# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, DC 20549**

# FORM 8-K

**Current Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of report (Date of earliest event reported): December 10, 2003**

# Nabi Biopharmaceuticals

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **000-04829** | **59-1212264** |
|---|---|---|
| **(State or other jurisdiction of incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

**5800 Park of Commerce Boulevard N.W., Boca Raton, FL 33487**

**(Address of principal executive offices, including zip code)**

**(561) 989-5800**

**(Registrant's telephone number, including area code)**

**Item 5. Other Events.**

The following information reflects several recent developments in our StaphVAX program:

- We continue to make progress towards the manufacture of StaphVAX consistency lots at Cambrex Bio Science Baltimore, Inc., or Cambrex Bio Science, to support the license application with the European Union, or EU, planned for the end of 2004. Capacity at Cambrex Bio Science can support the launch of StaphVAX in Europe and the initial launch in the U.S. Recognizing that the peak forecasted demand for StaphVAX is expected to be higher than the capacity at Cambrex Bio Science, we have decided to develop our own manufacturing capacity for StaphVAX. This will increase total vaccine manufacturing capacity and provide a second source of production for this product. We are evaluating the build-out of a vaccine manufacturing plant in an unused portion of our manufacturing facility in Boca Raton, Florida. This option would increase resource utilization at this facility. Simultaneously, we are conducting a search for an existing manufacturing facility close to our research and development location in Maryland. The decision between the two alternatives will be based primarily on cost and time-to-market adjusted for risk in both.
- We intend to initially file for licensure of StaphVAX in the EU with vaccine manufactured at the Cambrex Bio Science facility before the end of 2004. If the license is granted in the EU, a supplemental filing will be submitted for our manufacturing facility, allowing supply of StaphVAX from both facilities. For the U.S. filing for the licensure of StaphVAX, we intend to submit a license application by the end of 2005, based on both the Cambrex Bio Science facility as well as our own manufacturing facility.
- We recently increased the size of the confirmatory Phase III trial of StaphVAX from 3,000 to approximately 3,600 subjects to increase the trial's statistical power so that we can demonstrate statistical significance with a clinical reduction of 50% or more in types 5 and 8 *Staphylococcus aureus*, or *S. aureus*, infections through eight months post-vaccination. This is less than the 60% reduction rate used in the protocol for the previous Phase III trial.
- For licensure in the U.S., our plan to file a Biologics License Application, or BLA, with the FDA by the end of 2005 remains unchanged. The outside costs of the confirmatory Phase III trial are projected to total approximately $36 million and will be incurred from initiation of the trial in 2003 through its expected completion in the second half of 2005.
- The primary efficacy endpoint of the Phase III trial is a statistically significant reduction in types 5 and 8 *S. aureus* infections through eight months post-vaccination. A booster dose will also be administered eight months following the initial vaccination. Vaccine immunogenicity and efficacy will continue to be evaluated for an additional four to six months as secondary trial endpoints. Consequently, all patients enrolled in the trial will be followed for at least 12 months in total.

The following information concerns Gram-positive bacterial infections in Europe:

- There were approximately 2.4 million patients in Europe that acquired hospital based infections during the year 2000.
- *S. aureus* is the bacteria most responsible for bloodstream infections with an incidence rate above 35%.
- As reported by SENTRY, during the time period 1997-1999 the rate of Meticillin-resistant *S. aureus*, or MRSA, was 26.3% across Europe.

On November 26, 2003, we filed a registration statement (Registration No. 333-110813) on Form S-3 (the "Registration Statement") with the Securities and Exchange Commission for an underwritten public offering of 8,500,000 shares of our common stock, par value $0.10 per share. All shares will be offered by us. In addition, the underwriters will have an option to purchase up to an additional 1,275,000 shares of our common stock to cover any over-allotments. Lehman Brothers Inc. will act as bookrunner and Wachovia Securities, U.S. Bancorp Piper Jaffray and Harris Nesbitt Gerard will act as co-managers.

The following information was included in the Registration Statement and updates information previously set forth in our Annual Report on Form 10-K for the year ended December 28, 2002 and our subsequent filings under the Securities Exchange Act of 1934, as amended.

## RISK FACTORS

***Our initial Phase III clinical trial for StaphVAX did not achieve statistical significance for the specified end point and neither may our confirmatory Phase III clinical trial.***

In late 2000, we completed our initial Phase III placebo-controlled clinical trial for StaphVAX in hemodialysis patients with end-stage renal disease. The specified end point for this trial was a statistically significant reduction in *S. aureus* infections in end-stage renal disease patients after 12 months. The trial did not achieve this end point. In September 2003, we began enrollment for a Phase III clinical trial for StaphVAX with a primary efficacy end point at eight months post-vaccination. The results from this trial may not establish statistical significance for the eight-month end point. Our inability to achieve statistically significant results in our confirmatory Phase III clinical trial would adversely affect our future business, financial condition and results of operations.

***Our plan to commercialize StaphVAX initially in the EU may not be successful.***

We plan to file our first license application for StaphVAX in the EU by the end of 2004 using the centralized approval process. There can be no assurance that we will file a StaphVAX license application in the EU by the end of 2004 or that we will receive approval to begin commercial sales of the product in the EU by the end of 2005 or at all. Any delays in EU licensure or commercialization could adversely affect our market valuation and our financial position. We have no experience in obtaining licensure of vaccines in the EU or other markets. We have no direct experience marketing and selling biopharmaceutical products in the EU, and we also have no sales or marketing organization to sell and distribute StaphVAX in the EU.

***We may not realize the value of our acquisition of PhosLo.***

On August 4, 2003, we acquired the worldwide rights to PhosLo through the purchase of various intangible assets for $60.3 million in cash, 1.5 million shares of our common stock and an obligation to pay $30.0 million in cash over the period ending March 1, 2007. These intangible assets represent approximately one-third of the total assets reflected on our balance sheet at September 27, 2003. PhosLo is marketed to physicians caring for patients suffering kidney failure who have developed elevated phosphorus levels in their blood. This is a market in which we have no previous experience. PhosLo currently competes with two other products, a prescription medication and a non-prescription medication, and we are aware of a third competitive prescription product that may come to market. All of these products are or will be produced, marketed and sold by companies that have substantially greater financial and marketing resources than we have. If we do not achieve the necessary level of success in marketing PhosLo to recover the value of the intangible assets we acquired, we will be required to write down or write off some or all of the PhosLo intangible assets. If this occurs, our balance sheet and results of operations will be adversely affected.

***Our rights to three existing biopharmaceutical products may expire.***

Our rights to WinRho SDF expire in 2005. There can be no assurance that our rights to this product can be extended on terms that will be satisfactory to us.

We acquired our rights to Autoplex T from Baxter International Inc., or Baxter, under a consent decree of the Federal Trade Commission. Pursuant to this decree, Baxter is obligated to supply Autoplex T to us until May 2004, unless the consent decree is earlier terminated or we receive approval from the FDA to manufacture the product ourselves. We will not obtain approval from the FDA to manufacture Autoplex T by May 2004. We are unlikely to sell Autoplex T after May 2004.

Our rights to Aloprim expire in June 2004. We have an option to purchase the rights to distribute Aloprim in the territories now covered by the Aloprim agreement and to extend the obligation to supply this product to us for five years, subject to the negotiation of a mutually satisfactory supply agreement. Our inability to reach agreement on the terms of this supply agreement would interrupt our supply of Aloprim.

***We depend upon third parties to manufacture our products.***

We do not manufacture four of our five marketed products and depend upon third parties to manufacture these products for us. A failure by these manufacturers to timely meet our needs for these products could have a material adverse effect on our future business, financial condition and results of operations. This has occurred in the past. Our biopharmaceutical product sales were constrained in 2000 because of the inability of the contract manufacturer for WinRho SDF to supply product for a period of time. Since 2000, our ability to market Autoplex T and Aloprim has been adversely affected by our inability to obtain necessary quantities of these products.

Our research and development product pipeline principally involves conjugate vaccines. We currently rely on a third party to manufacture StaphVAX. We announced on October 9, 2003 that we have entered into an agreement for up to ten years with Cambrex Bio Science to manufacture StaphVAX. In so doing, we let expire agreements we had for several years with a different party to provide the services we will receive from Cambrex Bio Science. The agreement with Cambrex Bio Science contemplates that it will provide us with product for our clinical needs and for the initial commercial launch of StaphVAX but not for all of our forecasted needs if StaphVAX is a commercial success. Although we intend to develop or acquire an internal capacity to produce commercial quantities of StaphVAX, we will be dependent on Cambrex Bio Science and other third parties for the manufacture of StaphVAX and other products in our research and development pipeline. The failure of our contract manufacturers to supply us with sufficient amounts of product to meet our needs, or to renew their contracts with us on commercially reasonable terms, would have a material adverse effect on our future business, financial condition and results of operations.

