

BONE CARE INTERNATIONAL INC

Form S-3/A

April 29, 2004

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As filed with the Securities and Exchange Commission on April 29, 2004

Registration No. 333-113763

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Amendment No. 1
to
Form S-3
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933

Bone Care International, Inc.

(Exact name of registrant as specified in its charter)

Wisconsin

(State or other jurisdiction of incorporation or organization)

39-1527471

(I.R.S. Employer Identification No.)

1600 Aspen Commons
Middleton, Wisconsin 53562
(608) 662-7800

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Brian J. Hayden
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Middleton, Wisconsin 53562
(608) 662-7800

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement becomes effective.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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

SUBJECT TO COMPLETION, DATED APRIL 29, 2004

PROSPECTUS

4,500,000 Shares

Bone Care International, Inc.

Common Stock

\$ _____ per share

We are selling 4,000,000 shares of our common stock and the selling stockholder named in this prospectus is selling 500,000 shares. We will not receive any proceeds from the sale of the shares by the selling stockholder. We have granted the underwriters an option to purchase up to 675,000 additional shares of common stock to cover over-allotments.

Our common stock is quoted on the Nasdaq National Market under the symbol BCII. The last reported sale price of our common stock on the Nasdaq National Market on April 28, 2004 was \$25.11 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page 7.

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

	<u>Per Share</u>	<u>Total</u>
Public Offering Price	\$	\$
Underwriting Discount	\$	\$
Proceeds to Bone Care (before expenses)	\$	\$
Proceeds to the selling stockholder (before expenses)	\$	\$

The underwriters expect to deliver the shares to purchasers on or about _____, 2004.

Bear, Stearns & Co. Inc.

Citigroup

Robert W. Baird & Co.

First Albany Capital

Roth Capital Partners

, 2004

You should rely only on the information contained in or incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

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The terms "Bone Care", "Company", "we", "our" and "us" refer to Bone Care International, Inc. unless the context suggests otherwise. The term "investor" refers to a prospective investor. The term "Hectorol" refers to Hectorol® brand doxercalciferol.

Bone Care® is a registered trademark of Bone Care International, Inc. in the United States. Hectorol® is a registered trademark of Bone Care International, Inc. in the United States, the European Community, Japan and other selected countries. Hectorol is Bone Care's brand name for the active drug substance, doxercalciferol. This prospectus also includes trademarks of other companies.

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SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus. This summary is not complete and may not contain all of the information that investors should consider before investing in our common stock. Investors should read the entire prospectus carefully. This summary is not intended to be a complete description of the matters covered in this prospectus and is subject to, and qualified in its entirety by reference to the more detailed information and financial statements (including the notes thereto) included or incorporated by reference in this prospectus.

Bone Care International, Inc.

We are an emerging pharmaceutical company engaged in the discovery, development and commercialization of innovative therapeutic products to treat the unmet medical needs of patients with debilitating conditions and life-threatening diseases. Our current commercial and therapeutic focus is in nephrology utilizing Hectorol, our novel vitamin D hormone therapy, to treat secondary hyperparathyroidism in patients with moderate to severe chronic kidney disease and end-stage renal disease. Secondary hyperparathyroidism is a disease characterized by excessive secretion of parathyroid hormone which, if left untreated, can eventually result in cardiovascular disease, reduced immune system function, muscle weakness and bone mineral loss and fractures. The majority of patients with moderate to severe chronic kidney disease and most end-stage renal disease patients suffer from this disease. Hectorol, a safe and effective pro-hormone therapy in the management of secondary hyperparathyroidism in moderate to severe chronic kidney disease and end-stage renal disease, reduces elevated levels of parathyroid hormone while maintaining consistent levels of vitamin D with a low incidence of adverse events. Vitamin D therapies are currently used to treat patients with a variety of diseases, including kidney disease, osteoporosis and psoriasis, and research has shown that they may be useful in treating certain cancers such as prostate, breast and colon. Our principal clinical development programs focus on chronic kidney disease and hyperproliferative disorders such as cancer and psoriasis.

We have two products approved by the U.S. Food and Drug Administration (FDA): Hectorol Injection and Hectorol Capsules. Hectorol Injection and 2.5 mcg Hectorol Capsules are approved for the treatment of secondary hyperparathyroidism in end-stage renal disease. 0.5 mcg Hectorol Capsules are approved for the treatment of secondary hyperparathyroidism in moderate to severe chronic kidney disease. We obtained FDA approval for 2.5 mcg Hectorol Capsules in June 1999, and we began selling this orally administered product in the U.S. in October 1999. We obtained FDA approval for Hectorol Injection in April 2000. We launched this intravenous product in the U.S. in August 2000 and we received a national Medicare reimbursement code for Hectorol Injection in January 2002. The National Kidney Foundation estimates that as of 2003 there were approximately 300,000 end-stage renal disease patients in the U.S. and projects that this population will double by 2010. In April 2004 we obtained FDA approval for 0.5 mcg Hectorol Capsules to treat secondary hyperparathyroidism in moderate to severe chronic kidney disease prior to end-stage renal disease, or pre-dialysis. We intend to launch this product in July 2004. We are also developing Hectorol and other vitamin D hormones for expanded indications.

