

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

AMENDMENT NO. 1
TO
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

VICAL INCORPORATED
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

93-0948554
(I.R.S. Employer
Identification Number)

**10390 Pacific Center Court
San Diego, California 92121
(858) 646-1100**
(Address, including zip code, and telephone number, including
area code, of registrant's principal executive offices)

**Vijay B. Samant
President and Chief Executive Officer
Vical Incorporated
10390 Pacific Center Court
San Diego, California 92121
(858) 646-1100**
(Name, address, including zip code, and telephone number,
including area code, of agent for service)

**Copies to:
Frederick T. Muto, Esq.
L. Kay Chandler, Esq.
Cooley Godward LLP
4401 Eastgate Mall
San Diego, California 92121
(858) 550-6000**

**Approximate date of commencement of proposed sale to the public:
From time to time after the effective date of this registration statement.**

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)(5)
Preferred Stock, par value \$0.01 per share (3)	—	—
Common Stock, par value \$0.01 per share (3)	—	—
Total	\$50,000,000 (4)	\$4,045.00

(1) The proposed maximum aggregate offering price per each class of security will be determined from time to time by the registrant in connection with the issuance of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act.

(2) Calculated in accordance with Rule 457(o) under the Securities Act.

(3) Subject to note 4 below, there is being registered hereunder an indeterminate number of shares of common stock and preferred stock as may be sold from time to time by the registrant. Pursuant to Rule 416 and

Rule 457(i) under the Securities Act, the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions, or upon conversion of any preferred stock being registered under this registration statement.

- (4) In no event will the aggregate offering price of all securities issued from time to time pursuant to this registration statement exceed \$50,000,000. The securities registered hereunder may be sold separately or in combination with other securities registered hereunder.
- (5) Previously paid.

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

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

(Subject to completion, dated October 2, 2003)

PROSPECTUS

\$50,000,000

Vical Incorporated

Preferred Stock

Common Stock

We may offer and sell from time to time, at prices and on other terms that we will determine at the time of each offering:

- shares of preferred stock, or
- shares of common stock.

We will provide the specific terms of these securities in supplements to this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus and any prospectus supplement carefully before you invest.

Our common stock is quoted and traded on the Nasdaq National Market under the symbol "VICL."

Investing in our securities involves risks. See "Risk Factors" beginning on page 4.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

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

We will sell these securities directly to our stockholders or to purchasers or through agents on our behalf or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions or discounts.

The date of this prospectus is

You should rely only on the information contained or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different or inconsistent information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information appearing in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front cover of this prospectus or the prospectus supplement, or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any prospectus supplement. Our business, financial condition, results of operations and prospects may have subsequently changed.

TABLE OF CONTENTS

	Page
About this Prospectus	2
Summary of Our Business	3
Risk Factors	4
Forward-Looking Statements	14
Financial Ratios	15
Use of Proceeds	15
Description of Capital Stock	16

Plan of Distribution	20
Legal Matters	21
Experts	21
Where You Can Find More Information	21

Whenever we refer to "Vical," "we," "our" or "us" in this prospectus, we mean Vical Incorporated, unless the context suggests otherwise. When we refer to "you" or "yours," we mean the holders of the applicable series of securities.

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. Under this shelf registration process, we may sell common stock or preferred stock in one or more offerings up to a total dollar amount of \$50,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer to sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus or in documents incorporated by reference in this prospectus, other than information changing the basic terms of this offering or the securities offered. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus or in documents incorporated by reference in this prospectus, the statements made or incorporated by reference in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should carefully read both this prospectus and any prospectus supplement together with the additional information described under "Where You Can Find More Information" before buying any securities in this offering.

2

SUMMARY OF OUR BUSINESS

Our goal is to be an integrated biopharmaceutical company committed to the development and commercialization of vaccines and immunotherapies. We believe our unique DNA technology can be applied to the development of new and better medicines that improve people's lives. We, together with our network of licensees and collaborators, are currently developing a number of vaccine and therapeutic protein product candidates for the prevention or treatment of infectious diseases, cancer, and cardiovascular diseases. Our independent development programs include vaccines for cytomegalovirus, or CMV, and anthrax, as well as a novel immunotherapeutic for treatment of melanoma.

In addition to our independent drug development efforts, we license our intellectual property to other companies. This allows us to leverage our technologies for applications that may not be appropriate for our independent product development efforts. In addition, we pursue contract manufacturing opportunities to leverage our infrastructure and expertise in plasmid manufacturing, and to provide revenues that contribute to our independent research and development efforts.

Our headquarters are located at 10390 Pacific Center Court, San Diego, California 92121. Our telephone number is (858) 646-1100. We maintain an Internet website at www.vical.com. The reference to our Internet address does not constitute incorporation by reference of the information contained on our website.

Allovectin-7® and Leuvectin® are our trademarks. Any other brand names or trademarks appearing in this prospectus are the property of their respective owners.

3

RISK FACTORS

You should carefully consider the risks described below, together with all of the other information included in this prospectus, and in our other filings with the Securities and Exchange Commission, before deciding whether to invest in our securities. The risks described below are all material risks currently known, expected or reasonably foreseeable by us. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment.

None of our products has been approved for sale, and we have only one product candidate in Phase II clinical trials. If we do not develop commercially successful products, we may be forced to curtail or cease operations.

All of our potential products are either in research or development. We must conduct a substantial amount of additional research and development before any U.S. or foreign regulatory authority will approve any of our products. Very little data exists regarding the safety and efficacy of DNA-based vaccines or therapies. Results of our research and development activities may indicate that our potential products are unsafe or ineffective. In this case, regulatory authorities will not approve them.

For example, in 2002 we announced that the efficacy data from our low-dose Phase III registration trial with Allovectin-7® in patients with metastatic melanoma would not support a registration submission with the United States Food and Drug Administration, or FDA. We also announced in 2002 that further independent development of Allovectin-7® for head and neck cancer, and of Leuvectin® for kidney cancer and prostate cancer, was not justified in light of our other priorities. As a result, our only product candidate currently in clinical trials is high-dose Allovectin-7® for metastatic melanoma, which is currently in Phase II clinical trials.

