

LA JOLLA PHARMACEUTICAL CO

Form 424B5

February 20, 2004

Table of Contents

Filed Pursuant to Rule 424(b)(5)

Registrant No. 333-101499

PROSPECTUS SUPPLEMENT

(To Prospectus Dated December 12, 2002)

8,695,653 Shares

La Jolla Pharmaceutical Company

Common Stock

We are selling 8,695,653 shares of common stock. We have granted the underwriter an option, exercisable for up to 30 days from the date of this prospectus supplement, to purchase up to 1,304,347 additional shares of our common stock to cover over-allotments.

Our common stock is traded on the Nasdaq National Market under the symbol LJPC. On February 19, 2004, the last reported sale price of our common stock on the Nasdaq National Market was \$3.26 per share.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-3.

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 the accompanying prospectus. Any representation to the contrary is a criminal offense.

| | Per Share | Total |
|---|------------------|--------------|
| Public Offering Price | \$ 3.15 | \$27,391,307 |
| Underwriting Discount | \$0.189 | \$ 1,643,478 |
| Proceeds to La Jolla Pharmaceutical Company (before expenses) | \$2.961 | \$25,747,829 |

The underwriter is offering the shares of our common stock as described under the heading Underwriting beginning on page S-17. The shares will be ready for delivery on or about February 25, 2004.

PACIFIC GROWTH EQUITIES, LLC

Sole Underwriter

The date of this prospectus supplement is February 19, 2004

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS SUPPLEMENT

SUMMARY

RISK FACTORS

DESCRIPTION OF CAPITAL STOCK

DILUTION

USE OF PROCEEDS

UNDERWRITING

LEGAL MATTERS

EXPERTS

WHERE YOU CAN FIND MORE INFORMATION AND INCORPORATION BY REFERENCE

FORWARD-LOOKING STATEMENTS

ABOUT THIS PROSPECTUS

THE COMPANY

RECENT DEVELOPMENTS

RISK FACTORS

DESCRIPTION OF CAPITAL STOCK

USE OF PROCEEDS

PLAN OF DISTRIBUTION

LEGAL MATTERS

EXPERTS

FORWARD-LOOKING STATEMENTS

WHERE YOU CAN FIND MORE INFORMATION

Table of Contents

You should rely only on the information contained or incorporated by reference in this document. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information appearing in this prospectus supplement and the accompanying prospectus, as well as the information that we have previously filed with the Securities and Exchange Commission and incorporated by reference, is accurate only as of the date of the applicable document. The descriptions set forth in this prospectus supplement replace and supplement, where inconsistent, the description of the general terms and provisions set forth in the accompanying prospectus.

TABLE OF CONTENTS
PROSPECTUS SUPPLEMENT

| | Page |
|---|-------------|
| ABOUT THIS PROSPECTUS SUPPLEMENT | ii |
| SUMMARY | S-1 |
| RISK FACTORS | S-3 |
| DESCRIPTION OF CAPITAL STOCK | S-14 |
| DILUTION | S-16 |
| USE OF PROCEEDS | S-16 |
| UNDERWRITING | S-17 |
| LEGAL MATTERS | S-18 |
| EXPERTS | S-18 |
| WHERE YOU CAN FIND MORE INFORMATION AND INCORPORATION BY REFERENCE | S-18 |
| FORWARD-LOOKING STATEMENTS | S-19 |

PROSPECTUS

| | Page |
|-------------------------------------|-------------|
| ABOUT THIS PROSPECTUS | 1 |
| THE COMPANY | 1 |
| RECENT DEVELOPMENTS | 1 |
| RISK FACTORS | 2 |
| DESCRIPTION OF CAPITAL STOCK | 11 |
| USE OF PROCEEDS | 13 |
| PLAN OF DISTRIBUTION | 13 |
| LEGAL MATTERS | 15 |
| EXPERTS | 15 |
| FORWARD-LOOKING STATEMENTS | 15 |
| WHERE YOU CAN FIND MORE INFORMATION | 15 |

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement contains the terms of this offering. A description of our capital stock is contained in this prospectus supplement. This prospectus supplement, with the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, may add, update or change information in the accompanying prospectus. If information in this prospectus supplement, or the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, is inconsistent with the accompanying prospectus, this prospectus supplement, or the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, will apply and will supersede the information in the accompanying prospectus.

Please read and consider all information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus together with the additional information described under the section entitled "Where You Can Find More Information and Incorporation by Reference" in this prospectus supplement and the section entitled "Risk Factors" in this prospectus supplement before you make an investment decision.

This prospectus supplement and the accompanying prospectus do not constitute an offer or solicitation by anyone in any jurisdiction in which an offer or solicitation is not authorized or in which the person making an offer or solicitation is not qualified to do so, or to anyone to whom it is unlawful to make an offer or solicitation.

Table of Contents

SUMMARY

This is only a summary of the offering. It may not contain all of the information that may be important to you. To fully understand the investment you are contemplating, you should read this prospectus supplement, the prospectus and the detailed information incorporated into them by reference before you decide to make an investment. Unless the context otherwise requires, the terms we, us, and our refer to La Jolla Pharmaceutical Company, a Delaware corporation. Unless otherwise indicated, the information in this prospectus supplement assumes no exercise of the underwriter's over-allotment option.

The Company

La Jolla Pharmaceutical Company is a biopharmaceutical company focused on the research and development of highly specific therapeutic products for the treatment of certain life-threatening antibody-mediated diseases. These diseases, including autoimmune conditions such as lupus erythematosus (lupus) and antibody-mediated thrombosis, are caused by abnormal B cell production of antibodies that attack healthy tissues. Current treatments for these autoimmune disorders address only symptoms of the disease, or nonspecifically suppress the normal operation of the immune system, which often results in severe, negative side effects and hospitalization. We believe that our drug candidates, called Toleragens®, will treat the underlying cause of many antibody-mediated diseases without these severe, negative side effects.

Corporate Information

We are incorporated in the State of Delaware. Our principal executive offices are located at 6455 Nancy Ridge Drive, San Diego, California 92121 and our telephone number is (858) 452-6600.

Recent Developments

On February 18, 2003, we announced initial results from our Phase 3 clinical trial of Riquent®, our clinical drug candidate for the treatment of lupus renal disease. Although the trial did not reach statistical significance for its primary endpoint, time to renal flare, the Phase 3 trial results demonstrated that lupus patients treated with Riquent had significantly lower levels of antibodies to double-stranded DNA (dsDNA) than patients treated with a placebo. Data from the Phase 3 and Phase 2/3 studies demonstrated that lupus patients with sustained reductions in antibodies to dsDNA experienced fewer renal flares. In these two studies, two and four times as many Riquent-treated patients had sustained reductions compared with placebo-treated patients.

On May 5, 2003, we announced that, based upon our discussions with the United States Food and Drug Administration (the FDA), we planned to complete a New Drug Application (the NDA) for Riquent around the end of 2003.

On June 16, 2003, we announced the health-related quality of life results from our Phase 3 clinical trial of Riquent. Patients in our Phase 3 trial with sustained reductions in antibodies to dsDNA reported improved health-related quality of life and had a lower risk of Major SLE (systemic lupus erythematosus) flare compared with patients who did not have sustained reductions. Major SLE flare includes new or increased treatment with high-dose corticosteroids and/or cyclophosphamide or other immunosuppressive drugs, hospitalization, or death due to lupus. Similar results were also seen in our Phase 2/3 trial. We believe that these results support the pathogenicity or disease-causing ability of antibodies to dsDNA in lupus patients.

On July 24, 2003, we announced that, based upon discussions with the FDA, we may pursue an accelerated approval for Riquent under the Subpart H regulation. Under Subpart H, drugs in development for serious, life-threatening diseases with an unmet medical need can be approved on an accelerated basis if the FDA determines that the effect of the drug on a surrogate endpoint is reasonably likely to predict clinical benefit and that a post-marketing clinical trial can be successfully completed following drug approval which confirms the clinical benefit. As previously announced, in our Phase 3 and Phase 2/3 trials,

Table of Contents

patients treated with Riquent had significantly reduced levels of antibodies to dsDNA compared with patients treated with placebo. We believe that data from our clinical trials and the relevant medical literature would support the use of the level of antibodies to dsDNA as a surrogate endpoint that would be reasonably likely to predict clinical benefit.

On December 16, 2003, we announced that we had submitted the NDA for Riquent with the FDA.

On February 16, 2004, we announced that our NDA for Riquent had been accepted for review by the FDA. The acceptance of the NDA by the FDA indicates that the NDA is sufficiently complete to permit a substantive review of the application. Further discussions with the FDA will be needed to clarify whether any additional supportive information or studies will be required to support the approval of the NDA. The FDA will determine whether to approve Riquent, either on the basis of our clinical trial results or under Subpart H, and the conditions of any approval, after it has reviewed our NDA. We are currently in discussions with the FDA about the design and timing of a post-marketing clinical trial that would be required if Subpart H approval is pursued. We also are currently meeting with European regulatory authorities to discuss potential next steps for Riquent in Europe. There can be no guarantee that meetings with the FDA and other regulatory agencies can be held in a timely manner, or at all, or that our meetings with them will result in our being able to continue to develop Riquent. If for any reason our development efforts as to Riquent are terminated, it would have a material adverse effect on our business and future prospects.