In October 2003, the National Kidney Foundation published the Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. These guidelines, referred to as the K/DOQI guidelines, include recommendations for the treatment of bone disease and disorders of calcium and phosphorus metabolism which may encourage a shift in clinical practice to begin earlier treatment of patients with Stages 3 and 4 (moderate to severe) chronic kidney disease, in addition to Stage 5 (end-stage renal disease) chronic kidney disease. The National Kidney Foundation estimates that as of 2003 there were approximately 7,600,000 Stage 3 patients, 400,000 Stage 4 patients and 300,000 Stage 5 patients. According to the United States Renal Data System, approximately 65% of Stage 5 patients are treated with vitamin D hormone therapy. We believe that this potential shift in practice, together with our recently approved expanded indication for Hectorol Capsules, could expand the potential use of Hectorol to a broader range of chronic kidney disease patients.

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Recent Developments

On April 26, 2004, we announced that the FDA approved a new indication and strength for Hectorol Capsules. 0.5 mcg Hectorol Capsules are now approved for the treatment of secondary hyperparathyroidism in the earlier stages (Stages 3 and 4) of chronic kidney disease prior to end-stage renal disease.

On April 28, 2004, we announced our financial results for the third fiscal quarter ended March 31, 2004. We reported quarterly sales for Hectorol of \$11.6 million, compared to Hectorol sales of \$3.1 million for the third fiscal quarter of 2003, representing an increase of \$8.5 million, or 277 percent. Sales of Hectorol were \$28.9 million for the first nine months of fiscal 2004, an increase of \$16.7 million, or 136 percent from the same period of fiscal 2003.

Our net profit for the third fiscal quarter of 2004 was \$0.3 million, or \$0.02 per common share, compared with a net loss for the third fiscal quarter of 2003 of \$4.6 million, or \$0.33 per common share. The net loss for the first nine months of fiscal 2004 was \$2.3 million, or \$0.16 per common share, compared with a net loss of \$10.4 million, or \$0.73 per common share, for the same period of fiscal 2003. We ended the third fiscal quarter of 2004 with a total of \$12.9 million in cash and short and long-term investments, representing an increase of \$1.0 million over the total of \$11.9 million in cash and short and long-term investments at the end of the second fiscal quarter of 2004.

Business Strategy

Our strategy is to build a specialty pharmaceutical company with a strong distribution channel through research, development, commercialization and acquisition of key therapeutics. We plan to achieve these goals by:

expanding our sales and marketing infrastructure;

expanding the indications for Hectorol;

developing additional product offerings;

licensing and acquiring compounds that fit into our strategic plans; and

entering into strategic partnerships to globally commercialize our current products and assets or new products.

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Products and Pipeline

The following table summarizes the status of our products and our product development programs:

We have two FDA approved products: Hectorol Injection and Hectorol Capsules. Hectorol Injection and 2.5 mcg Hectorol Capsules are approved for the treatment of secondary hyperparathyroidism in end-stage renal disease. 0.5 mcg Hectorol Capsules are approved for the treatment of secondary hyperparathyroidism in moderate to severe chronic kidney disease.

We believe that Hectorol offers the following benefits:

Safe and Effective Treatment. Data obtained from our clinical trials have demonstrated that Hectorol is a safe and effective therapy for treating secondary hyperparathyroidism in moderate to severe chronic kidney disease and end-stage renal disease.

Oral Delivery that Expands Market Opportunities. Hectorol Capsules provide a safe, convenient and effective oral vitamin D therapy for the management of parathyroid hormone levels in patients with moderate to severe chronic kidney disease and end-stage renal disease. Oral Hectorol has the potential to be used in other clinical settings besides chronic kidney disease and end-stage renal disease.

A Pro-Hormone that Provides Consistent Levels of Natural Vitamin D Hormones. Hectorol is a vitamin D pro-hormone, an inactive vitamin D analog that is metabolized by the liver into two active and naturally occurring vitamin D hormones. Activated Hectorol is released into the bloodstream at a rate which mimics the normal physiologic production of active vitamin D hormones by normal kidneys. Normal physiologic blood levels of vitamin D hormones allow efficient regulation of parathyroid hormone secretion by the parathyroid glands with few side effects.

