NOVOSTE CORP /FL/
Form 10-K
March 31, 2003
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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2002.

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES ACT OF 1934.**

For the transition period _____ to _____ .

Commission File Number: 0-20727

NOVOSTE CORPORATION

(Exact Name of Registrant as Specified in Its Charter)

Florida	**59-2787476**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3890 Steve Reynolds Blvd., Norcross, GA	**30093**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone, including area code: (770) 717-0904

Securities registered pursuant to Section 12(b) of the Act: None

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

Common Stock, $.01 par value

(Title of Class)

Rights to Purchase Preferred Shares

(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 requirements for the past 90 days. Yes x No ¨

Indicate by check mark if disclosures 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 Exchange Act Rule 12b-2). Yes x No ¨

As of March 14, 2003, there were 16,351,953 shares of Common Stock outstanding. The aggregate market value of voting stock held by non-affiliates of the Registrant was approximately $71,882,455 based upon the closing sales price of the Common Stock on June 28, 2002 on the Nasdaq National Market. Shares of Common Stock held by each officer, director, and holder of five percent or more of the Common Stock outstanding as of June 28, 2002 have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily conclusive.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of Registrant s Proxy Statement for the 2003 Annual Meeting of Stockholders, which the Registrant intends to file not later than 120 days following December 31, 2002, are incorporated by reference to Part III of this Form 10-K Report.

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PART I.

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Cautionary Note Regarding Forward-Looking Statements

The forward-looking statements in this Form 10-K are made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934, as amended. Our operating results and financial condition have varied and may in the future vary significantly depending on a number of factors. Statements in this Form 10-K which are not strictly historical statements, including, without limitation, statements regarding management s expectations for future growth and plans and objectives for future management and operations, domestic and international marketing and sales plans, product plans and performance, research and development plans, management s assessment of market factors, as well as statements regarding our strategy and plans, constitute forward-looking statements that involve risks and uncertainties. In some cases these forward-looking statements can be identified by the use of words such as may, will, should, expect, project, predict, potential or the ne these words or comparable words. The factors listed under Certain Factors Which May Affect Future Results in Part I, Item 1 Business , among others, could cause actual results to differ materially from those contained in forward-looking statements made in this report and presented elsewhere by management from time to time. Such factors, among others, may have a material adverse effect upon our business, financial condition, and results of operations. We undertake no obligation to update publicly or revise any forward-looking statements, whether as a result of new information, future events or otherwise. Accordingly, you are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date on which they are made.

PART I

ITEM 1. BUSINESS

In this Form 10-K, Novoste, the Company, we, us and our refer to Novoste Corporation. Novoste®, Beta-Cath, Corona® and the Novoste® logo are trademarks of the Company.

General

Novoste, a Florida corporation, has developed the Beta-Cath System, a hand-held device to deliver beta, or low penetration, radiation to the site of a treated blockage in a coronary artery to decrease restenosis. Restenosis, the renarrowing of a previously treated artery, is the major limitation of percutaneous coronary angioplasty or PTCA, a procedure used by interventional cardiologists to open blocked coronary arteries. Coronary stents, metal tubes or coils permanently deployed at a blockage in a coronary artery, were developed to reduce the incidence of restenosis, however restenosis still occurs in greater than 15% of the patients who receive stents. In August 1998, we qualified to apply CE marking to the Beta-Cath System. CE marking is a regulatory approval and is a requirement to sell our device in most of the European Union and commenced the active marketing of our device there in January, 1999. On November 3, 2000, Novoste received U.S. marketing approval from the United States Food and Drug Administration (FDA) for the Beta-Cath System (30-millimeter source train) for use in patients suffering from in-stent restenosis , a condition in which previously placed coronary stents become clogged with new tissue growth. Novoste received additional approvals from the FDA for The Beta-Cath System with a 40-millimeter source train during 2001 and the 60-millimeter source train and smaller, next generation 3.5 French catheter and source train in early 2002.

Novoste was incorporated in Florida in 1987 and remained dormant until May 22, 1992 (date of inception) at which time it began operations. Novoste has its principal operations in the United States and sales and distribution in Western Europe, Canada, Asia and South America. Novoste markets it products through a direct sales force in the United States and a combination of direct sales representatives and independent

distributors in markets outside the United States. All of our revenues have been generated from the marketing of the Beta-Cath System and during 2002, 94% of net sales were generated in the United States. Information concerning revenues and long-lived assets by geographic area for the past three years may be found under Notes To Consolidated Financial Statements, Note 12. Segment Information.

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Available Information. Novoste files annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission (the SEC). You may read and copy any document the Company files at the SEC s public reference room at Room 1024, 450 Fifth Street, NW, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information on the public reference room. The SEC maintains a website that contains annual, quarterly and current reports, proxy statements and other information that issuers (including Novoste) file electronically with the SEC. The SEC s website is http://www.sec.gov.

Novoste s website is http://www.novoste.com. The Company makes available free of charge through its internet site its annual reports on Form 10-K; quarterly reports on Form 10-Q; current reports on Form 8-K; and any amendments to those reports filed or furnished pursuant to the Securities Exchange Act of 1934 (the Exchange Act) as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information on Novoste s website is not incorporated by reference into this report.

INDUSTRY OVERVIEW

Coronary Artery Disease. Coronary artery disease is the leading cause of death in the United States. More than 13 million people in the United States currently suffer from coronary artery disease, which is generally characterized by the progressive accumulation of plaque as a result of the deposit of cholesterol and other fatty materials on the walls of the arteries. The accumulation of plaque leads to a narrowing of the interior passage, or lumen, of the arteries, thereby reducing blood flow to the heart muscle. When blood flow to the heart muscle becomes insufficient, oxygen supply is restricted and a heart attack and death may result. Depending on the severity of the disease and other variables, patients will be treated either surgically with coronary artery bypass graft surgery or less invasively with a PTCA procedure.