The Offering

Common stock offered by us: 8,695,653 shares

Shares outstanding after the offering: 59,820,236 shares (61,124,583 shares if the underwriter exercises its over-allotment option in full)

Use of proceeds: We estimate that our net proceeds from this offering without exercise of the over-allotment option will be approximately \$25.6 million, after deducting the underwriting discount and estimated offering expenses. We intend to use the net proceeds from this offering to fund the development of Riquent and as further described in this prospectus supplement under the heading Use of Proceeds.

Risk factors: See the Risk Factors section and other information included in this prospectus supplement and the prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.

Nasdaq National Market symbol: LJPC

The number of shares outstanding after the offering is based on 51,124,583 shares of common stock outstanding as of February 17, 2004 and excludes 7,476,645 shares of common stock reserved at December 31, 2003 for issuance upon exercise of outstanding options under our equity incentive plans.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before purchasing the common stock offered hereby, you should carefully consider the risk factors set forth below, as well as the other information included in this prospectus supplement, the prospectus and the information incorporated by reference in them. Some of these factors have affected our financial condition and operating results in the past or are currently affecting us. All of these factors could affect our future financial condition or operating results. If any of the following risks actually occurs, our business could be harmed. If that happens, the trading price of our common stock could decline, and you may lose all or part of your investment.

I. Risk Factors Relating To La Jolla Pharmaceutical And The Industry In Which We Operate

If the continued development of Riquent is significantly delayed, our business and financial condition will be adversely affected and it may be difficult or impossible for us to survive.

The data from our Phase 2/3 and Phase 3 clinical trials of Riquent indicated that treatment with Riquent did not increase length of time to renal flare, the primary endpoint for the trials, in a statistically significant manner when compared with placebo. As a result, our ability to obtain regulatory clearance to market Riquent either in the United States or in Europe is uncertain, and we may be required to conduct additional clinical trials to demonstrate the safety and efficacy of Riquent. The uncertainty regarding the future development of Riquent may negatively affect our ability to raise necessary additional funding in the future. If the continued development of Riquent is significantly delayed for any reason, and if we are unable to timely raise additional funding, we may not have the financial resources to continue research and development of Riquent, LJP 1082, our drug candidate for the treatment of antibody-mediated thrombosis, or any other potential drug candidates, and it may be difficult or impossible for us to survive.

Results from our clinical trials may not be sufficient to obtain clearance to market Riquent or our other drug candidates in the United States or Europe on a timely basis, or at all.

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. In order to sell our products that are under development, we must first receive regulatory approval. To obtain regulatory approval, we must conduct clinical trials and toxicology studies that demonstrate that our drug candidates are safe and effective. The process of obtaining FDA and other regulatory approvals is costly, time consuming, uncertain and subject to unanticipated delays. The FDA and foreign regulatory authorities have substantial discretion in the approval process and may not agree that we have demonstrated that Riquent or LJP 1082 are safe and effective after we complete our clinical trials. If Riquent or LJP 1082 are ultimately not found to be safe and effective, we would be unable to obtain regulatory approval to manufacture, market and sell these drugs. In addition, in the course of the FDA's review of our NDA, the FDA could determine that the indication for Riquent is broader than anticipated and this may affect our ability to maintain the orphan drug designation for Riquent. Although our New Drug Application for Riquent has been accepted for review by the FDA, we can provide no assurances that the FDA will approve Riquent.

We may be required to design and conduct additional studies to further demonstrate the safety and efficacy of our drug candidates, which may result in significant expense and delay. The FDA and foreign regulatory authorities may require new or additional clinical trials because of inconclusive results from earlier clinical trials, including the Phase 2/3 and Phase 3 trials of Riquent, a possible failure to conduct clinical trials in complete adherence to FDA good clinical practice standards and similar standards of foreign regulatory authorities, the identification of new clinical trial endpoints, or the need for additional data regarding the safety or efficacy of our drug candidates. It is possible that the FDA or foreign regulatory authorities may not ultimately approve Riquent, LJP 1082 or our other drug candidates for commercial sale in any jurisdiction, even if future clinical results are positive.

Because Riquent is our only drug candidate for which we have completed a Phase 3 clinical trial, and because there is no guarantee that we would be able to develop an alternate drug candidate, our inability

Table of Contents

to obtain regulatory approval of Riquent would have a severe negative effect on our business, and we may not have the financial resources to continue research and development of Riquent, LJP 1082 or any other potential drug candidates.

We may be unsuccessful in obtaining accelerated approval for Riquent under the Subpart H regulation.

Although we may pursue accelerated FDA approval for Riquent under the Subpart H regulation, there can be no assurance that reductions in levels of antibodies to double-stranded DNA (dsDNA) will be deemed by the FDA to be a surrogate endpoint that is reasonably likely to predict clinical benefit, that we will be able to agree with the FDA about the design and timing of a post-marketing clinical trial, or that we will be able to successfully complete any post-marketing clinical trial. The success of any future clinical trial that we may be required to conduct as part of a Subpart H approval process will depend, in part, on our ability to locate and enroll patients meeting the criteria specified for such a trial. We may be required to commence patient enrollment or to complete patient enrollment milestones for a post-marketing clinical trial prior to any regulatory approval that we may receive. The enrollment process may take a significant amount of time and may require significant funding. Any delay in meeting patient enrollment requirements may impact our ability to obtain timely regulatory approval for Riquent, if at all. A post-marketing efficacy trial may involve significantly more patients than were involved in the Phase 3 trial of Riquent and may require significant time to complete. Even if the FDA approves Riquent under Subpart H, if we fail to successfully complete a post-marketing clinical trial, the FDA would have the authority to remove Riquent from the market. Because Riquent is our only drug candidate for which we have completed a Phase 3 clinical trial, and because there is no guarantee that we would be able to develop an alternate drug candidate, our inability to obtain or maintain regulatory approval of Riquent would have a severe negative effect on our business, and we may not have the financial resources to continue research and development of Riquent, LJP 1082 or any other potential drug candidates.

Our blood test to measure the binding affinity for Riquent has not been validated by independent laboratories and is likely to require regulatory review as part of the Riquent approval process.

In 1998, we developed a blood test that we believe can identify the lupus patients who are most likely to respond to Riquent. The blood test is designed to measure the strength of the binding between Riquent and a patient's antibodies. This affinity assay was used to identify, prospectively in the Phase 3 trial and retrospectively in the Phase 2/3 trial, the patients included in the efficacy analyses. Independent laboratories have not validated the assay, and the results of the affinity assay observed in our clinical trials of Riquent may not be observed in the broader lupus patient population. In addition, regulatory agencies will likely require that the assay be reviewed as part of the approval process of Riquent. The testing laboratory that will conduct the assay if Riquent is approved may also require additional regulatory approval. If additional regulatory approval of the testing laboratory is required, or if regulatory agencies do not concur with the use of the assay to identify potential patients for treatment with Riquent, the approval and possible commercialization of Riquent may be delayed or prevented.

If we are to obtain regulatory approval of Riquent, we must pass FDA inspection of our manufacturing facilities and processes.

In addition to demonstrating the safety and efficacy of Riquent in clinical trials, we must also pass FDA inspection of our manufacturing facilities in order to obtain FDA approval for the commercial use of Riquent. Before we can manufacture commercial product, we must validate our manufacturing facilities and processes to the satisfaction of the FDA. Although we have initiated the process of preparing for FDA inspection of our facilities and processes, we have never operated a manufacturing facility that has passed an FDA pre-approval inspection. If we are unable to pass the necessary inspections, the FDA will not approve Riquent for commercial use.

Table of Contents

We will need additional funds to support our operations.

Our operations to date have consumed substantial capital resources, and we may expend substantial amounts of capital resources for additional research, product development, pre-clinical testing and clinical trials of drug candidates. We may also devote substantial additional capital resources to establish commercial-scale manufacturing capabilities and to market and sell potential products. These expenses may be incurred prior to or after any regulatory approvals that we may receive. We will need to raise additional funds to finance our future operations. Our future capital requirements will depend on many factors, including:

- our ability to obtain regulatory approval for Riquent,
- continued scientific progress in our research and development programs,
- the size and complexity of our research and development programs,
- the scope and results of pre-clinical testing and clinical trials,
- the time and costs involved in applying for regulatory approvals,
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims,
- competing technological and market developments,
- our ability to establish and maintain collaborative research and development arrangements,
- our need to establish commercial manufacturing capabilities, and
- our ability to develop effective marketing and sales programs.