A Potentially Wider Therapeutic Window. We believe that there is indirect evidence through animal studies that Hectorol has a wider range, or therapeutic window, between a minimum effective dose and a dose with significant side effects, as compared to other vitamin D hormone therapies. A wider therapeutic window would improve safety and facilitate improved patient management.

We currently have two products in development, LR-103 and BCI-202, for the treatment of secondary hyperparathyroidism.

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In addition to having a role in parathyroid function and calcium and phosphorus metabolism, vitamin D hormones have an important role in regulating the growth and differentiation of skin, prostate, breast and colon cells. We are investigating the use of Hectorol Capsules, LR-103 and BCI-202 in diseases associated with hyperproliferative or neoplastic cell growth such as cancers of the prostate and breast and psoriasis.

Our principal executive offices are located at 1600 Aspen Commons, Middleton, Wisconsin 53562 and our telephone number is (608) 662-7800. Our web site is located at <http://www.bonecare.com>. Information on our website is not part of this prospectus.

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The Offering

Unless specifically stated, information in this prospectus assumes the underwriters will not exercise their over-allotment option and no other person will exercise any other outstanding options.

Common Stock offered by Bone Care 4,000,000 shares

Common Stock offered by Selling
Stockholder 500,000 shares

Common Stock outstanding after the
offering 18,339,485 shares

Use of proceeds We intend to use the proceeds from this offering for general corporate purposes, which we anticipate will include our efforts in one or more of the following areas: commercialization of 0.5 mcg Hecitorol Capsules in the pre-dialysis market, commercialization of Hecitorol in the dialysis market, development of alternative and secondary sources of supply of our products, development of non-renal clinical indications for Hecitorol, expansion of our research and development activities, and acquisition of complementary licenses, products, technologies or companies.

Nasdaq National Market symbol BCII

The number of shares of our common stock to be outstanding after this offering is based on the number of shares outstanding as of April 1, 2004, and excludes:

2,225,785 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of \$8.76 per share;

543,052 shares of common stock reserved for future grants under our stock option plans; and

up to 675,000 shares of common stock that the underwriters may purchase from us if they exercise their over-allotment option.

Risk Factors

You should consider the risk factors before investing in our common stock and the impact from various events which could adversely affect our business. See Risk Factors.

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You should read this summary financial data in conjunction with the discussion in Management's Discussion and Analysis of Financial Condition and Results of Operations and the financial statements and notes thereto included elsewhere in this prospectus. The statements of operations data set forth below for each of the years ended June 30, 2003, 2002 and 2001, and the balance sheet data as of June 30, 2003, 2002 and 2001 are derived from, and are qualified by reference to, the audited financial statements and notes thereto included elsewhere in this prospectus and should be read in conjunction with those financial statements and notes. The statements of operations data set forth below for the six months ended December 31, 2003 and 2002, and the balance sheet data as of December 31, 2003 and 2002 are derived from our financial statements which are unaudited but which in the opinion of management have been prepared on the same basis as the audited financial statements and include all adjustments necessary (consisting of normal recurring adjustments) for a fair presentation of the results for such periods. Interim results may not be indicative of results for the remainder of the year. Our historical results are not necessarily indicative of results to be expected for any future period.

	Year Ended June 30,			Six Months Ended December 31,	
	2001	2002	2003	2002	2003
(In thousands, except per share data)					
Statements of Operations Data:					
Product sales	\$ 5,997	\$ 14,991	\$ 19,518	\$ 9,160	\$ 17,241
Cost and expenses:					
Cost of product sales from related party			1,689		2,854
Cost of product sales from others	1,905	3,557	5,294	2,969	1,995
Research and development	4,556	5,739	6,019	3,371	3,446
Selling, general and administrative	9,859	13,856	18,768	8,946	11,628
	<u>16,320</u>	<u>23,152</u>	<u>31,770</u>	<u>15,286</u>	<u>19,923</u>
Loss from operations	(10,323)	(8,161)	(12,252)	(6,126)	(2,682)
Interest income, net	1,309	1,257	574	367	102
Net loss	<u>\$ (9,014)</u>	<u>\$ (6,904)</u>	<u>\$ (11,678)</u>	<u>\$ (5,759)</u>	<u>\$ (2,580)</u>
Net loss per common share-basic and diluted	<u>\$ (0.70)</u>	<u>\$ (0.49)</u>	<u>\$ (0.82)</u>	<u>\$ (0.41)</u>	<u>\$ (0.18)</u>
Shares used in computing basic and diluted net loss per common share	<u>12,884</u>	<u>14,084</u>	<u>14,175</u>	<u>14,157</u>	<u>14,270</u>

