BONE CARE INTERNATIONAL INC
Form 10-K
September 29, 2003

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO
SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED JUNE 30, 2003

COMMISSION FILE NUMBER 0-27854

BONE CARE INTERNATIONAL, INC.
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

WISCONSIN	39-1527471
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)
1600 ASPEN COMMONS MIDDLETON, WISCONSIN (Address of Principal Executive Offices)	53562 (Zip Code)

Registrant's Telephone Number, Including Area Code: (608) 662-7800

Securities registered pursuant to Section 12(b) of the Act:

NONE

Securities registered pursuant to Section 12(g) of the Act:

COMMON STOCK, WITHOUT PAR VALUE
PREFERRED STOCK PURCHASE RIGHTS
(Title of Class)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes [X] No [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [ ]

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Exchange Act).
Yes [X] No [ ]

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was $141,577,720 as of December 31, 2002, assuming solely for purposes of this calculation that all directors and executive officers of the registrant are "affiliates." This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of September 15, 2003, there were 14,283,130 shares of the Registrant's Common Stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Bone Care International, Inc., Proxy Statement for its 2003 Shareholders Meeting to be held on November 19, 2003 (Part III).

BONE CARE INTERNATIONAL, INC.

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FOR THE YEAR ENDED JUNE 30, 2003

In this Annual Report on Form 10-K, the "Company", "Bone Care," "we," "us" and "our" refer to Bone Care International, Inc., unless the context suggests otherwise.

Bone Care(R) and Hectorol(R) are registered trademarks of Bone Care International, Inc., in the U.S. A community trademark application for Hectorol is pending in the European Community Trademark Office, Japan, and selected other countries. Hectorol is the brand name for the active drug substance, doxercalciferol. This filing also includes trademarks of other companies.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. Statements relating to future net sales, costs of sales, other expenses, profitability, financial resources, or products and production schedules, or statements that predict or indicate future events and trends and which do not relate solely to historical matters identify forward-looking statements. Forward-looking statements are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and are based on management's beliefs as well as assumptions made by and information currently available to management. Accordingly, the Company's actual results may differ materially from those expressed or implied in such forward-looking statements due to known and unknown risks and uncertainties that exist in the Company's operations and business environment, including, among other factors:

- general economic and market conditions in the U.S., Europe and the rest of the world;
- our expectations and estimates concerning future financial performance, financing plans and the impact of competition;
- the ability of the Company and its supplier of Hectorol Injection to meet the Company's anticipated production schedule;
- technical risks associated with the development of new products, regulatory policies in the U.S. and other countries;
- risks associated with our ability to avoid or minimize delays in/or interruption of the manufacture and supply of our products, including the approvals of regulatory authorities in connection therewith;
- reimbursement policies of public and private health care payors;
- introduction and acceptance of new drug therapies;
- competition from existing products and from new products or technologies;
- the failure by the Company to produce anticipated cost savings or improve productivity;
- the timing and magnitude of capital expenditures and acquisitions; and

- other risk factors set forth under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this Annual Report.

In addition, in this Annual Report, the words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect" and similar expressions, as they relate to Bone Care, our business or our management, are intended to identify forward-looking statements.

Unless otherwise required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this filing. However, we acknowledge our obligation to disclose material developments related to previously disclosed information. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in the filing may not occur, and actual results could differ materially from those anticipated or implied in the forward-looking statements.

PART I

ITEM 1. BUSINESS

OVERVIEW

Bone Care International, Inc., is a specialty pharmaceutical company engaged in discovering, developing and commercializing improved vitamin D-hormone therapies to treat secondary hyperparathyroidism in patients with kidney (or renal) disease, and other diseases, including osteoporosis, psoriasis and cancers of the prostate, breast and colon. We were founded in 1984 as a subsidiary of Lunar Corporation, located in Madison, Wisconsin, and we were spun off from Lunar in 1996.

We licensed our first product, doxercalciferol or Hectorol, as it is known commercially, in 1987 from the University of Wisconsin, a leading vitamin D research center. Hectorol is a vitamin D-hormone replacement therapy approved by the U.S. Food and Drug Administration (FDA) in two formulations to treat secondary hyperparathyroidism in patients with end-stage renal disease, or ESRD. Hectorol is a safe and effective therapy for reducing elevated levels of parathyroid hormone (PTH) in blood in the management of secondary hyperparathyroidism, a disease characterized by excessive secretion of PTH. Hyperparathyroidism, if left untreated, can eventually result in cardiovascular compromise, reduced immunity, muscle weakness, bone loss and fractures. Virtually all ESRD patients suffer from secondary hyperparathyroidism. We obtained FDA approval for 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. We are also developing doxercalciferol and other vitamin D-hormones to expand indications and treat other diseases. We filed a supplemental New Drug Application with the FDA in December 2001 to treat secondary hyperparathyroidism in chronic kidney disease (CKD) patients. We received an "approvable letter" from the FDA in October 2002, for which we have provided our response. If approved, this would expand the approved indications for Hectorol Capsules.