We expect to incur substantial losses each year for at least the next several years as we continue our planned research, clinical development, manufacturing and marketing activities. If we ultimately receive regulatory approval for Riquent, LJP 1082 or our other drug candidates, our manufacturing, marketing and sales activities are likely to substantially increase our expenses and our need for additional working capital. We anticipate that our existing cash, investments and interest earned thereon plus the proceeds that we expect to receive from the shares of common stock that we are offering pursuant to this prospectus supplement will be sufficient to fund our operations as currently planned into the second quarter of 2005, assuming that we do not engage in any significant clinical trial or commercialization activities and further assuming that we do not enter into an agreement with a collaborative partner or engage in any other fundraising activities. However, the amounts expended by us may vary significantly, and it is possible that our cash requirements will exceed current projections and that we will therefore need additional financing sooner than currently expected. In the future, it is possible that we will not have adequate resources to support continuation of our business activities.

We may need to sell stock or assets, enter into collaborative agreements, reduce our operations, or merge with another entity to continue operations.

We actively seek additional funding, including through public and private financings and collaborative arrangements. Our choice of financing alternatives may vary from time to time depending on various factors, including the market price of our securities, conditions in the financial markets and the interest of other entities in strategic transactions with us. There can be no guarantee that additional financing will be available on favorable terms, if at all, whether through issuance of securities, collaborative arrangement, or otherwise. If adequate funds are not available, we may be required to delay, scale back or eliminate one or more of our research and development programs or obtain funds through arrangements with collaborative partners or others that require us to relinquish rights to our technologies or potential products. We also may be required to merge with another entity to continue our operations. Any one of these outcomes could have a negative impact on our ability to develop products or achieve profitability if our products are brought to market. If, and to the extent, we obtain additional funding through sales of securities, your

Table of Contents

investment in us will be diluted, and dilution can be particularly substantial when the price of our common stock is low.

Our limited manufacturing capabilities and experience could result in shortages of products for clinical studies and future sale, and our revenues and profit margin could be negatively affected.

Substantial capital investment in the expansion and build-out of our manufacturing facilities will be required to enable us to manufacture Riquent, if approved, in significant commercial quantities. We have limited manufacturing experience, and we may be unable to successfully transition to commercial production. In addition, we have never operated a manufacturing facility that has passed an FDA pre-approval inspection, and we will be required to manufacture Riquent pursuant to applicable FDA good manufacturing practices. Our inexperience could result in manufacturing delays or interruptions and higher manufacturing costs. This could negatively affect our ability to introduce products into the market on a timely and competitive basis and the subsequent sales of our products and our profit margins may be negatively affected.

We may enter into arrangements with contract manufacturing companies to expand our own production capacity in order to meet demand for our products or to attempt to improve manufacturing efficiency. If we choose to contract for manufacturing services, the FDA and comparable foreign regulators would have to approve the contract manufacturers prior to our use, and these contractors would be required to comply with strictly enforced manufacturing standards. We also enter into agreements with contractors to prepare our drug candidates for use by patients. If we encounter delays or difficulties in establishing or maintaining relationships with contractors to produce, package or distribute our finished products, if they are unable to meet our needs, if they are not approved by the regulatory authorities, or if they fail to adhere to applicable manufacturing standards, the introduction of our products into the market and the subsequent sales of these products would be negatively affected, and our profit margins and our ability to develop and deliver products on a timely and competitive basis may be negatively affected.

Our suppliers may not be able to provide us with sufficient quantities of materials that we may need to manufacture our products.

We rely on outside suppliers to provide us with specialized chemicals and reagents that we use to manufacture our drugs. In order to manufacture Riquent, LJP 1082 and our other drug candidates in sufficient quantities for our clinical trials and possible commercialization, our suppliers will be required to provide us with an adequate supply of chemicals and reagents. Our ability to obtain these chemicals and reagents is subject to the following risks:

our suppliers may not be able to increase their own manufacturing capabilities in order to provide us with a sufficient amount of material for our use,

some of our suppliers may be required to pass FDA inspection or obtain other regulatory approvals of their manufacturing facilities or processes, and they may be delayed or unable to do so,

the materials that our suppliers use to manufacture the chemicals and reagents which they provide us may be costly or in short supply, and

there may be a limited number of suppliers that are able to provide us with the chemicals or reagents that we use to manufacture our drugs.

If we are unable to obtain sufficient quantities of chemicals or reagents, the introduction of any products into the market and the subsequent sales of any products would be negatively affected, and our profit margins and our ability to develop and deliver products on a timely and competitive basis may be negatively affected.

Table of Contents

An interruption in the operation of our sole manufacturing facility could disrupt our operations.

We have only one drug manufacturing facility. A significant interruption in the operation of this facility, whether as a result of a natural disaster or other causes, could significantly impair our ability to manufacture drugs for our clinical trials or possible commercialization.

Even if we receive regulatory approval for our product candidates, we will be subject to ongoing regulatory obligations and review.

Following any regulatory approval of our product candidates, we will be subject to continuing regulatory obligations such as safety reporting requirements and additional post-marketing obligations, including regulatory oversight of the promotion and marketing of our products. In addition, we and any third-party manufacturers will be required to adhere to regulations setting forth current good manufacturing practices. These regulations cover all aspects of the manufacturing, testing, quality control and record keeping relating to our product candidates. Furthermore, we and any third-party manufacturers will be subject to periodic inspection by regulatory authorities. These inspections may result in compliance issues that would require the expenditure of financial or other resources to address. If we or any third-party manufacturers that we may engage fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

The size of the market for our potential products is uncertain.

We estimate that the number of people who suffer from lupus in the United States and Europe is approximately 1,000,000 and that those with renal impairment, which Riquent is designed to treat, is approximately 300,000. With respect to antibody-mediated thrombosis, which LJP 1082 is designed to treat, we estimate that there are approximately 1,000,000 to 2,000,000 patients in the United States and Europe. For example, within the estimated antibody-mediated thrombosis patient population, we believe that antiphospholipid antibodies contributed to approximately 10% of the approximate 4,000,000 strokes in 2002. However, there is limited information available regarding the actual size of these patient populations. In addition, it is uncertain whether the results from previous or future clinical trials of our drug candidates will be observed in broader patient populations, and the number of patients who may benefit from our drug candidates may be significantly smaller than the estimated patient populations. Furthermore, management of patients with renal disease by specialists other than nephrologists and immunologists is likely to reduce our ability to access patients who may benefit from Riquent.

Any regulatory approvals that we may obtain for our product candidates may be limited and subsequent issues regarding safety or efficacy could cause us to remove products from the market.

If the FDA or foreign regulatory authorities grant approval of any of our drug candidates, the approval may be limited to specific conditions or patient populations, or limited with respect to its distribution, including to specified facilities or physicians with special training or experience. The imposition of any of these restrictions or other restrictions on the marketing and use of Riquent could adversely affect any future sales of Riquent. Furthermore, even if a drug candidate is approved, it is possible that a subsequent issue regarding its safety or efficacy would require us to remove the drug from the market.

Our drugs may not achieve market acceptance.

Even if Riquent or our other drug candidates receive regulatory approval, patients and physicians may not readily accept our proposed methods of treatment. In order for Riquent or our other drug candidates to be commercially successful, we will need to increase the awareness and acceptance of our drug candidates among physicians, patients and the medical community. Riquent is designed to be administered weekly by intravenous injection. It is possible that providers and patients may resist an intravenously administered therapeutic. It is also possible that physician treatment practices may change and that the use of other drugs, either newly approved or currently on the market for other conditions, may become widely utilized

Table of Contents

by clinicians for the treatment of patients with lupus and reduce the potential use of Riquent in this patient population. In addition, if we are unable to manufacture drugs at an acceptable cost, physicians may not readily prescribe drugs that we may manufacture due to cost-benefit considerations when compared to other methods of treatment. If we are unable to achieve market acceptance for approved products, our revenues and potential for profitability will be negatively affected.

We lack experience in marketing products for commercial sale.

In order to commercialize any drug candidate approved by the FDA, we must either develop marketing and sales programs or enter into marketing arrangements with others. If we cannot do either of these successfully, we will not generate meaningful sales of any products that may be approved. If we develop our own marketing and sales capabilities, we will be required to employ a sales force, establish and staff a customer service department, and create or identify distribution channels for our drugs. We will compete with other companies that have experienced and well-funded marketing and sales operations. In addition, if we establish our own sales and distribution capabilities, we may experience delays and expenditures and have difficulty in gaining market acceptance for our drug candidates. We currently have no marketing arrangements with others. There can be no guarantee that, if we desire to, we will be able to enter into any marketing agreements on favorable terms, if at all, or that any such agreements will result in payments to us. If we enter into co-promotion or other marketing and sales arrangements with other companies, any revenues that we may receive will be dependent on the efforts of others. There can be no guarantee that these efforts will be successful.

We may not earn as much income as we hope due to possible changes in healthcare reimbursement policies.

The continuing efforts of government and healthcare insurance companies to reduce the costs of healthcare may reduce the amount of income that we can generate from sales of future products. For example, in certain foreign markets, pricing and profitability of prescription drugs are subject to government control. In the United States, we expect that there will continue to be a number of federal and state proposals to implement similar government controls. In addition, an increasing emphasis on managed care in the United States will continue to put pressure on drug manufacturers to reduce prices. Price control initiatives could reduce the revenue that we receive for any products we may develop and sell in the future.

