

not have sufficient cash to meet our obligations, while we could seek to obtain third-party financing to pay for any amounts due in cash upon such events, we cannot be sure that such third-party financing will be available on commercially reasonable terms, if at all. Our failure to repurchase the notes would constitute an event of default under the indenture under which we issued the notes, which would constitute a default under

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the terms of our existing credit facility and might constitute an event of default under the terms of our other indebtedness at that time.

The make-whole premium that may be payable upon conversion in connection with a fundamental change may not adequately compensate you for the lost option time value of your notes as a result of such change in control.

If you convert notes in connection with a fundamental change, we may be required to pay a make-whole premium by increasing the conversion rate. The make-whole payment is described under Description of the Notes Make-Whole Premium Upon a Fundamental Change. While the make-whole premium is designed to compensate you for the lost option time value of your notes as a result of a fundamental change, the make-whole amount is only an approximate of such lost value and may not adequately compensate you for such loss. In addition, in some other cases described below under Description of the Notes Make-Whole Premium Upon a Fundamental Change, there will be no such make-whole premium.

Because your right to require us to repurchase the notes is limited, the market price of the notes may decline if we enter into a transaction that is not a fundamental change under the indenture.

The term fundamental change is limited and may not include every event that might cause the market price of the notes to decline. The term fundamental change does not apply to transactions in which 95% of the consideration paid for our common stock, excluding cash payments for fractional shares and cash payments made in respect of dissenters appraisal rights, in a merger or similar transaction is publicly traded common stock. Our obligation to repurchase the notes upon a fundamental change may not preserve the value of the notes in the event of a highly leveraged transaction, reorganization, merger or similar transaction. See Description of the Notes Repurchase at Option of Holders Upon a Fundamental Change.

Conversion of the notes may dilute the ownership interest of existing stockholders, including holders who had previously converted their notes.

The conversion of some or all of the notes may dilute the ownership interests of existing stockholders, including holders who have previously converted their notes. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants because the conversion of the notes could depress the price of our common stock.

The conversion rate of the notes may not be adjusted for all dilutive events.

The conversion rate of the notes is subject to adjustment for certain events, including, among others, the issuance of stock dividends on our common stock, the issuance of rights or warrants to acquire shares of our common stock or securities convertible into shares of our common stock, subdivisions and combinations of our common stock, dividends of our capital stock, certain cash dividends and certain tender or exchange offers. The conversion rate will not be adjusted for other events, such as an issuance of shares of common stock for cash, that may adversely affect the trading price of the notes or our common stock. We cannot assure you that an event that adversely affects the value of the notes, but does not result in an adjustment to the conversion rate, will not occur.

If you hold notes, you are not entitled to any rights with respect to our common stock, but you are subject to all changes made with respect to our common stock.

If you hold notes, you are not entitled to any rights with respect to our common stock, including, without limitation, voting rights and rights to receive any dividends or other distributions on our common stock, but you are subject to all changes affecting the common stock. You will only be entitled to rights on the common stock if and when we deliver shares of common stock to you in exchange for your notes and in limited cases

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under the anti-dilution adjustments of the notes. For example, in the event that an amendment is proposed to our restated certificate of incorporation or bylaws requiring stockholder approval and the record date for determining the stockholders of record entitled to vote on the amendment occurs prior to delivery of the common stock, you will not be entitled to vote on the amendment, although you will nevertheless be subject to any changes in the powers or rights of our common stock.

You should consider the U.S. federal income tax consequences of owning the notes.

The U.S. federal income tax treatment of the conversion of the notes into our common stock is uncertain. You are urged to consult your tax advisors with respect to the U.S. federal income tax consequences resulting from the conversion of notes into our common stock.

You may have to pay taxes with respect to distributions on our common stock that you do not receive.

The conversion rate of the notes is subject to adjustment for certain events arising from stock splits and combinations, stock dividends and other actions by us that modify our capital structure. See Description of the Notes Conversion Rights. If the conversion rate is adjusted, under certain circumstances you may be deemed to have received a constructive dividend from us, resulting in ordinary income to you for U.S. federal income tax purposes, even though you would not receive any cash related to that adjustment and even though you might not exercise your conversion right. See Material U.S. Federal Income Tax Considerations.

An active trading market for the notes may not develop, and you may not be able to sell your notes at attractive prices or at all.

The notes are a new issue of securities for which there is currently no public market, and no active trading market might ever develop. If the notes are traded after their initial issuance, they may trade at a discount from their initial offering price, depending on prevailing interest rates, the market for similar securities, the price, and volatility in the price, of shares of our common stock, our performance and other factors. In addition, we do not know whether an active trading market will develop for the notes. To the extent that an active trading market does not develop, the liquidity and trading prices for the notes may be harmed.

We have no plans to list the notes on a securities exchange. We have been advised by the underwriter that it presently intends to make a market in the notes. However, the underwriter is not obligated to do so. Any market-making activity, if initiated, may be discontinued at any time, for any reason or for no reason, without notice. If the underwriter ceases to act as the market makers for the notes, we cannot assure you another firm or person will make a market in the notes.

The liquidity of any market for the notes will depend upon the number of holders of the notes, our results of operations and financial condition, the market for similar securities, the interest of securities dealers in making a market in the notes and other factors. An active or liquid trading market of the notes may not develop.

We expect that the trading price of the notes will be significantly affected by the trading price of our common stock.

Because the notes are convertible into shares of our common stock, volatility or depressed prices for our common stock could have a similar effect on the trading price of the notes. This may result in greater volatility in the trading price of the notes than would be expected for any non-convertible debt securities we may issue. Holders who receive our common stock upon conversion of the notes will also be subject to the risk of volatility and depressed prices of our common stock.