Additionally, we are in the early stages of research and development of vaccine candidates for infectious diseases such as CMV and anthrax. These vaccine candidates will require significant costs to advance through the development stages. If such vaccine candidates are advanced to clinical trials, the results of such trials may not support FDA approval. Even if approved, our products may not be commercially successful. If we fail to develop and commercialize our products, we may be forced to curtail or cease operations.

Our revenues partially depend on the development and commercialization of products by others to whom we have licensed our technology. If our collaborators or licensees are not successful or if we are unable to find collaborators or licensees in the future, we may not be able to derive revenues from these arrangements.

We have licensed our technology to corporate collaborators and licensees for the research, development and commercialization of specified product candidates. Our revenues partially depend upon the ability of these collaborators and licensees to successfully develop and commercialize products under these arrangements. Some collaborators or licensees may not succeed in their product development efforts or devote sufficient time or resources to the programs covered by these arrangements, causing us to derive little or no revenue from these arrangements. Our collaborators and licensees may also breach or terminate their agreements with us, and we may be unsuccessful in entering into and maintaining other collaborative arrangements for the development and commercialization of products using our technology.

We have a history of net losses. We expect to continue to incur net losses and we may not achieve or maintain profitability.

To date, we have not sold or received approval to sell any products. We do not expect to sell any products for the next several years. Our net losses were approximately \$27.9 million, \$9.2 million and

4

\$8.5 million for 2002, 2001 and 2000, respectively. As of June 30, 2003, we have incurred cumulative net losses totaling approximately \$104.3 million. Moreover, we expect that our net losses will continue and may increase for the foreseeable future. For 2003, we have forecast a net loss of between \$24 million and \$28 million. We may not be able to achieve our projected results, either because we generate lower revenues or lower investment income than expected, or we incur greater expenses than expected, or all of the above. We may never generate sufficient product revenue to become profitable. We also expect to have quarter-to-quarter fluctuations in revenues, expenses, and losses, some of which could be significant.

We may need additional capital in the future. If additional capital is not available, we may have to curtail or cease operations.

We may need to raise more money to continue the research and development necessary to bring our products to market and to establish marketing and additional manufacturing capabilities. We may seek additional funds through public and private stock offerings, government contracts and grants, arrangements with corporate collaborators, borrowings under lease lines of credit or other sources. We may not be able to raise additional funds on favorable terms, or at all. If we are unable to obtain additional funds, we may have to reduce our capital expenditures, scale back our development of new products, reduce our workforce or license to others products or technologies that we otherwise would seek to commercialize ourselves. The amount of money we may need will depend on many factors, including:

- The progress of our research and development programs,
- The scope and results of our preclinical studies and clinical trials, and
- The time and costs involved in:
 - Obtaining necessary regulatory approvals,
 - Filing, prosecuting and enforcing patent claims,
 - Scaling up our manufacturing capabilities, and
 - The commercial arrangements we may establish.

We anticipate that our available cash and existing sources of funding will be adequate to satisfy our operating needs through at least 2005.

The regulatory approval process is expensive, time consuming and uncertain, which may prevent us from obtaining required approvals for the commercialization of our products.

Our product candidates under development and those of our collaborators and licensees are subject to extensive and rigorous regulations by numerous governmental authorities in the United States and other countries. The regulations are evolving and uncertain. The regulatory process can take many years and require us to expend substantial resources. For example:

- The FDA has not established guidelines concerning the scope of clinical trials required for gene-based products,
- The FDA has provided only limited guidance on how many patients it will require to be enrolled in clinical trials to establish the safety and efficacy of gene-based products, and
- Current regulations are subject to substantial review by various governmental agencies.

5

Therefore, U.S. or foreign regulations could prevent or delay regulatory approval of our products or limit our ability to develop and commercialize our products. Delays could:

- Impose costly procedures on our activities,
- Diminish any competitive advantages that we attain, or
- Negatively affect our results of operations and cash flows.

We believe that the FDA and comparable foreign regulatory bodies will regulate separately each product containing a particular gene depending on its intended use. Presently, to commercialize any product we must sponsor and file a regulatory application for each proposed use. We then must conduct clinical studies to demonstrate the safety and efficacy of the product necessary to obtain FDA approval. The results obtained so far in our clinical trials may not be replicated in our ongoing or future trials. This may prevent any of our potential products from receiving FDA approval.

We use recombinant DNA molecules in our product candidates, and therefore we also must comply with guidelines instituted by the National Institutes of Health, or NIH, and its Office of Biotechnology Activities. The NIH could restrict or delay the development of our product candidates.

We understand that both the FDA and NIH are considering rules and regulations that would require public disclosure of commercial development data that is presently confidential. This potential disclosure of commercial confidential information, if implemented, may result in loss of advantage of competitive secrets.

A rule published in 2002 by the FDA, known commonly as the "Animal Rule," attempts to establish requirements for demonstrating effectiveness of drugs and biological products in settings where human clinical trials for efficacy are not feasible or ethical. The rule requires as conditions for market approval the demonstration of safety and biological activity in humans, and the demonstration of effectiveness under rigorous test conditions in up to two appropriate species of animal. We believe that with appropriate

guidance from the FDA, we may seek and win market approval under the Animal Rule for DNA-based products designed to treat or prevent a disease for which clinical efficacy trials in humans are neither feasible nor ethical, such as our DNA vaccine for anthrax. At the moment, however, we cannot guarantee that the Animal Rule will be applied to any of our products, or if applied, that its application would result in expedited development time or regulatory review.

Adverse events in the field of gene therapy, or with respect to our product candidates, may negatively impact regulatory approval or public perception of our products.

The death in 1999 of a patient undergoing a viral-delivered gene therapy at the University of Pennsylvania in an investigator-sponsored trial was widely publicized. In October 2002 and January 2003, two children in France who received retroviral-delivered ex vivo gene transfer for the treatment of X-linked Severe Combined Immunodeficiency Disease, called X-SCID or "bubble boy" syndrome, were diagnosed with leukemia that was caused by the integration of the viral delivery vehicle in or near a cancer-causing region of the children's genome. The FDA responded to these events in France by temporarily halting all U.S. clinical trials using retroviral vectors to transduce hematopoietic stem cells. Following public advisory committee review by experts in the field, the FDA allowed these trials in the U.S. to continue under careful scrutiny, because the potential benefit of the investigational gene therapy in patients with this life-threatening condition was believed to justify the risk.