We have a history of losses and may not become profitable.

We have incurred operating losses each year since our inception in 1989 and had an accumulated deficit of approximately \$184.0 million as of September 30, 2003. We expect to incur substantial losses each year for at least the next several years as we seek regulatory approval, conduct additional clinical trials of our drug candidates, and continue our research, clinical development, and manufacturing and marketing activities. In addition, assuming we ultimately receive favorable clinical results and FDA approval for Riquent, LJP 1082 or our other drug candidates, we will be required to develop commercial manufacturing capabilities and sales and marketing programs which may result in substantial additional losses. To achieve profitability we must, among other matters, complete the development of our products, obtain all necessary regulatory approvals and establish commercial manufacturing, marketing and sales capabilities. The amount of losses and the time required by us to reach sustained profitability are highly uncertain and we may never achieve profitability. We do not expect to generate revenues from the sale of Riquent, if approved, or our other products, if any, in the near term, and we may never generate product revenues.

Table of Contents

Our success in developing and marketing our drug candidates depends significantly on our ability to obtain patent protection for Riquent, LJP 1082 and any other developed products. In addition, we will need to successfully preserve our trade secrets and operate without infringing on the rights of others.

We depend on patents and other unpatented intellectual property to prevent others from improperly benefiting from products or technologies that we may have developed. As of December 31, 2002, we owned 98 issued patents and 93 pending patent applications covering various technologies and drug candidates including Riquent and LJP 1082. However, there can be no assurance that any additional patents will be issued, that the scope of any patent protection will be sufficient, or that any current or future issued patent will be held valid if subsequently challenged. There is a substantial backlog of biotechnology patent applications at the United States Patent and Trademark Office that may delay the review and issuance of any patents. The patent position of biotechnology firms like ours is highly uncertain and involves complex legal and factual questions, and no consistent policy has emerged regarding the breadth of claims covered in biotechnology patents or the protection afforded by these patents. Currently, we have a number of patent applications pending in the United States relating to our technology, as well as foreign counterparts to some of our United States patent applications. We intend to continue to file applications as believed appropriate for patents covering both our products and processes. There can be no assurance that patents will be issued from any of these applications, or that the scope of any issued patents will protect our technology.

We do not necessarily know if others, including competitors, have patents or patent applications pending that relate to compounds or processes that overlap or compete with our intellectual property. We are aware of one family of United States patents that contain claims covering subject matter that may conflict with some of our key patents and patent applications, and that may affect our ability to manufacture and sell our products in the future. If the United States Patent and Trademark Office or any foreign counterpart issues or has issued patents containing competitive or conflicting claims, and if these claims are valid, the protection provided by our existing patents or any future patents that may be issued could be significantly reduced, and our ability to prevent competitors from developing products or technologies identical or similar to ours could be negatively affected. In addition, the pharmaceutical and biotechnology industries have been greatly affected by time-consuming and expensive litigation regarding patents and other intellectual property rights. We may be required to commence, or may be made a party to, litigation relating to the scope and validity of our intellectual property rights or the intellectual property rights of others. Such litigation could result in adverse decisions regarding the patentability of our inventions and products, the enforceability, validity or scope of protection offered by our patents or our infringement of patents held by others. Such decisions could make us liable for substantial money damages, or could bar us from the manufacture, sale or use of certain products. Moreover, an adverse decision may also compel us to seek a license from a third party. There can be no guarantee, however, that we would be able to obtain licenses to these patents on commercially reasonable terms, if at all, or that we would be able to develop or obtain alternative technology. Our failure to obtain a license to a technology or process that may be required to develop or commercialize one or more of our drug candidates may have a material adverse effect on our business. The cost to us of any litigation or proceeding relating to patent or license rights, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of complex patent or licensing litigation more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of any patent or related litigation could have a material adverse effect on our ability to compete in the marketplace.

We also rely on unpatented intellectual property such as trade secrets and improvements, know-how, and continuing technological innovation. While we seek to protect these rights, it is possible that:

others, including competitors, will develop inventions relevant to our business,

our binding confidentiality agreements will be breached, and we will not have adequate remedies for such a breach, or

our trade secrets will otherwise become known or be independently discovered by competitors.

S-9

Table of Contents

We could incur substantial costs in defending suits brought against us by others for infringement of intellectual property rights or in prosecuting suits that we might bring against others to protect our intellectual property rights.

The technology underlying our products is uncertain and unproven.

All of our product development efforts are based on unproven technologies and therapeutic approaches that have not been widely tested or used. To date, no products that use our technology have been commercialized. Riquent and LJP 1082 have not been proven to be safe and effective in humans, and the technology on which they are based has been used only in our pre-clinical tests and clinical trials. Application of our technology to antibody-mediated diseases other than lupus and antibody-mediated thrombosis is in earlier research stages. Clinical trials of Riquent and LJP 1082 may be viewed as a test of our entire approach to developing therapies for antibody-mediated diseases. If Riquent or LJP 1082 does not work as intended, or if the data from our clinical trials indicates that Riquent or LJP 1082 is not safe and effective, the applicability of our technology for treating antibody-mediated diseases will be highly uncertain. As a result, there is a significant risk that our therapeutic approaches will not prove to be successful, and there can be no guarantee that our drug discovery technologies will result in any commercially successful products.

Future clinical trials may be delayed or halted.

Future clinical trials of Riquent or LJP 1082, trials of drugs related to these drugs, or clinical trials of other drug candidates may be delayed or halted. During the development of Riquent, our Phase 2/3 clinical study, in collaboration with Abbott Laboratories, was terminated before planned patient enrollment was completed. Future trials may be delayed or halted for various reasons, including:

the products are not effective,

patients experience severe side effects during treatment,

the trials are not conducted in accordance with applicable clinical practices,

patients do not enroll in the studies at the rate we expect, or

supplies of drug product are not sufficient to treat the patients in the studies.

If any future trials are delayed or halted, we may incur significant additional expenses, which could have a severe negative effect on our business.

Our research and development and operations depend in part on key employees. Losing these employees would have a negative effect on our product development and operations.

We are highly dependent on the principal members of our scientific and management staff, the loss of whose services would delay the achievement of our research and development objectives. This is because our key personnel, including Steven Engle, Dr. Matthew Linnik, Dr. Paul Jenn and Dr. Andrew Wiseman, have been involved in the development of Riquent, LJP 1082 and other drug candidates for several years and have unique knowledge of our drug candidates and of the technology on which they are based. In addition, we will be required to rely on other key members of our senior management team, including Bruce Bennett, Dr. Kenneth Heilbrunn, and William Welch, to assist us with growth and expansion into areas requiring additional expertise, such as clinical trials, regulatory approvals, manufacturing, marketing and sales. We expect that we will continue to require additional management personnel, and that our existing management personnel will be required to develop additional expertise.

Retaining our current personnel and recruiting additional personnel will be critical to our success.

Retaining our current key personnel and recruiting additional qualified personnel to perform research and development, clinical development, manufacturing, marketing and sales will be critical to our success. Because competition for experienced scientific, clinical, manufacturing, marketing and sales personnel

Table of Contents

among numerous pharmaceutical and biotechnology companies and research and academic institutions is intense, we may not be able to attract and retain these people. If we cannot attract and retain qualified people, our ability to conduct necessary clinical trials and to develop and sell our products may be negatively affected because, for instance, the trials may not be conducted properly, or the manufacturing or sales of our products may be delayed. In addition, we rely upon consultants and advisors to assist us in formulating our research and development, clinical, regulatory, manufacturing, marketing and sales strategies. All of our consultants and advisors have outside employment and may have commitments or consulting or advisory contracts with other entities that may limit their ability to contribute to our business.

Our freedom to operate our business or profit fully from sales of our products may be limited if we enter into collaborative agreements.

We may seek to collaborate with pharmaceutical companies to gain access to their research, drug development, manufacturing, marketing, sales and financial resources. However, we may not be able to negotiate arrangements with any collaborative partners on favorable terms, if at all. Any collaborative relationships that we enter into may include restrictions on our freedom to operate our business or may limit the sales of our products. If a collaborative arrangement is established, the collaborative partner may discontinue funding any particular program or may, either alone or with others, pursue alternative technologies or develop alternative drug candidates for the diseases we are targeting. Competing products, developed by a collaborative partner or to which a collaborative partner has rights, may result in the collaborative partner withdrawing support as to all or a portion of our technology.

Without collaborative arrangements, we must fund our own research, development, manufacturing, marketing and sales activities, which would accelerate the depletion of our cash and require us to develop our own manufacturing, marketing and sales capabilities. Therefore, if we are unable to establish and maintain collaborative arrangements and if other sources of cash are not available, we could experience a material adverse effect on our ability to develop products and, if developed and approved, to manufacture, market and sell them successfully.

