NORTHFIELD LABORATORIES INC /DE/
Form 424B2
May 13, 2004

PROSPECTUS SUPPLEMENT

(TO PROSPECTUS DATED JUNE 27, 2003)

1,954,416 SHARES

NORTHFIELD LABORATORIES INC.

COMMON STOCK

We are offering up to 1,954,416 shares of our common stock. In connection with this offering, we will pay fees and issue an unregistered warrant to purchase up to 58,632 shares of our common stock to SG Cowen & Co., LLC, as exclusive placement agent. See "Plan of Distribution" beginning on page S-7 of this prospectus supplement for more information regarding these arrangements.

Our common stock is quoted on the Nasdaq National Market under the symbol "NFLD." On May 12, 2004, the closing price of our common stock as quoted on the Nasdaq National Market was $13.18 per share.

OUR BUSINESS AND AN INVESTMENT IN OUR COMMON STOCK INVOLVES SIGNIFICANT RISKS. THESE RISKS ARE DESCRIBED UNDER THE CAPTION "RISK FACTORS" BEGINNING ON PAGE S-1.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS SUPPLEMENT OR ACCOMPANYING PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

	PER SHARE	MAXIMUM OFFERING
Public offering price	$12.00	$23,452,992
Placement agent fee	$ 0.84	$ 1,641,709
Proceeds, before expenses, to us	$11.16	$21,811,283

We estimate the total expenses of this offering, excluding the placement agent fee, will be approximately $100,000. The placement agent is not required to sell any specific number or dollar amount of the shares of common stock offered by this offering, but will use its commercially reasonable efforts to sell the shares of common stock offered. Pursuant to an escrow agreement between us, the placement agent and an escrow agent, certain funds received in payment for the shares sold in this offering will be wired to an interest bearing escrow account and held until we and the placement agent notify the escrow agent that the offering has closed, indicating the date on which the shares are to be delivered to the purchasers and the proceeds are to be delivered to us. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agent fee and net

proceeds to us, if any, in this offering are not presently determinable and may be substantially less than the maximum offering amounts set forth above.

SG COWEN & CO.

May 13, 2004

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THE PURPOSE OF THIS PROSPECTUS SUPPLEMENT IS TO PROVIDE SUPPLEMENTAL INFORMATION REGARDING NORTHFIELD LABORATORIES INC. IN CONNECTION WITH THE OFFERING. YOU SHOULD READ THIS PROSPECTUS SUPPLEMENT, ALONG WITH THE ACCOMPANYING PROSPECTUS, CAREFULLY BEFORE YOU INVEST. BOTH DOCUMENTS CONTAIN IMPORTANT INFORMATION YOU SHOULD CONSIDER WHEN MAKING YOUR INVESTMENT DECISION. THIS PROSPECTUS SUPPLEMENT MAY ADD, UPDATE OR CHANGE INFORMATION CONTAINED IN THE ACCOMPANYING PROSPECTUS.

YOU SHOULD RELY ONLY ON INFORMATION CONTAINED IN THIS PROSPECTUS SUPPLEMENT, THE ACCOMPANYING PROSPECTUS AND THE DOCUMENTS WE INCORPORATE BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS. WE HAVE NOT AUTHORIZED ANYONE TO PROVIDE YOU WITH INFORMATION THAT IS DIFFERENT. WE ARE OFFERING THE COMMON STOCK ONLY IN JURISDICTIONS WHERE SUCH OFFERS ARE PERMITTED. THE INFORMATION CONTAINED IN THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS IS ACCURATE ONLY AS OF THEIR RESPECTIVE DATES, REGARDLESS OF THE TIME OF DELIVERY OF THIS PROSPECTUS SUPPLEMENT AND THE ACCOMPANYING PROSPECTUS.

RISK FACTORS

The securities offered by this prospectus supplement involve a high degree of risk. You should consider the following risk factors when reviewing the information contained in this prospectus supplement. These risk factors replace and supercede in their entirety the "Risk Factors" beginning on page 4 of the

accompanying prospectus. You also should consider the other information incorporated by reference in this prospectus supplement. These risk factors may be supplemented and amended by any risk factors set forth in a later filed prospectus supplement.

RISKS RELATED TO OUR BUSINESS

WE ARE REQUIRED TO CONDUCT ADDITIONAL CLINICAL TRIALS IN THE FUTURE.

The results of our clinical trials conducted to date are not sufficient to demonstrate adequately the safety and effectiveness of PolyHeme in order to obtain approval from FDA for the commercial sale of PolyHeme. We have begun enrollment in a pivotal Phase III trial in which PolyHeme is being used for the first time in civilian trauma applications to treat severely injured patients before they reach the hospital. Under this protocol, treatment with PolyHeme begins at the scene of the injury and continues during transport to the hospital by ambulance. This trial is likely to be expensive and time-consuming and the timing of FDA review process is uncertain. We cannot ensure that we will be able to complete our clinical trials successfully or obtain FDA approval of PolyHeme, or that FDA approval, if obtained, will not include limitations on the indicated uses for which PolyHeme may be marketed. Our business, financial condition and results of operations are critically dependent on receiving FDA approval of PolyHeme. A significant delay in our planned clinical trials or a failure to achieve FDA approval of commercial sales of PolyHeme would have a material adverse effect on us and could result in the cessation of our business. We or FDA may in the future suspend clinical trials at any time if it is believed that the subjects participating in such trials are being exposed to unacceptable health risks.

OUR ACTIVITIES ARE AND WILL CONTINUE TO BE SUBJECT TO EXTENSIVE GOVERNMENT REGULATION.

Our research, development, testing, manufacturing, marketing and distribution of PolyHeme are, and will continue to be, subject to extensive regulation, monitoring and approval by FDA. The regulatory approval process to establish the safety and effectiveness of PolyHeme and the safety and reliability of our manufacturing process has already consumed several years and considerable expenditures. The data obtained from clinical trials are susceptible to varying interpretations, which could delay, limit or prevent FDA regulatory approval. The lack of established criteria for evaluating the effectiveness of blood substitute products could also delay or prevent FDA regulatory approval. In addition, delay or rejection could be caused by changes in FDA policies and regulations. We cannot ensure that, even after extensive clinical trials, regulatory approval will ever be obtained for PolyHeme. We will be required to file a Biologics License Application, or BLA, with FDA in order to obtain regulatory approval for the commercial sale of PolyHeme in the United States. Under FDA guidelines, FDA may comment upon the acceptability of a BLA following its submission. After a BLA is submitted there is an initial review by FDA to be sure that all of the required elements are included in the submission. There can be no assurance that the submission will be accepted for filing or that FDA may not issue a refusal to file, or RTF. If an RTF is issued, there is opportunity for dialogue between the sponsor and FDA in an effort to resolve all concerns. There can be no assurance that such a dialogue will be successful in leading to the filing of the BLA. If the submission is filed, there can be no assurance that the full review will result in product approval. Moreover, if regulatory approval of PolyHeme is granted, the approval may include limitations on the indicated uses for which PolyHeme may be marketed. Further, even if such regulatory approval is obtained, we do not presently have manufacturing facilities sufficient to produce commercial quantities of PolyHeme. In order to seek FDA approval of the sale of PolyHeme produced at its first commercial manufacturing facility, we may be required to conduct a portion of our clinical trials with product manufactured at that facility. Discovery of previously

unknown problems with PolyHeme or unanticipated problems with our manufacturing facilities, even after FDA approval of PolyHeme for commercial sale, may result in the imposition of significant restrictions, including withdrawal of

PolyHeme from the market. Additional laws and regulations may also be enacted which could prevent or delay regulatory approval of PolyHeme, including laws or regulations relating to the price or cost-effectiveness of medical products. Any delay or failure to achieve regulatory approval of commercial sales of PolyHeme is likely to have a material adverse effect on our financial condition. FDA continues to review products even after they receive agency approval. If and when FDA approves PolyHeme, its manufacture and marketing will be subject to ongoing regulation, including compliance with current good manufacturing practices, adverse event reporting requirements and FDA's general prohibitions against promoting products for unapproved or "off-label" uses. We are also subject to inspection and market surveillance by FDA for compliance with these and other requirements. Any enforcement action resulting from failure, even by inadvertence, to comply with these requirements could affect the manufacture and marketing of PolyHeme. In addition, FDA could withdraw a previously approved product from the market upon receipt of newly discovered information. FDA could also require us to conduct additional, and potentially expensive, studies in areas outside our approved indicated uses.