Coronary Artery Bypass Graft Surgery (CABG). Coronary artery bypass graft surgery, or CABG, was introduced as a treatment for coronary artery disease in the 1950 s. CABG is a highly invasive, open surgical procedure in which blood vessel grafts are used to bypass the site of a blocked artery, thereby restoring blood flow. CABG, still considered the most durable treatment for coronary artery disease, is generally the primary treatment for severe coronary artery disease involving multiple vessels. In addition, CABG is often a treatment of last resort for patients who have undergone other less invasive procedures like percutaneous transluminal coronary angioplasty, but require revascularization. However, CABG has significant limitations, including medical complications such as stroke, multiple organ dysfunction, inflammatory response, respiratory failure and post-operative bleeding, each of which may result in death. In addition, CABG is a very expensive procedure and requires a long recovery period. In the United States, the average cost of undergoing CABG, including hospital stay, is approximately $45,000; and the average recuperation period following discharge from the hospital is at least four to six weeks. In 2002, approximately 400,000 CABG procedures were performed in the United States. Several new minimally invasive surgical techniques have been commercialized which attempt to lessen the cost and trauma of CABG procedures while maintaining efficacy.

Percutaneous Transluminal Coronary Angioplasty (PTCA). Since its introduction in the late 1970s, PTCA has emerged as the principal less invasive alternative to CABG. PTCA is a procedure performed in a cardiac catheterization labs, commonly referred to cath labs, by an interventional cardiologist. During PTCA, a guidewire is inserted into a blood vessel through a puncture in the leg (or arm, in some cases) and guided through the vasculature to a diseased site in the coronary artery. A balloon-tipped catheter is then guided over the wire to the deposit of plaque or lesion occluding the artery. Once the balloon is positioned across the lesion inside the vessel, the balloon is inflated and deflated several times. Frequently, successively larger balloons are inflated at the lesion site, requiring the use of multiple balloon catheters. The inflation of the balloon cracks or reshapes the plaque and the arterial wall, thereby expanding the arterial lumen and increasing blood flow. However, the inflation of the balloon typically results in injury to the arterial wall. In 2002, it is estimated that about 1,000,000 PTCA procedures were performed in the United States and approximately 600,000 procedures were performed outside the United States. The average cost of each PTCA procedure in the United States is approximately $20,000, or less than one-half of the average cost of CABG. The length of stay and recuperation period are substantially less than those required for CABG.

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Though PTCA has grown rapidly as a highly effective, less invasive therapy to treat coronary artery disease, the principal limitation of PTCA is the high rate of restenosis, the renarrowing of a treated artery, which often requires reintervention. Studies have indicated that, within six months after PTCA, between 30% and 50% of PTCA patients experience restenosis.

Pathology of Restenosis. Restenosis is typically defined as the renarrowing of a treated coronary artery within six months of a revascularization procedure, such as PTCA, to less than 50% of its normal size. Restenosis is a vascular response to the arterial trauma caused by PTCA. Due to multiple mechanisms controlling vascular repair, restenosis may occur within a short period after a revascularization procedure or may develop over the course of months or years.

Restenosis that occurs within a day of a revascularization procedure is usually attributed to elastic recoil (acute loss of diameter) of the artery. Restenosis also may result from hyperplasia, which is the excessive proliferation of cells at the treatment site, or from vascular remodeling of the arterial segment, which is a slow contraction of a vessel wall. Hyperplasia is a physiological response to injury, similar to scarring, which occurs in wound healing. Vascular remodeling is a contraction of the vessel caused by a thickening of the outside wall of the artery. In response to an arterial injury from revascularization, the body sets off a biochemical response to repair the injured site and protect it from further harm. This response will include a signal to adjacent cells of the arterial wall to multiply. Often this cell proliferation goes unchecked, resulting in a much thicker and inelastic arterial wall and in reduced blood flow. Hyperplasia and vascular remodeling are the primary causes of restenosis.

Coronary Stenting. Coronary stents are expandable, implantable metal devices permanently deployed at a lesion site. Stents maintain increased lumen diameter by mechanically supporting the diseased site in a coronary artery. Of all the non-surgical treatments seeking to improve upon PTCA, stents have been the most successful in improving the outcome immediately following the procedure and reducing the incidence of restenosis. In a typical stent procedure, the artery is pre-dilated at the lesion site with a balloon catheter, and the stent is delivered to the site of the lesion and deployed with the use of a second balloon catheter which expands the stent and firmly positions it in place. This positioning may be followed by a third expansion, using a high-pressure balloon to fully deploy and secure the stent. Once placed, stents exert radial force against the walls of the coronary artery to enable the artery to remain open and functional.

Studies have concluded that the rate of restenosis in patients receiving coronary stents following PTCA is approximately 30% lower than in patients treated only by PTCA. Since their commercial introduction in the United States in 1994, the use of stents has grown rapidly, and it is estimated that they were utilized in over 75% of the approximately 1.6 million PTCA procedures performed in 2002.

Despite their rapid adoption, stents have certain drawbacks. The use of stents increases the cost of a PTCA procedure, especially when, as is often the case, two or more stents are used. In addition, studies have shown that restenosis still occurs in approximately 30% to 40% of the patients who receive stents following PTCA. This is commonly referred to as in-stent restenosis. Studies have shown that patients with in-stent restenosis often experience recurrent restenosis and as a result are prone to multiple revascularization procedures. Stents are also permanent implants which may result in unforeseen, long-term adverse effects, and cannot be used in cases where the coronary arteries are too tortuous or too narrow. Further, stents appear to be effective in reducing the frequency of restenosis resulting from elastic recoil and vascular remodeling, but they increase the degree of hyperplasia.