***We may not utilize the full capacity of our facility and have limited manufacturing capability and experience with our clinical product candidates, Altastaph and Civacir.***

We began commercial manufacture of Nabi-HB at our Boca Raton biopharmaceutical manufacturing facility in the fourth quarter of 2001 and intend to use this facility for the manufacture of our clinical product candidates, Altastaph and Civacir, and for the manufacture of products of other parties. For the foreseeable future, we will not utilize the full manufacturing capacity of the facility and there can be no assurance that we can operate the facility efficiently. There can be no assurance that we will have either our own products to manufacture or those of others to offset the cost of the facility's operation. Further, we have limited experience manufacturing our clinical product candidates. Our failure to manufacture our clinical product candidates successfully would have a material adverse effect on our future business, financial condition and results of operations.

***A disaster at our sole manufacturing facility would interrupt our manufacturing capability for the products produced there.***

Manufacturing products at a single site presents risks because a disaster, such as a fire or hurricane, may interrupt manufacturing capability. In such an event, we will have to resort to alternative sources of manufacturing that could increase our costs as well as result in significant delays while required regulatory approvals are obtained. Any such delays or increased costs could have a material adverse effect on our future business, financial condition and results of operations.

***Our sales of Nabi-HB are directly related to patient treatment protocols and the number of liver transplants performed in patients who are positive for hepatitus B virus, or HBV.***

Our sales of Nabi-HB are primarily for the care of HBV-positive liver transplant patients at the time of and for a period following liver transplant. The number of liver transplants that occurs depends on the number of livers available for transplant. The number of livers used for HBV-positive liver transplant candidates as well as the dosing of Nabi-HB may vary from time to time based on the following factors

- changes in overall organ availability,
- allocations of available organs to eligible potential recipients and
- changes in the treatment protocols applied to HBV-positive patients.

Each of these factors is outside our control. Sales of Nabi-HB will be adversely affected if patient treatment protocols change or the number of hepatitis B liver transplants decreases. Sales of Nabi-HB Intravenous, if it is licensed, will be similarly affected. This could have an adverse effect on our future results of operations and financial condition.

***We sell our products to a small number of customers; therefore, the loss of any major customer could have a material adverse effect on our results of operations or financial condition.***

We sell a significant portion of our biopharmaceutical products to pharmaceutical wholesalers and distributors. A loss of any major customer or a material reduction in such customer's purchases from us could have a material adverse effect on our results of operations and financial condition. We also maintain a significant receivable balance with each of these customers. If these customers become unable or unwilling to pay amounts owed to us, our financial condition and results of operations could be adversely affected.

Our antibody sales are concentrated among a few large pharmaceutical companies. During the 2000, 2001 and 2002 fiscal years, antibody sales to our top three customers collectively accounted for approximately 60%, 66%, and 74%, respectively, of our antibody sales. The loss of certain remaining major customers or a material reduction in these major customers' purchases of antibodies could have a material adverse effect upon our future business, financial condition and results of operations. If these customers are unable to comply with FDA or European Medicines Evaluation Agency, or EMEA, and other non-U.S. regulations, their manufacturing facilities may be temporarily closed, thereby reducing the need for the antibodies we provide. Plant closures and reductions in customers' production because of regulatory problems have occurred in recent years, and our financial performance has been adversely affected as a result. There can be no assurance that customer regulatory problems, which are not within our control, will not reoccur with an adverse impact on us in the future.

***Heightened concerns over antibody products and screening measures could adversely affect our antibody production.***

Our antibody collection centers and our customers for antibody products are subject to extensive regulation by the FDA and non-U.S. regulatory authorities. Concern over the safety of antibody products has resulted in the adoption of more rigorous screening procedures by regulatory authorities and manufacturers of antibody products. In prior years, these changes have resulted in significantly increased costs to us in providing non-specific and specialty antibodies to our customers. New procedures, which include a more extensive investigation into a donor's background, as well as more sensitive tests, also have disqualified numerous potential donors and discouraged other donors who may be reluctant to undergo the screening procedures. These more stringent measures could adversely affect our antibody production with a corresponding, adverse effect on our future business, financial condition and results of operations. In addition, our efforts to increase production to meet customer demand may result in higher costs to attract and retain donors.

***New treatments may reduce the demand for our antibodies and antibody based biopharmaceutical products.***

Most of the antibodies we collect, process and sell to our customers are used in the manufacture of biopharmaceutical products to treat certain diseases. Several companies are marketing and developing products to treat some of these diseases based on technology that would reduce or eliminate the need for human antibodies. Such products could adversely affect the demand for antibodies and antibody based biopharmaceutical products. We are unable to predict the impact of future technological advances on our business.

***A reduction in the availability of specialty antibodies could adversely affect our ability to manufacture an adequate amount of Nabi-HB or to fulfill contractual obligations.***

Our ability to manufacture Nabi-HB depends upon the availability of anti-HB specialty antibodies that we primarily obtain from our FDA-approved antibody collection centers. Similarly, we have contractual obligations to supply other specialty antibodies to third parties that we also obtain from our FDA-approved antibody collection centers. Specialty antibodies are more difficult to obtain than non-specific antibodies. Reduced availability of the necessary specialty antibodies would adversely affect our ability to manufacture an adequate amount of Nabi-HB or to fulfill our contractual obligations, with the result that our future business, financial condition and results of operations would suffer.

***We may not generate sufficient cash flow from our biopharmaceutical and antibody products or obtain financing necessary to fund our research and development activity at an appropriate level.***

We have incurred and expect to continue incurring significant expenses associated with our biopharmaceutical research and development activities, including the cost of clinical trials and marketing expenses. These expenses adversely affect our current ability to be profitable. Products under development may not generate sales for several years or at all. We do not have the financial resources to fund concurrently all of our biopharmaceutical product development programs to completion. Our ability to continue to fund all of our ongoing research and development activities depends on our ability to generate sales from our biopharmaceutical and antibody products or to obtain financing. There can be no assurance, therefore, that we will be able to continue to fund our research and development activities at the level required to commercialize all of our biopharmaceutical product development programs. If we are required to reduce the funding for certain of our research and development activities, this could have a material adverse effect on our future prospects.

***We may enter into strategic alliances that may not be successful and may adversely affect our ability to develop our products.***

We intend to pursue strategic alliances with third parties to develop and/or commercialize certain of our biopharmaceutical products. No assurance can be given that we will be successful in these efforts or, if successful, that our collaborative partners will conduct their activities in a timely manner. If we are not successful in our efforts, our ability to continue to develop our products may be affected adversely. Even if we are successful, if any of our collaborative partners violates or terminates their agreements with us or otherwise fails to conduct their collaborative activities in a timely manner, the development or commercialization of our products could be delayed. This might require us to devote significant additional resources to product development and commercialization or terminate certain development programs. In addition, there can be no assurance that disputes will not arise in the future with respect to the ownership of rights to any technology developed with third parties. These and other possible disagreements between our collaborative partners and us could lead to delays in the collaborative research, development or commercialization of certain products, or could require or result in litigation or arbitration, which would be time consuming and expensive and could have a material adverse effect on our future business, financial condition and results of operations.

***We may not be able to develop and commercialize new biopharmaceutical products successfully or in a timely manner, which could adversely impact our future operations.***

Our future success will depend on our ability to achieve scientific and technological advances and to translate such advances into commercially competitive products on a timely basis. Our biopharmaceutical products under development are at various stages, and substantial further development, pre-clinical testing and clinical trials will be required to determine their technical feasibility and commercial viability. Our proposed development schedules for these products may be affected by a variety of factors, including

- technological difficulties,
- competition,
- failure to obtain necessary regulatory approvals,
- failure to achieve desired results in clinical trials,
- proprietary technology positions of others,
- reliance on third parties for manufacturing,
- failure to market effectively,
- changes in government regulation and funding.