Because a number of companies compete with us, many of which have greater resources than we do, and because we face rapid changes in technology in our industry, we cannot be certain that our products will be accepted in the marketplace or capture market share.

Competition from domestic and foreign biotechnology companies, large pharmaceutical companies and other institutions is intense and is expected to increase. A number of companies and institutions are pursuing the development of pharmaceuticals in our targeted areas, many of which are very large, and have financial, technical, sales and distribution and other resources substantially greater than ours. The greater resources of these competitors could enable them to develop competing products more quickly than we are able to, and to market any competing product more quickly or effectively so as to make it extremely difficult for us to develop a share of the market for our products. These competitors also include companies that are conducting clinical trials and pre-clinical studies for the treatment of lupus and thrombosis. Our competitors may develop or obtain regulatory approval for products more rapidly than we do. Also, the biotechnology and pharmaceutical industries are subject to rapid changes in technology. Our competitors may develop and market technologies and products that are more effective or less costly than those being developed by us, or that would render our technology and proposed products obsolete or noncompetitive.

The use of Riquent, LJP 1082 and other potential products in clinical trials, as well as the sale of any approved products, may expose us to lawsuits resulting from the use of these products.

The use and possible sale of Riquent, LJP 1082 and other potential products may expose us to legal liability and generate negative publicity if we are subject to claims that our products harmed people. These claims might be made directly by patients, pharmaceutical companies, or others. We currently maintain \$10.0 million of product liability insurance for claims arising from the use of our products in clinical trials.

Table of Contents

However, product liability insurance is becoming increasingly expensive, and there can be no guarantee that we will be able to maintain insurance or that insurance can be acquired at a reasonable cost, in sufficient amounts, or with broad enough coverage to protect us against possible losses. Furthermore, it is possible that our financial resources would be insufficient to satisfy potential product liability or other claims. A successful product liability claim or series of claims brought against us could negatively impact our business and financial condition.

We face environmental liabilities related to certain hazardous materials used in our operations.

Due to the nature of our manufacturing processes, we are subject to stringent federal, state and local laws governing the use, handling and disposal of certain materials and wastes. We may have to incur significant costs to comply with environmental regulations if and when our manufacturing increases to commercial volumes. Current or future environmental laws may significantly affect our operations because, for instance, our production process may be required to be altered, thereby increasing our production costs. In our research activities, we use radioactive and other materials that could be hazardous to human health, safety or the environment. These materials and various wastes resulting from their use are stored at our facility pending ultimate use and disposal. The risk of accidental injury or contamination from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any resulting damages, and any such liability could exceed our resources. Although we maintain general liability insurance, we do not specifically insure against environmental liabilities.

II. Risk Factors Related Specifically To Our Stock

Our common stock price is volatile and may decline even if our business is doing well.

The market price of our common stock has been and is likely to continue to be highly volatile. Market prices for securities of biotechnology and pharmaceutical companies, including ours, have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. The following factors, among others, can have a significant effect on the market price of our securities:

- actions or decisions by the FDA and other comparable agencies,
- our clinical trial results,
- announcements of technological innovations or new therapeutic products by us or others,
- developments in patent or other proprietary rights,
- public concern as to the safety of drugs discovered or developed by us or others,
- future sales of significant amounts of our common stock by existing stockholders,
- developments concerning potential agreements with collaborators,
- comments by securities analysts and general market conditions, and
- government regulation.

The realization of any of the risks described in these Risk Factors could have a negative effect on the market price of our common stock.

In the future, our stock may be removed from listing on the Nasdaq quotation system and may not qualify for listing on any stock exchange, in which case it may be difficult to find a market in our stock.

If our stock is no longer traded on a national trading market, it may be more difficult for you to sell shares that you own, and the price of the stock may be negatively affected. Currently, our securities are traded on the Nasdaq National Market. Nasdaq has several continued listing requirements, including a minimum-trading price. Previously, we have received notice from Nasdaq that our stock price fell below this minimum trading price. Although we have since come back into compliance with this Nasdaq

Table of Contents

requirement, it is possible that we will fall out of compliance with this and/or other Nasdaq continued listing criteria at some point in the future. Failure to comply with any one of several Nasdaq requirements may cause our stock to be removed from listing on Nasdaq. Should this happen, we may not be able to secure listing on other exchanges or quotation systems. This would have a negative effect on the price and liquidity of our stock.

Future sales of our stock by existing stockholders could negatively affect the market price of our stock and make it more difficult for us to sell stock in the future.

Sales of our common stock in the public market, or the perception that such sales could occur, could result in a drop in the market price of our securities and make it more difficult for us to complete future equity financings on acceptable terms, if at all. As of September 30, 2003, there were:

Approximately 50,815,504 shares of common stock (excluding the shares offered hereby) that have been issued in registered offerings or were otherwise freely tradable in the public markets.

Approximately 72,348 shares of common stock eligible for resale in the public market pursuant to SEC Rule 144.

7,635,295 shares of common stock that may be issued on the exercise of outstanding stock options granted under our various stock option plans at a weighted average exercise price of \$4.72 per share.

Approximately 9,200,000 shares of common stock reserved under our incentive stock option and employee stock purchase plans which shares are covered by effective registration statements under the Securities Act of 1933, as amended (the "Securities Act"). Approximately 143,900 shares of common stock that may be issued on the exercise of outstanding stock options will be available for public resale under SEC Rule 144 pursuant to Rule 701 under the Securities Act.

Pursuant to a registration statement on Form S-3 filed on December 10, 2002, we registered an aggregate amount of \$125,000,000 of our common stock for issuance from time to time. After giving effect to the offering of common stock under this prospectus supplement, we may offer up to an aggregate amount of \$75,196,193 of our common stock (or, if the over-allotment option is exercised in full, \$71,087,500 of our common stock) under the registration statement in the future.

We cannot estimate the number of shares of common stock that may actually be resold in the public market because this will depend on the market price for our common stock, the individual circumstances of the sellers and other factors. We also have a number of institutional stockholders that own significant blocks of our common stock. If these stockholders sell significant portions of their holdings in a relatively short time, for liquidity or other reasons, the market price of our common stock could drop significantly.

Anti-takeover devices may prevent changes in our management.

We have in place several anti-takeover devices, including a stockholder rights plan, which may have the effect of delaying or preventing changes in our management or deterring third parties from seeking to acquire significant positions in our common stock. For example, one anti-takeover device provides for a board of directors that is separated into three classes, with their terms in office staggered over three year periods. This has the effect of delaying a change in control of our board of directors without the cooperation of the incumbent board. In addition, our bylaws require stockholders to give us written notice of any proposal or director nomination within a specified period of time prior to the annual stockholder meeting, establish certain qualifications for a person to be elected or appointed to the board of directors during the pendency of certain business combination transactions, and do not allow stockholders to call a special meeting of stockholders.

We may also issue shares of preferred stock without further stockholder approval and upon terms that our board of directors may determine in the future. The issuance of preferred stock could have the effect of making it more difficult for a third party to acquire a majority of our outstanding stock, and the holders

Table of Contents

of such preferred stock could have voting, dividend, liquidation and other rights superior to those of holders of our common stock.

We do not pay dividends and this may negatively affect the price of our stock.

We have not paid any cash dividends since our inception and do not anticipate paying any cash dividends in the foreseeable future. The future price of our common stock may be negatively affected by the fact that we have not paid dividends.

DESCRIPTION OF CAPITAL STOCK

The following is a description of our capital stock. The following summary of our amended and restated certificate of incorporation, amended and restated bylaws, and rights plan does not describe the certificate, the bylaws, or the rights plan entirely. We urge you to read our certificate, bylaws, and rights plan which are incorporated by reference herein. See *Where You Can Find More Information and Incorporation by Reference* on page S-18. On the date of this prospectus supplement, our authorized capital stock consists of 100,000,000 shares of common stock, \$0.01 par value per share, and 8,000,000 shares of preferred stock, \$0.01 par value per share.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote per share on all matters to be voted upon by our stockholders. The vote of the holders of a majority of the stock represented at a meeting at which a quorum is present is generally required to take stockholder action, unless a greater vote is required by law or specifically required by our certificate of incorporation or bylaws. Special stockholder meetings may be called only by the board of directors, the chairman of the board or the president. Our certificate of incorporation provides that our stockholders may not act by written consent. In addition, our bylaws include an advance notice procedure with regard to the nomination, other than by or at the direction of the board of directors, of candidates for election as directors and with regard to matters to be brought before an annual meeting or special meeting of stockholders.

Dividends and Other Rights. Holders of our common stock are entitled to receive, as when and if declared by the board of directors from time to time, such dividends and other distributions in cash, stock or property from our assets or funds legally available for such purposes subject to any dividend preferences that may be attributable to preferred stock that may be authorized. In the event of our liquidation, dissolution or winding up, after all liabilities and the holders of each series of preferred stock, if any, have been paid in full, the holders of our common stock are entitled to share ratably in all remaining assets available for distribution. Our common stock has no preemptive, subscription, redemption or conversion rights. There are no sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are, and all shares of our common stock outstanding on the closing of this offering will be, fully paid and non-assessable.