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An adverse rating of the notes may cause their trading prices to fall.

If a rating agency rates the notes, it may assign a rating that is lower than investors expectations. Rating agencies also may lower ratings on the notes in the future. If rating agencies assign a lower-than-expected rating or reduce, or indicate that they may reduce, their ratings in the future, the trading price of the notes could significantly decline.

We may issue additional shares of common stock and thereby materially and adversely affect the price of our notes.

We are not restricted from issuing additional shares of common stock during the life of the notes. If we issue additional shares of common stock, the price of our common stock, and in turn, the price of the notes may decline.

Our stock price may be volatile, and an investment in our stock could suffer a decline in value.

Our valuation and stock price since the beginning of trading after our initial public offering have had no meaningful relationship to current or historical earnings, asset values, book value or many other criteria based on conventional measures of stock value. The market price of our common stock will fluctuate due to factors including:

- product sales and profitability of Aldurazyme and Naglazyme and royalties received from Orapred;
- manufacture, supply or distribution of Aldurazyme, Naglazyme or Orapred;
- progress of our product candidates through the regulatory process;
- results of clinical trials, announcements of technological innovations or new products by us or our competitors;
- government regulatory action affecting our product candidates or our competitors drug products in both the U.S. and foreign countries;
- developments or disputes concerning patent or proprietary rights;
- general market conditions and fluctuations for the emerging growth and pharmaceutical market sectors;
- economic conditions in the U.S. or abroad;

broad market fluctuations in the U.S. or in the E.U.;

actual or anticipated fluctuations in our operating results; and

changes in company assessments or financial estimates by securities analysts.

In addition, the value of our common stock may fluctuate because it is listed on both the Nasdaq National Market and the Swiss Main Board. Listing on both exchanges may increase stock price volatility due to:

trading in different time zones;

different ability to buy or sell our stock;

different market conditions in different capital markets; and

different trading volume.

In the past, following periods of large price declines in the public market price of a company s securities, securities class action litigation has often been initiated against that company. Litigation of this type

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could result in substantial costs and diversion of management s attention and resources, which would hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

Anti-takeover provisions in our charter documents, our stockholders rights plan and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to the stockholders. Our anti-takeover provisions include provisions in our certificate of incorporation providing that stockholders meetings may only be called by the board of directors and provisions in our bylaws providing that the stockholders may not take action by written consent and requiring that stockholders that desire to nominate any person for election to the board of directors or to make any proposal with respect to business to be conducted at a meeting of our stockholders be submitted in appropriate form to our Secretary within a specified period of time in advance of any such meeting. Additionally, our board of directors has the authority to issue an additional 249,886 shares of preferred stock and to determine the terms of those shares of stock without any further action by our stockholders. The rights of holders of our common stock are subject to the rights of the holders of any preferred stock that may be issued. The issuance of preferred stock could make it more difficult for a third party to acquire a majority of our outstanding voting stock. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

In 2002, our board of directors authorized a stockholder rights plan and related dividend of one preferred share purchase right for each share of our common stock outstanding at that time. In connection with an increase in our authorized common stock, our board approved an amendment to this plan in June 2003. As long as these rights are attached to our common stock, we will issue one right with each new share of common stock so that all shares of our common stock will have attached rights. When exercisable, each right will entitle the registered holder to purchase from us one two-hundredth of a share of our Series B Junior Participating Preferred Stock at a price of $35.00 per 1/200 of a Preferred Share, subject to adjustment.

The rights are designed to assure that all of our stockholders receive fair and equal treatment in the event of any proposed takeover of us and to guard against partial tender offers, open market accumulations and other abusive tactics to gain control of us without paying all stockholders a control premium. The rights will cause substantial dilution to a person or group that acquires 15% or more of our stock on terms not approved by our board of directors. However, the rights may have the effect of making an acquisition of us, which may be beneficial to our stockholders, more difficult, and the existence of such rights may prevent or reduce the likelihood of a third party making an offer for an acquisition of us.

Our management will have broad discretion in how we use the net proceeds of this offering and the common stock offering.

We have not determined the specific allocation of the net proceeds from this offering and the concurrent common stock offering. Our management will have broad discretion over the use and investment of the net proceeds, and, accordingly, investors in this offering will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning management s specific intentions. Our management may spend a portion or all of the net proceeds in ways that our securityholders may not desire or that may not yield a favorable return. The failure of our management to apply the net proceeds from this offering and the concurrent common stock offering effectively could harm our business, financial condition and results of operations.

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RATIO OF EARNINGS TO FIXED CHARGES

We present below the ratio of our earnings to our fixed charges, which is computed by dividing earnings before taxes adjusted for fixed charges, minority interest and capitalized interest net of amortization by fixed charges. Fixed charges include interest expense and capitalized interest incurred, plus the portion of interest expense under operating leases deemed by us to be representative of the interest factor, plus amortization of the debt issuance costs.

	Year Ended December 31,				
	2005	2004	2003	2002	2001
Ratio of earnings to fixed charges					

For the years ended December 31, 2001, 2002, 2003, 2004 and 2005, no ratios are provided because earnings were insufficient to cover fixed charges. Earnings were inadequate to cover fixed charges by $57.4 million in 2001, $77.4 million in 2002, $76.4 million in 2003, $187.4 million in 2004 and $74.3 million in 2005.

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USE OF PROCEEDS

We expect to receive approximately $145.2 million from the sale of our notes in this offering, or $167.1 million if the underwriter exercises its overallotment option in full, after deducting the estimated underwriting discount and offering expenses that we are to pay. We estimate that the net proceeds from the common stock offering will be approximately $110.9 million, or $127.6 million if the underwriters exercise their overallotment option in full, after deducting the underwriting discount and our estimated offering expenses.