WE ARE A DEVELOPMENT STAGE COMPANY WITHOUT REVENUES OR PROFITS.

Northfield was founded in 1985 and is a development stage company. Since 1985, we have been engaged primarily in the development and clinical testing of PolyHeme. No revenues have been generated to date from commercial sales of PolyHeme. Our revenues to date have consisted solely of license fees. We cannot ensure that our clinical testing will be successful, that regulatory approval of PolyHeme will be obtained, that we will be able to manufacture PolyHeme at an acceptable cost and in appropriate quantities or that we will be able to successfully market and sell PolyHeme. We also cannot ensure that we will not encounter unexpected difficulties which will have a material adverse effect on us, our operations or our properties.

WE HAVE A HISTORY OF LOSSES, OUR FUTURE PROFITABILITY IS UNCERTAIN AND OUR FINANCIAL STATEMENTS ARE SUBJECT TO A GOING CONCERN EXPLANATORY PARAGRAPH BY OUR INDEPENDENT ACCOUNTANTS.

From Northfield's inception through February 29, 2004, we have incurred net operating losses totaling $120,438,163. We will require substantial additional expenditures to complete clinical trials, to pursue regulatory approval for PolyHeme, to establish commercial scale manufacturing processes and facilities, and to establish marketing, sales and administrative capabilities. These expenditures are expected to result in substantial losses for a least the next several years and are expected to substantially exceed our available capital resources. The expense and the time required to realize any product revenues or profitability are highly uncertain. We cannot ensure that we will be able to achieve product revenues or profitability on a sustained basis or at all. As a result of these factors, our independent accountants have included an explanatory paragraph in their audit opinion based on uncertainty regarding our ability to continue as a going concern.

WE WILL NEED TO RAISE ADDITIONAL CAPITAL TO CONTINUE OUR BUSINESS.

We intend to use the proceeds of this offering to fund certain post-enrollment activities in connection with our current clinical trials, the preparation and filing of a Biologics License Application with FDA, the preparation for the commercialization of our product and for other general corporate purposes. We expect that we will be required to raise capital, in

addition to the proceeds of this offering, to achieve commercial production of PolyHeme. Our future capital requirements will depend on many factors, including the scope and results of our clinical trials, the timing and outcome of regulatory reviews, administrative and legal expenses, the status of competitive products, the establishment of manufacturing capacity and the establishment of collaborative relationships. We cannot ensure that this additional funding will be available or, if it is available, that it can be obtained on terms and conditions we will deem acceptable. Our independent accountants have included an explanatory paragraph in their audit opinion based on uncertainty regarding our ability to continue as a going concern. A statement of this type may interfere with our ability to issue our securities to the public or in private transactions. Any additional funding derived from the sale of equity securities may result in significant dilution to our existing stockholders.

WE ARE DEVELOPING A SINGLE PRODUCT THAT IS SUBJECT TO A HIGH LEVEL OF TECHNOLOGICAL RISK.

Our operations have to date consisted primarily of the development and clinical testing of PolyHeme. We do not expect to realize product revenues unless we successfully develop and achieve commercial introduction of PolyHeme. We expect that such revenues, if any, will be derived solely from sales of PolyHeme. We also expect the use of PolyHeme to be limited primarily to the acute blood loss segment of the transfusion market. The biomedical field has undergone rapid and significant technological changes. Technological developments may result in PolyHeme becoming obsolete or non-competitive before we are able to recover any portion of the research and development and other expenses we have incurred to develop and clinically test PolyHeme. Any such occurrence would have a material adverse effect on us and our operations.

WE ARE NOT CERTAIN THAT WE WILL BE ABLE TO MANUFACTURE POLYHEME COMMERCIALLY.

Commercial-scale manufacturing of PolyHeme will require the construction of a manufacturing facility significantly larger than that currently being used to produce PolyHeme for our clinical trials. We have no experience in commercial-scale manufacturing, and there can be no assurance that we can achieve commercial-scale manufacturing capacity. It is also possible that we may incur substantial cost overruns and delays compared to existing estimates in building and equipping a commercial-scale manufacturing facility. Moreover, in order to seek FDA approval of the sale of PolyHeme produced at our first commercial manufacturing facility, we may be required to conduct a portion of our clinical trials with product manufactured at that facility. Accordingly, a delay in achieving scale-up of commercial manufacturing capabilities will have a material adverse effect on sales of PolyHeme. Additionally, the manufacture of PolyHeme will be subject to extensive government regulation. Among the conditions for marketing approval is that our quality control and manufacturing procedures conform to FDA's good manufacturing practice regulations. We cannot ensure that we will be able to obtain the necessary regulatory clearances or approvals to manufacture PolyHeme on a timely basis or at all.

THERE MAY BE LIMITATIONS IN THE SUPPLY OF THE STARTING MATERIAL FOR POLYHEME.

We currently purchase donated blood from The American Red Cross and Blood Centers of America for use as the starting material for PolyHeme. We have also entered into an agreement with hemerica, Inc., a subsidiary of Blood Centers of America, under which hemerica would supply us with up to 160,000 units per year of packed red cells, the source material for PolyHeme. We have not purchased any blood supplies under this agreement to date. We have plans to enter long-term supply arrangements with other blood collectors. We cannot ensure that we will be able to enter into satisfactory long-term arrangements with blood bank

operators, that the price we may be required to pay for starting material will permit us to price PolyHeme competitively or that we will be able to obtain an adequate supply of starting material. Additional demand for blood may arise from competing blood substitute products, some of which are derived from human blood, thereby limiting our available supply of starting material.

THERE ARE SIGNIFICANT COMPETITORS DEVELOPING SIMILAR PRODUCTS.

If approved for commercial sale, PolyHeme will compete directly with established therapies for acute blood loss and may compete with other technologies currently under development. We cannot ensure that PolyHeme will have advantages which will be significant enough to cause medical professionals to adopt it rather than continue to use established therapies or to adopt other new technologies or products. We also cannot ensure that the cost of PolyHeme will be competitive with the cost of established therapies or other new technologies or products. The development of blood substitute products is a rapidly evolving field. Competition is intense and expected to increase. Several companies have developed or are in the process of developing technologies which are, or in the future may be, the basis for products which will compete with PolyHeme. Certain of these companies are pursuing different approaches or means of accomplishing the therapeutic effects sought to be achieved through the use of PolyHeme. Some of these companies have substantially greater financial resources, larger research and development staffs, more extensive facilities and more experience than Northfield in testing, manufacturing, marketing and distributing medical products. We cannot ensure that one or more other companies will not succeed in developing technologies or products which

will become available for commercial use prior to PolyHeme, which will be more effective or less costly than PolyHeme or which would otherwise render PolyHeme obsolete or non-competitive. A bovine-source hemoglobin-based oxygen-carrier has been approved for human use in South Africa and a BLA is under review by FDA for its use in the United States.

WE DO NOT HAVE EXPERIENCE IN THE SALE AND MARKETING OF MEDICAL PRODUCTS.

If approved for commercial sale, we intend to market PolyHeme in the United States using our own sales force. We have no experience in the sale or marketing of medical products. Our ability to implement our sales and marketing strategy for the United States will depend on our ability to recruit, train and retain a marketing staff and sales force with sufficient technical expertise. We cannot ensure that we will be able to establish an effective marketing staff and sales force, that the cost of establishing such a marketing staff and sales force will not exceed revenues from the sale of PolyHeme or that our marketing and sales efforts will be successful.

THE MARKET MAY NOT ACCEPT OUR PRODUCT.