Some of our potential products may be administered to patients who are suffering from or vulnerable to diseases which can themselves be life-threatening. For example, one patient who had undergone treatment with Allovectin-7® for advanced metastatic melanoma died more than two months later of progressive disease and numerous other factors after receiving multiple other cancer therapies. The death was originally reported as unrelated to the treatment. Following an autopsy, the death was

6

reclassified as "probably related" to the treatment because the possibility could not be ruled out. We do not believe Allovectin-7® was a significant factor in the patient's death.

As another example, we may administer our developmental CMV vaccine to patients who are at risk of CMV reactivation. Likewise, our developmental anthrax vaccine may eventually be administered to patients who have been exposed to anthrax. Although we do not believe our vaccine candidates could cause the diseases they are designed to protect against, a temporal relationship between vaccination and disease onset could be perceived as causal.

These adverse events, and real or perceived risks, could result in greater government regulation and stricter labeling requirements for DNA-based vaccines or therapies, and may adversely impact market acceptance of some of our product candidates. Increased scrutiny in the field of gene therapy also may cause regulatory delays or otherwise affect our product development efforts or clinical trials.

Our patents and proprietary rights may not provide us with any benefit and the patents of others may prevent us from commercializing our products.

As of September 1, 2003, we had 23 patents issued in the U.S., seven patents issued in Europe, one of which was revoked and is under appeal, two patents issued in Japan, one of which was revoked and is under appeal, and a patent issued in Canada, which was withdrawn and is under appeal. We also have a number of pending patent applications in the U.S. and foreign countries.

We may not receive any patents from our current patent applications. Moreover, if patents are issued to us, governmental authorities may not allow claims sufficient to protect our technology and products. Finally, others may challenge or seek to circumvent or invalidate our patents. In that event, the rights granted under our patents may be inadequate to protect our proprietary technology or to provide any commercial advantage.

Once issued, we maintain our patents by paying maintenance fees to the patent office in each country when due. Where appropriate, we participate in legal proceedings to vigorously defend against the revocation or withdrawal of our patents. The scope and nature of these proceedings generally differ depending on the country in which they are initiated.

For example, our core DNA delivery technology is covered by patents that have been issued and revoked as a result of oppositions in Europe and Japan. In addition, our core DNA delivery technology is covered by a patent that was withdrawn from issuance as a result of a protest procedure in Canada. We are currently appealing the revocation or withdrawal from issuance of our patents in Europe, Japan and Canada, but if our appeals do not succeed, we may lose all or part of our proprietary protection on our product candidates in these countries or regions.

Some components of our gene-based product candidates are, or may become, patented by others. As a result, we may be required to obtain licenses to conduct research, to manufacture, or to market such products. Licenses may not be available on commercially reasonable terms, or at all, which may impede our ability to commercialize our products.

The legal proceedings to obtain and defend patents, and litigation of third-party claims of intellectual property infringement, could require us to spend money and could impair our operations.

Our success will depend in part on our ability to obtain patent protection for our products and processes, both in the United States and in other countries. The patent positions of biotechnology and pharmaceutical companies, however, can be highly uncertain and involve complex legal and factual questions. Therefore, it is difficult to predict the breadth of claims allowed in the biotechnology and pharmaceutical fields.

7

We also rely on confidentiality agreements with our corporate collaborators, employees, consultants and certain contractors to protect our proprietary technology. However, these agreements may be breached and we may not have adequate remedies for such breaches. In addition, our trade secrets may otherwise become known or independently discovered by our competitors.

Protecting intellectual property rights can be very expensive. Litigation will be necessary to enforce patents issued to us or to determine the scope and validity of third-party proprietary rights. Moreover, if a competitor were to file a patent application claiming technology also invented by us, we would have to participate in an interference proceeding before the United States Patent and Trademark Office to determine the priority of the invention. We may be drawn into interferences with third parties or may have to provoke interferences ourselves to unblock third-party patent rights to allow us or our licensees to commercialize products based on our technology. Litigation could result in substantial costs and the diversion of management's efforts regardless of the results of the litigation. An unfavorable result in litigation could subject us to significant liabilities to third parties, require disputed rights to be licensed or require us to cease using some technology.

Our products and processes may infringe, or be found to infringe, patents not owned or controlled by us. Patents held by others may require us to alter our products or processes, obtain licenses, or stop activities. If relevant claims of third-party patents are upheld as valid and enforceable, we could be prevented from practicing the subject matter claimed in the patents, or may be required to obtain licenses or redesign our products or processes to avoid infringement. In addition, we could be required to pay money damages. A number of genetic sequences or proteins encoded by genetic sequences that we are investigating are, or may become, patented by others. As a result, we may have

to obtain licenses to test, use or market these products. Our business will suffer if we are not able to obtain licenses at all or on terms commercially reasonable to us and we are not able to redesign our products or processes to avoid infringement.

We are currently involved in several legal proceedings involving our intellectual property rights. Our core DNA delivery technology was covered by a patent issued in Europe in 1998, which was subsequently opposed by seven companies under European patent procedures. This patent was revoked on formal grounds in October 2001 under an initial ruling by the Opposition Division of the European Patent Office, or EPO. In April 2002, we filed an appeal, which is still pending, seeking to overturn this initial ruling. Our core DNA delivery technology is also covered by a Canadian patent that was issued and then withdrawn after protests against its issuance were filed on behalf of an undisclosed party or parties in August and December 2001. We have responded to the protests and are awaiting further action by the Canadian Patent Office.

In addition, our core DNA delivery technology is covered by a Japanese patent that was published in January 2002 and thereafter revoked by the examining panel at the Japanese Patent Office, or JPO, on formal and substantive grounds. We filed a rebuttal response to the revocation which resulted in the maintenance of the patent. We have also received notice that four Trial for Invalidation, or TFI, requests against this patent were filed in the JPO by two companies. We intend to file responses to the TFI requests on or before the deadlines for each response.

We have licensed from the University of Michigan rights to various U.S. and international patents related to injection of DNA-based therapeutics into tumors that, for example, provide additional protection for Allovectin-7® and Leuvectin®. Included in this license is a European patent granted in March 2002. We have received notice from the EPO that one company filed an opposition in December 2002 alleging both formal and substantive grounds for revocation, and that the opposition was declared admissible in February 2003. We have submitted a rebuttal response to the opposition.