We intend to apply the net proceeds of these offerings towards the commercialization of our products; additional clinical trials of Phenoptin, BH_4 for other indications, Phenylase and Vibrilase; preclinical studies and clinical trials for our other product candidates; potential licenses and acquisitions of complementary technologies, products and companies; general corporate purposes, including acquisition costs related to the purchase of our facility located at 46 Galli Drive for which we are currently under contract; and working capital. We may also use a portion of the proceeds of these offerings to purchase some or all of our 3.50% convertible subordinated notes due 2008 pursuant to the redemption provisions of the indenture governing such notes whereby we have the right to call the notes beginning June 20, 2006 or in one or more privately negotiated transactions from time to time.

The time and amount of our actual expenditures are subject to change and will be based on many factors, including:

- the amount of cash actually generated in this offering and the concurrent common stock offering;
- the progress, timing and scope of our preclinical studies and clinical trials;
- the time and cost necessary to obtain regulatory approvals;
- the time and cost necessary to develop commercial manufacturing processes, including quality systems and to build or acquire manufacturing capability;
- the time and cost necessary to respond to technological and market developments; and
- any changes made or new developments in our existing collaborative, licensing and other commercial relationships or any new collaborative, licensing and other commercial relationships that we may establish.

We have discussions from time to time regarding potential acquisitions and licensing opportunities. Although we may use a portion of the net proceeds for this purpose, we currently have no material agreements or commitments in this regard. We reserve the right, at the sole discretion of our Board of Directors, to reallocate our use of proceeds in response to these and other factors. Until we use the net proceeds of this offering, we intend to invest the funds in investment grade, interest-bearing securities.

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PRICE RANGE OF COMMON STOCK

Our common stock is quoted on the Nasdaq National Market and traded on the SWX Swiss Exchange under the symbol BMRN. The following table shows the high and low sale prices for our common stock as reported by the Nasdaq National Market during the periods indicated:

	High	Low
Year Ended December 31, 2003		
First Quarter	$ 12.30	$ 5.79
Second Quarter	13.67	9.16
Third Quarter	10.89	7.00
Fourth Quarter	8.47	6.60
Year Ended December 31, 2004		
First Quarter	8.87	7.09
Second Quarter	8.12	5.53
Third Quarter	6.66	4.50
Fourth Quarter	6.49	3.87
Year Ended December 31, 2005		
First Quarter	6.41	4.40
Second Quarter	7.77	4.75
Third Quarter	9.47	7.02
Fourth Quarter	11.70	6.94
Year Ended December 31, 2006		
First Quarter (through March 23, 2006)	15.29	10.55

The last reported sale price of our common stock on the Nasdaq National Market on March 23, 2006 was $13.13 per share. As of March 14, 2006, there were 89 holders of record of our common stock. Additionally, as of March 14, 2006, options to acquire 8,049,183 shares of our common stock were outstanding under our stock option plans.

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CAPITALIZATION

The following table shows:

- our actual capitalization as of December 31, 2005; and
- our capitalization as adjusted to give effect to both our issuance and sale of $150,000,000 aggregate principal amount of notes in this offering, and our concurrent issuance of 9,000,000 shares of common stock in the common stock offering at the public offering price of $13.00 per share, after deducting the underwriting discount and estimated offering expenses payable by us.

	As of December 31, 2005	
(in thousands, except for share and per share data)	**Actual**	**As Adjusted**
Cash, cash equivalents and short-term investments and cash balances relating to long term debt[1]	$ 64,841	$ 320,969
Long-term debt, including current portion		
2.50% senior subordinated convertible notes due 2013	$	$ 150,000
3.50% convertible subordinated notes due 2008	125,000	125,000
Acquisition obligation, net of discount	78,350	78,350
Equipment and facility loan	20,909	20,909
Total long-term debt	$ 224,259	$ 374,259
Stockholders equity		
Common stock, par value $0.001 per share: 150,000,000 shares authorized; 74,301,610 shares issued and outstanding, actual and 83,301,610 shares issued and outstanding, as adjusted	$ 75	$ 84
Additional paid-in capital	485,570	596,460
Accumulated other comprehensive loss	(16)	(16)
Accumulated deficit	(563,091)	(563,091)
Total stockholders equity/(deficit)	$ (77,462)	$ 33,437
Total capitalization	$ 146,797	$ 407,696

(1) Cash, cash equivalents, short-term investments and cash balances relating to long-term debt includes $17.0 million of cash balances relating to long-term debt that is a portion of the $25.0 million that we are required to keep on deposit with the lender pursuant to the terms of the equipment and facility loan that we entered into in May 2004.

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The table above assumes no exercise of the underwriters overallotment option in this offering or the concurrent common stock offering. In addition, the number of shares of our common stock in the actual and as adjusted columns in the table above excludes:

- 6,968,569 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $8.60 per share as of December 31, 2005;
- 8,922,198 shares of our common stock issuable upon the conversion of our $125.0 million 3.50% convertible subordinated notes due 2008; and
- shares of common stock reserved for issuance upon conversion of the senior subordinated convertible notes being offered by us in this offering.

The table set forth above assumes that none of the proceeds from this offering or the concurrent common stock offering will be applied to the purchase of our 3.50% convertible subordinated notes due 2008.

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DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We currently intend to retain any future earnings to finance operations and the expansion of our business and do not intend to declare or pay cash dividends on our capital stock in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors and will depend upon our results of operations, financial condition, current and anticipated cash needs, contractual restrictions, restrictions imposed by applicable law and other factors that our Board of Directors deems relevant.