We anticipate that the market price for PolyHeme, if FDA approval is received, will exceed the cost of transfused blood. Competitors may also develop new technologies or products which are more effective or less costly than PolyHeme. We cannot ensure that the price of PolyHeme, considered in relation to PolyHeme's expected benefits, will be perceived by health care providers and third party payors as cost-effective, or that the price of PolyHeme will be competitive with transfused blood or with other new technologies or products. Our results of operations may be adversely affected if the price of PolyHeme is not considered cost-effective or if PolyHeme does not otherwise receive market acceptance.

OUR PATENTS AND OTHER PROPRIETARY RIGHTS MAY NOT PROTECT OUR TECHNOLOGY.

Our ability to compete effectively with other companies will depend, in part, on our ability to protect and maintain the proprietary nature of our technology. We cannot be certain as to the degree of protection offered by our patents or as to the likelihood that additional patents in the United States and certain other countries will be issued based upon pending patent applications. Patent applications in the United States are maintained in secrecy until patents are issued. We cannot be certain that we were the first creator of the inventions covered by our patents or pending patent applications or that we were the first to file patent applications for our inventions. The high costs of enforcing patent and other proprietary rights may also limit the degree of protection afforded to us. We also rely on unpatented proprietary technology, and we cannot ensure that others may not independently develop the same or similar technology or otherwise obtain access to our proprietary technology. We cannot ensure that our patents or other proprietary rights will be determined to be valid or enforceable if challenged in court or administrative proceedings or that we will not become involved in disputes with respect to the patents or proprietary rights of third parties. An adverse outcome from these proceedings could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to stop using this technology, any of which would result in a material adverse effect on our results of operations.

OUR PROFITABILITY WILL BE AFFECTED IF WE INCUR PRODUCT LIABILITY CLAIMS IN EXCESS OF OUR INSURANCE COVERAGE.

The testing and marketing of medical products, even after FDA approval, have an inherent risk of product liability. We maintain limited product liability insurance coverage for our clinical trials in the total amount of $10 million. However, our profitability will be adversely affected by a successful product liability claim in excess of our insurance coverage. We cannot guarantee that product liability insurance will be available in the future or be available on reasonable terms.

WE DEPEND ON THE SERVICES OF A LIMITED NUMBER OF KEY PERSONNEL.

Our success is highly dependent on the continued services of a limited number of skilled managers and scientists. The loss of any of these individuals could have a material adverse effect on us. In addition, our

success will depend, among other factors, on the recruitment and retention of additional highly skilled and experienced management and technical personnel. We cannot ensure that we will be able to retain existing employees or to attract and retain additional skilled personnel on acceptable terms given the competition for such personnel among numerous large and well-funded pharmaceutical and health care companies, universities and non-profit research institutions.

HEALTH CARE REFORM AND CONTROLS ON HEALTH CARE SPENDING MAY LIMIT THE PRICE WE CAN CHARGE FOR POLYHEME AND THE AMOUNT WE CAN SELL.

The federal government and private insurers have considered ways to change, and have changed, the manner in which health care services are provided in the United States. Potential approaches and changes in recent years include controls on health care spending and the creation of large purchasing groups. In the future, it is possible that the government may institute price controls and limits on Medicare and Medicaid spending. These controls and limits might affect the payments we collect from sales of our product. Assuming we succeed in bringing PolyHeme to market, uncertainties regarding future health care reform and private market practices could affect our ability to sell PolyHeme in large

quantities at profitable pricing.

UNCERTAINTY OF THIRD-PARTY REIMBURSEMENT COULD AFFECT OUR PROFITABILITY.

Sales of medical products largely depend on the reimbursement of patients' medical expenses by governmental health care programs and private health insurers. There is no guarantee that governmental health care programs or private health insurers will reimburse our sales of PolyHeme, or permit us to sell our product at high enough prices to generate a profit.

RISKS RELATED TO THE OFFERING

OUR STOCK PRICE COULD BE VOLATILE AND YOUR INVESTMENT COULD SUFFER A DECLINE IN VALUE.

The market price of our common stock has fluctuated significantly in response to a number of factors, many are which are beyond our control, including:

- regulatory developments relating to our PolyHeme blood substitute product;
- announcements by us relating to the results of our clinical trials of PolyHeme;
- developments relating to our efforts to obtain additional financing to fund our operations;
- announcements by us regarding transactions with potential strategic partners;
- announcements relating to blood substitute products being developed by our competitors;
- changes in industry trends or conditions;
- our issuance of additional debt or equity securities; and
- sales of significant amounts of our common stock or other securities in the market.

In addition, the stock market in general, and the Nasdaq National Market and the biotechnology industry market in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of listed companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, securities class action litigation has often been instituted following periods of volatility in the market price of a company's securities. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of our management's attention and resources.

ANTI-TAKEOVER PROVISIONS CONTAINED IN OUR CHARTER AND BYLAWS COULD DISCOURAGE POTENTIAL TAKEOVER ATTEMPTS.

Our certificate of incorporation contains a "fair price" provision which requires approval of the holders of at least 80% of our voting stock, excluding shares held by certain interested stockholders and their affiliates, as a condition to mergers or certain other business combinations with, or proposed

by, any holder of 15% or more of our voting stock, except in cases where approval of our disinterested directors is obtained or certain minimum price criteria and other procedural requirements are satisfied. In addition, our board of directors has the authority, without further action by our stockholders, to fix the rights and preferences and issue shares of preferred stock. These provisions, and other provisions of our certificate of incorporation and bylaws and Delaware law, may have the effect of deterring hostile takeovers or delaying or preventing changes in our control or management, including transactions in which stockholders might otherwise receive a premium for their shares over the then prevailing market prices.

THERE IS A LARGE NUMBER OF SHARES THAT MAY BE SOLD IN THE MARKET FOLLOWING THIS OFFERING, WHICH MAY DEPRESS THE MARKET PRICE OF OUR COMMON STOCK.

Sales of a substantial number of shares of our common stock or securities convertible into or exercisable for our common stock in the public market following this offering could cause the market price of our common stock to decline. If there are more shares of common stock offered for sale than buyers are willing to purchase, then the market price of our common stock may decline to a market price at which buyers are willing to purchase the offered shares of common stock and sellers remain willing to sell the shares. All of the shares sold in the offering will be freely tradeable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates" as defined in Rule 144 of the Securities Act and the shares underlying the warrant issued to the placement agent.

YOU WILL EXPERIENCE IMMEDIATE AND SUBSTANTIAL DILUTION.

The public offering price of the securities offered hereby is likely to be substantially higher than the book value per share of our common stock. Investors purchasing common stock in this offering may, therefore, incur immediate dilution in net tangible book value per share of common stock. Investors will also incur additional dilution upon the exercise of outstanding stock options and warrants. See "Dilution" for a more detailed discussion of the dilution you will incur in this offering.

USE OF PROCEEDS

Unless we inform you otherwise, we intend to use the proceeds of this offering to fund certain post-enrollment activities in connection with our current clinical trials, the preparation and filing of a Biologics License Application with FDA, the preparation for the commercialization of our product and for other general corporate purposes. Pending any specific application, we may initially invest funds in short-term marketable securities.