Positive results for a product in a clinical trial do not necessarily assure that positive results will be obtained in future clinical trials or that we will obtain government approval to commercialize the product. In addition, any delay in the development, introduction or marketing of our products under development could result either in such products being marketed at a time when their cost and performance characteristics might not be competitive in the marketplace or in a shortening of their commercial lives. There can be no assurance that our biopharmaceutical products under development will prove to be technologically feasible or commercially viable or that we will be able to obtain necessary regulatory approvals and licenses on a timely basis, if at all. Our failure to develop and commercialize successfully our biopharmaceutical products in a timely manner and obtain necessary regulatory approvals could have a material adverse effect on our future operations. In particular, our failure to obtain regulatory approval for StaphVAX on a timely basis could adversely affect our market valuation.

***The market may not be receptive to our products upon their introduction.***

There can be no assurance that any of our products in development will achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including

- the receipt of regulatory approvals,
- any limited indications of regulatory approvals,
- the establishment and demonstration in the medical community of the clinical efficacy and safety of our products and their potential advantages over existing treatment methods,
- the prices of such products and
- the reimbursement policies of government and third-party payers.

The failure of our product pipeline to gain market acceptance could have a material adverse effect on our future business, financial condition and results of operations.

***We are unable to pass through certain cost increases to our antibody product customers with which we have supply contracts.***

A significant amount of our antibodies are sold under contracts that extend for periods up to five years. Certain contracts do not permit us to increase prices during the contract term except to reflect changes in customer specifications and new governmental regulations. If our costs of collecting antibodies under these contracts rise for reasons other than changes in customer specifications and new governmental regulations, we are unable to pass on these cost increases to our antibody product customers except with the customer's consent.

***An increase in the supply of or a decrease in the demand for antibody products could materially and adversely affect our future business, financial condition and results of operations.***

The worldwide supply of antibodies has fluctuated historically. Future changes in government regulation relating to the collection, fractionation and use of antibodies or any negative public perception about the antibody collection process or the safety of products derived from blood or antibodies could further adversely affect the overall supply of or demand for antibodies. Increases in supply or decreases in demand of antibody products could have a material adverse effect on our future business, financial condition and results of operations.

***If we fail to comply with extensive regulations enforced by the FDA, EMEA and other agencies, the sale of our current products and the commercialization of our product candidates would be prevented or delayed.***

Research, pre-clinical development, clinical trials, manufacturing and marketing of our products are subject to extensive regulation by various government authorities. The process of obtaining FDA, EMEA and other required regulatory approvals is lengthy and expensive, and the time required for such approvals is uncertain. The approval process is affected by such factors as

- the severity of the disease,
- the quality of submission,
- the clinical efficacy and safety,
- the strength of the chemistry and manufacturing control of the process,

- the manufacturing facility compliance,
- the availability of alternative treatments and
- the risks and benefits demonstrated in clinical trials.

Regulatory authorities also may require post-marketing surveillance to monitor potential adverse effects of our products or product candidates. Congress or the FDA in specific situations can modify the regulatory process. Many of our clinical trials are at a relatively early stage and, except for Nabi-HB, WinRho SDF, PhosLo, Aloprim, Autoplex T and certain non-specific and specialty antibody products, no approval from the FDA or any other government agency for the manufacturing or marketing of any other products under development has been granted. There can be no assurance that we will be able to obtain the necessary approvals to manufacture or market any of our pipeline products. Failure to obtain additional regulatory approvals of products currently marketed or regulatory approval for products under development could have a material adverse effect on our future business, financial condition and results of operations. Once approved, a product's failure to comply with applicable regulatory requirements could, among other things, result in warning letters, fines, suspension or revocation of regulatory approvals, product recalls or seizures, operating restrictions, injunctions and criminal prosecutions.

Although we do not have material sales of our biopharmaceutical products outside the U.S. today, our goal is to expand our global presence for these products. Distribution of our products outside the U.S. is subject to extensive government regulation. These regulations, including the requirements for approvals or clearance to market, the time required for regulatory review and the sanctions imposed for violations, vary from country to country. There can be no assurance that we will obtain regulatory approvals in such countries or that we will not be required to incur significant costs in obtaining or maintaining these regulatory approvals. In addition, the export by us of certain of our products that have not yet been cleared for domestic commercial distribution may be subject to FDA export restrictions. Failure to obtain necessary regulatory approvals, the restriction, suspension or revocation of existing approvals or any other failure to comply with regulatory requirements would have a material adverse effect on our future business, financial condition and results of operations.

Our U.S. manufacturing, antibody collection, labeling, storage and distribution activities also are subject to strict regulation and licensing by the FDA. Our biopharmaceutical manufacturing facility in Boca Raton, Florida is subject to periodic inspection by the FDA, the EMEA and other regulatory authorities and from time to time, we may receive notices of deficiencies from these agencies as a result of such inspections. Our antibody collection centers in the U.S. also are subject to periodic inspection by the FDA, the EMEA and other regulatory authorities and from time to time, we may receive notices of deficiencies from these agencies as a result of such inspections. Our failure, or the failure of our biopharmaceutical manufacturing facility or our antibody collection centers, to continue to meet regulatory standards or to remedy any deficiencies could result in corrective action by the FDA, including closure of our biopharmaceutical manufacturing facility or one or more antibody collection centers and fines or penalties. New regulations may be enacted and existing regulations, their interpretation and enforcement, are subject to change. Therefore, there can be no assurance that we will be able to continue to comply with any regulations or that the costs of such compliance will not have a material adverse effect on our future business, financial condition and results of operations.

***We may be subject to costly and damaging liability claims relating to antibody contamination and other claims.***

Antibodies we collect, antibody based products we manufacture, antibody based products we market and antibody based products our customers manufacture run the risk of being contaminated with viruses. As a result, suits may be filed against our customers and us claiming that the plaintiffs became infected with a virus as a result of using contaminated products. Such suits have been filed in the past related to contaminated antibodies, and in a number of suits we were one of several defendants. No assurance can be given that additional lawsuits relating to infection with viruses will not be brought against us by persons who have become infected with viruses from antibody based products.

Pharmaceutical and biotechnology companies are increasingly subject to litigation, including class action suits, and governmental and administrative investigations and proceedings related to product pricing and marketing

practices. We have been named as one of over 40 pharmaceutical and biotechnology defendants in three class action lawsuits. There can be no assurance that lawsuits based on other causes of action will not be filed or that we will be successful in the defense of any or all existing or potential future lawsuits. Defense of suits can be expensive and time consuming, regardless of the outcome, and an adverse result in one or more suits could have a material adverse effect on our future business, financial condition and results of operations.

***We may not be able to maintain sufficient product liability and directors and officers insurance to cover claims against us.***

Product liability and directors and officers insurance for the biopharmaceutical industry is generally expensive to the extent it is available at all. There can be no assurance that we will be able to maintain such insurance on acceptable terms or that we will be able to secure increased coverage if the commercialization of our products progresses, or that existing or future claims against us will be covered by our product liability insurance. Moreover, there can be no assurance that the existing coverage of our insurance policy and/or any rights of indemnification and contribution that we may have will offset existing or future claims. A successful claim against us with respect to uninsured liabilities or in excess of insurance coverage and not subject to any indemnification or contribution could have a material adverse effect on our future business, financial condition and results of operations. Further, if we were unable to obtain directors and officers liability insurance, it could affect adversely our ability to attract and retain directors and senior officers.

***We may not be able to maintain sufficient property insurance on our facilities in Florida.***

We maintain significant real property assets in Florida. Property insurance for companies with a high concentration of property assets in Florida is generally expensive to the extent it is available at all. There can be no assurance that we will be able to maintain such insurance on acceptable terms or that we will be able to secure increased coverage if the value of our property increases.

***We may not be able to raise necessary additional capital on acceptable terms, if at all.***

We may need to raise additional capital to increase funding of our product research, development and marketing activities or to acquire additional products. We may seek additional funding through public or private equity or debt financing, collaborative arrangements with strategic partners or from other sources. There can be no assurance, however, that additional financing will be available on acceptable terms, if at all. If adequate funds are not available, we may have to defer certain investments in the areas of research, product development, manufacturing, marketing activity or business development, or otherwise modify our business strategy, and our future business and future prospects could be materially and adversely affected.

***We may not maintain compliance with our credit agreement.***

We may not maintain compliance with the covenants required by our credit agreement. This potential non-compliance may limit our ability to access funds under the credit agreement without receipt of a waiver from the lender, which may not be given. In addition, our borrowing base, as defined in the credit agreement, is limited by eligible accounts receivable and inventory balances. If funds are not available to us under our credit agreement due to non-compliance with debt covenants or borrowing base limitations, we may have to defer certain investments in the areas of research, product development, manufacturing, marketing activity or business development, or otherwise modify our business strategy, and our future business and future prospects could be materially and adversely affected.