Vascular Brachytherapy vs. Drug Coated Stents. Vascular brachytherapy is the delivery of radiation within blood vessels. Studies conducted by Novoste and other companies using radiation to treat in-stent restenosis led to FDA approval and the subsequent introduction of vascular brachytherapy (VBT) devices in 2000 and 2001. These devices, which deliver a dose of radiation to the site of restenosis, have proven to reduce in-stent restenosis, but because of the complexity of using radiation in the cath lab, other companies have been researching coatings and treatments to coronary stents that could also reduce restenosis and would possibly be

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more acceptable to a medical community already experienced at using stents. One of the drug coated stents has continued development in its current configuration and is believed to be likely to receive its approval in the second quarter of 2003 (as discussed further in Competition; Rapid Technological Change). Other companies are seeking to test multiple drug coatings in an effort also to produce a competitive coated stent. While not completely effective, it is believed that drugs will reduce the rate of in-stent restenosis from approximately 15% down below 10%. Novoste believes, however, that the early clinical data is not representative of the wide variety of patients that will be treated by the wide variety of physicians in typical commercial settings. Novoste believes that many of those patients who do suffer from restenosis will still benefit from treatment with vascular brachytherapy. Since the price of drug coated stents is projected to be about three times the price of traditional bare metal stents, from an economic standpoint it also may not be practical or possible for many hospitals to use drug-coated stents on all their patients. Novoste believes the cost benefit of only using vascular brachytherapy on the low percentage of failed stents is currently the most attractive financial alternative for the health care system.

The Novoste Solution

The Beta-Cath System has been shown to reduce the incidence of restenosis in patients who are being treated for blocked stents, or in-stent restenosis. The administration of localized beta radiation reduces restenosis rates by inhibiting hyperplasia and vascular remodeling. Radiation has been used therapeutically in medicine for more than 50 years in the treatment of proliferative cell disorders, such as cancer. Cancer therapy has primarily involved the use of gamma radiation, which is highly penetrating and may be hazardous unless handled and used with great care. By contrast, beta radiation is far less penetrating and easier to use and shield than gamma radiation while still delivering a sufficient dose to the treated coronary arteries. We view beta radiation as well-suited for intracoronary use following PTCA in a blocked stent, where the objective is to treat the coronary artery with minimal exposure to adjacent tissues.

The Beta-Cath System is designed to fit well with techniques currently used by interventional cardiologists in the cath lab. It is a hand-held device that hydraulically delivers beta radiation sources through a closed-end catheter to the area of the coronary artery injured by the immediately preceding PTCA procedure. To facilitate easy placement of the catheter, it is advanced over the same guidewire used in the PTCA procedure. After the administration of the prescribed radiation dose to a lesion site, which takes less than five minutes per lesion, the radiation sources are hydraulically returned to the hand-held transfer device. We are able to reuse the radiation isotopes for up to a eighteen months due to the long half-life of Strontium-90, the isotope used in the Novoste device.

Our Business Strategy

Our objective is to maintain our leadership position in the vascular brachytherapy market and to generate additional revenue and profits by leveraging our distribution network and our ability to execute product development and clinical trials. Elements of our strategy include:

Maintaining our vascular brachytherapy market leadership position by offering additional enhancements and catheter options to the Beta-Cath System. We ve responded to customer demand in 2002 by introducing a next generation small-diameter catheter and source train, the longest radiation treatment length (60mm) available in a single dwell time and the option of a longer catheter length for the convenience of remaining outside the sterile field for non-cath lab personnel. We plan to offer additional enhancements throughout 2003 to enable interventional cardiologists greater ability to treat in-stent restenosis.

Improving our financial performance by applying our resources to products that can generate near term revenue and profits. We are also improving our enterprise resource-planning infrastructure to provide the necessary information to operate efficiently and reduce costs. Focusing on the preservation of our existing cash balances and operating profitably will allow us to fund our operating and product development activities internally.

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Expanding into the peripheral markets for growth. We plan to focus our development and leverage our vascular brachytherapy technology into larger peripheral markets treating arterial-venous (A-V) dialysis grafts and femoral-popliteal (fem-pop) disease where drug-coated stents are not likely to be a competitive threat. We are already enrolling patients in our BRAVO A-V Graft trial and our MOBILE Fem-Pop trial. See Product Development on Clinical Trials.

Our goals and strategies are aimed at creating a global company that is recognized for innovative, clinically superior and economically beneficial therapeutic solutions for the treatment of vascular disease. Our vision is to be the recognized leader in providing simple solutions to complex interventional therapies.

Beta-Cath System Design and Advantages

The primary components of the Beta-Cath System are: radiation source train, transfer devices and delivery catheter.

Radiation Source Train. The beta radiation administered by the Beta-Cath System emanates from a train of several miniature sealed sources containing Strontium-90 (Strontium/Yttrium), a beta-emitting radioisotope. We currently manufacture trains in 2 diameters and in 30mm, 40mm and 60mm lengths, with the longer length intended for use on longer lesions. The use of beta, rather than gamma, radiation is intended to make the Beta-Cath System safer (less radiation exposure to cath lab personnel and shorter patient treatment dwell times versus Gamma) and easier to use in the cath lab environment. In addition, due to the long half-life (approximately 28 years) of Strontium-90, and because the source train will not come into contact with a patient s blood or tissue, the radiation sources are reused for up to eighteen months and deliver a consistent dose in a short period. Beta radiation from the Strontium-90 source is easily shielded from health care workers by the use of approximately one-half-inch-thick quartz in the transfer device.

Transfer Device. The transfer device is a multiple-use, hand-held instrument used to deliver, retrieve and then store the radiation sources when not in use. The transfer device:

transfers the radiation sources to and from the delivery catheter via a proprietary hydraulic delivery system;

contains a radiation source sensing system which is interlocked with a gating system to prevent the radiation sources from exiting the transfer device until the delivery catheter is locked in place and to prevent removal of the delivery catheter from the transfer device prior to the return of the radiation sources to the device; and

shields the beta radiation from health care workers when the radiation source train is housed inside it.