BACKGROUND

D-hormones are produced in the body from vitamin D that is either ingested or generated in the skin from sunlight exposure. D-hormones have essential roles in human health; they regulate (1) parathyroid hormone secretion by the parathyroid glands, (2) the absorption of calcium by the small intestine, (3) muscle function, and (4) the proliferation and maturation of several types of normal and abnormal cells. D-hormone deficiency in CKD occurs when the kidneys are unable to produce adequate active D-hormones. Without sufficient active D-hormone levels, PTH secretion is increased and calcium absorption in the small intestine is reduced, leading to hypocalcemia and eventually to bone disease.

Hyperparathyroidism is a disease characterized by excessive secretion of PTH by the parathyroid glands. The medical community classifies hyperparathyroidism as either "primary" or "secondary," depending on the underlying cause. Primary hyperparathyroidism is less common and is caused by a disorder in one or more of the parathyroid glands, usually a tumor. Surgical removal of the affected parathyroid glands is the only effective treatment. Secondary hyperparathyroidism is the more common type of hyperparathyroidism and is caused by diseases unrelated to the parathyroid glands. It is seen in varying severity in virtually all ESRD patients, in whom normal kidney function is lost and dialysis is required for survival. Secondary hyperparathyroidism in renal disease generally continues to worsen unless treated with D-hormone therapy.

The goals of D-hormone therapy in this setting are to decrease blood PTH levels and to normalize blood calcium, thereby treating or preventing bone disease, and other adverse effects of elevated PTH. There are other vitamin D-hormones on the market which have been approved for the treatment of secondary hyperparathyroidism and are competing with Hectorol. The two key competing products in the U.S. approved by the FDA are calcitriol and paricalcitol. The challenge in administering vitamin D hormone therapy is to deliver a sufficient dose to be effective without causing toxic side effects including:

- Excessive phosphorus and/or calcium in the blood, which increases the risk that mineral deposits will develop in soft tissues, such as in the heart and arteries, contributing to cardiac disease, or in the kidneys, accelerating kidney failure in CKD patients.

- Excessive phosphorus in the blood, which stimulates secretion of PTH by the parathyroid glands and exacerbates secondary hyperparathyroidism.

- Excessive calcium in the urine, which increases the risk that calcium-rich deposits will develop in the kidneys and accelerate kidney failure in CKD patients.

Due to the risks of these side effects, D-hormones are customarily administered at low dosages. Starting dosages are increased cautiously, to minimize the chance of these toxic side effects and optimize therapeutic response. The pharmacokinetic profiles of calcitriol and paricalcitol typically demonstrate supraphysiological spikes occurring rapidly after administration, followed by trough levels at concentrations below the physiologic range of activated vitamin D. This is in contrast to the relatively constant blood levels of D-hormones that are maintained in individuals with normal kidney function without side effects, yielding consistent, efficient regulation of PTH secretion.

Currently U.S. physicians and dialysis providers favor intravenous products because of several factors: (1) Medicare reimbursement is only available for intravenous products; (2) repeated oral delivery of active D-hormones promotes their breakdown in the intestine, thereby increasing intestinal absorption of calcium and reducing the amount delivered to the parathyroid glands; and (3) healthcare professionals can assure patient compliance with drug administration at the time of dialysis.

THE BONE CARE SOLUTION

We have two FDA approved products to treat secondary hyperparathyroidism in ESRD patients: Hectorol Injection and Hectorol Capsules. Hectorol offers:

- 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 ESRD patients. In these trials, Hectorol reduced blood levels of PTH in more than 90% of the treated patients with minimal side effects. Based on these and other trials, we believe that Hectorol compares favorably to competitive D-hormones, including calcitriol and paricalcitol; however, we have not performed comparative trials to demonstrate these conclusions.