***Our patents and proprietary rights may not provide sufficient protection, and patents of other companies could prevent us from developing and marketing our products.***

The patent positions of biopharmaceutical firms generally are highly uncertain and involve complex legal and factual questions. There can be no assurance that existing patent applications will result in issued patents, that we will be able to obtain additional licenses to patents of others or that we will be able to develop additional patentable technology of our own. We cannot be certain that we were the first creator of inventions covered by our patents or pending patent applications or that we were the first to file patent applications for such inventions. There can be no assurance that any patents issued to us will provide us with competitive advantages or will not be challenged by others. Furthermore, there can be no assurance that others will not independently develop similar products, or, if patents are issued to us, design around such patents.

A number of pharmaceutical companies, biotechnology companies, universities and research institutions have filed patent applications or received patents relating to products or processes competitive with or similar to ours. Some of these applications or patents may compete with our applications or conflict in certain respects with claims made under our applications. Such a conflict could result in a significant reduction of the coverage of our patents, if issued. In addition, if patents that contain competitive or conflicting claims are issued to others and such claims are ultimately determined to be valid, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. If any licenses are required, there can be no assurance that we will be able to obtain any such licenses on commercially favorable terms, if at all. Our failure to obtain a license to any technology that we may require in order to commercialize our products could have a material adverse effect on our future business, financial condition and results of operations. Litigation, which could result in substantial cost to us, may also be necessary to enforce any patents issued to us or to determine the scope and validity of third-party proprietary rights.

We also rely on secrecy to protect our technology, especially where patent protection is not believed to be appropriate or obtainable. We maintain strict controls and procedures regarding access to and use of our proprietary technology and processes. However, there can be no assurance that these controls or procedures will not be violated, that we would have adequate remedies for any violation, or that our trade secrets will not otherwise become known or be independently discovered by competitors.

***We compete with larger, better financed and more mature pharmaceutical and biotechnology companies, which are capable of developing new products and approaches that could make our products obsolete.***

Competition in the development of biopharmaceutical products is intense, both from pharmaceutical and biotechnology companies, and is expected to increase. Many of our competitors have greater financial resources and larger research and development staffs than we have, as well as substantially greater experience in developing products, obtaining regulatory approvals, and manufacturing and marketing biopharmaceutical products. We compete with our competitors

- to develop products,
- to acquire products and technologies and
- to attract and retain qualified scientific personnel.

There can be no assurance that our competitors may succeed in developing technologies and products that are more effective or affordable than those that we are developing. In addition, one or more of our competitors may achieve product commercialization of or patent protection for competitive products earlier than us, which would preclude or substantially limit sales of our products. Further, several companies are attempting to develop and market products to treat certain diseases based upon technology that would lessen or eliminate the need for human antibodies. The successful development and commercialization by any of our competitors of any such product could have a material adverse effect on our future business, financial condition and results of operations.

***There are potential limitations on third-party reimbursement and other pricing-related matters that could reduce the sales of our products and may delay or impair our ability to generate sufficient revenues.***

Our ability to commercialize our biopharmaceutical products and related treatments depends in part upon the availability of, and our ability to obtain adequate levels of, reimbursement from government health administration authorities, private healthcare insurers and other organizations. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products, and there can be no assurance that adequate third-party payer coverage will be available, if at all. Inadequate levels of reimbursement may prohibit us from maintaining price levels sufficient for realization of an adequate return on our investment in developing new biopharmaceutical products and could result in the termination of production of otherwise commercially viable products.

In the U.S., government and other third-party payers are increasingly attempting to contain healthcare costs by limiting both the coverage and level of reimbursement for new products approved for marketing by the FDA and by refusing, in some cases, to provide any coverage for disease indications for which the FDA has not granted marketing approval. Also, the trend towards managed healthcare in the U.S. and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of healthcare services and products, as well as legislative proposals to reform healthcare or reduce government insurance programs, may all result in lower prices for our products. The cost containment measures that healthcare providers are instituting and the impact of any healthcare reform could have an adverse effect on our ability to sell our products and may have a material adverse effect on our future business, financial condition and results of operations.

There can be no assurance that reimbursement in the U.S. or other markets will be available for our products, or, if available, will not be reduced in the future, or that reimbursement amounts will not reduce the demand for, or the price of, our products. The unavailability of government or third-party reimbursement or the inadequacy of the reimbursement for medical treatments using our products could have a material adverse effect on our future business, financial condition and results of operations. Moreover, we are unable to forecast what additional legislation or regulation, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation or regulation would have on our future business.

## BUSINESS

### Overview

We apply our knowledge of the human immune system to commercialize and develop products that address serious, unmet medical needs. We have a broad portfolio of marketed biopharmaceutical products with growing revenues that generate cash flow to support the development of our clinical product candidates and our research programs. Our clinical product pipeline is composed of novel vaccines and antibody based biopharmaceutical products that are designed to prevent and treat infectious and addictive diseases, such as *S. aureus* infections, hepatitis B and hepatitis C, and nicotine addiction. We have exclusive rights to commercialize all of our clinical development candidates.

Through our own specialty sales force we market five biopharmaceutical products: PhosLo for the control of hyperphosphatemia in end-stage renal disease patients, Nabi-HB for the prevention of hepatitis B infections, WinRho SDF for the treatment of acute, chronic and HIV-related ITP, Aloprim for the treatment of chemotherapy-induced hyperuricemia, or high uric acid levels, and Autoplex T for the treatment of hemophilia A patients who have developed inhibitors to factor VIII. We have filed a BLA for the use of an intravenous formulation of Nabi-HB to prevent reinfection with hepatitis B disease in HBV-positive liver transplant patients. Sales of our biopharmaceutical products for the nine months ended September 28, 2002 and September 27, 2003 were $61.8 million and $75.4 million, respectively.

We have four product candidates in clinical development: StaphVAX, Altastaph, Civacir and NicVAX. Our lead clinical candidate is StaphVAX, a vaccine designed to prevent *S. aureus* infections. We have initiated a confirmatory Phase III clinical trial of StaphVAX to support a BLA filing in the U.S. by the end of 2005. In addition, we plan to file a Marketing Authorization Application, or MAA, in the EU by the end of 2004 for regulatory approval to market StaphVAX for the prevention of *S. aureus* bacteremia for up to 40 weeks in end-stage renal disease patients on hemodialysis. This filing will be based on efficacy data at 40 weeks obtained from our previously completed Phase III clinical trial for StaphVAX. We believe that the potential global market for products to prevent *S. aureus* and other Gram-positive infections is approximately $1-$2 billion.

### Our Marketed and Development Products

| Products | Indication/Intended Use | Status |
|---|---|---|
| PhosLo | Hyperphosphatemia | Marketed |
| Nabi-HB | Post-exposure prevention of hepatitis B infection | Marketed |
| Nabi-HB Intravenous | Prevention of reinfection with hepatitis B in liver transplant patients | BLA filed in U.S.;<br>Orphan Drug Designation |
| WinRho SDF | ITP | Marketed |
| Aloprim | Chemotherapy-induced hyperuricemia | Marketed |
| Autoplex T | Hemophilia A | Marketed |
| *Clinical Development* | | |
| StaphVAX | Long-term protection against S. aureus infections | Phase III confirmatory trial in U.S.; Application for licensure in EU planned for late 2004 |
| Altastaph | Immediate protection against S. aureus infections | Phase II trial in very low birth-weight newborns; Phase I/II trial in adults with persistent S. aureus infections |
| Civacir | Prevention of reinfection with hepatitis C in liver transplant patients | Phase I/II trial; Orphan Drug Designation |
| NicVAX | Nicotine addiction | Phase II trial in U.S.; Phase I/II trial in Europe |

In addition to our biopharmaceutical product portfolio, we collect specialty and non-specific antibodies that are used in our manufacture of Nabi-HB and our antibody based clinical products in development. In September 2001, we sold the operating assets of a majority of our antibody collection centers and our testing laboratory for $156.3 million in cash. We retained nine centers to supply our antibody requirements for the manufacture and development of our antibody based products. We also supply specialty and non-specific antibodies to pharmaceutical and diagnostic companies.