A lawsuit was filed against us in July 2003 by the Wisconsin Alumni Research Foundation, or WARF, in the United States District Court for the Western District of Wisconsin. This lawsuit concerns the interpretation of payment provisions of a license agreement that we entered into with WARF in

8

1991, and payments made under this agreement. WARF seeks a declaratory judgment as to the correct interpretation of the payment provisions of the agreement and additional compensation from us, the amount of which is unspecified in WARF's complaint. We have counterclaimed, likewise seeking a declaratory judgment as to the correct interpretation of the payment provisions of the agreement and a return of amounts overpaid to WARF under this agreement in excess of \$1.5 million.

Competition and technological change may make our product candidates and technologies less attractive or obsolete.

We compete with companies, including major pharmaceutical and biotechnology firms, that are pursuing other forms of treatment or prevention for diseases that we target. We also may experience competition from companies that have acquired or may acquire technology from universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions which may prevent us from successfully commercializing products.

Some of our competitors are established companies with greater financial and other resources. Other companies may succeed in developing products and obtaining FDA approval faster than we do, or in developing products that are more effective than ours. While we will seek to expand our technological capabilities to remain competitive, research and development by others will seek to render our technology or products obsolete or noncompetitive or result in treatments or cures superior to any therapeutics developed by us. Additionally, even if our product development efforts are successful, and even if the requisite regulatory approvals are obtained, our products may not gain market acceptance among physicians, patients, healthcare payers and the medical communities. If any of our products do not achieve market acceptance, we may lose our investment in that product, which could have a material adverse impact on our operations.

The method of administration of some of our product candidates can cause adverse events in patients, including death.

Some of our potential products are designed to be injected directly into malignant tumors. There are medical risks inherent in direct tumor injections. For example, in clinical trials of Allovectin-7®, attending physicians have punctured patients' lungs in less than one percent of procedures, requiring hospitalization. In addition, a physician administering Allovectin-7® in an investigator-sponsored clinical trial inadvertently damaged tissue near the heart of a patient, which may have precipitated the patient's death. These events are reported as adverse events in our clinical trials. These risks may adversely impact market acceptance of some of our product candidates.

If we lose our key personnel or are unable to attract and retain additional personnel, we may not be able to pursue collaborations or develop our own products.

We are highly dependent on our principal scientific, manufacturing, clinical, regulatory and management personnel, including Vijay B. Samant, our President and Chief Executive Officer, and David C. Kaslow, our Chief Scientific Officer. The loss of the services of these individuals might significantly delay or prevent the achievement of our objectives. We do not maintain "key person" life insurance on any of our personnel. We depend on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We face competition for qualified individuals from other companies, academic institutions, government entities and other organizations in attracting and retaining personnel. To pursue our product development plans, we may need to hire additional management personnel and additional scientific personnel to perform research and development, as well as personnel with expertise in clinical trials, government regulation and manufacturing. We have not had any problem attracting and retaining key personnel and qualified staff in the recent past. Also, to our knowledge, no key personnel or qualified staff plans to retire or leave us in the near future.

9

However, due to the reasons noted above, we may not be successful in hiring or retaining qualified personnel.

A significant portion of our revenue is derived from agreements with government agencies, which are subject to termination and uncertain future funding.

We have entered into agreements with government agencies, such as the NIH, and we intend to continue entering into these agreements in the future. Our business is partially dependent on the continued performance by these government agencies of their responsibilities under these agreements, including adequate continued funding of the agencies and their programs. We have no control over the resources and funding that government agencies may devote to these agreements, which may be subject to annual renewal and which generally may be terminated by the government agencies at any time. Government agencies may fail to perform their responsibilities under these agreements. We may also be unsuccessful in entering into additional agreements with government agencies.

We have limited experience in manufacturing our product candidates in commercial quantities. We may not be able to comply with applicable manufacturing regulations or produce sufficient product for contract or commercial purposes.

The commercial manufacturing of vaccines and other biological products is a time-consuming and complex process, which must be performed in compliance with the FDA's current Good Manufacturing Practices, or GMP, regulations. Our experience in manufacturing our product candidates and the products of others has been limited to production of research and clinical trial supplies under less rigorous clinical GMP, or cGMP, regulations. We may not be able to comply with the GMP regulations, and our manufacturing process may be subject to delays, disruptions or quality control problems. In addition, we must complete the installation and validation of a large-scale fermenter

and related purification equipment in order to produce the quantities of product expected to be required under certain contract manufacturing agreements or for commercial purposes. We do not have any experience in manufacturing at this scale. Noncompliance with the GMP regulations, the inability to complete the installation or validation of our large-scale equipment, or other problems with our manufacturing process may limit or delay the development or commercialization of our product candidates, and cause us to breach our contract manufacturing arrangements.

We may initially depend on third parties to manufacture our product candidates commercially.

We may initially depend on collaborators, licensees or other third parties to manufacture our product candidates in commercial quantities. We may be unable to enter into any arrangement for the commercial manufacture of our product candidates, and any arrangement we secure may not meet our requirements for manufacturing quality or quantity. Our dependence on third parties for the commercial manufacture of our product candidates may also reduce our profit margins and our ability to develop and deliver products in a timely manner.

We have no marketing or sales experience, and if we are unable to develop our own sales and marketing capability, we may not be successful in commercializing our products.

Our current strategy is to market our proprietary products directly in the United States, but we currently do not possess pharmaceutical marketing or sales capabilities. In order to market and sell our proprietary products, we will need to develop a sales force and a marketing group with relevant pharmaceutical experience, or make appropriate arrangements with strategic partners to market and sell these products. Developing a marketing and sales force is expensive and time-consuming and could delay any product launch. If we are unable to successfully employ qualified marketing and sales personnel or develop other sales and marketing capabilities, our business will be harmed.

10

Healthcare reform and restrictions on reimbursement may limit our returns on potential products.

Our ability to earn sufficient returns on our products will depend in part on the extent to which reimbursement for our products and related treatments will be available from:

- Government health administration authorities,
- Government agencies procuring biodefense products for military or public use, including some for which we may become a sole-source vendor,
- Private health coverage insurers,
- Managed care organizations, and
- Other organizations.

If we fail to obtain appropriate reimbursement, we could be prevented from successfully commercializing our potential products.