	As of June 30,			As of December 31,	
	2001	2002	2003	2002	2003
(In thousands)					
Balance Sheet Data:					
Cash and cash equivalents	\$ 1,843	\$ 2,024	\$ 3,065	\$ 2,253	\$ 2,328
Marketable securities	15,080	18,437	13,625	16,685	8,650
Long-term securities	14,424	3,720	913	1,939	911
Long-term liabilities			650	438	
Shareholders' equity	38,098	32,024	20,443	26,231	18,455

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RISK FACTORS

You should consider carefully the risks described below before making a decision to buy our common stock. The risks and uncertainties described below are not the only ones facing our company. If any of the following risks actually occur, our business, financial condition or results of operations would likely suffer. In that event, the trading price of our common stock could decline, and you may lose all or part of your investment. You should also refer to the other information contained in or incorporated by reference into this prospectus, including the financial statements and related notes.

Risks Related to Our Business

Our business is at an early stage of development and we do not have a significant history for you to evaluate us on.

Our business is at an early stage of commercialization and product development, and historically has not had significant revenues or positive cash flow. Even if we are able to achieve positive cash flow from operations, we will face many challenges as we strive to maintain profitability. Hectorol Injection is approved for one indication and Hectorol Capsules are approved for two indications. Our product candidates and any expansion of indications for our current products will require extensive research and development and clinical testing before we can submit a new drug application to the FDA. In addition, we have not commercialized Hectorol in foreign markets. The successful commercialization of Hectorol or any of our other product candidates will require significant further research, testing, development and regulatory approvals and additional investment. There can be no assurance that we will be successful in any of our commercialization efforts. Our experience with, and history in, conducting these activities has been limited. Any predictions you make about our future success or viability may not be as accurate as they would be if we had a longer operating history.

We have a history of losses and our losses may continue.

We have incurred losses since we began operating. As of December 31, 2003, our accumulated deficit was \$55,778,286. To date, we have primarily spent our funds on product development and more recently on sales, marketing and manufacturing expenses incurred to commercialize Hectorol Injection and Hectorol Capsules. In fiscal year 2004 and subsequent fiscal years, we plan to make large expenditures to manufacture, market and sell Hectorol and to develop other products, which may result in losses in future periods. These expenditures include costs associated with continuing our research and development, performing clinical trials for new products, expanding our patent portfolio and seeking U.S. and foreign regulatory approvals for Hectorol, and business development activities. The amount of these expenditures is difficult to forecast accurately. It is possible, depending on the rate at which our revenues increase and our marketing, research and development, and other business development activities expand, that our losses will continue. Our ability to generate revenues in the near future will depend primarily on our ability to continue to obtain products manufactured by third parties and on our success in marketing and selling Hectorol Injection and Hectorol Capsules. We do not know whether we will achieve profitability or, if we do, whether we will be able to sustain profitability.

We currently derive all of our revenue from Hectorol, and expect to do so for the foreseeable future. If sales of Hectorol decrease, our results of operations will be significantly adversely affected.

We currently derive all of our revenue from the sale of Hectorol. In June 1999, we received FDA approval to market 2.5 mcg Hectorol Capsules in the U.S. to manage secondary hyperparathyroidism in kidney dialysis patients and began selling 2.5 mcg Hectorol Capsules in October 1999. In April 2000, we received FDA approval to market Hectorol Injection to manage secondary hyperparathyroidism in dialysis patients and began selling Hectorol Injection in the U.S. in August 2000. In April 2004 we obtained FDA approval for 0.5 mcg Hectorol Capsules to manage secondary hyperparathyroidism in pre-dialysis patients with moderate to severe chronic kidney disease and we intend to begin selling this product in the U.S. in July 2004. We believe that sales of Hectorol Capsules and Hectorol Injection will continue to constitute

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a significant portion of our total revenues for the foreseeable future. Accordingly, any factor adversely affecting sales of Hectorol, such as the introduction by other companies of generic equivalents of Hectorol or alternatives to Hectorol or any delay in marketing for pre-dialysis, may have a material adverse effect on our results of operations. There can be no assurance that the vitamin D hormone market will not decline in the future.

We may not be able to commercialize our existing or new products if we do not enter into successful strategic alliances or other marketing arrangements.