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DESCRIPTION OF THE NOTES

This description highlights some information concerning the notes to be sold in this offering. We have included in this description what we believe is the most important information concerning the notes. However, this description may not contain all of the information that is important to you. Important information is incorporated by reference into this prospectus supplement. To understand the notes fully, you should read carefully the entire prospectus supplement and the accompanying prospectus, including Risk Factors, the incorporated consolidated financial statements and related notes and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

The notes will be issued under a supplemental indenture. The supplemental indenture supplements the indenture between us and Wilmington Trust Company, as trustee. We refer to the supplemental indenture together with the indenture, as the indenture. Copies of the form of indenture and the notes will be made available to prospective investors in the notes upon request to us.

We have summarized portions of the indenture and the notes below. This summary is not complete and is subject to, and qualified by references to, all of the provisions of the indenture and the notes. We urge you to read the indenture and the notes because they define your rights as a holder of the notes. Capitalized terms not defined in this description have the meanings given them in the indenture. In this section, BioMarin, we, our and us each refers only to BioMarin Pharmaceutical Inc. and not to any existing or future subsidiary.

General

The notes are our unsecured, senior subordinated obligations and are convertible into our common stock as described under Conversion Rights below. The notes are limited to an aggregate principal amount of $150,000,000 (or $172,500,000 if the underwriter exercises its overallotment option in full) and will mature on March 29, 2013.

The notes bear interest at the rate of 2.50% per year from the date of issuance of the notes, or from the most recent date to which interest had been paid or provided for. Interest is payable semi-annually in arrears on September 29 and March 29 of each year, commencing September 29, 2006 to holders of record at the close of business on the preceding September 14 and March 14, respectively. Interest is computed on the basis of a 360-day year comprised of twelve 30-day months. In the event of the maturity, conversion or purchase by us at the option of the holder of a note, interest ceases to accrue on the note under the terms of, and subject to the conditions of, the indenture.

Principal is payable, and notes may be presented for conversion, registration of transfer and exchange, without service charge, at our office or agency in New York, New York, which is initially the office or agency of the trustee in New York, New York.

The indenture does not contain any financial covenants or any restrictions on the payment of dividends, the incurrence of senior debt (as defined below) or other indebtedness, or the issuance or repurchase of securities by us. The indenture does not contain any covenants or other provisions to protect holders of the notes in the event of a highly leveraged transaction or a change of control, except to the extent described under Make-Whole Premium Upon a Fundamental Change and Repurchase at Option of Holders Upon a Fundamental Change below.

Ranking

The notes will be unsecured obligations and will be:

- subordinated in right of payment, as provided in the indenture, to the prior payment in full of all of our existing and future senior debt,

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equal in right of payment with all of our existing and future senior subordinated debt, and

senior in right of payment to all of our existing and future subordinated debt, including, without limitation, our $125.0 million 3.50% convertible subordinated notes due 2008.

As of March 14, 2006, we had $113.0 million of senior debt outstanding. The indenture does not restrict the incurrence by us or our existing or future subsidiaries of indebtedness or other obligations. The term senior debt means all the

principal of,

premium, if any, on,

interest, including all interest accruing subsequent to the commencement of any bankruptcy or similar proceeding, whether or not a claim for post-petition interest is allowable as a claim in any such proceeding, on,

rent payable on,

termination payments with respect to or in connection with, and

fees, costs, expenses and other amounts accrued or due on or in connection with,

our Indebtedness (as defined below), whether outstanding on the date of the indenture or subsequently created, incurred, assumed, guaranteed or in effect guaranteed by us, including all deferrals, renewals, extensions or refundings of, or amendments, modifications or supplements to, the preceding, except for:

any Indebtedness that by its terms expressly provides that such indebtedness shall not be senior in right of payment to the notes or expressly provides that such indebtedness is equal with or junior in right of payment to the notes, and

any Indebtedness between or among us or any of our subsidiaries, a majority of the voting stock of which we directly or indirectly own.

The term senior subordinated debt means, with respect to us, the notes and any other indebtedness of ours that specifically provides that such indebtedness is to have the same rank as the notes in right of payment and is not subordinated by its terms in right of payment to any indebtedness or other obligations of ours that is not senior indebtedness.

The term Indebtedness means, with respect to any person:

all indebtedness, obligations and other liabilities, contingent or otherwise, of that person:

for borrowed money, including obligations in respect of overdrafts, foreign exchange contracts, currency exchange agreements, interest rate protection agreements, and any loans or advances from banks, whether or not evidenced by notes or similar instruments, or

evidenced by bonds, notes or other instruments for the payment of money, or

incurred in connection with the acquisition of any property, services or assets, whether or not the recourse of the lender is to the whole of the assets of such person or to only a portion thereof, other than any account payable or other accrued current liability or obligation to trade creditors incurred in the ordinary course of business in connection with the obtaining of materials or services;

all reimbursement obligations and other liabilities, contingent or otherwise, of that person with respect to letters of credit, bank guarantees, bankers acceptances, surety bonds, performance bonds or other guaranty of contractual performance;

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all obligations and liabilities, contingent or otherwise, in respect of:

leases of such person required, in conformity with generally accepted accounting principles, to be accounted for as capitalized lease obligations on the balance sheet of such person, and

any lease or related documents, including a purchase agreement, in connection with the lease of real property which provides that such person is contractually obligated to purchase or cause a third party to purchase the leased property and thereby guarantee a minimum residual value of the leased property to the landlord and the obligations of such person under such lease or related document to purchase or to cause a third party to purchase the leased property;

all obligations of such person, contingent or otherwise, with respect to an interest rate or other swap, cap or collar agreement or other similar instrument or agreement or foreign currency hedge, exchange, purchase or similar instrument or agreement;

all direct or indirect guaranties or similar agreements by that person in respect of, and obligations or liabilities, contingent or otherwise, of that person to purchase or otherwise acquire or otherwise assure a creditor against loss in respect of, indebtedness, obligations or liabilities of another person of the kind described in the first four bullet points above;

any indebtedness or other obligations described in the first four bullet points above secured by any mortgage, pledge, lien or other encumbrance existing on property which is owned or held by such person, regardless of whether the indebtedness or other obligation secured thereby shall have been assumed by such person; and

any and all deferrals, renewals, extensions, refinancings, replacements, restatements and refundings of, or amendments, modifications or supplements to, any indebtedness, obligation or liability of the kind described in any of the six bullet points above.