**Our Strategy**

The key elements of our business strategy are as follows

- *Continue to increase sales of our higher-margin biopharmaceutical products and the percentage these products represent of our total revenues.* We have successfully transitioned to a biopharmaceutical products company. We have grown our biopharmaceutical revenues each year since 2000. For the nine months ended September 28, 2002 and September 27, 2003 biopharmaceutical products represented 44.8% and 58.6% of our total sales, respectively. In the third quarter of 2003, biopharmaceutical products represented 72.4% of our total sales. We believe that the increasing percentage of our total revenues generated by sales of biopharmaceutical revenues reflects our increasing emphasis on our biopharmaceutical products business.
- *Expedite initial commercialization of StaphVAX by seeking EU approval for use in end-stage renal disease patients on hemodialysis.* After a series of discussions with various EU regulatory agencies, we have decided to file an MAA with the EU by the end of 2004 for regulatory approval to market StaphVAX for the prevention of *S. aureus* bacteremia for up to 40 weeks in end-stage renal disease patients on hemodialysis. This filing will be based on efficacy data obtained from our previously completed Phase III clinical trial that demonstrated a reduction in *S. aureus* bacteremia in those patients for up to 40 weeks. By using these data to support licensure, we will file two years earlier than we originally planned.
- *Obtain regulatory approval of a broad indication for StaphVAX for use in at-risk adults in the U.S. and the EU.* We commenced our confirmatory Phase III clinical trial for StaphVAX in September 2003. We recently increased the size of this trial from 3,000 to approximately 3,600 subjects to increase the trial's statistical power so that we can demonstrate statistical significance with a clinical reduction of 50% or more in types 5 and 8 *S. aureus* infections. The primary efficacy end point of this trial is to reduce the incidence of *S. aureus* bacteremia and secondary infections caused by bacteremia for up to eight months after vaccination. Our plan to file with the FDA for approval of a broad indication for StaphVAX by the end of 2005 remains unchanged. We also plan to file a supplement to the MAA dossier with the EU in the fourth quarter of 2005 incorporating data from the confirmatory Phase III clinical trial to apply for an expansion of the initial proposed indication.
- *Use cash flow from marketed products to contribute to the continued development of our clinical pipeline.* We expect to continue to generate meaningful revenues from our currently marketed biopharmaceutical products. We use the cash flow generated from sales of these products to contribute to the continued development of our product candidates in clinical development. By using cash flow from our marketed products to finance our clinical development programs, we intend to continue to reduce our need for external sources of financing.
- *Leverage our marketing expertise from our currently marketed products to advance commercial acceptance of PhosLo and products that emerge from our proprietary clinical pipeline.* We have an experienced specialty sales force that has successfully grown sales of our biopharmaceutical products. In August 2003, we acquired worldwide rights to PhosLo, which is sold in the nephrology market. We intend to use our sales force to grow sales of PhosLo and enhance our presence in this market. We believe that the experience we gain with nephrologists, the physicians who prescribe PhosLo, will enable us to build rapidly initial sales of StaphVAX.

**Currently Marketed Products**

*PhosLo [Calcium Acetate].* PhosLo is a prescription phosphate binder indicated for the control of hyperphosphatemia in end-stage renal disease patients. When given with food, PhosLo combines with dietary phosphorus to form insoluble calcium-phosphate complexes that are eliminated from the body, thereby reducing phosphorus absorption and lowering blood phosphorus levels. Controlling elevated phosphorus levels in dialysis patients with chronic kidney disease is critical because these patients are unable to eliminate excess phosphorus on their own. Elevated levels of phosphorus are associated with significant increases in illness and may result in death. In addition, elevated levels of phosphorus and calcium-phosphorus product have been associated with coronary calcification. We acquired worldwide rights to PhosLo in August 2003. We currently market PhosLo in the U.S. and plan to seek PhosLo registration and commercialization initially in the EU. Based upon customer demand, we anticipate reporting net sales of PhosLo of approximately $10.0 million to $11.0 million for the period August 5, 2003 through December 27, 2003.

According to the U.S. Renal Disease Service, or USRDS, as of December 2000, 382,000 patients in the U.S. met the criteria of chronic end-stage renal disease. The USRDS also projects that the population of end-stage renal disease patients will grow to over 650,000 patients in the U.S. by 2010. This growth in the number of chronic renal dialysis patients is largely attributable to increases in patients with diseases such as diabetes and hypertension, the primary causes of kidney failure, the overall aging of the U.S. population and increased life expectancy for dialysis patients. Based on our interviews with nephrologists, we believe that most dialysis patients are likely to experience elevated phosphorus levels during any 12-month period and therefore will require phosphate binder therapy to control their blood phosphorus levels for a period of time.

We believe that PhosLo has distinct competitive advantages over its principal competitors, Renagel and calcium carbonate products such as TUMS. In October 2003, the National Kidney Foundation issued the K/DOQI guidelines. The K/DOQI guidelines establish the primary goal of phosphate binder therapy to maintain the phosphorus levels in the blood below 5.5mg/dL and the calcium-phosphorus product below 55 mg/dL. We believe that PhosLo is the phosphate binder that best meets the K/DOQI guidelines.

In November 2003, the study: Treatment of Hyperphosphatemia in Hemodialysis Patients: The Calcium Acetate Renagel Evaluation (CARE Study) was presented. The results of this randomized, double-blind, controlled clinical trial, which compared the efficacy of calcium acetate (PhosLo) and sevelamer (Renagel (sevelamer hydrochloride)), show that patients treated with PhosLo were able to control blood phosphorus more effectively than patients treated with Renagel, the only other prescription drug currently indicated for the treatment of hyperphosphatemia in the U.S. In addition, patients treated with PhosLo achieved target phosphorus and calcium-phosphorus product levels more often and for longer periods of time than patients treated with Renagel. In addition to marked differences in efficacy, the mean daily cost of treatment with PhosLo in this study was $2.14 compared to $11.70 for Renagel. On an annualized basis, assuming continuous use, this would translate into $781 in projected treatment costs for PhosLo compared to $4,270 for Renagel, a potential cost-savings of $3,489 per year for patients treated with PhosLo.

PhosLo is distinct from calcium carbonate products, typically over-the-counter products such as TUMS in the U.S. or prescription calcium carbonate products in the EU. Although many chronic end-stage renal disease patients in the U.S. use over-the-counter calcium carbonate products to treat elevated phosphorus levels for reasons of cost, calcium carbonate products do not meet the K/DOQI guidelines due to the comparatively lower phosphate binding activity of calcium carbonate. As a result of this reduced activity, calcium carbonate products would be expected to result in calcium loads that fail to meet K/DOQI guidelines for non-dietary calcium absorption.

*Nabi-HB [Hepatitis B Immune Globulin (Human)]*. Nabi-HB is a human polyclonal antibody product indicated to prevent hepatitis B following accidental exposure to HBV. We believe the majority of our Nabi-HB sales are for intravenous use to prevent reinfection with hepatitis B disease in HBV-positive liver transplant patients. Currently, Nabi-HB is not indicated for this use. We have submitted a briefing document to European regulators, and we plan to seek regulatory approval for Nabi-HB in certain European countries using the mutual recognition process. We plan to submit our first license application for Nabi-HB in Europe in the first half of 2004. Sales of Nabi-HB for the nine months ended September 28, 2002 and September 27, 2003 were $25.5 million and $26.3 million, respectively.

In November 2002, we submitted a BLA to the FDA for an intravenous formulation of Nabi-HB to prevent hepatitis B disease in HBV-positive liver transplant patients. Nabi-HB Intravenous has received Orphan Drug Designation from the FDA, entitling us to marketing exclusivity for this indication for a period of seven years. In January 2003, we received notification that the FDA had accepted our BLA for Nabi-HB Intravenous for priority review. We received a complete response letter from the FDA in May 2003 requesting supplemental data and information but no additional clinical trials. We responded to the complete response letter in August 2003. In addition, we are gathering longer-range follow-up data from previously completed clinical trials, which we will provide to the FDA. We anticipate a response from the FDA during the first half of 2004.

HBV is a major health concern globally. The Hepatitis B Foundation currently estimates that one out of 20 people in the U.S. has been infected with HBV. The U.S. Centers for Disease Control, or CDC, currently estimates that in the U.S. alone there are an estimated 1.25 million chronic hepatitis B carriers, 78,000 new hepatitis B infections per year, and 5,000 individuals who die annually from hepatitis B or its complications. Chronic HBV infection is a frequent cause of end-stage liver disease and is present in approximately 10%-15% of liver transplant patients. Moreover, during surgery and in the period immediately following transplant surgery patients do not have any other treatment options to prevent reinfection of the transplanted liver. Reinfection of the transplanted liver is almost inevitable after surgery in HBV-positive patients.