As part of our business strategy, we plan to establish strategic partnerships, alliances and commercialization arrangements with partners who can penetrate geographic markets and compete in therapeutic areas where we have no current or planned sales presence. In addition, we may seek to enter into strategic alliances or collaborations in connection with the development or commercialization of new products. We have been in discussions with several potential collaborators but have not entered into any agreements. We may not be able to negotiate collaborative arrangements on acceptable terms, if at all. If we are not able to establish collaborative arrangements, we will have to either delay further development of some of our programs or increase our expenditures and undertake the development activities at our own expense. We may encounter significant delays in commercializing our products or find that the development, manufacture or sale of our products is hindered due to the absence of collaborative agreements.

We have no experience establishing and maintaining collaborative agreements. In the event that we are able to enter into collaborative agreements, such agreements may pose additional risks, including the following:

the terms of our contracts with our collaborators may not be favorable to us in the future;

a collaborator with marketing and distribution rights to one or more of our products may not commit enough resources to the marketing and distribution of such products;

disputes with our collaborators may arise, leading to delays in or termination of the development or commercialization of our products, or resulting in significant litigation or arbitration;

contracts with our collaborators may fail to provide significant remedies if one or more of them fail to perform;

our contracts with collaborators may be terminated and we may not be able to replace our collaborators;

in some circumstances, if a collaborator terminates an agreement, or if we are found to be in breach of our obligations, we may be unable to secure all of the necessary intellectual property rights and regulatory approval to continue developing the same compound or product; and

our collaborators could independently develop, or develop with third parties, products that compete with ours.

If we make any acquisitions, we will incur a variety of costs and may never realize the anticipated benefits.

If appropriate opportunities become available, we may attempt to acquire licenses, technologies, products or companies that we believe fit strategically with our business. We currently have no understandings, commitments or arrangements with respect to any such acquisitions. If we do undertake any transaction of this sort, the process of integrating an acquired license, technology, product or company may result in operating difficulties and expenditures and may absorb significant management attention that would otherwise be available for our ongoing business development plans. Moreover, we may never realize the anticipated benefits of any acquisition. Future acquisitions could result in in-process research and development expenses, potentially dilutive issuances of equity securities, the incurrence of debt, contingent

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liabilities and/or impairment of goodwill and amortization or impairment of other intangible assets, which could adversely affect our business, financial condition and results of operations.

We have limited experience commercializing our products and may not be able to successfully do so.

To date, our experience in commercializing our products has been limited to marketing Hectorol to treat patients with end-stage renal disease. In order to successfully commercialize Hectorol or any other products, we will need to have adequate sales, marketing and distribution capabilities in place. Our sales force has been limited in number, current product experience and training. We have only recently begun to expand our sales force and marketing capabilities, and our efforts to expand may not be successful. We may not be able to attract skilled sales/marketing personnel in a timely manner or at all. In addition, we may not be able to maintain a commercial infrastructure with the technical expertise to support manufacturing oversight, product release and distribution capabilities. If we are unsuccessful in our commercialization efforts, our growth prospects will be diminished.

We lack sufficient long-term data regarding the safety and efficacy of Hectorol and we could find that our long-term data do not support our current clinical findings which may limit our efforts to commercialize Hectorol.

Hectorol is supported by less than five years of patient follow-up, and therefore, we could discover that our current clinical results cannot be supported by actual long-term clinical experience. If longer-term patient studies or clinical experience indicate that treatments with our products do not provide patients with sustained benefits, our sales could significantly decline. If longer-term patient studies or clinical experience indicate that our procedures cause tissue or muscle damage, motor impairment or other negative effects, we could be subject to significant liability. We are not certain how long it may take for patients to show significant increases in side effects. Further, because some of our data have been produced in studies that are not randomized and involved small patient groups, our data may not be reproduced in wider patient populations.

We have not conducted prospective clinical trials comparing Hectorol and competitive vitamin D hormone therapies in end-stage renal disease. We, and others not affiliated with us, have compared the toxicity and efficacy of Hectorol to some other vitamin D hormone therapies (1- α -calcidol and calcitriol) in rats and mice. We cannot be sure, however, that the results of additional clinical trials will prove that our assumptions, based on animal studies, are correct as applied to humans. Hectorol may not compare favorably to existing or new vitamin D hormone therapies. If Hectorol or our future products do not prove to be superior to competing products, we may face severe difficulties and may incur greater marketing expenses. If additional clinical trials prove that Hectorol is inferior to competitive vitamin D hormone therapies, we may be forced to suspend our efforts to commercialize Hectorol and to delay or suspend our planned efforts to develop Hectorol for additional indications.

If the medical community does not accept our products, our business will suffer.