Delivery Catheter. The delivery catheter is a single-use, multi-lumen catheter that provides a pathway for the radiation sources to be rapidly delivered to and retrieved from the coronary arterial segment to be treated. The delivery catheter is positioned by advancing it over the same guidewire used during the immediately preceding PTCA procedure. The radiation sources are delivered and retrieved through a dual-lumen closed hydraulic circuit, which uses a fluid-filled standard syringe to create the hydraulic pressure. We currently sell two versions of the catheter in the United States: the Beta-Cath 5.0 French(F) System which fits over the guidewire used in the PTCA procedure, commonly known as an over the wire catheter and our next generation 3.5F distal monorail rapid exchange version which we refer to as the Beta-Cath 3.5F System.

The Beta-Cath System is used in a cath lab by an interventional cardiologist in conjunction with a radiation oncologist or designated authorized user. The cardiologist places the delivery catheter into the patient s vasculature until the catheter reaches the targeted site. The radiation oncologist operates the transfer device to deliver the radiation source train hydraulically to the end of the catheter in a matter of seconds. The radiation sources remain at the targeted site for less than five minutes to deliver a predetermined dose of radiation. The

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radiation sources are then returned by the use of positive hydraulic pressure applied through a different lumen of the delivery catheter. Upon completion of each procedure, the train of radiation sources is stored safely inside the transfer device. At the end of the day, the transfer device is delivered to a designated radiation storage site within the hospital for safekeeping. We believe the Beta-Cath System is cost-effective, principally by reducing the need for costly revascularization procedures often required following treatment of in-stent restenosis.

We believe the Beta-Cath System has the following advantages:

Excellent economic cost benefit. The Beta-Cath System is applied only when and where it is needed to treat in-stent restenosis lessions.

Site-specific Therapy. The Beta-Cath System is designed to confine radiation exposure to the targeted intervention area.

Short Procedure Times. The Beta-Cath System is designed to enhance patient safety and comfort, as well as to promote productivity in the cath lab, by delivering the recommended dosage in less than five minutes of radiation exposure per lesion.

Utilization of Existing PTCA Techniques. Although intracoronary radiation is a new concept in coronary artery disease treatment, the hand-held Beta-Cath System is designed to be easily adopted and used by the interventional cardiologist. The Beta-Cath System is very similar to other catheter-based tools used by the cardiologist.

Multiple-Use System. The radiation source train can be reused for numerous patients, due to the long half-life of the isotope and because the source train does not come into contact with the patient s blood. As a result, inventory planning is very straightforward, and last minute treatment decisions can be made.

Ease of Use and Accuracy of Dosing. The Beta-Cath System is a hand-held device that is easy to operate. Because of the long half-life of our radiation source, prescribed treatment times will remain constant over the approved shelf life of the isotope. Vascular brachytherapy systems that utilize short half-life isotopes are likely to require complex case-by-case dose calculations based on the current decay state of the isotope. In addition, they require frequent inventory replacement due to their short half-lives.

Designed for Safety. The Beta-Cath System utilizes localized beta radiation, which results in total body radiation exposure significantly less than that received during routine x-ray during PTCA or during treatment with a gamma radiation device. Other safety mechanisms include: a closed-source train lumen, special locking mechanisms to connect the delivery catheter to the transfer device and sufficient shielding in the transfer device to protect health care workers from beta radiation exposure. In addition, the beta radiation sources are delivered and, following the administration of the prescribed dose, retrieved hydraulically in a matter of seconds, thereby minimizing exposure to adjacent tissue.

PRODUCT DEVELOPMENT AND CLINICAL TRIALS

We are engaged in ongoing product development to introduce new products to provide simple solutions to complex interventional therapies. In addition, we seek to enhance the effectiveness, ease of use, safety and reliability of our Beta-Cath System and to expand the applications for which its uses are appropriate.

Clinical trials are administered by our internal clinical and regulatory staff. We also use consultants to monitor the clinical sites and to assist in training and have engaged independent contract research organizations and consultants to compile data from the trials and to perform statistical and reimbursement analyses.

Research and development expenses, which include the cost of clinical trials, for the years ended December 31, 2002, 2001, and 2000 were approximately $13.3 million, $12.7 million and $17.1 million, respectively. We have conducted numerous clinical trials to provide the basis for approval by the FDA of several versions of the Beta-Cath System.

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Additional Beta-Cath System Approvals

During 2001, Novoste applied to the FDA for approval to market two additional Beta-Cath System products. The Beta-Cath 3.5F System, Novoste s next generation smaller diameter catheter system received marketing approval from the FDA in February, 2002. The Beta-Cath 3.5F System, offered with both a 30mm and 40mm radiation source train, is a smaller diameter vascular brachytherapy catheter approved for the treatment of in-stent restenosis. Due to its lower profile, the 3.5F System should be able to treat areas unable to be addressed with the current 5F System.

Marketing approval for the 60mm Beta-Cath System was received from the FDA in March 2002. The 60mm device is designed to treat long, diffuse in-stent restenosis. Approval of the 60-mm device was based on the results of a 139 patient subset (RENO Long) of the 1,098 patient RENO (**RE**gistry **NO**voste) European registry trial. An analysis was performed on the RENO Long group and compared to a placebo control group selected from the **W**ashington **R**adiation for **I**n-**S**tent Restenosis **T**rials (WRIST / LONG WRIST (n=94)). These data demonstrated a 75% reduction in Target Vessel Revascularization (TVR) rate (14.9% vs. 60.6%) and a 72% reduction in Major Adverse Cardiac Event (MACE) rate (17.9% vs. 64.9%) for the subset of patients receiving Sr-90 beta radiation compared to this placebo control group. The average lesion length for the RENO Long patient subset was 35.3 mm (site reported) compared to the average lesion length of 28.0 mm in the WRIST / LONG WRIST placebo control group.