*WinRho SDF [Rho(D) Immune Globulin Intravenous (Human)]*. WinRho SDF is a human polyclonal antibody based product approved and marketed for the treatment of ITP, an autoimmune disease that manifests itself in abnormally low platelet levels, thrombocytopenia, resulting in excessive bleeding. We began exclusive marketing of WinRho SDF in the U.S. in 1995 under a license and distribution agreement with Cangene Corporation, or Cangene. We pay a royalty to Cangene equal to approximately half of the net profits from sales of WinRho SDF. Sales of WinRho SDF for the nine months ended September 28, 2002 and September 27, 2003 were $26.8 million and $37.6 million, respectively.

ITP is recognized by the appearance of purple patches on the body caused by bleeding into the skin and mucus membranes. In ITP, the body's immune system produces antibodies that attach to platelets causing them to be removed from circulation, primarily by the spleen. Because platelets are required for blood clotting, as platelet counts decrease, the incidence of bleeding episodes increases. In certain cases, such as severe trauma or spontaneous intracranial hemorrhage, the bleeding can be life threatening. The Platelet Disorder Support Association currently estimates that approximately 30,000 people develop ITP in the U.S. each year. In children, the disease is usually acute at onset and is often resolved with treatment in six months. In adults, the onset is gradual and rarely resolves itself without treatment. ITP can occur as either a primary disease or secondary to another underlying disease such as HIV or lupus. Chronic thrombocytopenia is currently estimated to occur in about 10% of HIV-infected patients and in about one third of patients with AIDS.

***Other Products***

*Aloprim [(Allopurinol sodium) for injection]*. Aloprim is indicated for the treatment of chemotherapy-induced hyperuricemia in patients with leukemia, lymphoma or solid organ tumors. Complications associated with chemotherapy-induced hyperuricemia in these patients include renal failure. Aloprim is targeted to those patients who develop chemotherapy-induced hyperuricemia and are not treatable by oral therapies. Based on 2002 data from the American Cancer Society, there are approximately 90,000 patients annually suffering from leukemia and lymphoma in the U.S. that could potentially be at risk for developing chemotherapy-induced hyperuricemia. We acquired certain rights to distribute Aloprim from DSM Pharmaceuticals, or DSM, in June 1999 and currently have the exclusive right to distribute Aloprim in the U.S. We pay a royalty to DSM equal to a percentage of the net profits from sales of Aloprim. The royalty rate varies based on the level of annual sales.

*Autoplex T [Anti-Inhibitor Coagulant Complex, Heat Treated]*. Autoplex T is a blood clotting agent used to treat hemophilia A patients who have developed inhibitors to factor VIII. Hemophilia A is a blood clotting disorder characterized by a lack of functional coagulation factor VIII. Physicians typically treat hemophilia A by replacing the deficient factor with either recombinant clotting factor VIII or human factor VIII. In most cases, replacement therapy is effective in stopping bleeding episodes. However, the treatment of hemophilia A is complicated when an inhibitor or antibody is produced in response to outside sources of factor VIII. These antibodies neutralize infused factor VIII, rendering the patient at risk for excessive bleeding episodes. We acquired exclusive rights to distribute Autoplex T in the U.S., Canada and Mexico from Baxter in May 1997; however, these rights expire in May 2004.

**Clinical Development Products**

We have a significant pipeline of biopharmaceutical products under development. Our research and development pipeline products consist of vaccines for long-term protection and antibody based biopharmaceutical products for immediate short-term protection from blood infections caused by Gram-positive bacteria such as *S. aureus*, *S. epidermidis* and *Enterococci*, antibody based biopharmaceutical products for the treatment and/or prevention of various diseases, including hepatitis B and hepatitis C, and a vaccine for treating and preventing nicotine addiction.

***Gram-positive Infections Program***

According to current CDC estimates, more than two million patients in the U.S. each year contract an infection as a result of exposure to a pathogen while receiving care in a hospital. Within the approximately 5,400 acute care hospitals in the U.S., *S. aureus* is the leading cause of hospital-acquired bloodstream infections. With its capacity to cause serious complications and its increasing resistance to most antibiotics, *S. aureus* has become a critically dangerous pathogen. *S. aureus* can spread from the blood to the bones or the inner lining of the heart and its valves, or cause abscesses in internal organs such as the lungs, kidneys and brain. Patients who are most at risk for these infections include surgical patients, trauma or burn victims, newborns whose immune systems are not yet developed and people with chronic illnesses such as chronic skin diseases, diabetes, cancer and lung diseases or kidney diseases. People whose immune systems are suppressed due to disease, drugs or radiation therapy also are more susceptible to these bacterial infections.

Staphylococcal infections are difficult to treat because the bacteria that cause them are highly virulent and in many cases resistant to currently available antibiotics. This rise of antibiotic resistance has markedly curtailed options for treating *S. aureus* infections.

*StaphVAX (Staphylococcus aureus Polysaccharide Conjugate Vaccine)*. We are developing StaphVAX for patients who are at high risk of *S. aureus* infection and who are able to respond to a vaccine by producing their own antibodies. In the U.S. alone there are estimated to be 12 million of these patients. StaphVAX is intended to stimulate a patient's immune system to produce antibodies to *S. aureus* that provide active, long-term protection from the bacteria. StaphVAX targets *S. aureus* types 5 and 8, which are responsible for approximately 85% of *S. aureus* infections.

StaphVAX is an investigational polysaccharide conjugate vaccine based on patented vaccine technology licensed from the Public Health Service/NIH on terms that provide exclusivity for seven years following FDA approval. StaphVAX represents a novel approach to the prevention of *S. aureus* infections. StaphVAX contains surface polysaccharides found in the outer coating of *S. aureus* types 5 and 8. The polysaccharide molecules are linked, or conjugated, in the vaccine with a non-toxic, carrier protein derived from the bacteria *Pseudomonas aeruginosa*. Once given the vaccine, the patient's immune system produces proteins, called antibodies, which bind to *S. aureus* on subsequent exposure to the bacteria. These antibodies help the immune system to identify the *S. aureus* bacteria while it is in the blood, or bacteremia, and eliminate it. Since these antibodies bind to several sites on the bacteria's surface polysaccharides, we believe that the bacteria will be unable to develop resistance to the antibodies as it has to antibiotics.

Potential at-risk patient populations who may benefit from the use of StaphVAX include

- patients such as the elderly and those suffering chronic diseases including end-stage renal disease, congestive heart failure, chronic obstructive pulmonary disease and diabetics who are expected to have long stays in medical or extended care facilities,
- patients undergoing planned surgery who can be vaccinated in advance, for whom *S. aureus* infections can have serious consequences,
- prosthetic surgery and vascular graft patients who are at long-term risk of *S. aureus* infections due to their implants,
- chronic osteomyelitis patients, spinal cord injury and spinal fusion patients and
- hematology/oncology patients undergoing chemotherapy.

*S. aureus* infection rates in these high-risk populations range from 1-10%, and result in longer hospital stays, higher death rates, increased illness and significantly higher medical costs.

In September 2003, we began enrollment in a confirmatory Phase III clinical trial for StaphVAX with a prospectively defined primary efficacy end point at eight months post-vaccination. This trial will be double-blind, placebo-controlled and randomized. Enrollment for this trial is expected to be completed by mid-2004. We recently increased the size of the trial from 3,000 to approximately 3,600 subjects to increase the trial's statistical power so that we can demonstrate statistical significance with a clinical reduction of 50% or more in types 5 and 8 *S. aureus* infections. We estimate that we will incur outside clinical trial costs of approximately $36.0 million over the period from initiation of the trial through conclusion of the trial in the second half of 2005. In this confirmatory Phase III clinical trial, we also will administer a booster dose eight months following the initial vaccination and subjects will be monitored for an additional four to six months as secondary end points. Consequently, patients will be followed for at least 12 months in total. We plan to file a BLA by the end of 2005.

In September 2003, we also announced the completion of a clinical study in 40 healthy volunteers to compare the immune system response (immunogenicity) to vaccine manufactured at a contract manufacturer's site with the response achieved in previous trials using the vaccine manufactured in our research and development pilot plant. The study showed immunogenicity and safety at least equivalent to the immunogenicity seen in clinical studies with vaccine manufactured at our pilot plant. The study demonstrated that we can transfer the manufacturing process for StaphVAX was reproducible and scalable. We have started the process of transferring the StaphVAX manufacturing process to Cambrex Bio Science, our contract manufacturer for the manufacture of StaphVAX.