Any senior debt will continue to be senior debt and will be entitled to the benefits of the subordination provisions irrespective of any amendment, modification or waiver of any of its terms.

The indenture will provide that in the event of any payment or distribution of our assets upon our dissolution, winding up, liquidation or reorganization, the holders of our senior debt shall first be paid in respect of all senior debt in full in cash or other payment satisfactory to the holders of senior debt before we make any payments of principal of, or premium, if any, and interest on the notes. In addition, if the notes are accelerated because of an event of default, the holders of any senior debt would be entitled to payment in full in cash or other payment satisfactory to the holders of senior debt of all obligations in respect of senior debt before the holders of the notes are entitled to receive any payment or distribution. Under the indenture, we must promptly notify holders of senior debt if payment of the notes is accelerated because of an event of default.

The indenture will further provide that if any default by us has occurred and is continuing in the payment of principal of, premium, if any, or interest on, rent or other payment obligations in respect of, any senior debt, then no payment shall be made on account of principal of, premium, if any, or interest on the notes until all such payments due in respect of that senior debt have been paid in full in cash or other payment satisfactory to the holders of that senior debt.

Because of these subordination provisions, if we become insolvent, funds which we would otherwise use to pay the holders of notes will be used to pay the holders of senior debt. As a result of these payments, our general creditors may recover less, ratably, than holders of senior debt and

such general creditors may recover more, ratably, than holders of notes.

The notes are effectively subordinated to all existing and future liabilities of our subsidiaries. Any right we have to receive assets of our existing subsidiary or any future subsidiaries upon the latter s liquidation or reorganization (and the consequent right of the holders of the notes to participate in those assets) will be

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effectively subordinated to the claims of that subsidiary s creditors, except to the extent that we are ourselves 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 on the ability of our existing subsidiary or any future subsidiaries to incur indebtedness or other liabilities. As of March 14, 2006, our existing subsidiaries had no indebtedness outstanding (excluding intercompany debt and liabilities and accounts payable in the ordinary course of business).

We will be obligated to pay reasonable compensation to the trustee and to indemnify the trustee on terms reasonably satisfactory to it against any losses, liabilities or expenses it incurs in connection with its duties relating to the notes. The trustee s claims for such payments will be senior to those of holders of the notes in respect of all funds collected or held by the trustee.

Conversion Rights

Holders may convert their notes into shares of our common stock at any time prior to the stated maturity, unless the notes have been previously redeemed or purchased. For each $1,000 principal amount of the notes surrendered for conversion, a holder may convert any outstanding notes into our common stock at an initial conversion rate of 60.3318 shares of our common stock per note, equal to an initial conversion price of approximately $16.58. Upon conversion in connection with a fundamental change, we will pay a make-whole premium to holders of notes upon the conversion of their notes.

The conversion rate and the equivalent conversion price in effect at any given time are referred to as the applicable conversion rate and the applicable conversion price, respectively, and will be subject to adjustment as described below. A holder may convert fewer than all of such holder s notes so long as the amount of notes converted is an integral multiple of $1,000 principal amount.

Upon conversion of a note, a holder will not receive any cash payment of interest (unless in certain circumstances such conversion occurs between a regular record date and the interest payment date to which it relates) and we will not adjust the conversion rate to account for accrued and unpaid interest. Our delivery to the holder of the full number of shares of our common stock into which the note is convertible, together with any cash payment for such holder s fractional shares, will be deemed to satisfy our obligation to pay the principal amount of the note and our obligation to pay accrued and unpaid interest. As a result, any accrued but unpaid interest to the conversion date is deemed to be cancelled, extinguished and forfeited upon conversion. For a discussion of the tax treatment to you of receiving our common stock upon conversion, see Material U.S. Federal Income Tax Considerations.

If a holder converts notes, we will pay any documentary, stamp or similar issue or transfer tax due on the issuance of shares of our common stock upon the conversion, unless the tax is due because the holder requests the shares to be issued or delivered to a person other than the holder, in which case the holder will pay that tax.

If a holder wishes to exercise its conversion right, such holder must deliver an irrevocable duly completed conversion notice, together, if the notes are in certificated form, with the certificated security, to the conversion agent along with appropriate endorsements and transfer documents, if required, and pay any transfer or similar tax, if required. The conversion agent will, on the holder s behalf, convert the notes into shares of our common stock. Holders may obtain copies of the required form of the conversion notice from the conversion agent. A certificate, or a book-entry transfer through The Depository Trust Company, New York, New York, or DTC, for the number of full shares of our common stock into which any notes are converted, together with a cash payment for any fractional shares, will be delivered through the conversion agent as soon as practicable, but no later than the fifth business day, following the conversion date. The trustee will initially act as the conversion agent.

If a holder has already delivered a purchase notice as described under Repurchase at Option of Holders Upon a Fundamental Change with respect to a note, however, the holder may not surrender that note for conversion until the holder has withdrawn the purchase notice in accordance with the indenture.

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Holders may surrender their notes for conversion to shares of our common stock at the applicable conversion rate at any time prior to the close of business on the second business day immediately preceding the stated maturity date. The notes and the shares issuable upon conversion of the notes will be registered under the Securities Act on the date the notes are issued. We will use our best efforts to ensure that, upon conversion of the notes, the shares so issued will be registered. In the event that, despite our best efforts, we are unable to deliver registered shares, we may issue unregistered shares upon conversion of the notes.