DILUTION

Our net tangible book value at February 29, 2004 was $22,116,021, or $1.16 per share of common stock. Net tangible book value per share represents total tangible assets less total liabilities divided by the number of outstanding shares of our common stock on February 29, 2004. Assuming that we issue an aggregate of 1,954,416 shares of our common stock at a public offering price of $12.00 per share, with estimated net proceeds to us (after assumed commissions and expenses) of $21,711,283, our pro forma net tangible book value at February 29, 2004 would have been $43,827,304, or $2.09 per share. This represents an immediate

increase in the tangible book value of $0.93 per share to our existing stockholders and an immediate dilution of $9.91 per share to new investors

purchasing common stock in this offering, as illustrated in the following table:

Public offering price per share		$12.00
Net tangible book value per share as of February 29, 2004	$1.16	
Increase per share attributable to new investors	$0.93	
Pro forma net tangible book value per share after offering		$ 2.09
Dilution per share to new investors		$ 9.91

The computations in the table above assume (i) no exercise of any outstanding stock options or warrants after February 29, 2004 and (ii) no exercise of the unregistered warrant to be issued to the placement agent for this offering. At February 29, 2004, there were options and warrant outstanding to purchase a total of 1,368,259 shares of our common stock at a weighted average exercise price of $8.44 per share. If any of these options or warrants are exercised, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

We are offering the shares of our common stock through a placement agent. Subject to the terms and conditions contained in the placement agent agreement dated May 12, 2004, SG Cowen & Co., LLC has agreed to act as the placement agent for the sale of up to 1,954,416 shares of our common stock. The placement agent is not purchasing or selling any shares by this prospectus supplement or accompanying prospectus, nor is it required to arrange the purchase or sale of any specific number or dollar amount of the shares, but has agreed to use commercially reasonable efforts to arrange for the sale of all 1,954,416 shares.

The placement agent agreement provides that the obligations of the placement agent are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain opinions, letters and certificates from our counsel, our independent auditors and us.

Confirmations and definitive prospectuses will be distributed to all investors who agree to purchase shares of the common stock, informing investors of the closing date as to such shares. We currently anticipate that closing of the sale of 1,954,416 shares of common stock will take place on or about May 18, 2004. Investors will also be informed of the date on which they must transmit the purchase price into our account.

On the scheduled closing date, the following will occur:

- each investor will transfer to us funds in the amount of the purchase price, and

- the placement agent will be paid its fee.

We will pay the placement agent a commission equal to 7% of the gross proceeds of the sale of shares of common stock in the offering. In addition, on the closing date of this offering, we will issue to the placement agent a warrant to purchase up to 3% of the aggregate number of shares of our common stock sold in this offering. The placement agent's warrant will become exercisable beginning one year after the closing date of this offering at a per share exercise price equal to $13.73 subject to adjustments, and will expire five years from the closing date of this offering. The placement agent's warrant and underlying shares of common stock will be restricted from sale, transfer, assignment or hypothecation for a period of one year from the closing date of

this offering, in compliance with Rule 2710 of the Conduct Rules of the National Association of Securities Dealers, Inc. The total amount of compensation paid to the placement agent upon completion of this offering will not exceed 8% of the maximum gross proceeds of the offering.

We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act of 1933 and liabilities arising from breaches of representations and warranties contained in the placement agent agreement. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

We, along with our executive officers and directors, have agreed to certain lock-up provisions with regard to future sales of our common stock for a period of 60 days, in the case of Northfield, and 90 days, in the case of our directors and executive officers, after the offering as set forth in the placement agent agreement.

The placement agent agreement with SG Cowen & Co., LLC and the placement agent's warrant are included as exhibits to our Current Report on Form 8-K filed with the Securities and Exchange Commission on May 13, 2004, which are incorporated by reference into this prospectus supplement and the accompanying prospectus.

LEGAL MATTERS

The validity of the issuance of the shares of common stock offered hereby will be passed upon by our counsel, Baker & McKenzie in Chicago, Illinois. Brown Raysman Millstein Felder & Steiner LLP in New York, New York is acting as counsel for the placement agent in connection with various legal matters relating to the shares of common stock offered hereby.

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

PROSPECTUS

$50,000,000

NORTHFIELD LABORATORIES INC.

COMMON STOCK

PREFERRED STOCK

DEPOSITARY SHARES

STOCK PURCHASE CONTRACTS

WARRANTS

DEBT SECURITIES

THE SECURITIES OFFERED BY THE PROSPECTUS INVOLVE A HIGH DEGREE OF RISK.

SEE "RISK FACTORS" BEGINNING ON PAGE 4.

We will provide you with the specific terms of the particular securities being offered in supplements to this prospectus. You should read this prospectus and each related supplement carefully before you invest. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

Our common stock is quoted on the Nasdaq Stock Market's National Market System under the symbol "NFLD." The last reported sale price of our common stock on June 24, 2003 was $8.39 per share.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this Prospectus is June 27, 2003.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process. Using this process, we may offer the securities described in this prospectus in one or more offerings with a total initial offering price of up to $50,000,000 or an equivalent amount in one or more foreign currencies. We may sell these securities separately or in units. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide you a prospectus supplement that will contain information about the specific terms of that particular offering. The prospectus supplement may also add, update or change information contained in this prospectus. To obtain additional information that may be important to you, you should read the exhibits filed by us with the registration statement of which this prospectus is a part or our other filings with the SEC. You also should read this prospectus and any prospectus supplement together with the additional information described below under "Where You Can Find More Information."

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You can read and copy any materials we file with the SEC at its Public Reference Room at 450 Fifth Street, N.W., Washington, D.C.

20549. You can obtain information about the operations of the SEC Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains information we file electronically with the SEC, which you can access over the Internet at www.sec.gov. You may also access the information we file electronically with the SEC through our website at www.northfieldlabs.com.

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede some of this information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 until we sell all of the securities covered by this prospectus. The documents we incorporate by reference are:

- our Annual Report on Form 10-K for the year ended May 31, 2002;

- our Quarterly Reports on Form 10-Q for the quarters ended August 31, 2002, November 30, 2002 and February 28, 2003; and

- the description of our common stock contained in our Registration Statement on Form 8-A, Registration No. 33-76856, filed with the SEC on March 24, 1994, including any amendments or reports filed for the purpose of updating this description.

You may request a copy of these filings (other than an exhibit to the filings unless we have specifically incorporated that exhibit by reference into the filing), at no cost, by writing or telephoning us at the following address:

Northfield Laboratories Inc. 1560 Sherman Avenue Suite 1000 Evanston, Illinois 60201-4800
(847)864-3500

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. We may only use this prospectus to sell securities if it is accompanied by a prospectus supplement. We are only offering the securities in states where the offer is permitted. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents.

FORWARD-LOOKING INFORMATION

This prospectus and the documents we incorporate by reference contain forward-looking statements concerning, among other things, our prospects, clinical and regulatory developments affecting our potential product and our business strategies. These forward-looking statements are identified by the use of such terms as "intends," "expects," "plans," "estimates," "anticipates," "should" and "believes" and are in certain cases followed by a cross reference to "Risk Factors."

These forward-looking statements involve risks and uncertainties. Actual results may differ materially from those predicted by the forward-looking statements because of various factors and possible events, including those discussed under "Risk Factors." Because these forward-looking statements involve risks and uncertainties, actual results may differ significantly from those

predicted in these forward-looking statements. You should not place undue weight on these statements. These statements speak only as of the date of this prospectus or, in the case of any document incorporated by reference, the date of that document.

All subsequent written and oral forward-looking statements attributable to Northfield or any person acting on our behalf are qualified by the cautionary statements in this section. We will have no obligation to revise these forward-looking statements.

OUR BUSINESS

Northfield Laboratories Inc. is a leader in the development of a safe and effective alternative to transfused blood for use in the treatment of acute blood loss. Our PolyHeme(R) blood substitute product is a solution of chemically modified hemoglobin derived from human blood. PolyHeme simultaneously restores lost blood volume and hemoglobin levels and is designed for rapid, massive infusion. PolyHeme requires no cross- matching, and is therefore immediately available and compatible with all blood types. PolyHeme has an extended shelf life compared to blood. We believe PolyHeme is the only blood substitute in development that has been safely infused in clinical trials in sufficient quantities to be useful in the treatment of urgent, large volume blood loss in trauma and surgical settings, with a particular focus on situations where donated blood is not immediately available.

We have conducted Phase II and Phase III clinical trials of PolyHeme at multiple locations in the United States in trauma and emergency surgical applications, in elective surgical procedures, and as life-saving therapy in situations of compassionate use. The observations in these trials have demonstrated the potential clinical utility of PolyHeme in the treatment of urgent blood loss and life-threatening hemoglobin levels. In these trials in hospitalized trauma patients, PolyHeme significantly improved survival compared to historical control patients who did not receive blood. Our trials have involved high dosage and rapid infusion of PolyHeme in situations that are life-threatening and where massive blood loss routinely occurs. We believe that this application addresses the largest world-wide clinical need and has the greatest market opportunity. We believe we are the only company in our field with an oxygen-carrying blood substitute that has been rapidly infused at such high doses -- as much as 20 units (1,000 grams) or twice the blood volume of the average adult.