- Oral Delivery that Expands Market Opportunities. Hectorol Capsules provide a safe, convenient and effective oral vitamin D therapy for the management of PTH levels in patients with ESRD. Oral Hectorol has the potential to be used in other clinical settings besides ESRD. Intravenous D-hormone products are used only in hemodialysis patients under medical supervision. Competitive intravenous D-hormones may be less well suited for oral delivery because they are fully active on delivery, which can cause certain cells lining the small intestine to absorb too much calcium and phosphorus, leading to side effects. Hectorol, on the other hand, is an inactive pro-hormone that, after oral delivery, is not immediately available to these intestinal cells.

- A Pro-Hormone that Provides Consistent Levels of Natural 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 D-hormones. Activated Hectorol is released into the bloodstream at a rate which mimics the normal physiologic production of active D-hormones by normal kidneys. Normal physiologic blood levels of D-hormones allow efficient regulation of PTH secretion by the parathyroid glands with few side effects.

- A Potentially Wider Therapeutic Window. We believe that there is indirect evidence 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 D-hormone therapies. Animal studies have demonstrated that Hectorol has fewer side effects than calcitriol or alfacalcidol when delivered at doses of equivalent potency. No clinical trials directly comparing Hectorol to any other D-hormone therapy in ESRD patients have been conducted. We have not conducted any comparative trials of D-hormones in any human subjects. A wider therapeutic window would improve safety and facilitate patient management.

OUR STRATEGY

Our strategy is to develop new D-hormone products and commercialize our two approved products, Hectorol Injection and Hectorol Capsules, by:

- Expanding Our Sales and Marketing Infrastructure. We will continue to develop our internal sales and marketing capabilities to compete in

the $400 million D-hormone market in the U.S. for ESRD patients and for related markets that could be effectively addressed with a small, highly targeted sales and marketing effort. We will seek to establish mutually beneficial alliances or marketing agreements with partners who can rapidly penetrate geographic markets and therapeutic areas where we have no current or planned sales presence.

- Competitively Pricing Hectorol. On a per treatment basis, Hectorol Injection is priced similar to the older D-hormone, calcitriol, but below the more recently launched D-hormone, paricalcitol. Hectorol Capsules also represent an attractive alternative for patients on home dialysis who do not receive IV therapy. While oral D-hormone therapies are not currently reimbursed by Medicare, they are favored outside of the U.S. We are currently the only company with both an oral and intravenous D-hormone product approved for treatment of dialysis patients in the U.S., and we believe we are well positioned to compete in the marketplace if Medicare reimbursement dynamics change in the future.

- Expanding the Approved Indications for Hectorol Capsules. We filed a supplemental New Drug Application with the FDA in December 2001 to treat secondary hyperparathyroidism in CKD (pre-ESRD) patients. We do not have plans to request FDA approvals for other new indications in the next two years.

- Developing Additional Product Offerings. We will continue to use our research, clinical and regulatory expertise to seek to develop our other patented D-hormones for targeted diseases, such as osteoporosis in elderly patients, as well as for psoriasis and cancers where vitamin D therapy may be of benefit, such as cancers of the prostate, breast and colon.

OUR PRODUCTS

Our objective is to discover, develop and commercialize vitamin D-hormone therapies with improved safety and efficacy profiles to treat a variety of diseases where current treatments are either unavailable or inadequate. Comparative studies in several animal species have demonstrated that our vitamin D technologies potentially have an improved therapeutic index as compared to other vitamin D analogs. In pre-clinical models, Hectorol and/or LR-103 are 3 to 30 times less toxic when administered at doses with equivalent potency as compared to calcitriol and/or alfacalcidol. Additional animal studies have shown that, unlike Hectorol and LR-103, competitive D-hormone therapies cause significant calcium deposits in the kidneys when delivered in doses equivalent to those used to treat patients. We cannot be certain, however, that additional clinical studies will support our conclusion that Hectorol and LR-103 have wider therapeutic windows than other D-hormone therapies.

HECTOROL INJECTION

We developed Hectorol Injection for use in the estimated 340,000 ESRD patients in the U.S. Our FDA submission included data from two Phase III trials, which included a total of 70 patients and consisted of an eight-week monitoring period in which no D-hormone therapies were given, followed by a 12-week period in which patients received open-label treatment with Hectorol Injection at hemodialysis. The study endpoint for effectiveness was the observed reduction in

blood PTH levels, and the endpoints for safety were the observed rates of hypercalcemia and hyperphosphatemia. In both trials, after 12 weeks of open-label treatment, mean blood PTH levels were reduced 40% to 50%. These reductions were statistically significant (p