There are efforts by governmental and third-party payers to contain or reduce the costs of healthcare through various means. We expect that there will continue to be a number of legislative proposals to implement government controls. The announcement of proposals or reforms could impair our ability to raise capital. The adoption of proposals or reforms could impair our business.

Certain portions of the Health Insurance Portability and Accountability Act of 1996, or HIPAA, became effective in 2003 and may complicate the process by which clinical trials may be initiated, however the specific nature and degree of impact are not yet known.

Additionally, third-party payers are increasingly challenging the price of medical products and services. If purchasers or users of our products are not able to obtain adequate reimbursement for the cost of using our products, they may forego or reduce their use. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products, and whether adequate third-party coverage will be available.

We use hazardous materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled storage, use and disposal of hazardous materials, biological hazardous materials and radioactive compounds. The hazardous materials we use include certain compressed gases, flammable liquids, acids and bases, and other toxic compounds. We are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of materials and waste products. Although we believe that our safety procedures for handling and disposing of these hazardous materials comply with the standards prescribed by law and regulation, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance on acceptable terms, or at all. We could be required to incur significant costs to comply with current or future environmental laws and regulations.

We may have significant product liability exposure.

We face an inherent business risk of exposure to product liability and other claims in the event that our technologies or products are alleged to have caused harm. We also have potential liability for products manufactured by us on a contract basis for third parties. These risks are inherent in the development and manufacture of chemical and pharmaceutical products. Although we currently maintain product liability insurance in the amount of \$10 million in the aggregate, this insurance

11

coverage may not be sufficient, and we may not be able to obtain sufficient coverage in the future at a reasonable cost. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the commercialization of any products developed by us or our collaborators, or our ability to manufacture products for third parties. To date, no product liability claims have been filed against us. However, if we are sued for any injury caused by our technology or products, or by third-party products that we manufacture, our liability could exceed our insurance coverage and total assets.

Our stock price could continue to be highly volatile and you may not be able to resell your shares at or above the price you pay for them.

The market price of our common stock, like that of many other life sciences companies, has been and is likely to continue to be highly volatile. During the three year period ended on October 1, 2003, our closing stock price has ranged from \$2.23 to \$24.50. The following factors, among others, could have a significant impact on the market

price of our common stock:

- The results of our preclinical studies and clinical trials or those of our collaborators, licensees or competitors or for gene therapies in general,
- Evidence or lack of evidence of the safety or efficacy of our potential products or those of our collaborators, licensees or competitors,
- The announcement by us or our collaborators, licensees or competitors of technological innovations or new products,
- Developments concerning our patent or other proprietary rights or those of our collaborators, licensees or competitors, including litigation and challenges to our proprietary rights,
- Other developments with our collaborators or licensees,
- Geopolitical developments, natural or man-made disease threats, or other events beyond our control,
- U.S. and foreign governmental regulatory actions,
- Changes or announcements in reimbursement policies,
- Concern as to the safety of our potential products,
- Period-to-period fluctuations in our operating results,
- Market conditions for life science stocks in general,
- Changes in the collective short interest in our stock,
- Changes in estimates of our performance by securities analysts, and
- Our cash balances, need for additional capital, and access to capital.

We are at risk of securities class action litigation due to our expected stock price volatility.

In the past, stockholders have brought securities class action litigation against a company following a decline in the market price of its securities. This risk is especially acute for us because life science companies have experienced greater than average stock price volatility in recent years and, as a result, have been subject to, on average, a greater number of securities class action claims than companies in other industries. To date, we have not been subject to class action litigation. However, we may in the future be the target of this litigation. Securities litigation could result in substantial costs and divert our management's attention and resources, and could seriously harm our business.

12

The ability of our investors to seek remedies against Arthur Andersen LLP, who audited some of the financial statements included in this prospectus, may be significantly limited.

Our annual financial statements for the years ended December 31, 2001 and 2000, which are incorporated by reference in this prospectus, were audited by Arthur Andersen LLP. We dismissed Arthur Andersen as our independent public accountants effective April 16, 2002. After reasonable efforts, we were unable to obtain Arthur Andersen's written consent to incorporate by reference its report dated February 1, 2002 with respect to these audited financial statements. The absence of this consent may limit the ability of investors to seek remedies against Arthur Andersen for any untrue statement of a material fact contained in these financial statements, or any omission of a material fact required to be stated in these financial statements. In addition, as a practical matter, any claims that may be available under federal securities laws against auditing firms may not be available against Arthur Andersen due to the diminished amount of assets of Arthur Andersen that are or in the future may be available for claims.

Anti-takeover provisions in our stockholder rights plan, our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Pursuant to the terms of our stockholder rights plan, we have distributed a dividend of one preferred stock purchase right for each outstanding share of common stock. These rights will cause substantial dilution to the ownership of a person or group that attempts to acquire us on terms not approved by our board of directors. Our certificate of incorporation and bylaws include other anti-takeover provisions, such as a classified board of directors, a prohibition on stockholder actions by written consent, the authority of our board of directors to issue preferred stock without stockholder approval, and supermajority voting requirements for specified actions. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. These provisions may delay or prevent an acquisition of us, even if the acquisition may be considered beneficial by some stockholders. In addition, they may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

The preferred stock we are offering may not develop an active public market, which could depress its resale price.

The preferred stock we are offering will be a new issue of securities for which there is currently no trading market. We cannot predict whether an active trading market for our preferred stock will develop or be sustained. If an active trading market were to develop, our preferred stock could trade at prices that may be lower than its initial offering price.

The issuance of preferred stock could adversely affect our common stockholders.

The issuance of preferred stock could adversely affect the voting power of holders of our common stock, and reduce the likelihood that our common stockholders will receive dividend payments and payments upon liquidation. The issuance of preferred stock could also decrease the market price of our common stock, or have terms and conditions that could discourage a takeover or other transaction that might involve a premium price for our shares or that our stockholders might believe to be in their best interests.

13

FORWARD-LOOKING STATEMENTS

Any statements in this prospectus about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. You can identify these forward-looking statements by the use of words or phrases such as "believe," "may," "could," "will," "estimate," "continue," "anticipate," "intend," "seek," "plan," "expect," "should," and "would."