New Products and Applications

Future development efforts will focus on modifying the Beta-Cath System for use in peripheral applications, such as arterial-venous shunts and the femoral arteries. There can be no assurance that we will be successful in developing these or other products or that clinical trials will prove that the product is safe and effective for the treatment or therapy.

BRAVO TRIAL

In June 2002, Novoste received approval for an investigational device exemption (IDE) application to the FDA for its CORONA System to treat non-thrombotic arterial-venous dialysis graft stenosis. In February 2002, Novoste received approval for a major modification to the BRAVO trial to include thrombotic arterial-venous dialysis graft stenosis. More than 220,000 people in the U.S. currently undergo long-term dialysis for end stage renal disease and a majority of these patients rely on arterial-venous dialysis grafts for vascular access. Unfortunately, these grafts are associated with a very low patency rate of 40 60% at one year and many of these grafts require interventional therapy to maintain patency. There is evidence that the stenosis is due to intimal hyperplasia formation at the graft site as a result of turbulent blood flow, increased pressure and cyclical stretching of the vein wall, and therefore may be an ideal target for vascular brachytherapy.

The BRAVO (**B**eta **R**adiation for treatment of **A**rterial-**V**enous graft **O**utflow) trial IDE, approved by the FDA, is a prospective, randomized, multi-center, placebo-controlled trial investigating the safety and efficacy of the CORONA System to treat venous outflow stenosis in arterial-venous dialysis grafts.

The BRAVO trial protocol will include 215 patients who will be assigned at random after either conventional treatment or conventional treatment plus radiation. The trial is expected to be performed in 30 sites in North America. We anticipate completion of the enrollment of the 215 patients in the second half of 2003. Provided the trial is successful we intend to file, in 2004, an application to obtain pre-market approval

from the FDA to sell the CORONA System in the United States for the treatment of venous outflow stenosis in arterial-venous dialysis grafts. Approval from the FDA, if any, would likely not be obtained any earlier than six months after submission.

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MOBILE TRIAL

Novoste is developing the CORONA System to deliver Beta vascular brachytherapy to treat patients with peripheral artery disease (restricted blood flow in the upper legs). Novoste believes that there is currently no effective treatment of diffuse peripheral artery disease, which can range from debilitating by limiting a patient s ability to walk without pain, all the way to amputation, for patients who suffer from this disease. Symptomatic peripheral artery disease affects over 1.25 million patients annually in the U.S. The CORONA System differs from the Beta-Cath System by the addition of a balloon-based delivery system which allows for the treatment of large 4mm 8mm diameter vessels.

In December 2001, Novoste began its **M**obile **MO**re **p**atency with **B**eta **I**n the **L**ower **E**xtremity trial. The MOBILE trial will include 410 patients from 30 sites in North America and Europe. Patients will be assigned at random for either standard percutaneous catheter-based revascularization therapy followed by vascular brachytherapy or standard therapy alone.

SALES AND MARKETING

Novoste has its U.S. sales and marketing management located in our corporate office in Norcross, Georgia and our European operation is located in Krefeld, Germany.

We have recruited, trained and deployed a qualified and experienced sales organization made up of field management, sales representatives and clinical trainers. Our marketing organization is also made up of professionals experienced in cardiology and vascular medicine as well as medically applied radiation. At the end of the year, the Sales and Marketing organization consisted of 69 employees.

We market and sell directly into the markets of the U.S. and most of Europe and Canada and we work through our distributor network for the rest of the world where the market conditions are viable for our technology.

Novoste directs its sales and marketing efforts primarily at the prominent domestic and international cardiac catheterization laboratories that perform the majority of the interventional cardiology procedures. We believe that these hospitals control the majority of procedures and will utilize new coronary technologies such as the Beta-Cath System for treating restenosis. Our sales and marketing strategy includes developing and maintaining a close working relationship with its customers in order to assess and satisfy their needs for products and services. All customers must be trained, proctored and certified, pursuant to FDA requirements, by Novoste before they are eligible to do cases independently.

We also periodically meet with clinicians to share ideas regarding the marketplace, existing products, procedure techniques, products under development and existing or proposed research projects.

Our direct sales activities require contact with all of the medical specialists involved in vascular brachytherapy: cardiologists, radiation therapists and medical physicists as well as hospital administration, which results in a lengthy sales process. In addition to our multidiscipline sales force calling on these customers, we have a team of medical physicists who help the hospitals through this licensing process with both the NRC and agreement states. Amended licenses are required by every hospital before vascular brachytherapy can be performed.

We expect the existing sales force, supplemented by additional expertise for the particular application, will distribute future products currently in development or by additional personnel required to properly support the market.

We are not dependent on any single customer, and no single customer accounted for more than 10% of revenue in 2002.

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Manufacturing, Sources of Supply and Scale-up

Our manufacturing operations are required to comply with the FDA s quality system regulations, which included an inspection of our manufacturing facilities prior to pre-market approval of the Beta Cath System. In addition, certain international markets have quality assurance and manufacturing requirements that may be more or less rigorous than those in the United States. Specifically, we are subject to the compliance requirements of ISO 9001 certification and CE mark directives in order to produce products for sale in Europe. We received ISO 9001/EN 46001 certification from our European notified body in April 1998. We are subject to periodic inspections by regulatory authorities to ensure such compliance. See Government Regulation. We conduct quality audits of suppliers and we are establishing a supplier certification program. All suppliers of components must also be in compliance with Novoste s requirements and the FDA s quality system regulations.

Beta Radiation Source Train Suppliers

Beginning in 1996, Novoste contracted with Bebig Isotopentechnik Medizintechnik (Bebig), a German corporation, to equip a production site for the production of radioactive sealed Strontium-90 seed trains.