The success of our products depends on acceptance of those products by the medical community, which is based on a number of factors including:

perceptions about the safety and efficacy of our products;

cost-effectiveness of our products relative to competing products;

availability of reimbursement for our products from government or third-party payors; and

effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

If doctors and patients do not use our products, we may not become profitable. We cannot predict how quickly, if at all, the medical community will accept our products or the extent to which these products will be used. If we encounter difficulties introducing our products into our targeted markets, our operating results and business may be substantially impaired.

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Reimbursement for Hectorol or any future products could be reduced or modified.

Sales of our products will depend, in part, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar health care management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. These health care management organizations and third-party payors are increasingly challenging the prices charged for medical products and services and frequently require predetermined discounts from list prices. Additionally, the containment of health care costs has become a priority of federal and state governments, and the prices of drugs have been targeted in this effort. Our current and potential products may not be considered cost effective, and reimbursement to the consumer may not be available or sufficient to allow us to sell our products on a competitive basis. Legislation and regulations affecting reimbursement for our products have recently changed and may change at any time, including in ways that are adverse to us. Currently, only Hectorol Injection is eligible to be reimbursed under Medicare but there is no guarantee as to the level of this reimbursement or whether it will continue at all. Any reduction in Medicare or other third-party payor reimbursements could have a negative effect on our operating results.

Failure to raise additional funds in the future may delay or eliminate some or all of our efforts to develop, manufacture and sell Hectorol and any of our future products.

Based upon our current plans, we believe that, without the proceeds of this offering, we have sufficient funds to meet our operating expenses and capital requirements for at least the next twelve months. Thereafter, we may need to raise additional capital to fund our operations. Additional required financing may not be available on satisfactory terms, if at all. If we are unable to obtain financing in the future, we may have to seek alternative sources of capital or re-evaluate our operating plans, or we may be required to delay, reduce or eliminate some or all of our research and development activities or sales and marketing efforts, in which case our operating results and business may be substantially impaired.

Our expenditures on sales and marketing, research and development, regulatory, quality and compliance activities have been substantial to date and are planned to increase in the future. We cannot be sure that our estimates of expenditures for Hectorol and the development of our other new products will be accurate. The scope and amount of our liquidity and capital requirements will depend upon many factors, including the extent to which Hectorol gains market acceptance, the progress and success of our clinical trials, the timing and cost involved in obtaining regulatory approvals, the timing and cost of developing sales and marketing programs, our ability to enter into strategic alliances, manufacturing and research and development activities and competitive developments.

We currently have no manufacturing capabilities so we must rely exclusively on suppliers who are outside of our control to manufacture our products, including Hectorol.

The manufacture of pharmaceutical products requires significant expertise, oversight, and capital investment. We do not have the internal capability to manufacture pharmaceutical products, and we currently use others to formulate, manufacture and package Hectorol and other drug candidates and manufacture our active pharmaceutical ingredient. Our manufacturers are required to adhere to current Good Manufacturing Practices regulations enforced by the FDA. Our dependence upon others to manufacture our active pharmaceutical ingredient and products may adversely affect our profit margins and our ability to develop and commercialize products on a timely and competitive basis. Delays or difficulties with contract manufacturers in manufacturing active pharmaceutical ingredient and producing, packaging or distributing our products would adversely affect the results of operations of Hectorol or introduction of other products. If we were to need to seek alternative sources of supply, we may be unable to enter into alternative supply arrangements on commercially acceptable terms, if at all. Any disruption of these activities could impede our ability to sell our products, which would significantly reduce our results of operations.

All of our suppliers have FDA inspected facilities that are required to operate under current Good Manufacturing Practices regulations established by the FDA. In December 2001, Akorn, Inc. (previously

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the sole manufacturer of Hectorol Injection) halted production of Hectorol Injection until such time as certain general deviations from the FDA's current Good Manufacturing Practices could be remediated. The FDA's site inspection, which concluded in February 2003, resulted in additional inspectional observations that preclude submission of a supplement with respect to the manufacture and process improvements at Akorn. Accordingly, supply of Hectorol Injection was constrained from December 2002 to March 2003. We entered into a manufacturing agreement with Draxis Pharma Inc., a subsidiary of Draxis Health Inc., to serve as a manufacturer of Hectorol Injection and began commercial distribution in March 2003. There is no assurance that Draxis will have sufficient production capacity to meet future demand or that Draxis will perform its contractual obligations.

We purchase our active pharmaceutical ingredient for Hectorol from a sole supplier, although we are currently in the process of obtaining regulatory approval for an additional supplier. We rely on one supplier to formulate Hectorol Capsules and another supplier to package Hectorol Capsules. In addition, one of our suppliers is located in the Middle East, a geographic location subject to increased political instability, which could disrupt or halt the operations of this supplier. Although we believe that other suppliers may be available, any change in suppliers could cause an increase in cost, a delay in manufacturing, and a possible loss of sales, any of which would affect operating results adversely. All of our current suppliers are, and any future suppliers will be, subject to extensive government regulation by the FDA and other comparable foreign regulators.