After a series of discussions with various EU regulatory agencies, we have decided to file an MAA with the EU by the end of 2004 based on the efficacy data obtained from our previously completed Phase III clinical trial, using the centralized registration procedure. Based on the results of these discussions, we intend to file for regulatory approval to market StaphVAX for the prevention of *S. aureus* bacteremia for up to 40 weeks in end-stage renal disease patients on hemodialysis. If the MAA is approved, we would be granted simultaneous regulatory approval to market StaphVAX for this indication throughout the EU. We also plan to file a supplement to the MAA dossier with the EU in the fourth quarter of 2005 incorporating data from the confirmatory Phase III clinical trial currently underway in the U.S. These data, together with safety and immune response data from immunogenicity clinical trials in other at-risk patient populations such as patients undergoing orthopedic or cardiothoracic surgery, will be used to apply for an expansion of the initial proposed indication to an indication for the prevention of *S. aureus* bacteremia and secondary infections caused by bacteremia in at-risk adults.

We completed our initial Phase III double-blind, placebo-controlled and randomized clinical trial for StaphVAX in hemodialysis patients with end-stage renal disease in late 2000. We targeted this patient population because of its relatively high infection rate and because it is at long-term risk of infection and could maximally benefit from the protection that a vaccine may afford. A total of 1,804 patients were included in the clinical trial. Half the enrolled patients were vaccinated with StaphVAX and half received a placebo. The clinical trial population was evaluated at intervals for up to a year to evaluate vaccine safety and *S. aureus* infection rates. The results of the trial showed that a single injection of StaphVAX was safe and showed a statistically significant reduction in the incidence of *S. aureus* bacteremia by almost 60% through 10 months post-vaccination. The reduction in bacteremia one year after vaccination was 26%. The decrease in effect from 10 to 12 months was associated with declining levels of antibodies. No significant side effects attributable to the vaccine were noted. The results in end-stage renal disease patients are especially relevant because these patients are severely immune-compromised and therefore, generally respond poorly to vaccines. Based upon previous clinical trials in healthy volunteers, immune-competent patients who are at risk for *S. aureus* infections are expected to respond more favorably with higher levels of antibody to StaphVAX than end-stage renal disease patients. The significance of the results of this trial was confirmed by publication in the New England Journal of Medicine in February 2002.

To build on the results of our previous Phase III clinical trial completed in 2000, we conducted a booster trial in 2001, giving a second dose of StaphVAX to 77 hemodialysis patients who received an initial dose of the vaccine. The booster trial was designed to evaluate whether patients at long-term risk could respond to a booster dose of the vaccine. The trial demonstrated that a booster dose of the vaccine given to previously vaccinated hemodialysis patients increased the concentration of the vaccine-specific antibodies against *S. aureus*. The trial results suggest that periodic booster doses of StaphVAX can be administered to increase and sustain antibody levels for patients at chronic risk of *S. aureus* infection. The average antibody concentrations reached after the booster vaccination were above what our scientists believe to be a protective level, although not as high as those following the first dose of vaccine. In addition, antibody levels decreased more gradually over time after the booster vaccination than following the initial dose.

*Altastaph [Staphylococcus aureus Immune Globulin (Human)]*. Altastaph is an investigational human polyclonal antibody product that contains high levels of specific antibodies to *S. aureus* types 5 and 8. These antibodies are collected from the plasma of healthy donors who have been vaccinated with StaphVAX at our antibody collection centers. In contrast to StaphVAX, which is intended to provide long-term protection against *S. aureus* infection, we are initially developing Altastaph to provide short-term protection to patients at immediate risk of infection, or who have compromised immune systems and cannot respond effectively to a vaccine. High-risk populations that could benefit from a product such as Altastaph include very low birth-weight newborns, trauma patients and patients in intensive care and burn units. This type of protection or treatment may be cost-effective because antibodies in a single dose of Altastaph persist in the bloodstream for a number of weeks and can be available to provide protection for the entire risk period. We are also exploring the use of Altastaph as a therapeutic agent for use in patients with persistent *S. aureus* infections.

In July 2003, we initiated a randomized, double-blind, placebo-controlled Phase II clinical trial for short-term protection against *S. aureus* types 5 and 8 in very low birth-weight newborns, with birth weights between 500 and 1500 grams, in 20 neonatology centers throughout the U.S. Newborns will be randomly selected to receive Altastaph or placebo and followed up to 42 days for safety and incidence of infections. We have also initiated a placebo-controlled, double-blind Phase I/II clinical trial of Altastaph in adults with persistent *S. aureus* infections. We also will monitor clearance and recurrence of infections. We anticipate reporting data from these clinical trials by the end of 2004.

In 1999, we successfully completed a multi-dose Phase I/II clinical trial of Altastaph in very low birth-weight newborns that demonstrated its safety and the presence of measurable antibodies to *S. aureus* at a variety of dosage levels. The trial indicated that titers of the specific anti-staph antibodies are dose-related. Even the lowest dose of 500 mg/kg of Altastaph resulted in antibody titers that pre-clinical models and clinical trials with StaphVAX indicate may be protective against infection.

*Next Generation Products and Other Anti-Bacterial Vaccines in Development.* We have identified and patented an antigen, type 336, found on a serotype of *S. aureus*, that accounts for more than 90% of types 5 and 8 *S. aureus* clinical infections, or about 10-12% of all clinically significant *S. aureus* infections. We have identified, purified and characterized the type 336 antigen and have prepared a prototype conjugate vaccine that is capable of protecting animals from challenge with clinical isolates of the serotype. During 1998, we were issued a U.S. patent on the type 336 antigen. Included in the patent were claims relating to vaccines made from type 336 antigen and monoclonal and polyclonal antibodies reactive to the antigen. Patents for type 336 antigen and its use are being pursued worldwide. The second generation of StaphVAX is expected to contain type 336 antigen in addition to *S. aureus* types 5 and 8 antigens. A second generation of Altastaph is expected to contain type 336 antibodies in addition to *S. aureus* types 5 and 8 antibodies. We expect these second-generation vaccines to provide coverage for greater than 95% of all clinically significant *S. aureus* infections.

*S. epidermidis* and *Enterococcus faecalis* are the two other clinically significant Gram-positive bacteria that cause hospital-acquired infections. We intend to extend product coverage to these two Gram-positive bacteria in subsequent generations of StaphVAX and Altastaph. We have been issued two patents containing claims covering both a *S. epidermidis* vaccine and human monoclonal and polyclonal antibodies and have filed patent applications on selected enterococcal antigens. Prototypical *S. epidermidis* and enterococcal vaccines produced by us have been shown to induce antibodies that are protective in animal models and facilitate elimination of bacteria by the same type of immune system response as StaphVAX.

***Other Programs***

*Civacir [Hepatitis C Immune Globulin (Human)]*. Civacir is an investigational human polyclonal antibody product that contains antibodies to hepatitus C virus, or HCV. Pre-clinical studies indicate that Civacir contains antibodies that are neutralizing to HCV. We are developing Civacir to prevent hepatitis C disease in HCV-positive liver transplant patients.

HCV has significant social impact because it causes chronic infections in a large percentage of those infected and often results in severe illness and death in later stages of the disease. Chronic HCV infection is a frequent cause of end-stage liver disease in North America and Europe and is present in approximately one third of patients undergoing liver transplants. Moreover, during surgery and in the period immediately following, these patients have no treatment options to prevent reinfection of the transplanted liver. Reinfection of the transplanted liver is almost inevitable within weeks to months after surgery and can occur within days of transplantation. HCV infection also contributes to frequent hospitalizations and failure of the transplanted liver when it occurs in transplant patients. The CDC currently estimates that there are approximately 2.7 million individuals in the U.S. chronically infected with HCV, and the WHO estimates 170 million individuals worldwide are infected with HCV.

The NIH is funding and conducting a Phase I/II clinical trial of Civacir in HCV-positive liver transplant patients at six study sites in the U.S. This trial is a three-armed, randomized, controlled clinical study evaluating two dose levels of Civacir. In this trial the NIH is evaluating the safety of dosing patients with Civacir during and after transplant surgery. The NIH is also evaluating the level of HCV-specific antibodies in trial subjects following dosing, as well as liver enzyme levels, a measure of liver damage, and HCV levels in the transplanted livers. The

results of this trial will help us determine the safety of Civacir in this patient population and define the efficacy markers that may be important in subsequent Phase II and III clinical trials. We anticipate receiving the data from the trial in early 2004. The data will then be used to define our continued development strategy with Civacir. Civacir has received Orphan Drug Designation from the FDA.