On June 20, 2001, the Company entered into a new manufacturing and supply agreement with Bebig to manufacture and supply the Company with seed trains. The agreement supercedes all prior agreements with Bebig and neither the Company nor Bebig have any rights or obligations under any of the previous agreements. During each calendar year under the four-year contract, the Company guarantees to pay to Bebig minimum annual payments. All product purchases are credited against the annual guaranteed payment. In the event that the Company does not purchase product to exceed the annual guaranteed payment, the deficiency will be due and payable to Bebig within thirty days after the end of each one-year contract period. At December 31, 2002, the Company exceeded the annual guaranteed payment.

Bebig is required to comply with various regulatory requirements with respect to the supply of radiation sources. Bebig has agreed to manufacture Strontium-90 seed trains at an agreed-upon base price.

On October 14, 1999, Novoste signed a development and manufacturing supply agreement with AEA Technologies QSA GmbH for a second source of radioactive seed trains and for the development of smaller diameter radiation seed trains. The agreement provided for the construction of a production line to be finished in two phases. The first phase, the design phase, was completed in February 2001 and the second phase, the construction phase, was completed in October 2002 by using the design equipment to produce the smaller diameter radiation source. The completion of the first phase provided Novoste with access to a limited supply of the smaller diameter radiation source. Payments to cover the cost of this production line were paid as construction progressed.

Significant proportions of key components and processes relating to the Company s products are purchased from single sources due to technology, availability, price, quality, and other considerations. Key components and processes currently obtained from single sources include isotopes, protective tubing for catheters, proprietary connectors, and certain plastics and electronic components used in the design and manufacture of the transfer device. In the event a supply of a key single-sourced material or component was delayed or curtailed, Novoste s ability to produce the related product in a timely manner could be adversely affected. Novoste attempts to mitigate these risks by working closely with key suppliers regarding the Company s product needs and the maintenance of strategic inventory levels.

Supply of Other Components by Third Parties

Through 2002, Novoste relied on Plexus Corporation as third party manufacturer for the hand-held transfer device. During 2002, Novoste began a project to manufacture the transfer devices at its Norcross location. FDA approval is expected for this manufacturing change in the summer of 2003. While the Company believes it will

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be better positioned to control transfer device design, lead time, product availability and overall transfer device cost, our inability to obtain sub-assemblies and components from suppliers could have a material adverse effect on our ability to manufacture the Beta-Cath System and, therefore, on our ability to market the Beta-Cath System. The Company will continue its efforts to mitigate the risks associated with this issue by continued careful review and proactive control of its inventories, and ensuring adequate safety stock of both finished devices and components is maintained

Patents and Proprietary Technology

Our policy is to protect our proprietary position by, among other methods, filing United States and foreign patent applications. We were issued United States Patent No. 5,683,345 on November 4, 1997, Patent No. 5,899,882 on May 4, 1999, No. 6,013,020 on January 11, 2000, No. 6,261,219 on July 17, 2001 and Patent No. 6,306,074 on October 23, 2001, all of which relate to both or either the Beta-Cath System with an over-the-wire catheter of the Beta Cath System with a rapid exchange catheter. We also have several additional United States applications pending covering aspects of our Beta-Cath System. With respect to the above identified United States Patents and our other pending United States patent applications, we have filed, or will file in due course, counterpart applications in the European and certain other regions or countries.

Like other firms that engage in the development of medical devices, we must address issues and risks relating to patents and trade secrets. United States Patent Nos. 5,683,345; 5,899,882; 6,013,020; 6,261,219 and 6,306,074 may not offer any protection to us because competitors may be able to design functionally equivalent devices that do not infringe these patents. Any of the patients may also be reexamined, invalidated or circumvented. In addition, claims under our other pending applications may not be allowed, or if allowed, may not offer any protection or may be reexamined, invalidated or circumvented. In addition, competitors may have or may obtain patents that will prevent, limit or interfere with our ability to make, use or sell our products in either the United States or international markets.

We received a letter from NeoCardia, L.L.C., dated July 7, 1995, in which NeoCardia notified us that it was the exclusive licensee of United States Patent No. 5,199,939, or the Dake patent, and requested that we confirm that our products did not infringe the claims of the Dake patent. On August 22, 1995 our patent counsel responded on our behalf that we did not infringe the Dake patent.

The United States Patent and Trademark Office later reexamined the Dake patent. In the reexamination proceeding some of the patent claims were amended and new claims were added. We have concluded, based upon advice of patent counsel, that our Beta-Cath System does not infringe any claim of the Dake patent as reexamined.

In May 1997, Guidant Corporation (Guidant) acquired NeoCardia together with the rights under the Dake patent. Guidant currently markets and distributes products that compete with the Beta-Cath System and has significantly greater capital resources than Novoste. Novoste does not believe that its products infringe the Dake patent or that an action by Guidant for infringement would have merit.

The medical device industry has been characterized by extensive litigation regarding patents and other intellectual property rights. Companies in the medical device industry have employed intellectual property litigation to gain a competitive advantage. There can be no assurance that we will not become subject to patent-infringement claims or litigation or interference proceedings declared by the United States Patent and Trademark Office to determine the priority of inventions. The defense and prosecution of intellectual property suits, or interference proceedings and related legal and administrative proceedings are both costly and time-consuming. Litigation may be necessary to enforce our patents, to protect our trade secrets or know-how or to determine the enforceability, scope and validity of the proprietary rights of others. Any litigation or interference proceedings will result in substantial expense to us and significant diversion of effort by our technical and management

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personnel. An adverse determination in litigation or interference proceedings to which we may become a party could subject us to significant liabilities to third parties, require us to seek licenses from third parties, require us to redesign our products or processes to avoid infringement or prevent us from selling our products in certain markets, if at all. Although patent and intellectual property disputes regarding medical devices have often been settled through licensing or similar arrangements, costs associated with such arrangements may be substantial and could include significant ongoing royalties.