While we currently do not intend to manufacture any products ourselves, we may choose to do so in the future. If we were to manufacture products ourselves, we would need substantial additional financing to build manufacturing facilities and to hire and train qualified personnel. We also would be subject to additional regulatory requirements and would be subject to risks associated with delays or difficulties encountered in manufacturing a product. We may not be able to manufacture any products successfully or in a cost-effective manner.

If we are unable to receive approval of our Phase IV commitments for Hectorol Capsules from the FDA or are otherwise required to meet any additional FDA obligation with respect to Hectorol Injection, our operating results and business will be substantially impaired.

After initial FDA or other health authority approval has been obtained, further studies, including Phase IV post-marketing studies, may be required to provide additional data on safety. The FDA or other regulatory authorities may also require post-marketing reporting to monitor the side effects of a drug. Results of post-marketing requirements may limit the marketing of such products.

The FDA allowed us to market 2.5 mcg Hectorol Capsules to end-stage renal disease patients, but required us to complete post-approval Phase IV research and development pertaining to the analysis of this product and its active ingredients by July 2000. We have completed and submitted the results of our Phase IV commitments for 2.5 mcg Hectorol Capsules to the FDA. We do not know if the FDA will be fully satisfied with our response or will require additional future Phase IV commitments. In addition, in connection with our recent FDA approval of 0.5 mcg Hectorol Capsules, the FDA required us to commit to complete, by April 2006, a post-marketing Phase IV study of 0.5 mcg Hectorol Capsules in pediatric patients ages 5 through 18 with Stage 3 or 4 chronic kidney disease, pre-dialysis. We are also required to complete, by February 2007, a post-marketing Phase IV study of 0.5 mcg Hectorol Capsules in adult vitamin D sufficient patients with Stage 3 or 4 chronic kidney disease to address recommendations made in the K/DOQI guidelines. Lastly, we are required to complete, by June 2008, a post-marketing Phase IV carcinogenicity study in a single species. We do not know if we will be able to timely complete these studies, if the FDA will be satisfied with the results or if the FDA will require additional post-marketing commitments.

We cannot assure you that we will obtain regulatory approvals for Hectorol or any of our future products.

Obtaining required regulatory approvals may take several years to complete and consume substantial capital resources. There can be no assurance that the FDA or any other regulatory authority will act

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quickly or favorably on any of our current or future requests for product approval, or that the FDA or any other regulatory authority will not require us to provide additional data that we do not currently anticipate to obtain product approvals. We cannot apply for FDA approval to market our future products until we successfully complete pre-clinical and clinical trials. If we are not able to obtain regulatory approvals for use of our future products, or if the patient populations for which they are approved are not sufficiently broad, the commercial success of these products could be limited.

We filed an investigational new drug application in September of 2003 for LR-103. Our investigational new drug will be tested in refractory cancer patients. Several factors could prevent successful completion or cause significant delays of these trials, including an inability to enroll the required number of patients or failure to demonstrate adequately that the product is safe and effective for use in humans. If safety problems develop, we or the FDA could stop our trials before completion.

Our failure to obtain regulatory approvals in foreign jurisdictions would prevent us from marketing our products abroad.

We may also market our products in international markets, including the European Union and Japan. In order to do so, we must obtain separate regulatory approvals from these other foreign jurisdictions. The regulatory approval processes differ among these jurisdictions. Approval in any one jurisdiction does not ensure approval in a different jurisdiction. Hectorol has not been approved for marketing by any governmental entity outside of the U.S. except for 2.5 mcg Hectorol Capsules which are approved in Canada. We will require substantial additional funds to develop the product, conduct clinical trials and gain the necessary regulatory approvals for Hectorol Injection, Hectorol Capsules or other products in foreign countries. As a result, in order to commercialize our products outside the U.S. we will need to invest additional resources or enter into arrangements with partners.

Our success depends on our key personnel, the loss of whom could impair our business.

Our success depends upon our ability to attract and retain qualified personnel including our management, scientific, regulatory, sales, marketing and financial personnel. Pharmaceutical companies, academic and government organizations, research institutions and other entities compete for the services of qualified personnel. We may not be able to attract and retain such personnel. Furthermore, our anticipated growth and expansion into areas and activities requiring additional expertise will require additional personnel.

Our failure to expand our management systems and controls to support anticipated growth could harm our business.