*NicVAX (Nicotine Conjugate Vaccine)*. NicVAX is an investigational vaccine to prevent and treat nicotine addiction that uses a conjugate vaccine technology similar to StaphVAX and other anti-bacterial vaccines in our pipeline. NicVAX is designed to cause the immune system to produce antibodies that bind to nicotine and prevent it from entering the brain. The stimulus in the brain that is caused by nicotine is therefore no longer present. Preclinical studies showed that vaccination with NicVAX can prevent nicotine from reaching the brain and block the effects of nicotine, including effects that can lead to addiction or can reinforce and maintain addiction.

In August 2003, we announced the initiation of a Phase II dose response, double-blind, placebo-controlled, randomized clinical trial in 63 smokers who have expressed a desire to quit smoking. The trial, which is designed to observe safety, specific nicotine antibody levels and the rate of smoking cessation in trial participants in response to vaccination with NicVAX, is being conducted at three sites in the U.S. This trial is funded in part by a grant from the National Institute on Drug Abuse, or NIDA. In addition, in February 2003, we initiated a placebo controlled, double-blind Phase I/II clinical trial of NicVAX in smokers, ex-smokers and non-smokers in collaboration with researchers at the University of Maastricht in The Netherlands. The primary intent of this trial is to evaluate the development of specific nicotine antibody levels and safety of the vaccine in study participants. Both studies are fully enrolled. We expect to report the full results from The Netherlands trial by the first quarter of 2004 and from the U.S. trial by the second half of 2004.

In 2002, we completed a placebo-controlled, double-blind Phase I clinical trial of a single dose of NicVAX in healthy, non-smoker volunteers with the assistance of funding from NIDA. The intent of the trial was to evaluate the safety and immunogenicity of the vaccine. Analysis of blood samples from the participants showed that a single dose of vaccine resulted in a rapid immune response and generated nicotine-specific antibodies. Local reactions to vaccination were generally mild to moderate, temporary and required no therapeutic intervention. Antibody levels were detected within 7-14 days of vaccination and were either maintained or continued to increase through at least 60 days post-vaccination.

**Supply and Manufacturing**

We manufacture Nabi-HB in our biopharmaceutical manufacturing facility in Boca Raton, Florida. Additionally, we manufacture clinical lots of our investigational products, Altastaph and Civacir, in this facility. We are considering modifying an unused portion of our Boca Raton facility to manufacture commercial quantities of StaphVAX.

All of our marketed products other than Nabi-HB are manufactured for us by third parties. PhosLo is manufactured for us by Braintree Laboratories, Inc. under an agreement that can be extended until 2018. PhosLo is also manufactured for us by another third-party manufacturer. WinRho SDF is manufactured for us by Cangene under an agreement that terminates in 2005. Aloprim is manufactured for us by DSM under an agreement that terminates in 2004, although we intend to exercise an option to extend that agreement. Baxter supplies Autoplex T to us under a contract that ends in May 2004.

In October 2003 we signed a ten-year agreement with Cambrex Bio Science for the contract manufacturing and commercial supply of StaphVAX.

**Competition**

PhosLo competes with Renagel, a product marketed by Genzyme Corporation, and calcium carbonate products such as TUMS.

There is one antibody based therapy for prevention of hepatitis B post exposure currently on the market that competes with Nabi-HB. We believe that Nabi-HB has achieved a significant share of the U.S. market for the product.

WinRho SDF is the first and only $Rh_oD$ antibody based biopharmaceutical product approved for the treatment of ITP. We believe that WinRho SDF has a significant and growing share of the U.S. market for ITP treatment. Competing therapies include steroids, intravenous immune globulin and splenectomy (a surgical procedure to remove the spleen). Rituxan also is being used to treat refractory ITP patients.

Aloprim is the first intraveneous allopurinol therapy available for the treatment of chemotherapy-induced hyperuricemia. Aloprim provides a therapeutic option for patients that cannot tolerate oral allopurinol therapy. In 2002, a new competitive agent using a different mechanism of action was introduced into this market.

Autoplex T competes in the anti-inhibitor segment of the hemophilia A market. There are two significant biopharmaceutical products currently on the market that compete with Autoplex T.

**Intellectual Property**

Our success depends in part on our ability to maintain our rights to our existing marketed biopharmaceutical products and our ability to obtain patent protection for product candidates in clinical development. Currently, we have 31 granted patents and 62 patent applications pending.

***Marketed products***

We have two patents granted in the U.S., one patent granted in Canada and one patent application pending in the U.S. relating to PhosLo. The granted patents contain claims directed to methods of using calcium acetate in an orally ingested form to inhibit gastrointestinal absorption of phosphorus. The claims of the granted patent are directed to methods for the use of PhosLo for our approved application with end-stage renal disease patients. Patent coverage for these claims expires in April 2007. We also have a U.S. patent granted and a U.S. patent application pending with claims to a second-generation, phosphorus-binding composition that comprises calcium acetate in #0 or #2 size capsule form. The capsules are characterized by an enhanced ease of patient use and, as a result, improved treatment management. This granted U.S. patent expires in April 2021 and any patent granted on the pending U.S. patent application would expire in October 2022.

***Products in clinical development***

We have 25 patents issued and 38 patent applications pending relating to our Gram-positive infectious disease program. We have several U.S. and non-U.S. patents granted or pending for various *Staphylococcus* and *Enterococcus* antigens. With respect to *Staphylococcus*, the patents and pending patent applications relate both to polysaccharide antigens—our "336" *S. aureus* antigen and "Type I" *S. epidermidis* antigen—and to a glycopeptide antigen common to *S. epidermidis*, *S. haemolyticus* and *S. hominis*. Our pending patent applications relate to *Enterococcus* and describe polysaccharide antigens from *E. faecalis* and *E. faecium*, respectively. Currently, we are pursuing claims to one of the *E. faecalis* antigens.

With regard to *S. epidermidis*, our two issued U.S. patents and many non-U.S. issued patents contain claims to vaccines and hyperimmune globulins against *S. epidermidis* surface antigen. Most of these patents expire in 2016. Our four granted U.S. patents and two non-U.S. patents in our *S. aureus* program contain claims directed to vaccines, antibody based therapies, methods of preparing antigen and diagnostic assays and kits against surface antigens of *S. aureus*. These patents all expire in September 2016. Additional patent applications still pending include claims directed to the antigens, as well as to compositions, or conjugates, of the antigens, vaccines containing the antigens, antibodies to the antigens, and immunotherapy and diagnostic methods using the antigens and/or the antibodies to the antigens. In addition, we have filed a U.S. patent application covering methods directed to the use of StaphVAX, among other compositions. These two applications, which address a method of protecting a human being with a compromised immune system from *Staphylococcal* or *Enterococcal* bacterial infection, include claims that prescribe our use of proprietary antigens. The applications also encompass a method for the use of types 5 and 8 *S. aureus* antigens.

In addition, we have one U.S. patent and one U.S. and three non-U.S. patent applications pending that contain claims directed to a pharmaceutical composition containing a ßglucan and intravenous hyperimmune globulin, which can be specific for a given pathogenic microorganism. This combination produces an unexpected antimicrobial effect that is greater than that obtained when either the ßglucan or the intravenous hyperimmune globulin is used separately.

Our patent portfolio for technology related to the NicVAX product concerns both compositions and therapeutic methodology for treating or preventing nicotine addiction. In particular, we have three issued patents and 21 applications pending in the U.S. and abroad. Our patent claims are directed to compositions, or conjugates, that comprise nicotine linked to a carrier protein and to the methods for the use of these conjugates to treat or prevent nicotine addiction. We also have claims to a pharmaceutical composition that contains anti-conjugate antibodies, as well as to methods for using those antibodies against nicotine addiction.

***Trade Secrets and Trademarks***

We rely on unpatented proprietary technologies in the development and commercialization of our products. We also depend upon the unpatentable skills, knowledge and experience of our scientific and technical personnel, as well as those of our advisors, consultants and other contractors. To help protect our proprietary know-how, we often use trade secret protection and confidentiality agreements to protect our interests. We require employees, consultants and advisors to enter into agreements that prohibit the disclosure of confidential information and where applicable require disclosure and assignment to us of the ideas, developments, discoveries and inventions that arise from their activities for us.

We own or license trademarks associated with each of our products, including several national and foreign trademark registrations, or common law rights, for each of our marketed and development products.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

NABI BIOPHARMACEUTICALS

Date: December 10, 2003

By: /S/ MARK SMITH

Name: Mark L. Smith
Title: Senior Vice President, Finance, Chief Financial Officer, Chief Accounting Officer and Treasurer