On March 5, 2003, we received clearance from the U.S. Food and Drug Administration, or FDA, to proceed with a pivotal Phase III trial in which PolyHeme will be used for the first time in civilian, urban trauma settings to treat severely injured patients in hemorrhagic shock before they reach the hospital. Under this protocol, treatment with PolyHeme will begin at the scene of the injury or in the ambulance and continue during transport and the initial 12 hour post-injury period in the hospital. Since blood is not presently carried in ambulances, the use of PolyHeme in this setting has the potential to improve survival and thereby address a critical, unmet medical need.

On June 11, 2003, we received a response from FDA on our request for Special Protocol Assessment, or SPA, for our urban ambulance trial, confirming that agreement had been reached on the primary endpoints for the protocol and the concepts for clinical indications those endpoints would support. An SPA represents acknowledgement and confirmation of a mutual agreement between a clinical trial sponsor and FDA that successful completion of the proposed trial will form the primary basis for an efficacy claim in a marketing application for product approval. Such agreements become part of the administrative record and

may only be changed by mutual agreement of the parties, or if FDA identifies a substantial scientific issue relevant to safety or efficacy after the trial has begun.

We are currently in contact with over 30 potential clinical sites in an effort to complete the trial at the earliest possible date. We anticipate that approximately 20 Level I trauma centers throughout the United States will eventually participate in the PolyHeme trial, which has an expected enrollment of 720 patients. The process of public disclosure and community consultation required under the regulations is underway at a number of potential trial sites across the country.

Our principal executive offices are located at 1560 Sherman Avenue, Suite 1000, Evanston, Illinois 60201-4800, and our telephone number is (847) 864-3500. We maintain an Internet web site at www.northfieldlabs.com. The information contained on our web site, or on other web sites linked to our web site, is not a part of this prospectus.

RISK FACTORS

The securities offered by this prospectus involve a high degree of risk. You should consider the following risk factors when reviewing the information contained in this prospectus. You also should consider the other information incorporated by reference in this prospectus. These risk factors may be supplemented and amended by any risk factors set forth in a prospectus supplement.

RISKS RELATED TO OUR BUSINESS

WE ARE REQUIRED TO CONDUCT ADDITIONAL CLINICAL TRIALS IN THE FUTURE.

The results of our clinical trials conducted to date are not sufficient to demonstrate adequately the safety and effectiveness of PolyHeme in order to obtain approval from FDA for the commercial sale of PolyHeme. We are preparing to commence enrollment a pivotal Phase III trial in which PolyHeme will be used for the first time in civilian trauma applications to treat severely injured patients before they reach the hospital. Under this protocol, treatment with PolyHeme will begin at the scene of the injury and continue during transport to the hospital by ambulance. This trial is likely to be expensive and time-consuming and the timing of FDA review process is uncertain. We cannot ensure that we will be able to complete our clinical trials successfully or obtain FDA approval of PolyHeme, or that FDA approval, if obtained, will not include limitations on the indicated uses for which PolyHeme may be marketed. Our business, financial condition and results of operations are critically dependent on receiving FDA approval of PolyHeme. A significant delay in our planned clinical trials or a failure to achieve FDA approval of commercial sales of PolyHeme would have a material adverse effect on us and could result in the cessation of our business. We or FDA may in the future suspend clinical trials at any time if it is believed that the subjects participating in such trials are being exposed to unacceptable health risks.

OUR ACTIVITIES ARE AND WILL CONTINUE TO BE SUBJECT TO EXTENSIVE GOVERNMENT REGULATION.

Our research, development, testing, manufacturing, marketing and distribution of PolyHeme are, and will continue to be, subject to extensive regulation, monitoring and approval by FDA. The regulatory approval process to establish the safety and effectiveness of PolyHeme and the safety and reliability of our manufacturing process has already consumed several years and

considerable expenditures. The data obtained from clinical trials are susceptible to varying interpretations, which could delay, limit or prevent FDA regulatory approval. The lack of established criteria for evaluating the effectiveness of blood substitute products could also delay or prevent FDA regulatory approval. In addition, delay or rejection could be caused by changes in FDA policies and regulations. We cannot ensure that, even after extensive clinical trials, regulatory approval will ever be obtained for PolyHeme. We will be required to file a Biologics License Application, or BLA, with FDA in order to obtain regulatory approval for the commercial sale of PolyHeme in the United States. Under FDA guidelines, FDA may comment upon the acceptability of a BLA following its submission. After a BLA is submitted there is an initial review by FDA to be sure that all of the required elements are included in the submission. There can be no assurance that the submission will be accepted for filing or that FDA may not issue a refusal to file, or RTF. If an RTF is issued, there is opportunity for dialogue between the sponsor and FDA in an effort to resolve all concerns. There can be no assurance that such a dialogue will be successful in leading to the filing of the BLA. If the submission is filed, there can be no assurance that the full review will result in product approval. Moreover, if regulatory approval of PolyHeme is granted, the approval may include limitations on the indicated uses for which PolyHeme may be marketed. Further, even if such regulatory approval is obtained, we do not presently have manufacturing facilities sufficient to produce commercial quantities of PolyHeme. In order to seek FDA approval of the sale of PolyHeme produced at its first commercial manufacturing facility, we may be required to conduct a portion of our clinical trials with product manufactured at that facility. Discovery of previously unknown problems with PolyHeme or unanticipated problems with our manufacturing facilities, even after FDA approval of PolyHeme for commercial sale, may result in the imposition of significant restrictions, including withdrawal of PolyHeme from the market. Additional laws and regulations may also be enacted which could prevent or delay regulatory approval of PolyHeme, including laws or regulations relating to the price or cost-effectiveness

of medical products. Any delay or failure to achieve regulatory approval of commercial sales of PolyHeme is likely to have a material adverse effect on our financial condition. FDA continues to review products even after they receive agency approval. If and when FDA approves PolyHeme, its manufacture and marketing will be subject to ongoing regulation, including compliance with current good manufacturing practices, adverse event reporting requirements and FDA's general prohibitions against promoting products for unapproved or "off-label" uses. We are also subject to inspection and market surveillance by FDA for compliance with these and other requirements. Any enforcement action resulting from failure, even by inadvertence, to comply with these requirements could affect the manufacture and marketing of PolyHeme. In addition, FDA could withdraw a previously approved product from the market upon receipt of newly discovered information. FDA could also require us to conduct additional, and potentially expensive, studies in areas outside our approved indicated uses.

WE ARE A DEVELOPMENT STAGE COMPANY WITHOUT REVENUES OR PROFITS.

Northfield was founded in 1985 and is a development stage company. Since 1985, we have been engaged primarily in the development and clinical testing of PolyHeme. No revenues have been generated to date from commercial sales of PolyHeme. Our revenues to date have consisted solely of license fees. We cannot ensure that our clinical testing will be successful, that regulatory approval of PolyHeme will be obtained, that we will be able to manufacture PolyHeme at an acceptable cost and in appropriate quantities or that we will be able to successfully market and sell PolyHeme. We also cannot ensure that we will not encounter unexpected difficulties which will have a material adverse effect on us, our operations or our properties.

WE WILL NEED TO RAISE ADDITIONAL CAPITAL TO CONTINUE OUR BUSINESS.