Classified Board of Directors. Our certificate of incorporation and bylaws provide for a classified board of directors. Our board is classified into three classes, each as nearly equal in number as possible. At each annual meeting, the successors to the class of directors whose term expire at that meeting are elected for a term of office to expire at the third succeeding annual meeting after their election or until their successors have been duly elected and qualified. Delaware law provides that, unless the certificate of incorporation provides otherwise, directors serving on a classified board of directors may be removed only for cause. Our certificate of incorporation does not provide otherwise. Therefore, our directors may only be removed for cause. The affirmative vote of the holders of 75% or more of the total voting power of all outstanding shares of voting stock would be required to amend our certificate of incorporation or bylaws to remove the classified board provisions.

Rights Plan. Each outstanding share of our common stock is accompanied by a right to purchase our preferred stock, our common stock or the common stock of a successor company pursuant to the terms

Table of Contents

of a rights agreement. Please refer to the discussion entitled "La Jolla Pharmaceutical Company Rights Plan" below.

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation's voting stock. Delaware law, the existence of our rights agreement, and the provisions of our certificate of incorporation and bylaws may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent. American Stock Transfer & Trust Company is the Transfer Agent and Registrar for the shares of our common stock.

Preferred Stock

Our board of directors has the authority, without further action by stockholders, to issue up to 8,000,000 shares of preferred stock in one or more series and to fix the powers, designations, rights, preferences, privileges, qualifications, and restrictions thereof, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preferences and sinking fund terms, any or all of which may be greater than the rights of our common stock. Our board of directors, without further stockholder approval, can issue preferred stock with voting, conversion, and other rights that could adversely affect the voting power and other rights of the holders of common stock. The issuance of preferred stock in certain circumstances may have the effect of delaying, deferring or preventing a change in control of La Jolla Pharmaceutical Company, may discourage bids for our common stock at a premium over the market price of the common stock, and may adversely affect the market price of our common stock. As of the date of this prospectus supplement, there are no shares of our preferred stock outstanding.

We have filed a certificate of designation with the Secretary of State of the State of Delaware which designates 100,000 shares of preferred stock as Series A Junior Participating Preferred Stock in connection with our stockholder rights plan, as described below. We refer to our Series A Junior Participating Preferred Stock as our Series A Preferred Shares. Except to the extent that a right to purchase our Series A Preferred Shares accompanies each share of our common stock, no shares of our preferred stock are covered by this prospectus supplement.

La Jolla Pharmaceutical Company Rights Plan

On November 19, 1998, our board of directors authorized and declared a dividend of one right for each share of our common stock. On December 3, 1998, we entered into a rights agreement with American Stock Transfer & Trust Company, as rights agent, and filed a Certificate of Designation with the State of Delaware regarding our Series A Preferred Shares. The Company paid the rights dividend to the holders of record of common stock as of the close of business on December 18, 1998. Common stock certificates issued after December 18, 1998, and prior to the Distribution Date (as defined in the rights agreement), contain a notation incorporating the rights agreement by reference. The rights agreement was amended as of July 21, 2000 to eliminate the concept of "continuing directors" in response to a clarification of Delaware law and to amend the definition of an acquiring person. Currently, there are no separate rights certificates. Each right is attached to each share of our common stock and trades automatically with the common stock. Rights will not be separable from common stock or exercisable, unless specified events described in the rights agreement occur. Upon the occurrence of the events described in the rights agreement, the rights will separate from the common stock and may thereafter become exercisable to purchase additional securities.

Table of Contents**DILUTION**

The net tangible book value of our common stock on September 30, 2003 was \$41.9 million, or approximately \$0.82 per share, based on 50,887,852 shares outstanding. Net tangible book value per share represents the amount of our total tangible assets, less our total liabilities, divided by the total number of shares of our common stock outstanding. Dilution in net tangible book value per share to new investors represents the difference between the amount per share paid by purchasers of shares of our common stock in this offering and the net tangible book value per share of our common stock immediately afterwards. Without taking into account any other changes in net tangible book value after September 30, 2003, other than to give effect to the sale of 8,695,653 shares of common stock offered by us at a public offering price of \$3.15 per share and after deducting the underwriting discount and estimated offering expenses payable by us, our net tangible book value would have been \$67.5 million, or approximately \$1.13 per share based on 59,583,505 shares outstanding. This represents an immediate increase in net tangible book value of \$0.31 per share to existing stockholders and an immediate dilution in net tangible book value of \$2.02 per share to new investors.

| | | |
|--|--------|-----------|
| Public offering price per share | | \$3.15 |
| Net tangible book value per share as of September 30, 2003 | \$0.82 | |
| Increase per share attributable to new investors | 0.31 | |
| | <hr/> | |
| As adjusted net tangible book value per share after the offering | | 1.13(1) |
| | | <hr/> |
| Dilution in net tangible book value per share to new investors | | \$2.02(1) |
| | | <hr/> |

- (1) If the over-allotment of 1,304,347 shares is included, the net tangible book value per share after the offering would be \$1.17, representing an immediate increase in net tangible book value to existing stockholders of \$0.35 per share and a dilution in net tangible book value to new investors of \$1.98 per share.

This table excludes 7,635,295 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2003, at a weighted average exercise price of \$4.72 per share (4,528,200 were exercisable as of September 30, 2003 and the balance become exercisable in the future based upon continued employment) and any shares that we may issue in the future pursuant to the registration statement of which this prospectus supplement forms a part.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of our common stock will be approximately \$25.6 million, after deducting the underwriting discount and estimated offering expenses. If the underwriter exercises its over-allotment option in full, we estimate that the net proceeds will be approximately \$29.5 million. We intend to use the net proceeds we receive to fund the continued research and development of our potential products, to expand and validate our existing facilities, processes and infrastructures, and for other general corporate purposes. The amounts and timing of expenditures may vary significantly depending on several factors, including the time and costs of obtaining regulatory approvals, the progress of our research and development efforts, the results of our clinical trials, our future capital expenditures, our need to develop commercial marketing and sales capabilities, and our ability to generate revenues in the future.

Table of Contents**UNDERWRITING**

We have entered into an underwriting agreement with Pacific Growth Equities, LLC with respect to the shares being offered by this prospectus supplement. Subject to the terms and conditions stated in the underwriting agreement, we have agreed to sell to Pacific Growth Equities, LLC, as underwriter, and Pacific Growth Equities, LLC has agreed to purchase from us, 8,695,653 shares of our common stock. If the underwriter sells more shares than the above number, the underwriter has an over-allotment option, which is exercisable within 30 days of the date of this prospectus supplement, to buy up to an additional 1,304,347 shares from us at the public offering price less the underwriting discounts and commissions to cover these sales. The option may be exercised only once after the initial sale of shares in this offering.

The underwriting agreement provides that the obligation of the underwriter to purchase the shares included in this offering is subject to approval of legal matters by counsel and to other conditions. The underwriter is obligated to purchase all of the shares of common stock offered hereby if any of the shares are purchased.

The underwriter proposes to offer the shares of common stock at the public offering price set forth on the cover page of this prospectus supplement. If all of the shares are not sold by the underwriter at the initial offering price, the underwriter may change the public offering price and other selling terms. In connection with the sale of the shares of common stock offered hereby, the underwriter will be deemed to have received compensation in the form of underwriting discounts.

We and our directors and executive officers have agreed, subject to certain limited exceptions, not to, without the prior written consent of the underwriter, directly or indirectly, offer, pledge, sell, contract to sell, grant any option to purchase, grant any security interest, hypothecate, or otherwise dispose of any shares of our common stock or other capital stock or any securities convertible into, derivative of or exercisable or exchangeable for or any rights to purchase or acquire our common stock, owned directly or indirectly, for a period of 90 days after the date of this prospectus supplement. The foregoing will not prohibit us from issuing our equity securities pursuant to our equity incentive plans existing or authorized on the date of this prospectus supplement.

The following table shows the underwriting discounts and commissions that we will pay in connection with this offering assuming both no exercise and full exercise of the underwriter's over-allotment option to purchase up to an additional 1,304,347 shares.

| | No Exercise | Full Exercise |
|-----------|--------------------|----------------------|
| Per Share | \$ 0.189 | \$ 0.189 |
| Total | \$ 1,643,478 | \$ 1,890,000 |

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make because of any of those liabilities.

We estimate that the total expenses of this offering, including legal, accounting, printing, Nasdaq, transfer agent and other miscellaneous fees and expenses, but not including the underwriting discount, will be \$152,500 and will be payable by us.

The underwriter has performed investment banking and advisory services for us from time to time for which it has received customary fees and expenses. The underwriter may, from time to time, engage in transactions with and perform services for us in the ordinary course of its business.

The underwriter has advised us that it may engage in activities that stabilize, maintain or otherwise affect the price of the shares, including:

stabilizing transactions,

short sales, and

Table of Contents

purchases to cover positions created by short sales.