Furthermore, there can be no assurance that the necessary licenses would be available to us on satisfactory terms, if at all, or that we could redesign our products or processes to avoid infringement. Any adverse determination in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing and selling our products, which would have a material adverse effect on our business, financial condition and results of operations.

Patent applications in the United States and patent applications in foreign countries are maintained in secrecy for a period after the earliest claimed priority date. Publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries and the filing of related patent applications. Patents issued and patent applications filed relating to medical devices are numerous. Accordingly, there can be no assurance that current and potential competitors, many of which have substantial resources and have made substantial investments in competing technologies, or other third parties have not or will not file applications for, or have not or will not receive, patents and will not obtain additional proprietary rights relating to products made, used or sold or processes used or proposed to be used by us.

We have developed certain of our patent and proprietary rights relating to the Beta-Cath System in conjunction with Emory University Hospital, a leader in the research of intravascular radiation therapy. To obtain the exclusive rights to commercialize the Beta-Cath System for the treatment of restenosis, we entered into a license agreement with Emory. Under this agreement, Emory assigned to us all of Emory s rights to one United States patent application and exclusively licensed to us its rights under another United States application and related technology. Emory made no representation or warranty with respect to its ownership of the assigned patent application, and made only limited representations as to its ownership of the licensed patent application and related technology. Under the agreement Emory will be entitled to royalty payments based upon net sales of the Beta-Cath System. The term of the agreement runs through the later of (i) the date the last patent covered by the agreement expires or (ii) January 2016 (unless earlier terminated as provided in the agreement). Any inventions developed jointly by our personnel and Emory during the term of the license agreement are owned jointly by Emory and us. If Emory terminated the agreement as a result of our failure to pay such royalties or any other breach of our obligations under such agreement, our rights to use jointly owned patents (including the United States Patent No. 5,899,882) would become non-exclusive and we would have no rights to use future patents owned exclusively by Emory. In addition, if we breach our obligations under the license agreement, we could be required by Emory to cooperate in licensing the pending jointly-owned United States patent application and our foreign counterparts to third parties so that they would be able to commercialize and sell the Beta-Cath System.

All of the physicians on staff at Emory who were involved in the development of the Beta-Cath System, have assigned their rights in the technology, if any, to Emory and/or Novoste. In addition, we have entered into a license agreement with one of the physicians and under the terms of this agreement, he is entitled to receive a royalty on the net sales of the Beta-Cath System (excluding consideration paid for the radioactive isotope), up to a maximum, over the term of the agreement, of $5,000,000.

We employ a full time manager of intellectual property to prepare invention records and to coordinate the prosecution of new intellectual property. We obtain confidentiality and invention assignment agreements in connection with employment, consulting and advisory relationships. These agreements generally provide that all confidential information developed or made known to the individual by us during the course of the individual s relationship with us, is to be kept confidential and not disclosed to third parties, except in specific circumstances. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for us in the event of unauthorized use, transfer or disclosure of such information or inventions.

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Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our proprietary technology, and we may not be able to meaningfully protect our rights in unpatented proprietary technology.

COMPETITION; RAPID TECHNOLOGICAL CHANGE

Competition in the medical device industry, and specifically the markets for cardiovascular devices, is intense and characterized by extensive research and development efforts and rapidly advancing technology. New developments in technology could render vascular brachytherapy noncompetitive.

Many of our competitors and potential competitors have substantially greater resources than we do and also have greater resources and expertise in the area of research and development, obtaining regulatory approvals, manufacturing and marketing. Our competitors and potential competitors may succeed in developing, marketing and distributing technologies and products that are more effective than those we will develop and market or that would render our technology and products obsolete or noncompetitive. Additionally, many of the competitors have the capability to bundle a wide variety of products in sales to cath labs. We may be unable to compete effectively against such competitors and other potential competitors in terms of manufacturing, marketing, distribution, sales and servicing.

Both J&J and Guidant offer vascular brachytherapy products that compete directly with Novoste Beta-Cath System and both have substantially greater capital resources and greater resources and experience at introducing new products than does Novoste. J&J s product, the CHECKMATE System, is a gamma radiation vascular brachytherapy device. Although the CHECKMATE System received approval at the same time as our Beta-Cath System, we believe the Beta-Cath System competes effectively against the CHECKMATE System because of the ease of use of beta radiation over gamma. In November 2001, Guidant received FDA approval to market the GALILEO Intravascular Radiotherapy System. The GALILEO System is a beta radiation system as is the Beta-Cath System and the Company competes with Guidant based upon price and product performance. For 2002 the Beta-Cath System maintained approximately 60% of the vascular brachytherapy market worldwide.

Many of these same companies and others are researching coatings and treatments to coronary stents, commonly referred to as drug eluting stents, which could reduce restenosis and would possibly be more acceptable to a medical community already experienced at using stents. Their development represents a potentially revolutionary advance in cardiovascular treatment. During 2002 drug eluting stents began to enter the European market and we anticipate initial US entry in the second quarter of 2003. We expect these introductions to reduce the use of metallic stents in the US and, if the reduction of in-stent restenosis is significant, it could have a negative impact on the ultimate acceptability of vascular brachytherapy

GOVERNMENT REGULATION

United States

Our Beta-Cath System is regulated in the United States as a medical device. The manufacture and sale of medical devices intended for commercial distribution are subject to extensive governmental regulations in the United States. Medical devices are regulated in the United States by the FDA under the Federal Food, Drug, and Cosmetic Act (the FDC Act) and generally require pre-market clearance or pre-market approval prior to commercial distribution. In addition, certain material changes or modifications to medical devices also are subject to FDA review and clearance or approval. The FDA regulates the clinical testing, manufacture, packaging, labeling, storage, distribution and promotion

of medical devices. Noncompliance with applicable requirements can result in, among other things, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, failure of the government to grant pre-market clearance or pre-market approval for devices, withdrawal of marketing approvals, a recommendation by the FDA that we not be permitted to enter into government contracts, and criminal prosecution. The FDA also has the authority to request

repair, replacement or refund of the cost of any device manufactured or distributed.