These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and so are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Among the factors that could cause actual results to differ materially from those anticipated in the forward-looking statements are risks and uncertainties associated with our development programs and business and finances, including but not limited to the risk that our drug candidates will not successfully proceed through clinical trials or that later stage clinical trials will not show that they are effective in treating humans; adverse determinations by regulatory and governmental authorities; dependence on licensees and collaborators who could terminate their relationships with us at any time; uncertainties relating to patent protection and intellectual property rights of third parties; the impact of competitive products and technological changes; our ability to raise additional capital and the cost of the capital; and other material risks described under "Risk Factors" in this prospectus and in our other SEC filings.

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

14

FINANCIAL RATIOS

Our ratios of combined fixed charges and preference dividends to earnings are as follows for the periods indicated:

	Six Months Ended June 30, 2003	Year Ended December 31,				
		2002	2001	2000	1999	1998
Ratio of combined fixed charges and preference dividends to earnings	—	—	—	—	—	—

For the years ended December 31, 2002, 2001, 2000, 1999 and 1998 and the six months ended June 30, 2003, our earnings were insufficient to cover fixed charges by \$27,932,494, \$9,239,991, \$8,516,873, \$6,909,217, \$7,480,507 and \$13,947,023, respectively. Fixed charges consist of interest expense, including capitalized interest, on all debt, amortized premiums, discounts and capitalized expenses related to indebtedness and estimated interest included in rental expense. For the periods indicated above and as of the date of this prospectus, we have had no preference securities outstanding.

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, including clinical trials, research and development expenses, general and administrative expenses, manufacturing expenses, and potential acquisitions of companies and technologies that complement our business. Pending their application, we expect to invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities.

15

DESCRIPTION OF CAPITAL STOCK

General

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 40,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. To date, our board of directors has designated 40,000 of the 5,000,000 authorized shares of preferred stock as Series A participating preferred stock reserved for issuance under our stockholder rights plan, as described below. As of August 5, 2003, we had 20,091,344 shares of our common stock outstanding held of record by approximately 460 stockholders, and no shares of our preferred stock were outstanding.

This prospectus contains a general description of our capital stock and stockholder rights plan. For a more detailed description, you should read our certificate of incorporation and bylaws, our stockholder rights plan and the applicable provisions of the Delaware General Corporation Law, or DGCL.

When we offer to sell a particular series of these securities, we will describe the specific terms of the series in a supplement to this prospectus. Accordingly, for a complete description of the terms of any series of securities, you must refer to both the specific description of the series in the prospectus supplement relating to that series and the general description of the securities described in this prospectus. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Subject to preferences that may be applicable to any of our outstanding preferred stock, the holders of common stock are entitled to receive ratably the dividends, if any, that may be declared from time to time by our board of directors out of funds legally available for such dividends. In the event of a liquidation, dissolution or winding up of Vical, the holders of our common stock would be entitled to share ratably in all assets remaining after payment of liabilities and the satisfaction of any liquidation preferences granted to the holders of any outstanding shares of preferred stock. Holders of our common stock have no preemptive rights and no conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to our common stock. All the outstanding shares of common stock are, and the shares offered by this prospectus, when issued and paid for, will be validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of any shares of our preferred stock.

Preferred Stock

To date, our board of directors has designated 40,000 shares of preferred stock as Series A participating preferred stock reserved for issuance under our stockholder rights plan, none of which were issued and outstanding as of August 5, 2003. Under our certificate of incorporation, our board of directors is authorized to issue additional shares of our preferred stock from time to time, in one or more classes or series, without stockholder approval. Prior to the issuance of shares of each class or series, our board of directors is required by the DGCL and our certificate of incorporation to adopt resolutions and file a certificate of designation with the Delaware Secretary of State. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions of that class or series, including the following:

- the number of shares constituting each class or series,
- voting rights,

16

- rights and terms of redemption, including sinking fund provisions,
- dividend rights and rates,
- terms concerning the distribution of assets,
- conversion or exchange terms,
- redemption prices, and
- liquidation preferences.

All shares of preferred stock offered by this prospectus, when issued and paid for, will be validly issued, fully paid and nonassessable and will not have any preemptive or subscription rights.

We will describe in a prospectus supplement relating to the class or series of preferred stock being offered the following terms:

- the title and stated value of the preferred stock,
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock,
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock,
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate,
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period,
- the procedures for auction and remarketing, if any, for the preferred stock,
- the provisions for a sinking fund, if any, for the preferred stock,
- the provision for redemption, if applicable, of the preferred stock,
- any listing of the preferred stock on any securities exchange,
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period,
- voting rights, if any, of the preferred stock,
- whether interests in the preferred stock will be represented by depository shares,
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock,
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs,
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs, and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Stockholder Rights Plan

On March 20, 1995, our board of directors adopted a stockholder rights plan. Under the stockholder rights plan, a dividend of one preferred stock purchase right was declared for each

17

outstanding share of our common stock. In addition, a preferred stock purchase right is attached to each share of common stock issued during the term of the stockholder rights plan. Each right entitles the holder to buy one one-thousandth of a share of our Series A participating preferred stock at an exercise price of \$50.00, subject to specified adjustments.

Our Series A participating preferred stock is nonredeemable and junior to any other series of preferred stock we may issue, unless otherwise provided in the terms of the other series of preferred stock. If the Series A participating preferred stock is issued under the terms of our stockholder rights plan, the holders of Series A participating

preferred stock:

- would vote together with our common stock, and would be entitled to 1,000 votes per share,
- would be entitled to a preferential quarterly dividend per share equal to the greater of \$100 or 1,000 times the dividend declared per each share of common stock,
- in the event of a liquidation, dissolution or winding up of Vical, would be entitled to a liquidation payment per share equal to the greater of \$1,000 or 1,000 times the payment made per each share of common stock, and
- in the event of a merger, consolidation or other transaction in which shares of common stock are exchanged, would be entitled to receive an amount per share equal to 1,000 times the amount and type of consideration received per share of common stock.

Initially, each preferred stock purchase right is transferred automatically with the related share of common stock, and is not exercisable. The rights will separate from the common stock, and become exercisable, upon the acquisition by a person or affiliated group of, or ten days following the commencement or public announcement of a tender or exchange offer for, 15% or more of the voting power of our outstanding voting securities.