We intend to use the proceeds of this offering to fund our planned clinical trials and ongoing business operations and for other general corporate purposes. We will be required to raise capital, in addition to the proceeds of this offering, to achieve commercial production of PolyHeme. Our future capital requirements will depend on many factors, including the scope and results of our clinical trials, the timing and outcome of regulatory reviews, administrative and legal expenses, the status of competitive products, the establishment of manufacturing capacity and the establishment of collaborative relationships. We cannot ensure that this additional funding will be available or, if it is available, that it can be obtained on terms and conditions we will deem acceptable. If we are unable to raise additional capital, our independent accountants may qualify their audit opinions based on uncertainty regarding our ability to continue as a going concern. A qualification of this type may interfere with our ability to issue our securities to the public or in private transactions. Any additional funding derived from the sale of equity securities may result in significant dilution to our existing stockholders.

WE ARE DEVELOPING A SINGLE PRODUCT THAT IS SUBJECT TO A HIGH LEVEL OF TECHNOLOGICAL RISK.

Our operations have to date consisted primarily of the development and clinical testing of PolyHeme. We do not expect to realize product revenues unless we successfully develop and achieve commercial introduction of PolyHeme. We expect that such revenues, if any, will be derived solely from sales of PolyHeme. We also expect the use of PolyHeme to be limited primarily to the acute blood loss segment of the transfusion market. The biomedical field has undergone rapid and significant technological changes. Technological developments may result in PolyHeme becoming obsolete or non-competitive before we are able to recover any portion of the research and development and other expenses we have incurred to develop and clinically test PolyHeme. Any such occurrence would have a material adverse effect on us and our operations.

WE ARE NOT CERTAIN THAT WE WILL BE ABLE TO MANUFACTURE POLYHEME COMMERCIALLY.

Commercial-scale manufacturing of PolyHeme will require the construction of a manufacturing facility significantly larger than that currently being used to produce PolyHeme for our clinical trials. We have no experience in commercial scale manufacturing, and there can be no assurance that we can achieve commercial-scale manufacturing capacity. It is also possible that we may incur substantial cost overruns and delays compared to existing estimates in building and equipping a commercial-scale manufacturing facility.

Moreover, in order to seek FDA approval of the sale of PolyHeme produced at our first commercial manufacturing facility, we may be required to conduct a portion of our clinical trials with product manufactured at that facility. Accordingly, a delay in achieving scale-up of commercial manufacturing capabilities will have a material adverse effect on sales of PolyHeme. Additionally, the manufacture of PolyHeme will be subject to extensive government regulation. Among the conditions for marketing approval is that our quality control and manufacturing procedures conform to FDA's good manufacturing practice regulations. We cannot ensure that we will be able to obtain the necessary regulatory clearances or approvals to manufacture PolyHeme on a timely basis or at all.

THERE MAY BE LIMITATIONS IN THE SUPPLY OF THE STARTING MATERIAL FOR POLYHEME.

We currently purchase donated blood from The American Red Cross and Blood

Centers of America for use as the starting material for PolyHeme. We have also entered into an agreement with hemerica, Inc., a subsidiary of Blood Centers of America, under which hemerica would supply us with up to 160,000 units per year of packed red cells, the source material for PolyHeme. We have not purchased any blood supplies under this agreement to date. We have plans to enter long-term supply arrangements with other blood collectors. We cannot ensure that we will be able to enter into satisfactory long-term arrangements with blood bank operators, that the price we may be required to pay for starting material will permit us to price PolyHeme competitively or that we will be able to obtain an adequate supply of starting material. Additional demand for blood may arise from competing blood substitute products, some of which are derived from human blood, thereby limiting our available supply of starting material.

THERE ARE SIGNIFICANT COMPETITORS DEVELOPING SIMILAR PRODUCTS.

If approved for commercial sale, PolyHeme will compete directly with established therapies for acute blood loss and may compete with other technologies currently under development. We cannot ensure that PolyHeme will have advantages which will be significant enough to cause medical professionals to adopt it rather than continue to use established therapies or to adopt other new technologies or products. We also cannot ensure that the cost of PolyHeme will be competitive with the cost of established therapies or other new technologies or products. The development of blood substitute products is a rapidly evolving field. Competition is intense and expected to increase. Several companies have developed or are in the process of developing technologies which are, or in the future may be, the basis for products which will compete with PolyHeme. Certain of these companies are pursuing different approaches or means of accomplishing the therapeutic effects sought to be achieved through the use of PolyHeme. Some of these companies have substantially greater financial resources, larger research and development staffs, more extensive facilities and more experience than Northfield in testing, manufacturing, marketing and distributing medical products. We cannot ensure that one or more other companies will not succeed in developing technologies or products which will become available for commercial use prior to PolyHeme, which will be more effective or less costly than PolyHeme or which would otherwise render PolyHeme obsolete or non-competitive. A bovine-source hemoglobin-based oxygen-carrier has been approved for human use in South Africa and a BLA is under review by FDA for its use in the United States.

WE DO NOT HAVE EXPERIENCE IN THE SALE AND MARKETING OF MEDICAL PRODUCTS.

If approved for commercial sale, we intend to market PolyHeme in the United States using our own sales force. We have no experience in the sale or marketing of medical products. Our ability to implement our sales and marketing strategy for the United States will depend on our ability to recruit, train and retain a marketing staff and sales force with sufficient technical expertise. We cannot ensure that we will be able to establish an effective marketing staff and sales force, that the cost of establishing such a marketing staff and sales force will not exceed revenues from the sale of PolyHeme or that our marketing and sales efforts will be successful.

WE HAVE A HISTORY OF LOSSES AND OUR FUTURE PROFITABILITY IS UNCERTAIN.

From Northfield's inception through February 28, 2003, we have incurred net operating losses totaling $107,142,000. We will require substantial additional expenditures to complete clinical trials, to pursue

regulatory approval for PolyHeme, to establish commercial scale manufacturing processes and facilities, and to establish marketing, sales and administrative

capabilities. These expenditures are expected to result in substantial losses for at least the next several years. The expense and the time required to realize any product revenues or profitability are highly uncertain. We cannot ensure that we will be able to achieve product revenues or profitability on a sustained basis or at all.

THE MARKET MAY NOT ACCEPT OUR PRODUCT.

We anticipate that the market price for PolyHeme, if FDA approval is received, will exceed the cost of transfused blood. Competitors may also develop new technologies or products which are more effective or less costly than PolyHeme. We cannot ensure that the price of PolyHeme, considered in relation to PolyHeme's expected benefits, will be perceived by health care providers and third party payors as cost-effective, or that the price of PolyHeme will be competitive with transfused blood or with other new technologies or products. Our results of operations may be adversely affected if the price of PolyHeme is not considered cost-effective or if PolyHeme does not otherwise receive market acceptance.

OUR PATENTS AND OTHER PROPRIETARY RIGHTS MAY NOT PROTECT OUR TECHNOLOGY.

Our ability to compete effectively with other companies will depend, in part, on our ability to protect and maintain the proprietary nature of our technology. We cannot be certain as to the degree of protection offered by our patents or as to the likelihood that additional patents in the United States and certain other countries will be issued based upon pending patent applications. Patent applications in the United States are maintained in secrecy until patents are issued. We cannot be certain that we were the first creator of the inventions covered by our patents or pending patent applications or that we were the first to file patent applications for our inventions. The high costs of enforcing patent and other proprietary rights may also limit the degree of protection afforded to us. We also rely on unpatented proprietary technology, and we cannot ensure that others may not independently develop the same or similar technology or otherwise obtain access to our proprietary technology. We cannot ensure that our patents or other proprietary rights will be determined to be valid or enforceable if challenged in court or administrative proceedings or that we will not become involved in disputes with respect to the patents or proprietary rights of third parties. An adverse outcome from these proceedings could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to stop using this technology, any of which would result in a material adverse effect on our results of operations.

OUR PROFITABILITY WILL BE AFFECTED IF WE INCUR PRODUCT LIABILITY CLAIMS IN EXCESS OF OUR INSURANCE COVERAGE.

The testing and marketing of medical products, even after FDA approval, have an inherent risk of product liability. We maintain limited product liability insurance coverage for our clinical trials in the total amount of $10 million. However, our profitability will be adversely affected by a successful product liability claim in excess of our insurance coverage. We cannot guarantee that product liability insurance will be available in the future or be available on reasonable terms.