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In the United States, medical devices are classified into one of three classes (Class I, II or III) on the basis of the controls deemed necessary by the FDA to reasonably assure their safety and effectiveness. Under FDA regulations Class I devices are subject to general controls (for example, labeling, pre-market notification and adherence to good manufacturing practices or quality systems regulations) and Class II devices are subject to general and special controls (for example, performance standards, postmarket surveillance, patient registries, and FDA guidelines). Class III is the most stringent regulatory category for medical devices. Generally, Class III devices are those that must receive pre-market approval by the FDA after evaluation of their safety and effectiveness (for example, life-sustaining, life-supporting or implantable devices, or new devices that have not been found substantially equivalent to other Class II legally marketed devices). The Beta-Cath System is a Class III device, which required the FDA s pre-market approval prior to its commercialization, which occurred November 2000.

A pre-market approval application must be supported by valid scientific evidence, which typically includes extensive data, including preclinical and human clinical trial data to demonstrate safety and effectiveness of the device. If human clinical trials of a device are required and the device is a significant risk device, the sponsor of the trial, usually the manufacturer or the distributor of the device, is required to file an investigational device exemption application with the FDA and obtain FDA approval prior to commencing human clinical trials. The investigational device exemption application must be supported by data, typically including the results of animal and laboratory testing. If the investigational device exemption application is approved by the FDA and one or more appropriate Institutional Review Boards, human clinical trials may begin at a specific number of investigational sites with a specific number of patients, as approved by the FDA.

The pre-market approval application must also contain the results of all relevant bench tests, laboratory and animal studies, a complete description of the device and its components, and a detailed description of the methods, facilities and controls used to manufacture the device. In addition, the submission should include the proposed labeling, advertising literature and training methods (if required).

If the FDA s evaluation of the pre-market approval application is favorable, the FDA will either issue an approval letter or an approvable letter, containing a number of conditions, which must be satisfied in order to secure the final approval of the pre-market approval application. When and if those conditions have been fulfilled to the satisfaction of the FDA, the agency will issue a letter approving a pre-market approval application authorizing commercial marketing of the device for certain indications. If the FDA s evaluation of the pre-market approval application or manufacturing facilities is not favorable, the FDA will deny approval of the pre-market approval application or issue a not approvable letter. The FDA may also determine that additional clinical trials are necessary, in which case approval of the pre-market approval application could be delayed for several years while additional clinical trails are conducted and submitted in an amendment to the pre-market approval application.

The process of obtaining a pre-market approval and other required regulatory approvals can be expensive, uncertain and lengthy, and we may be unsuccessful in obtaining approvals to market future products. The Company anticipates submitting applications for pre-market approval for the use of radiation in treating femoral-popliteal (fem-pop) disease and arterial-venous (A-V) dialysis grafts after the completion of their respective clinical trials. The FDA may not act favorably or quickly on any of our submissions. We may encounter significant difficulties and costs in our efforts to obtain additional FDA approvals that could delay or preclude us from selling new products in the United States. Furthermore, the FDA may request additional data or require that we conduct further clinical studies, causing us to incur substantial cost and delay. In addition, the FDA may impose strict labeling requirements, onerous operator training requirements or other requirements as a condition of our pre-market approval, any of which could limit our ability to market new products. Labeling and marketing activities are subject to scrutiny by the FDA and, in certain circumstances, by the Federal Trade Commission. FDA enforcement policy strictly prohibits the marketing of FDA cleared or approved medical devices for unapproved uses, further, if a company wishes to modify a product after FDA approval of a pre-market approval,

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including any changes that could affect safety or effectiveness, additional approvals will be required by the FDA. Such changes include, but are not limited to new indications for use, the use of a different facility to manufacture, changes to process or package the device, changes in vendors to supply components, changes in manufacturing methods, changes in design specifications and certain labeling changes.

Any products we manufacture or distribute pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the use of the device. Device manufacturers are required to register their establishments and list their devices with the FDA and certain state agencies, and are subject to periodic inspections by the FDA and those state agencies. The Food, Drug, and Cosmetic Act requires device manufacturers to comply with good manufacturing practices regulations, called the quality systems regulations (QSR). The QSR require that medical device manufacturers comply with various quality control requirements pertaining to design controls, purchasing contracts, organization and personnel; device and manufacturing process design; buildings, environmental control, cleaning and sanitation; equipment and calibration of equipment; medical device components; manufacturing specifications and processes; reprocessing of devices; labeling and packaging; in-process and finished device inspection and acceptance; device failure investigations; and recordkeeping requirements including compliance files. The FDA enforces these requirements through periodic inspections of medical device manufacturing facilities. In addition, a set of regulations known as the medical device reporting regulations obligates manufacturers to inform the FDA whenever information reasonably suggests that one of its devices may have caused or contributed to a death or serious injury, or when one of its devices malfunctions and, if the malfunction were to recur, the device would be likely to cause or contribute to a death or serious injury.

Labeling and promotional activities are also subject to scrutiny by the FDA. Among other things, labeling violates law if it is false or misleading in any respect or it fails to contain adequate directions for use. Moreover, any labeling claims that exceed the representations approved by the FDA will violate the Food, Drug and Cosmetic Act.

Our product advertising is also subject to regulation by the Federal Trade Commission under the Federal Trade Commission Act, which prohibits unfair methods of competition and unfair or deceptive acts or practices in or affecting commerce, including the dissemination of any false or misleading advertisement pertaining to medical devices. Under the Federal Trade Commission s substantiation doctrine, an advertiser is required to have a reasonable basis for all product claims at the time claims are first used in advertising or other promotions. What constitutes a &#14