Each preferred stock purchase right entitles its holder, other than the person or affiliated group acquiring 15% or more of the voting power of our outstanding voting securities, to purchase:

- shares of our common stock with a market value of twice the exercise price of the right, or
- in the event of a merger, business combination or other transaction in which 50% or more of our assets or earning power are sold, shares of the common stock of the surviving company in the transaction having a market value of twice the exercise price of the right.

We may redeem the preferred stock purchase rights at a price of \$0.01 per right in specified circumstances, including at any time before a person or affiliated group acquires 15% or more of the voting power of our outstanding voting securities. Also, at any time after such an acquisition occurs, but before the person or affiliated group acquires 50% or more of the voting power of our outstanding voting securities, our board of directors may exchange all or part of the preferred stock purchase rights for one share of common stock per right, or other consideration as may be determined by our board.

The stockholder rights plan is intended to protect stockholders in the event of an unsolicited attempt to acquire us. As a result, the stockholder rights plan could have the effect of delaying, deferring or preventing transactions that our stockholders may deem to be in their best interests, including those in which they may receive a premium for their shares.

The above description of our stockholder rights plan is intended as a summary only. For a more detailed description, you should read our stockholder rights agreement dated March 20, 1995 with First Interstate Bank of California. To obtain a copy of the stockholder rights agreement, please see the section of this prospectus entitled "Where You Can Find More Information."

Anti-Takeover Provisions

In addition to our stockholder rights plan, there are provisions of the DGCL, our certificate of incorporation and our bylaws that could have the effect of delaying, deferring or preventing an acquisition of Vical, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the ability of our stockholders to remove current management or approve transactions that our stockholders may deem to be in their best interests.

Delaware Law. We are subject to Section 203 of the DGCL, which restricts our ability to enter into a business combination with an interested stockholder for a period of three years. Generally, a business combination means a merger, asset sale or other transaction resulting in a financial benefit to the stockholder. An interested stockholder means a stockholder who, together with that stockholder's affiliates and associates, owns 15% or more of our outstanding voting stock. These restrictions do not apply if:

- before the date a stockholder becomes an interested stockholder, our board of directors approves either the business combination or the transaction in which the stockholder becomes an interested stockholder,
- upon consummation of the transaction in which the stockholder becomes an interested stockholder, the interested stockholder owns at least 85% of our voting stock outstanding at the time the transaction commenced, subject to exceptions, or
- on or after the date a stockholder becomes an interested stockholder, the business combination is both approved by our board of directors and authorized at an annual or special meeting of our stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock not owned by the interested stockholder.

Certificate of Incorporation and Bylaws. Some provisions of our certificate of incorporation and bylaws could also have anti-takeover effects. These provisions:

- provide for a board comprised of three classes of directors with each class serving a staggered three-year term,
- authorize our board of directors to issue preferred stock from time to time, in one or more classes or series, without stockholder approval,
- require the approval of at least two-thirds of our outstanding voting stock to amend specified provisions of our certificate of incorporation,
- require the approval of at least two-thirds of our total number of authorized directors, or two-thirds of our outstanding voting stock, to amend our bylaws,
- provide that special meetings of our stockholders may be called only by our Chief Executive Officer, or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors, and
- do not include a provision for cumulative voting for directors (under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares may be able to ensure the election of one or more directors).

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Mellon Investor Services LLC. Its address is 400 South Hope Street, 4th Floor, Los Angeles, CA 90071 and its telephone number is (800) 522-6645.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus in any of three ways (or in any combination):

- to or through underwriters or dealers,
- directly to a limited number of purchasers or to a single purchaser, or
- through agents.

The prospectus supplement will set forth the terms of the offering of the securities covered by this prospectus, including:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them,
- any over-allotment options under which underwriters may purchase additional securities from us,
- any underwriting discounts or commissions or agency fees and other items constituting underwriters' or agents' compensation,
- the initial public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers, and
- any securities exchanges or markets on which the securities may be listed.

Any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Underwriters may offer and sell the offered 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. If underwriters are used in the sale of any securities in a firm commitment public offering, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to conditions specified in the applicable underwriting agreement, but the underwriters will be obligated to purchase all of the securities if they purchase any of the securities. We may use underwriters with whom we have a material relationship. We will name the underwriter in the prospectus supplement and describe the nature of any such relationship.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to the agent. Generally, any agent will act on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be

obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Regulation M prohibits stabilizing transactions in an "at the market" offering. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the applicable securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Cooley Godward LLP, San Diego, California.

EXPERTS

The balance sheet of Vical Incorporated as of December 31, 2002, and the related statements of operations, stockholders' equity and cash flows for the year ended December 31, 2002, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent accountants, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The balance sheets of Vical Incorporated as of December 31, 2001 and 2000, and the related statements of operations, stockholders' equity and cash flows for the years

ended December 31, 2001 and 2000, have been incorporated by reference herein and in the registration statement in reliance upon the report of Arthur Andersen LLP, independent accountants, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

Arthur Andersen LLP have not consented to the inclusion of their report in this prospectus, and we have not obtained their consent to do so in reliance upon Rule 437a of the Securities Act. The absence of this consent may limit recovery against Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statement of a material fact, or any omission to state a material fact required to be stated, in the financial statements audited by Arthur Andersen LLP. Also, as a practical matter, Arthur Andersen LLP's ability to satisfy any claims may be limited due to events arising out of their conviction on federal obstruction of justice charges.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act, and file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any

21

reports, proxy statements and other information we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 to obtain information on the operation of the SEC's public reference room. You may also access information we file electronically with the SEC by visiting the SEC's Internet website at www.sec.gov.

We are incorporating by reference some information about us that we file with the SEC. We are disclosing important information to you by referencing these filed documents. Any information that we reference this way is considered part of this prospectus. The information in this prospectus supersedes information incorporated by reference that we have filed with the SEC prior to the date of this prospectus, while information that we file with the SEC after the date of this prospectus that is incorporated by reference will automatically update and supersede information in this prospectus.