Stabilizing transactions consist of bids or purchases made, pursuant to Regulation M under the Securities Act, for the purpose of preventing or retarding a decline in the market price of the shares while this offering is in progress. Stabilizing transactions may include making short sales of the shares, which involves the sale by the underwriter of a greater number of shares than it is required to purchase in this offering, and purchasing shares from us or in the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriter's over-allotment option referred to above, or may be naked shorts, which are short positions in excess of that amount.

The underwriter may close out any covered short position either by exercising its over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriter will consider, among other matters, the price of the shares available for purchase in the open market compared to the price at which the underwriter may purchase shares pursuant to the over-allotment option. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriter creates a naked short position, it will purchase shares in the open market to cover the position.

Purchases to cover short positions and stabilizing transactions may have the effect of preventing or slowing a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. Neither we nor the underwriter makes any representation or prediction as to the effect that the transactions described may have on the price of the shares. The underwriter has advised us that stabilizing bids, short sales and open market purchases may be effected on the Nasdaq National Market or otherwise and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter may distribute prospectuses electronically.

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP of Orange County, California will issue an opinion with respect to the validity of the issuance of the shares of common stock being issued hereby. Certain legal matters will be passed upon for the underwriter by Howard, Rice, Nemerovski, Canady, Falk & Rabkin, A Professional Corporation of San Francisco, California.

EXPERTS

The consolidated financial statements of La Jolla Pharmaceutical Company appearing in La Jolla Pharmaceutical Company's Annual Report (Form 10-K) for the year ended December 31, 2002, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION AND

INCORPORATION BY REFERENCE

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (the SEC). You may read and copy any document we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may also obtain copies from the SEC's public reference room by mail at prescribed rates. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference room. Our SEC filings

Table of Contents

are also available to the public from the SEC's web site at <http://www.sec.gov>. Information about La Jolla Pharmaceutical Company is also available to the public from our website at <http://www.ljpc.com>.

The SEC allows us to incorporate by reference the information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede information in this prospectus supplement. We incorporate by reference the documents listed below and any future filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, until this offering is completed:

1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 2002;
2. Our Proxy Statement filed on April 11, 2003 for our 2003 Annual Meeting of Stockholders;
3. Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2003, June 30, 2003, and September 30, 2003;
4. Our Current Reports on Form 8-K filed on February 18, February 24, March 4, March 13, April 1, April 10, May 5, June 3, June 17, June 19, July 24, August 12, August 13, September 22, October 17, October 28, November 17, December 3, and December 16, 2003, February 17, 2004, and our Current Report on Form 8-K/A filed on August 1, 2003;
5. The description of our common stock contained in our Registration Statements on Form 8-A, filed on June 2, 1994, December 4, 1998, and January 26, 2001; and
6. All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of the offering of the shares offered by this prospectus supplement.

Each person to whom a copy of this prospectus supplement is delivered may request a copy of any or all of the information incorporated by reference in this prospectus supplement, including the exhibits to any filings incorporated by reference herein, at no cost by writing or telephoning us at the following address or telephone number:

Corporate Secretary

La Jolla Pharmaceutical Company
6455 Nancy Ridge Drive
San Diego, California 92121
(858) 452-6600

You should rely only on the information contained in this prospectus supplement. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front of this prospectus supplement.

FORWARD-LOOKING STATEMENTS

We have made forward-looking statements in this prospectus supplement that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements include information concerning our possible or assumed future results of operations and statements preceded by, followed by, or that include the words believes, expects, anticipates, intends, plans, estimates or similar expressions.

Forward-looking statements involve risks, uncertainties and assumptions. Actual results may differ materially from those expressed in these forward-looking statements. You are cautioned not to put undue reliance on any forward-looking statements. Except as may be required by law, we do not have any

Table of Contents

intention or obligation to update forward-looking statements after we distribute this prospectus supplement. These statements appear in a number of places in this prospectus supplement and include statements regarding our intentions, plans, strategies, beliefs or current expectations and those of our directors or our officers with respect to, among other matters:

actions or decisions by the FDA or comparable agencies,

the results of our clinical trials,

our financial prospects,

our financing plans,

trends affecting our financial condition or operating results,

our strategies for growth, operations, and product development and commercialization, and

conditions or trends in or factors affecting the biotech industry.

You should understand that a number of factors could cause our results to differ materially from those expressed in the forward-looking statements. The information incorporated by reference or provided in this prospectus supplement identifies important factors that could cause such differences. Those factors include, among others, the high cost and uncertainty of technology and drug development, which can result in loss of profitability and long delays in getting products to market.

Table of Contents

PROSPECTUS

\$125,000,000

La Jolla Pharmaceutical Company

Common Stock

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission utilizing a shelf registration process. Under this shelf registration process, we may sell our common stock described in this prospectus in one or more offerings. Each time we sell securities, we will provide specific terms of the offering in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any of our securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

The aggregate public offering price of all securities sold under this prospectus will not exceed \$125,000,000.

Our common stock is traded on the Nasdaq National Market under the symbol LJPC.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 2.

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 December 12, 2002

Table of Contents

No person is authorized to give any information or to make any representations other than those contained or incorporated by reference in this prospectus, and, if given or made, such information or representations must not be relied upon as having been authorized. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall, under any circumstances, create any implication that there has been no change in our affairs since the date hereof or that the information contained or incorporated by reference herein is correct as of any time subsequent to the date of such information.

TABLE OF CONTENTS

| | |
|-------------------------------------|----|
| ABOUT THIS PROSPECTUS | 1 |
| THE COMPANY | 1 |
| RECENT DEVELOPMENTS | 1 |
| RISK FACTORS | 2 |
| DESCRIPTION OF CAPITAL STOCK | 11 |
| USE OF PROCEEDS | 13 |
| PLAN OF DISTRIBUTION | 13 |
| LEGAL MATTERS | 15 |
| EXPERTS | 15 |
| FORWARD-LOOKING STATEMENTS | 15 |
| WHERE YOU CAN FIND MORE INFORMATION | 15 |

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement we filed with the SEC pursuant to a shelf registration process. Under this shelf registration process, we may sell the securities described in this prospectus up to a total dollar amount of \$125,000,000. Each time we sell securities, we will describe in a prospectus supplement, which we will deliver with this prospectus, specific information about the offering. In each prospectus supplement we will include the following information:

- the amount of common stock which we propose to sell,
- the public offering price of the common stock,
- the names of the underwriters or agents, if any, through or to which we will sell the common stock,
- any compensation of those underwriters or agents,
- information about any securities exchanges or automated quotation systems on which the common stock will be listed or traded, and
- any other material information about the offering and sale of the common stock.

In addition, the prospectus supplement may add, update or change the information contained in this prospectus.

THE COMPANY

La Jolla Pharmaceutical Company is a biopharmaceutical company focused on the research and development of highly specific therapeutic products for the treatment of certain life-threatening antibody-mediated diseases. These diseases, including autoimmune conditions such as lupus erythematosus (lupus) and antibody-mediated thrombosis, are caused by abnormal B cell production of antibodies that attack healthy tissues. Current treatments for these autoimmune disorders address only symptoms of the disease, or nonspecifically suppress the normal operation of the immune system, which often results in severe, negative side effects and hospitalization. We believe that our drug candidates, called Toleragens®, will treat the underlying cause of many antibody-mediated diseases without these severe, negative side effects.

We are incorporated in the State of Delaware. Our principal executive offices are located at 6455 Nancy Ridge Drive, San Diego, California 92121 and our telephone number is (858) 452-6600.

RECENT DEVELOPMENTS

We completed enrollment in our Phase III clinical trial of LJP 394 for the treatment of lupus renal disease on November 11, 2002. Our study physicians are currently conducting final patient visits, which we expect to be completed in December 2002. After the completion of the patient visits, our Phase III trial of LJP 394 will be finished and we will collect and audit final data from the trial sites prior to unblinding and analysis. We currently plan to report initial results from the Phase III trial in early 2003, which could be as early as February.

On October 27, 2002, we announced the preliminary results from our first clinical trial evaluating our experimental drug candidate, LJP 1082, for the treatment of antibody-mediated stroke, heart attack, deep-vein thrombosis and recurrent miscarriage. The Phase I/II trial was a randomized, placebo-controlled study that was designed to evaluate the safety and activity of a single dose of LJP 1082. Based on an initial assessment of the trial data, the drug was well tolerated at all five dose levels. Following treatment with a single 50 or 200 mg dose, antibodies to LJP 1082 were reduced in some patients. This study is the first of several that may be required to establish, among other matters, appropriate dose regimes.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the following risk factors related to our common stock offered by this prospectus and to our business and operations. You should also carefully consider the other information in this prospectus and in the documents incorporated by reference before you decide to purchase our securities. Some of these factors have affected our financial condition and operating results in the past or are currently affecting us. All of these factors could affect our future financial condition or operating results. If any of the following risks actually occurs, our business could be harmed. If that happens, the trading price of our common stock could decline, and you may lose all or part of your investment.