WE DEPEND ON THE SERVICES OF A LIMITED NUMBER OF KEY PERSONNEL.

Our success is highly dependent on the continued services of a limited number of skilled managers and scientists. The loss of any of these individuals could have a material adverse effect on us. In addition, our success will depend, among other factors, on the recruitment and retention of additional highly skilled and experienced management and technical personnel. We cannot ensure that we will be able to retain existing employees or to attract and

retain additional skilled personnel on acceptable terms given the competition for such personnel among numerous large and well-funded pharmaceutical and health care companies, universities and non-profit research institutions.

HEALTH CARE REFORM AND CONTROLS ON HEALTH CARE SPENDING MAY LIMIT THE PRICE WE CAN CHARGE FOR POLYHEME AND THE AMOUNT WE CAN SELL.

The federal government and private insurers have considered ways to change, and have changed, the manner in which health care services are provided in the United States. Potential approaches and changes in recent years include controls on health care spending and the creation of large purchasing groups. In the future, it is possible that the government may institute price controls and limits on Medicare and Medicaid spending. These controls and limits might affect the payments we collect from sales of our product. Assuming we succeed in bringing PolyHeme to market, uncertainties regarding future health care reform and private market practices could affect our ability to sell PolyHeme in large quantities at profitable pricing.

UNCERTAINTY OF THIRD-PARTY REIMBURSEMENT COULD AFFECT OUR PROFITABILITY.

Sales of medical products largely depend on the reimbursement of patients' medical expenses by governmental health care programs and private health insurers. There is no guarantee that governmental health care programs or private health insurers will reimburse our sales of PolyHeme, or permit us to sell our product at high enough prices to generate a profit.

RISKS RELATED TO THE OFFERING

OUR STOCK PRICE COULD BE VOLATILE AND YOUR INVESTMENT COULD SUFFER A DECLINE IN VALUE.

The market price of our common stock has fluctuated significantly in response to a number of factors, many are which are beyond our control, including:

- regulatory developments relating to our PolyHeme blood substitute product;
- announcements by us relating to the results of our clinical trials of PolyHeme;
- developments relating to our efforts to obtain additional financing to fund our operations;
- announcements by us regarding transactions with potential strategic partners;
- announcements relating to blood substitute products being developed by our competitors;
- changes in industry trends or conditions;
- our issuance of additional debt or equity securities; and
- sales of significant amounts of our common stock or other securities in the market.

In addition, the stock market in general, and the Nasdaq National Market and the biotechnology industry market in particular, have experienced

significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of listed companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, securities class action litigation has often been instituted following periods of volatility in the market price of company's securities. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of our management's attention and resources.

ANTI-TAKEOVER PROVISIONS CONTAINED IN OUR CHARTER AND BYLAWS COULD DISCOURAGE POTENTIAL TAKEOVER ATTEMPTS.

Our certificate of incorporation contains a "fair price" provision which requires approval of the holders of at least 80% of our voting stock, excluding shares held by certain interested stockholders and their affiliates, as a condition to mergers or certain other business combinations with, or proposed by, any holder of 15% or more of our voting stock, except in cases where approval of our disinterested directors is obtained or certain minimum price criteria and other procedural requirements are satisfied. In addition, our board of directors has the authority, without further action by our stockholders, to fix the rights and preferences and issue shares of preferred stock. These provisions, and other provisions of the our certificate of incorporation and bylaws and

Delaware law, may have the effect of deterring hostile takeovers or delaying or preventing changes in our control or management, including transactions in which stockholders might otherwise receive a premium for their shares over the then prevailing market prices.

THERE IS A LARGE NUMBER OF SHARES THAT MAY BE SOLD IN THE MARKET FOLLOWING THIS OFFERING, WHICH MAY DEPRESS THE MARKET PRICE OF OUR COMMON STOCK.

Sales of a substantial number of shares of our common stock or securities convertible into or exercisable for our common stock in the public market following this offering could cause the market price of our common stock to decline. If there are more shares of common stock offered for sale than buyers are willing to purchase, then the market price of our common stock may decline to a market price at which buyers are willing to purchase the offered shares of common stock and sellers remain willing to sell the shares. All of the shares sold in the offering will be freely tradeable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates" as defined in Rule 144 of the Securities Act.

YOU WILL EXPERIENCE IMMEDIATE AND SUBSTANTIAL DILUTION.

The public offering price of the securities offered hereby is likely to be substantially higher than the book value per share of our common stock. Investors purchasing common stock in this offering may, therefore, incur immediate dilution in net tangible book value per share of common stock. Investors will also incur additional dilution upon the exercise of outstanding stock options and warrants. See "Dilution" for a more detailed discussion of the dilution you will incur in this offering.

USE OF PROCEEDS

Unless we inform you otherwise in the prospectus supplement, we intend to use the proceeds of this offering to fund our planned clinical trials and ongoing business operations and for other general corporate purposes. Pending any specific application, we may initially invest funds in short-term marketable

securities.

RATIO OF EARNINGS TO FIXED CHARGES AND PREFERENCE DIVIDENDS

We reported no revenues or earnings during our last five fiscal years. During this period, we did not have any debt or related interest expense and were not a party to any capital lease arrangements. No preference securities were outstanding during this period.

DILUTION

Our net tangible book value at February 28, 2003 was $10,504,000, or $.74 per share of common stock. Net tangible book value per share represents total tangible assets less total liabilities divided by the number of outstanding shares of our common stock on February 28, 2003. Assuming that we issue an aggregate of $50 million of common stock at an assumed public offering price of $8.39 per share (the last reported sale price of our common stock on the Nasdaq National Market on June 24, 2003), with estimated net proceeds to us (after assumed commissions and expenses) of $46,375,000, our pro forma net tangible book value at February 28, 2003 would have been $56,879,000 or $2.81 per share. This represents an immediate increase in the tangible book value of $2.07 per share to our existing stockholders and an immediate dilution of $5.58 per share to new investors purchasing common stock in this offering, as illustrated in the following table:

Assumed public offering price per share(1).....		$8.39
Net tangible book value per share as of February 28, 2003.....	$0.74	
Increase per share attributable to new investors.....	$2.07	
Pro forma net tangible book value per share after offering.....		$2.81
Dilution per share to new investors.....		$5.58

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(1) We assumed an offering price of $8.39 per share based on the last reported sale price of the common stock on the Nasdaq National Market on June 24, 2003. The assumed offering price of the common stock at the time any common stock is offered hereby may differ significantly from the offering price assumed for purposes of this prospectus.

The computations in the table above assume no exercise of any outstanding stock options after February 28, 2003. At February 28, 2003, there were options outstanding to purchase a total of 958,000 shares of our common stock at a weighted average exercise price of $9.62 per share. If any of these options are exercised, there will be further dilution to new investors.

If the securities offered hereby are common stock, the prospectus supplement will include a revised dilution table setting forth any increase in net tangible book value to existing stockholders and any dilution to new investors based on the proposed number of shares of common stock to be offered and the public offering price at the time of such offering.

DESCRIPTION OF THE SECURITIES WE MAY OFFER

We may offer up to $50,000,000 of common stock, preferred stock, depositary shares, stock purchase contracts, warrants and debt securities, in one or more offerings and in any combination. A prospectus supplement, which we will provide each time we offer securities, will describe the specific amounts, prices and terms of these securities.

We may sell the securities to or through underwriters, dealers or agents or directly to purchasers. We, as well as any persons acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers or agents involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

COMMON STOCK

We may issue shares of our common stock either alone or underlying other registered securities convertible into or exercisable or exchangeable for shares of our common stock. Holders of our common stock are entitled to receive dividends declared by our board of directors out of funds legally available for the payment of dividends, subject to rights, if any, of preferred stock holders. Currently, we do not pay a dividend. The holders of our common stock are entitled to one vote per share and are not entitled to cumulative voting rights for the election of our directors. The holders of our common stock have no preemptive rights.