Holders of notes at the close of business on a regular record date will receive payment of interest payable on the corresponding interest payment date notwithstanding the conversion of such notes at any time after the close of business on the applicable regular record date. Notes surrendered for conversion by a holder during the period from the close of business on any regular record date to the opening of business on the next interest payment date must be accompanied by payment of an amount equal to the interest that the holder is to receive on the notes; *provided*, *however*, that no such payment need be made (1) if we have specified a purchase date following a fundamental change that is after a record date and on or prior to the next interest payment date, (2) only to the extent of overdue interest, if any overdue interest exists at the time of conversion with respect to such note, or (3) if conversion occurs after the last record date prior to the maturity date.

Adjustment of Conversion Price

The initial conversion rate will be adjusted for certain events, including:

- the issuance of our common stock as a dividend or distribution on our common stock;
- certain subdivisions and combinations of our common stock;
- the issuance to all or substantially all holders of our common stock of certain rights or warrants to purchase our common stock (or securities convertible into our common stock) at less than (or having a conversion price per share less than) the current market price of our common stock;
- the dividend or other distribution to all or substantially all holders of our common stock of shares of our capital stock (other than common stock) or evidences of our indebtedness or our assets (including securities, but excluding those rights and warrants referred to above and dividends and distributions in connection with a reclassification, change, consolidation, merger, combination, sale or conveyance resulting in a change in the conversion consideration pursuant to the second succeeding paragraph or dividends or distributions paid exclusively in cash);
- dividends or other distributions consisting exclusively of cash to all or substantially all holders of our common stock; and
- payments to holders of our common stock pursuant to a tender or exchange offer made by us or any of our subsidiaries.

In the event that we pay a dividend or make a distribution on shares of our common stock consisting of capital stock of, or similar equity interests in, as described in the fourth bullet point above, a subsidiary or other business unit of ours, the conversion rate will be adjusted based on the market value of the securities so distributed relative to the market value of our common stock, in each case based on the average sale prices of those securities for the 10 trading days commencing on and including the fifth trading day after the date on which ex-dividend trading commences for such dividend or distribution on the Nasdaq National Market or such other national or regional exchange or market on which the securities are then listed or quoted.

If any adjustment of the conversion rate would be less than 1% of the then effective rate, such adjustment shall be carried forward and adjustment with respect thereto made at the time of and together with any subsequent adjustment which, together with the original adjustment shall aggregate at least 1% of the then effective conversion rate; provided, however, that any carry forward amount shall be paid to the holder upon conversion regardless of the 1% threshold.

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Under the provisions of our Rights Agreement (as defined below) holders will receive, and if we implement a new stockholder rights plan, this new rights plan must provide that upon conversion of the existing notes the holders will receive, in addition to the common stock issuable upon such conversion, the rights under such rights plan unless the rights have separated from the common stock before the time of conversion, in which case the conversion rate will be adjusted as if we distributed to all holders of our common stock, shares of our capital stock, evidences of indebtedness or assets as described above, subject to readjustment in the event of the expiration, termination or redemption of such rights.

Except as stated above, the conversion rate will not be adjusted for the issuance of our common stock or any securities convertible into or exchangeable for our common stock or carrying the right to purchase any of the foregoing.

In the case of:

- any recapitalization, reclassification or change of our common stock, other than changes resulting from a subdivision or combination,
- a consolidation, merger or combination involving us,
- a sale, conveyance or lease to another corporation of all or substantially all of our property and assets, or
- any statutory share exchange,

in each case as a result of which holders of our common stock are entitled to receive stock, other securities, other property or assets (including cash or any combination thereof) with respect to or in exchange for our common stock, the holders of the notes then outstanding will be entitled thereafter to convert those notes into the kind and amount of shares of stock, other securities or other property or assets (including cash or any combination thereof) which they would have owned or been entitled to receive upon such business combination had such notes been converted into our common stock immediately prior to such business combination. We may not become a party to any such transaction unless its terms are consistent with the preceding. None of the foregoing provisions shall affect the right of a holder of notes to convert its notes into shares of our common stock prior to the effective date of such transaction.

In the event holders of our common stock have the opportunity to elect the form of consideration to be received in such business combination, we will make adequate provision whereby the holders of the notes shall have a reasonable opportunity to elect the form of consideration into which all of the notes, treated as a single class, shall be convertible from and after the effective date of such business combination. Such determination shall be based on the weighted average of elections made by holders of the notes who participate in such determination, shall be subject to any limitations to which all of the holders of our common stock are subject, such as pro-rata reductions applicable to any portion of the consideration payable in such business combination and shall be conducted in such a manner as to be completed by the date which is the earliest of (a) the deadline of elections to be made by our stockholders, and (b) two trading days prior to the anticipated effective date. We will provide notice of the opportunity to determine the form of such consideration, as well as notice of the determination made by holders of the notes (and the weighted average of elections) by issuing a press release and providing a copy of such notice to the trustee. In the event the effective date is delayed beyond the initially anticipated effective date, holder of the notes may be given the opportunity to make subsequent similar determinations in regard to such delayed effective date.

If we make a distribution of property to holders of our common stock that would be taxable to them as a dividend for U.S. federal income tax purposes and the conversion rate is increased, this increase would generally be deemed to be the receipt of taxable income by U.S. holders (as

defined in Material U.S. Federal Income Tax Considerations) of the notes and would generally result in withholding taxes for non-U.S. holders (as defined in

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Material U.S. Federal Income Tax Considerations). Because this deemed income would not give rise to any cash from which any applicable withholding tax could be satisfied, we may offset any such withholding tax applicable to non-U.S. holders against cash payments of interest payable on the notes. See Material U.S. Federal Income Tax Considerations Consequences to U.S. Holders Constructive Dividends and Consequences to Non-U.S. Holders Dividends.