Sustaining our growth has placed significant demands on management and our administrative, operational, information technology, financial and personnel resources. Accordingly, our future operating results will depend on the ability of our officers and other key employees to continue to implement and improve our operational, quality compliance, regulatory support and financial control systems, and effectively expand, train and manage our employee base. We may not be able to manage our growth successfully, which could seriously harm our operating results and business.

Risks Related to Our Industry

We have many competitors, several of which have significantly greater financial and other resources.

We face competition from several companies that are focused on developing vitamin D hormone therapies, particularly to treat secondary hyperparathyroidism and hyperproliferative diseases. We also compete with other companies that produce vitamin D hormones and vitamin D hormone analogs for international marketplaces where these treatments have already been approved for secondary hyperparathyroidism and hyperproliferative diseases. Competition may increase further as additional companies begin to enter our markets and/or modify their existing products to compete directly with ours. Companies also compete indirectly with us utilizing different therapeutic approaches. Many of our competitors have

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substantially greater financial, research and development and marketing resources than we do and may be better equipped to develop, manufacture and market products. Our competitors include companies that market products that compete with Hectorol Injection and Hectorol Capsules and may in the future include companies that are developing vitamin D hormone therapies to treat cancer or psoriasis.

Our competitors may have broad product lines which allow them to negotiate exclusive, long-term supply contracts and offer comprehensive pricing for their products. Broader product lines may also provide our competitors with a significant advantage in marketing competing products to group purchasing organizations and other managed care organizations that are increasingly seeking to reduce costs through centralized purchasing. Greater financial resources and product development capabilities may allow our competitors to respond more quickly to new or emerging technologies and changes in customer requirements that may render our products obsolete. These technological developments may result in Hectorol becoming obsolete or non-competitive.

If our competitors develop more effective and/or affordable products, or achieve earlier patent protection or product commercialization than we do, our operations will likely be negatively affected.

We also face competition for marketing, distribution and collaborative development agreements, for establishing relationships with academic and research institutions, and for licenses to intellectual property. In addition, academic institutions, government agencies and other public and private research organizations also may conduct research, seek patent protection and establish collaborative arrangements for discovery, research, clinical development and marketing of products similar to ours. These companies and institutions compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our programs.

Our products and development activities are subject to extensive government regulation, which could make it more expensive and time-consuming for us to conduct our business and could adversely affect the manufacturing and marketing of our products.

Any new drug product, including any new indication for Hectorol, must undergo lengthy and rigorous clinical testing and other extensive, costly and time-consuming procedures mandated by the FDA and foreign regulatory authorities. We may elect to delay or cancel our anticipated regulatory submissions for new indications for Hectorol or proposed new products for a number of reasons, including:

- unanticipated clinical testing results;
- lack of sufficient resources;
- changes in, or adoption of, new FDA regulations;
- unanticipated enforcement of existing regulations or guidelines;
- an inability to enroll the required number of patients in trials;
- unexpected technological developments; and
- developments by our competitors.

The FDA continues to review products even after they receive FDA approval. The manufacture, distribution and marketing of Hectorol is subject to extensive ongoing regulation, including compliance with the FDA's current Good Manufacturing Practices, adverse event reporting requirements and the FDA's general prohibitions against promoting products for off-label uses, or uses not listed on the FDA-approved labeling. We and our manufacturers also are subject to inspection and market surveillance by the FDA for compliance with these and other requirements. Failure to comply with these requirements could result in:

- warning letters;
- finer;

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civil penalties;

injunctions;

recall or seizure of products;

total or partial suspension of production;

refusal of the government to grant approvals; or

withdrawal of existing approvals and criminal prosecution.

Any such enforcement action could adversely affect the manufacturing and marketing of our products.

We must also comply with numerous federal, state and local laws, regulations and recommendations relating to safe working conditions, current Good Laboratory Practices and the experimental use of animals. Additionally, products using inventions that are fully or partially funded by federal research grants are subject to government rights. We cannot predict the extent of government regulation or the impact of new governmental regulations which might have an adverse effect on the discovery, development, production and marketing of our products, and require us to incur significant costs to comply with the regulations.

Our customer base is highly concentrated and if we lose any of our customers, our business could be materially harmed.

Our customers primarily consist of wholesale distributors of pharmaceutical products. Five individual wholesale distributors represented 95% of our net revenues for the six months ended December 31, 2003, with the largest of those distributors representing 43% of net revenues. The loss or bankruptcy of any of these customers could materially and adversely affect our results of operations and financial condition.

We are exposed to product liability risks which may exceed our existing coverage and could result in significant liabilities and costly litigation.

Our business exposes us to potential product liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical products. The use of our products in the marketplace and the use of our products and drug candidates in clinical trials ma