PREFERRED STOCK AND DEPOSITARY SHARES

We may issue preferred stock, in one or more series, alone or underlying other registered securities convertible into or exercisable or exchangeable for shares of our preferred stock. Our board of directors or a committee designated by the board will determine the dividend, voting and conversion rights and other provisions of the preferred stock at the time of sale. Each series of preferred stock will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of liquidation, dissolution or the winding up of Northfield, voting rights and conversion rights. We may also issue fractional shares of preferred stock that will be represented by depositary shares and depositary receipts. Each particular series of depositary shares will be more fully described in the prospectus supplement that will accompany this prospectus.

WARRANTS

We may issue warrants for the purchase of common stock, preferred stock, depositary shares or debt securities. We may issue warrants independently or together with other securities. The specific terms of any warrants will be described in the prospectus supplement that will accompany this prospectus.

STOCK PURCHASE CONTRACTS

We may issue stock purchase contracts, including contracts obligating holders to purchase from us, and us to sell to the holders, a specified number of securities, at a future date or dates, or similar contracts issued on a "prepaid" basis, which in each case are referred to herein as "stock purchase contracts." The price per share of securities and the number of shares of securities may be fixed at the time the stock purchase contracts are issued or may be determined by reference to a specific formula set forth in the stock purchase contracts. The stock purchase contracts will require either the stock

purchase price be paid at the time the stock purchase contracts are issued or that payment be made at a specified future date. The stock purchase contracts also may require us to make periodic payments to the holders of the stock purchase contracts or vice versa, and such payments may be unsecured or refunded on some basis. The specific terms of any stock purchase contracts will be described in the prospectus supplement that will accompany this prospectus.

DEBT SECURITIES

GENERAL

We may issue secured or unsecured obligations in the form of either senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as "debt securities." The senior unsecured debt securities will have the same rank as all of our other unsecured unsubordinated debt. The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the senior debt securities. We may issue debt securities that are convertible into or exchangeable for shares of common stock or other securities or property.

The senior and subordinated debt securities will be issued under separate indentures between a trustee and us. We have summarized the general features of the debt securities to be governed by the indentures. These indentures have been filed as exhibits or will be incorporated by reference into the registration statement that we have filed with the SEC of which this prospectus is a part. We encourage you to read these indentures. Instructions on how you can get copies of these documents are provided above in "Where You Can Find More Information."

GENERAL INDENTURE PROVISIONS THAT APPLY TO SENIOR AND SUBORDINATED DEBT

The following general indenture provisions will apply to any senior and subordinated debt securities:

- each indenture allows debt to be issued in series with terms particular to each series;

- neither indenture limits the amount of debt that we may issue or generally provides holders any protection should we engage in a highly leveraged transaction;

- the indentures allow us to merge or to consolidate with another U.S. entity or convey, transfer or lease our properties and assets substantially as an entirety to another U.S. entity, as long as certain conditions are met. If these events occur, the other company will be required to assume our responsibilities on the debt securities, and we will be released from all liabilities and obligations, except in the case of a lease;

- the indentures provide that the trustee and we may generally amend the indenture with the consent of holders of a majority of the total principal amount of the debt outstanding in any series to change certain of our obligations or your rights concerning the debt. However, to change the payment of principal, interest or adversely affect the right to convert or certain matters, every holder in that series must consent; and

- we may discharge the indentures and defease restrictive covenants by depositing sufficient funds with the trustee to pay the obligations when due, as long as certain conditions are met. The trustee would pay all amounts due to you on the debt from the deposited funds.

EVENTS OF DEFAULT

Each of the following is an event of default under the indentures:

- principal not paid when due;
- any sinking fund payment not made when due;
- failure to pay interest for 30 days;
- covenants not performed for 90 days after notice; and
- certain events of bankruptcy, insolvency or reorganization of Northfield.

A prospectus supplement may describe deletions of, or changes or additions to, the events of default.

REMEDIES

Upon an event of default, other than a bankruptcy, insolvency or reorganization, the trustee or holders of 25 percent of the principal amount outstanding in a series may declare the outstanding principal, plus accrued interest, if any, immediately payable. However, the holders of a majority in principal amount may, under certain circumstances, rescind this action.

INDENTURE PROVISIONS THAT APPLY ONLY TO THE SUBORDINATED DEBT SECURITIES

The subordinated indenture provides that the subordinated debt securities will be subordinated to all senior debt as defined in the subordinated indenture.

PLAN OF DISTRIBUTION

We may sell the offered securities in and outside the United States through underwriters, dealers or agents or directly to purchasers. The prospectus supplement will set forth the following information:

- the terms of the offering;
- the names of any underwriters, dealers or agents;
- the purchase price;
- the net proceeds to us;
- any delayed delivery arrangements;
- any underwriting discounts and other items constituting underwriters' compensation;
- the initial public offering price;
- any discounts or concessions allowed, reallowed or paid to dealers; and
- any commissions paid to agents.

If we use underwriters in the sale of the offered securities, the underwriters will acquire the securities for their own account. The underwriters

may resell the securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer the securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless we inform you otherwise in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to conditions, and the underwriters will be obligated to purchase all the securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers.

During and after an offering through underwriters, the underwriters may purchase and sell the securities in the open market. These transactions may include overallotment and stabilizing transactions and purchases

to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, in which selling concessions allowed to syndicate members or other broker-dealers for the offered securities sold for their account may be reclaimed by the syndicate if the offered securities are repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered securities, which may be higher than the price that might otherwise prevail in the open market. If commenced, these activities may be discontinued at any time. If we use dealers in the sale of securities, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The dealers participating in any sale of our securities may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. We will include in the prospectus supplement the names of the dealers and the terms of the transaction.

We may sell the securities directly. In that event, no underwriters, dealers or agents would be involved. We may also sell the securities through agents we designate from time to time. In the prospectus supplement, we will name any agent involved in the offer or sale of the offered securities, and we will describe any commissions payable by us to the agent. Unless we inform you otherwise in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment. We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. We will describe the terms of any of these sales in the prospectus supplement.

The total amount of compensation paid to the underwriters or placement agents upon completion of this offering will not exceed 8% of the maximum gross proceeds of the offering.

We may have agreements with the underwriter, dealers and agents to indemnify them against civil liabilities, including liabilities under the Securities Act, or to contribute with respect to payments that the underwriter, dealers or agents may be required to make. Underwriters, dealers and agents may engage in transactions with us or may perform services for us in the ordinary course of their businesses.

Underwriters, dealers and agents participating in a sale of securities may be deemed to be underwriters as defined in the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions under

the Securities Act.

LEGAL MATTERS

The validity of the securities offered herein will be passed upon for us by Baker & McKenzie, Chicago, Illinois. If the securities are distributed in an underwritten offering, the underwriters will be advised by their own legal counsel with respect to any offering.

EXPERTS

The financial statements of Northfield Laboratories Inc. as of May 31, 2002, and for each of the years in the three-year period ended May 31, 2002 and for the cumulative period from June 19, 1985 (inception) have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent certified public, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

With respect to the unaudited interim financial information of the periods ended August 31, 2002, November 30, 2002 and February 28, 2003, incorporated by reference herein, the independent certified public accountants have reported that they applied limited procedures in accordance with professional standards for a review of such information. However, their separate reports included in Northfield Laboratories Inc.'s quarterly reports on Form 10-Q for the quarters ended August 31, 2002, November 30, 2002 and February 28, 2003, incorporated by reference herein, state that they did not audit and they do not express an opinion on that interim financial information. Accordingly, the degree of reliance on their reports on such information should

be restricted in light of the limited nature of the review procedures applied. The accountants are not subject to the liability provisions of Section 11 of the Securities Act of 1933 for their report on the unaudited interim financial information because that report is not a "report" or a "part" of the registration statement prepared or certified by the accountants within the meaning of Sections 7 and 11 of the Act.

1,954,416 SHARES

NORTHFIELD LABORATORIES INC.

COMMON STOCK

PROSPECTUS SUPPLEMENT

SG COWEN & CO.

May 13, 2004