We incorporate by reference the following documents we have filed, or may file, with the SEC:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2002,
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2003 and June 30, 2003,
- our Current Reports on Form 8-K filed on May 6, 2003, May 16, 2003 and July 31, 2003,
- the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on January 8, 1993, and the description of the preferred stock purchase rights for Series A participating preferred stock contained in our Registration Statement on Form 8-A filed with the SEC on March 24, 1995, and
- all documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before termination of this offering.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing us at the following address or telephoning us at the following phone number:

Vical Incorporated
10390 Pacific Center Court
San Diego, California 92121
(858) 646-1100

22

PART II INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

Our estimated expenses in connection with the issuance and distribution of the securities being registered, other than underwriting discounts and commissions, are as set forth in the following table:

SEC Registration Fee	\$	4,045
Printing and Engraving Expenses	\$	50,000*
Legal Fees and Expenses	\$	50,000*
Accounting Fees and Expenses	\$	25,000*
Miscellaneous	\$	15,000*
Total	\$	144,045*

*Estimated

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law generally allows us to indemnify directors and officers for all expenses, judgments, fines and amounts in settlement actually paid and reasonably incurred in connection with any proceedings so long as such party acted in good faith and in a manner reasonably believed to be in or not opposed to our best interests and, with respect to any criminal proceedings, if such party had no reasonable cause to believe his or her conduct to be unlawful. Indemnification may only be made by us if the applicable standard of conduct set forth in Section 145 has been met by the indemnified party upon a determination made (i) by our board of directors by a majority vote of the directors who are not parties to such proceedings, even though less than a quorum, (ii) if there are no such directors, or if such directors so direct, by independent legal counsel in a written opinion or (iii) by the stockholders.

Article X of our Restated Certificate of Incorporation provides for indemnification of our directors and officers, and Article V of our Bylaws provides for indemnification of our directors, officers, employees and other agents, to the maximum extent permitted by the Delaware General Corporation Law. We have entered into indemnification agreements with our officers and directors. In addition, we maintain a policy providing directors' and officers' liability insurance.

Item 16. Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed

II-1

that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that subparagraphs (a)(1)(i) and (a)(1)(ii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) The undersigned registrant hereby undertakes that, for the purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered herein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to existing provisions or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

(d) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

II-2

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on October 2, 2003.

VICAL INCORPORATED

By: /s/ VIJAY B. SAMANT

Vijay B. Samant
President, Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL MEN AND WOMEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Vijay B. Samant and Martha J. Demski, and each of them, his or her true and lawful attorneys-in-fact and agents, each with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign and all amendments, including post-effective amendments, to this registration statement, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Amendment No. 1 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ VIJAY B. SAMANT</u> Vijay B. Samant	President, Chief Executive Officer and Director (Principal Executive Officer)	October 2, 2003
<u>/s/ MARTHA J. DEMSKI</u> Martha J. Demski	Chief Financial Officer (Principal Financial and Accounting Officer)	October 2, 2003
<u>/s/ R. GORDON DOUGLAS*</u> R. Gordon Douglas	Chairman of the Board of Directors	October 2, 2003
<u>/s/ M. BLAKE INGLE*</u> M. Blake Ingle	Director	October 2, 2003

II-3

<u>/s/ PATRICK F. LATTERELL*</u> Patrick F. Latterell	Director	October 2, 2003
<u>/s/ GARY A. LYONS*</u> Gary A. Lyons	Director	October 2, 2003
<u>/s/ ROBERT C. MERTON*</u> Robert C. Merton	Director	October 2, 2003

*By: /s/ MARTHA J. DEMSKI

Martha J. Demski
Attorney-in-Fact

II-4

EXHIBIT INDEX

Exhibit Number	Description
1.1*	Underwriting Agreement
4.1(1)	Restated Certificate of Incorporation
4.2(2)	Amended and Restated Bylaws
4.3(3)	Specimen Common Stock Certificate
4.4(4)	Rights Agreement dated as of March 20, 1995, between the Company and First Interstate Bank of California

- 5.1*** Opinion of Cooley Godward LLP
 - 12.1*** Statement Regarding the Computation of Ratio of Combined Fixed Charges and Preference Dividends to Earnings
 - 23.1*** Consent of Cooley Godward LLP (reference is made to Exhibit 5.1 hereto)
 - 23.2** Consent of KPMG LLP
 - 23.3*** Consent of Arthur Andersen LLP
 - 24.1*** Power of Attorney (reference is made to the signature pages hereto)
-

* To be filed by amendment or incorporated by reference in connection with the offering of the securities.

** Filed herewith.

*** Previously filed.

- (1) Incorporated by reference to Exhibit 3.1(i) filed with the Company's Registration Statement on Form S-3 (No. 33-95812) filed on August 15, 1995.
 - (2) Incorporated by reference to Exhibit 3.1(ii) filed with the Company's Registration Statement on Form S-3 (No.33-95812) filed on August 15, 1995.
 - (3) Incorporated by reference to Exhibit 4.1 filed with the Company's Registration Statement on Form S-3 (No. 33-95812) filed on August 15, 1995.
 - (4) Incorporated by reference to Exhibit 4.2 filed with the Company's Annual Report on Form 10-K for the year ended December 31, 1994.
-

QuickLinks

[TABLE OF CONTENTS](#)

[ABOUT THIS PROSPECTUS](#)

[SUMMARY OF OUR BUSINESS](#)

[RISK FACTORS](#)

[FORWARD-LOOKING STATEMENTS](#)

[FINANCIAL RATIOS](#)

[USE OF PROCEEDS](#)

[DESCRIPTION OF CAPITAL STOCK](#)

[PLAN OF DISTRIBUTION](#)

[LEGAL MATTERS](#)

[EXPERTS](#)

[WHERE YOU CAN FIND MORE INFORMATION](#)

[PART II INFORMATION NOT REQUIRED IN PROSPECTUS](#)

[Item 14. Other Expenses of Issuance and Distribution](#)

[Item 15. Indemnification of Directors and Officers](#)

[Item 16. Exhibits](#)

[Item 17. Undertakings](#)

[SIGNATURES](#)

[POWER OF ATTORNEY](#)

[EXHIBIT INDEX](#)

[QuickLinks](#) -- Click here to rapidly navigate through this document

Exhibit 23.2

Independent Auditors' Consent

The Board of Directors
Vical Incorporated:

We consent to the use of our report dated February 6, 2003, with respect to the balance sheet of Vical Incorporated as of December 31, 2002, and the related statements of operations, stockholders' equity, and cash flows for the year then ended incorporated by reference herein and to the reference to our firm under the heading "Experts" in the prospectus.

/s/ KPMG LLP

San Diego, California
October 1, 2003

QuickLinks

[Exhibit 23.2](#)