We may from time to time, to the extent permitted by law, increase the conversion rate of the notes by any amount for any period of at least 20 days. In that case we will give at least 15 days notice of such increase. We may make such increase in the conversion rate, in addition to those set forth above, as our board of directors deems advisable to avoid or diminish any income tax to holders of our common stock resulting from any dividend or distribution of stock (or rights to acquire stock) or from any event treated as such for income tax purposes.

Make-Whole Premium Upon a Fundamental Change

If a fundamental change, other than a fundamental change described under the third bullet point under the definition of a change of control described below under Repurchase at Option of Holders Upon a Fundamental Change, occurs, in certain circumstances, we will pay a make-whole premium upon the conversion of the notes in connection with any such transaction by increasing the conversion rate on such notes. The make-whole premium will be in addition to, and not in substitution for, any cash, securities or other assets otherwise due to holders of notes upon conversion. The make-whole premium will be determined by reference to the table below and is based on the date on which the fundamental change becomes effective, referred to as the effective date, and the price, referred to as the stock price, paid, or deemed to be paid, per share of our common stock in the transaction constituting the fundamental change, subject to adjustment as described below. If holders of our common stock receive only cash in the fundamental change, the stock price shall be the cash amount paid per share. In all other cases, the stock price shall be the average closing sale price of our common stock for the 15 trading days immediately prior to but not including the effective date.

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The following table shows what the make-whole premium would be for each hypothetical stock price and effective date set forth below, expressed as additional shares of common stock per $1,000 principal amount of notes.

	Effective Date							
Stock Price on Effective Date	**3/29/06**	**3/29/07**	**3/29/08**	**3/29/09**	**3/29/10**	**3/29/11**	**3/29/12**	**3/29/13**
$13.00	16.5913	16.5913	16.5913	16.5913	16.5913	16.5913	16.5913	0.0000
15.00	12.6663	12.9378	13.1829	13.3647	13.3613	12.9979	11.7576	0.0000
17.50	9.2976	9.3644	9.3828	9.3121	9.0334	8.3743	6.8025	0.0000
20.00	6.9641	6.9180	6.8082	6.6020	6.1983	5.4322	3.8758	0.0000
22.50	5.3608	5.1665	4.9946	4.7229	4.2680	3.5059	2.1229	0.0000
25.00	4.8289	4.3311	3.7837	3.3693	2.9181	2.2103	1.0502	0.0000
27.50	4.3856	3.9347	3.4421	2.8881	2.2799	1.5994	0.8419	0.0000
30.00	4.0272	3.6079	3.1567	2.6464	2.0829	1.4645	0.7716	0.0000
35.00	3.4457	3.0987	2.7100	2.2684	1.7843	1.2508	0.6581	0.0000
40.00	3.0253	2.7037	2.3724	1.9884	1.5626	1.0952	0.5748	0.0000
45.00	2.6976	2.4108	2.1138	1.7707	1.3932	0.9751	0.5093	0.0000
50.00	2.4278	2.1705	1.8893	1.5955	1.2573	0.8796	0.4620	0.0000
55.00	2.2023	1.9778	1.7196	1.4547	1.1416	0.7975	0.4225	0.0000
60.00	2.0281	1.8157	1.5732	1.3353	1.0485	0.7362	0.3879	0.0000
70.00	1.7303	1.5553	1.3565	1.1486	0.8969	0.6317	0.3330	0.0000
80.00	1.5176	1.3630	1.1852	1.0087	0.7874	0.5537	0.2902	0.0000
90.00	1.3574	1.2119	1.0617	0.8946	0.6991	0.4902	0.2581	0.0000
100.00	1.2186	1.0957	0.9566	0.8038	0.6285	0.4413	0.2323	0.0000

The hypothetical stock prices and additional share amounts set forth above are based on a common stock price of $13.00 per share on March 23, 2006 and an initial conversion price of $16.58 per share.

The actual stock price and effective date may not be set forth on the table, in which case:

- if the actual stock price on the effective date is between two stock prices on the table or the actual effective date is between two effective dates on the table, the make-whole premium will be determined by a straight-line interpolation between the make-whole premiums set forth for the two stock prices and the two effective dates on the table based on a 365-day year, as applicable.

- if the stock price on the effective date exceeds $100.00 per share, subject to adjustment as described below, no make-whole premium will be paid.

- if the stock price on the effective date is less than $13.00 per share, subject to adjustment as described below, no make-whole premium will be paid.

The stock prices set forth in the first column of the table above will be adjusted as of any date on which the conversion rate of the notes is adjusted. The adjusted stock prices will equal the stock prices applicable immediately prior to such adjustment multiplied by a fraction, the numerator of which is the conversion rate immediately prior to the adjustment giving rise to the stock price adjustment and the denominator of which is the conversion rate as so adjusted. The number of additional shares set forth in the table above will be adjusted in the same manner as

the conversion rate as set forth above under Conversion Rights, other than by operation of an adjustment to the conversion rate by adding the make-whole premium as described above.

A conversion of the notes by a holder will be deemed for these purposes to be in connection with a fundamental change if the conversion notice is received by the conversion agent on or subsequent to the date 20

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calendar days prior to the date announced by us as the anticipated effective date of the fundamental change but before the close of business on the business day immediately preceding the related repurchase date. We will notify holders of notes of the anticipated effective date of any fundamental change as promptly as practicable following the date we publicly announce such fundamental change, but in no event less than 20 days prior to such date.

Notwithstanding the foregoing, in no event will the conversion rate exceed 76.9231 per $1,000 principal amount of notes, subject to adjustments in the same manner as the conversion rate.

The additional shares will be delivered upon the later of the settlement date for the conversion and promptly following the effective date of the fundamental change transaction.

Our obligation to pay the make-whole premium may constitute a penalty under applicable contract law, and therefore its enforceability cannot be assured.

Repurchase at Option of Holders Upon a Fundamental Change

If a fundamental change occurs, each holder of notes will have the right to require us to repurchase all or any portion of that holder s notes that is equal to $1,000 or a whole multiple of $1,000, on the date that is 45 days after the date we give notice at a repurchase price, payable in cash, equal to 100% of the principal amount of the notes to be repurchased, together with interest accrued and unpaid to, but excluding, the repurchase date.

As promptly as practicable following the date we publicly announce such transaction, but in no event less than 20 days prior to the anticipated effective date of a fundamental change, we are required to give notice to all holders of notes, as provided in the indenture, of the occurrence of the fundamental change and of their resulting repurchase right. We must also deliver a copy of our notice to the trustee. To exercise the repurchase right, a holder of notes must deliver prior to or on the 30th day after the date of our notice irrevocable written notice to the trustee of the holder s exercise of its repurchase right, together with the notes with respect to which the right is being exercised. We will also disseminate a press release through Dow Jones & Company, Inc. or Bloomberg Business News announcing the occurrence of the fundamental change or publish that information in a newspaper of general circulation in New York City or on our website, or through such other public medium as we deem appropriate at that time.

A fundamental change will be deemed to have occurred upon a change of control or a termination of trading, each as defined below.

A change of control will be deemed to have occurred at such time after the original issuance of the notes when the following has occurred:

- the acquisition by any person, including any syndicate or group deemed to be a person under Section 13(d)(3) of the Securities Exchange Act of 1934, as amended (Exchange Act), of beneficial ownership, directly or indirectly, through a purchase, merger or other acquisition transaction or series of transactions of shares of our capital stock entitling that person to exercise 50% or

more of the total voting power of all shares of our capital stock entitled to vote generally in elections of directors, other than any acquisition by us, any of our subsidiaries or any of our employee benefit plans;

our consolidation or merger with or into any other person, any merger of another person into us, or any conveyance, transfer, sale, lease or other disposition of all or substantially all of our properties and assets to another person, other than:

any transaction

that does not result in any reclassification, conversion, exchange or cancellation of outstanding shares of our capital stock, and

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pursuant to which holders of our capital stock immediately prior to the transaction have the entitlement to exercise, directly or indirectly, 50% or more of the total voting power of all shares of our capital stock entitled to vote generally in the election of directors of the continuing or surviving person immediately after the transaction; or

any merger solely for the purpose of changing our jurisdiction of incorporation and resulting in a reclassification, conversion or exchange of outstanding shares of common stock solely into shares of common stock of the surviving entity;

during any consecutive two-year period, individuals who at the beginning of that two-year period constituted our board of directors, together with any new directors whose election to our board of directors, or whose nomination for election by our stockholders, was approved by a vote of a majority of the directors then still in office who were either directors at the beginning of such period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority of our board of directors then in office; or

our stockholders pass a resolution approving a plan of liquidation or dissolution.

However, a change in control will not be deemed to have occurred if, in the case of a merger or consolidation, at least 95% of the consideration (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 notes become convertible solely into such common stock.

A termination of trading will be deemed to have occurred if our common stock or other common stock into which the notes are convertible is neither listed for trading on a U.S. national securities exchange nor approved for listing on Nasdaq or any similar U.S. system of automated dissemination of quotations of securities prices, or traded in over-the-counter securities markets, and no American Depositary Shares or similar instruments for such common stock are so listed or approved for listing in the U.S.

The beneficial owner shall be determined in accordance with Rule 13d-3 promulgated by the SEC under the Exchange Act. The term person includes any syndicate or group which would be deemed to be a person under Section 13(d)(3) of the Exchange Act.

Rule 13e-4 under the Exchange Act requires the dissemination of certain information to security holders if an issuer tender offer occurs and may apply if the repurchase option becomes available to holders of the notes. We will comply with this rule to the extent applicable at that time.

We may, to the extent permitted by applicable law, at any time purchase the notes in the open market or by tender at any price or by private agreement. Any note so purchased by us may, to the extent permitted by applicable law, be reissued or resold or may be surrendered to the trustee for cancellation. Any notes surrendered to the trustee may not be reissued or resold and will be canceled promptly.

The preceding provisions would not necessarily protect holders of the notes if highly leveraged or other transactions involving us occur that may adversely affect holders.

Our ability to repurchase notes upon the occurrence of a fundamental change is subject to important limitations. The occurrence of a fundamental change could cause an event of default under, or be prohibited or limited by, the terms of existing or future senior debt. As a result, any repurchase of the notes would, absent a waiver, be prohibited under the subordination provisions of the indenture until the senior debt is paid in full.

Further, we cannot assure you that we would have the financial resources, or would be able to arrange financing, to pay the repurchase price for all the notes that might be delivered by holders of notes seeking to

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exercise the repurchase right. Any failure by us to repurchase the notes when required following a fundamental change would result in an event of default under the indenture, whether or not such repurchase is permitted by the subordination provisions of the indenture. Any such default may, in turn, cause a default under existing or future senior debt. See Ranking above.

No Stockholder Rights for Holders of Notes

Holders of notes, as such, will not have any rights as our stockholders (including, without limitation, voting rights and rights to receive any dividends or other distributions on shares of our common stock), except in limited circumstances described above under Adjustment of Conversion Rate.