I. Risk Factors Relating to La Jolla Pharmaceutical and the Industry in Which We Operate

Our drug candidates may not perform well in clinical trials. Without successful clinical trials, we will not be able to market or sell any products.

In order to sell our products that are under development, we must first receive regulatory approval. To obtain regulatory approval, we must conduct clinical trials and toxicology studies that demonstrate that our products are safe and effective. Although we believe LJP 394 and LJP 1082 are promising, they may not be found to be safe or effective in ongoing or future clinical trials and studies and results from previous trials and studies may not be observed in current or future trials and studies.

If LJP 394 and LJP 1082 are ultimately not found to be safe and effective, we would be unable to obtain regulatory approval to manufacture, market and sell these drugs. Because LJP 394 is our only drug candidate that has advanced to Phase III clinical trials, and because there is no guarantee that we would be able to develop an alternate drug candidate, our inability to commercialize LJP 394 would have a severe negative effect on our business, and we may not have the financial resources to continue research and development of LJP 394, LJP 1082 or any other potential drug candidates.

Results from our clinical trials may not be sufficient to obtain clearance to market LJP 394 or our other drug candidates in the United States or Europe on a timely basis, or at all.

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. The process of obtaining United States Food and Drug Administration and other regulatory approvals is costly, time consuming, uncertain and subject to unanticipated delays. The FDA and foreign regulatory authorities have substantial discretion in the approval process. The FDA may refuse to approve an application for approval of a drug candidate if it believes that applicable regulatory criteria are not satisfied. The FDA and foreign regulatory authorities may not agree that we have demonstrated that LJP 394 or LJP 1082 are safe and effective after we complete our clinical trials.

Even if the results of clinical trials are positive, the FDA and foreign regulatory authorities may require us to design and conduct additional studies to further demonstrate the safety and efficacy of our drugs, which may result in significant expense and delay. The FDA and foreign regulatory authorities may require new or additional clinical trials because of inconclusive results from earlier clinical trials, a possible failure to conduct clinical trials in complete adherence to FDA good clinical practice standards and similar standards of foreign regulatory authorities, the identification of new clinical trial endpoints, or the need for additional data regarding the safety or efficacy of our drug candidates. Moreover, if the FDA or foreign regulatory authorities grant regulatory approval of a product, the approval may be limited to specific indications or patient populations, or limited with respect to its distribution. It is possible that the FDA or foreign regulatory authorities may not ultimately approve LJP 394, LJP 1082 or our other drug candidates for commercial sale in any jurisdiction, even if clinical results are positive. In addition, even if a drug candidate is approved, it is possible that a subsequent issue regarding its safety or efficacy would require us to remove the drug from the market.

Table of Contents

Because LJP 394 is our only drug candidate that has advanced to Phase III clinical trials, and because there is no guarantee that we would be able to develop an alternate drug candidate, our inability to obtain regulatory approval of LJP 394 would have a severe negative effect on our business, and we may not have the financial resources to continue research and development of LJP 394, LJP 1082 or any other potential drug candidates.

To obtain regulatory approval of LJP 394, the FDA must approve our manufacturing facilities and processes.

In addition to demonstrating the safety and efficacy of LJP 394, we must obtain FDA approval of our manufacturing facilities in order to obtain FDA approval for the commercial use of LJP 394. As part of the approval process, we must also validate our manufacturing facility and processes to the satisfaction of the FDA. Although we have initiated the process of validating and obtaining FDA approval for our facilities and processes, we have never operated an FDA-approved manufacturing facility. If we are unable to obtain the necessary approvals, the FDA will not approve LJP 394 for commercial use.

Our blood test to measure the binding affinity for LJP 394 has not been validated by independent laboratories and will likely require regulatory approval as part of the LJP 394 approval process.

In 1998, we developed a blood test that we believe can identify the lupus patients who are most likely to respond to LJP 394. The blood test is designed to measure the strength of the binding between LJP 394 and a patient's antibodies. This affinity assay was used to identify the patients who will be included in the efficacy analysis of the Phase III trial of LJP 394. The assay has not been validated by independent laboratories, and the results of the affinity assay observed in our clinical trials of LJP 394 may not be observed in the broader lupus patient population. In addition, regulatory agencies will likely require that the assay be reviewed and approved as part of the approval process of LJP 394. Furthermore, the testing laboratory conducting the assay may require additional regulatory approval. If additional regulatory approval of the testing laboratory is required, the approval and possible commercialization of LJP 394 may be delayed.

The technology underlying our products is uncertain and unproven.

All of our product development efforts are based on unproven technologies and therapeutic approaches that have not been widely tested or used. To date, no products that use our technology have been commercialized. LJP 394 and LJP 1082 have not been proven to be safe and effective in humans, and the technology on which they are based has been used only in our pre-clinical tests and clinical trials. Application of our technology to antibody-mediated diseases other than lupus and antibody-mediated thrombosis is in earlier research stages. Clinical trials of LJP 394 and LJP 1082 may be viewed as a test of our entire approach to developing therapies for antibody-mediated diseases. If LJP 394 or LJP 1082 does not work as intended, or if the data from our clinical trials indicates that LJP 394 or LJP 1082 is not safe and effective, the applicability of our technology for treating antibody-mediated diseases will be highly uncertain. As a result, there is a significant risk that our therapeutic approaches will not prove to be successful, and there can be no guarantee that our drug discovery technologies will result in any commercially successful products.

Future clinical trials may be delayed or halted.

Future clinical trials of LJP 394 or LJP 1082, trials of drugs related to these drugs, or clinical trials of other drug candidates may be delayed or halted. During the development of LJP 394, our Phase II/ III clinical study, in collaboration with Abbott Laboratories, was terminated before planned patient enrollment was completed. Future trials may be delayed or halted for various reasons, including:

the products are not effective,

patients experience severe side effects during treatment,

Table of Contents

patients do not enroll in the studies at the rate we expect, or

supplies of drug product are not sufficient to treat the patients in the studies.

If any future trials are delayed or halted we may incur significant additional expenses, which could have a severe negative effect on our business.

We have a history of losses and may not become profitable.

We have incurred operating losses each year since our inception in 1989 and had an accumulated deficit of approximately \$140.4 million as of September 30, 2002. Our future losses are likely to exceed those experienced in prior years due to our continued clinical development of drug candidates, increased manufacturing activities, which may include the production of LJP 394 for an open-label follow-on study and the production of LJP 1082 for clinical and toxicology studies, and continued research and development efforts. In addition, assuming we receive favorable clinical results and FDA approval for LJP 394, we will be required to develop commercial manufacturing capabilities and sales and marketing programs. To achieve profitability we must, among other matters, complete the development of our products, obtain all necessary regulatory approvals and establish commercial manufacturing, marketing and sales capabilities. We expect to incur significant losses each year for at least the next several years as our clinical trial, research, development, manufacturing, marketing and sales activities increase. The amount of losses and the time required by us to reach sustained profitability are highly uncertain and we may never achieve profitability. We do not expect to generate revenues from the sale of LJP 394, if approved, until at least 2004, or our other products, if any, for several years, and we may never generate product revenues.

We will need additional funds to support our operations and may need to reduce operations, sell stock or assets, enter into collaborative agreements or merge with another entity to continue operations.

Our operations to date have consumed substantial capital resources, and we will continue to expend substantial and increasing amounts of capital for research, product development, pre-clinical testing and clinical trials of drug candidates. Assuming that we receive favorable clinical results and regulatory approval for our drug candidates, we may also devote substantial capital resources to establish commercial-scale manufacturing capabilities and to market and sell potential products. We will need to raise additional funds to finance our future operations. Our future capital requirements will depend on many factors, including:

- continued scientific progress in our research and development programs,
- the size and complexity of our research and development programs,
- the scope and results of pre-clinical testing and clinical trials,
- the time and costs involved in applying for regulatory approvals,
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims,
- competing technological and market developments,
- our ability to establish and maintain collaborative research and development arrangements,
- our need to establish commercial manufacturing capabilities, and
- our ability to develop marketing and sales programs.

We expect to incur substantial and increasing losses each year for at least the next several years as our clinical trial, research, development and manufacturing activities increase. If we receive regulatory approval for LJP 394, LJP 1082 or our other drug candidates, our manufacturing, marketing and sales activities are likely to substantially increase our expenses and our need for working capital. We anticipate that our existing cash, investments and interest earned thereon will be sufficient to fund our operations as currently planned into the fourth quarter of 2003, assuming that we do not undertake significant commercialization activities for LJP 394 such as building inventory for launch or hiring a sales force.

Table of Contents

However, the amounts expended by us may vary significantly, and it is possible that our cash requirements will exceed current projections and that we will therefore need additional financing sooner than currently expected. In the future, it is possible that we will not have adequate resources to support our business activities.

We actively seek additional funding, including through public and private financings and collaborative arrangements. Our choice of financing alternatives may vary from time to time depending on various factors, including the market price of our securities, conditions in the financial markets and the interest of other entities in strategic transactions with us. There can be no guarantee that additional financing will be available on favorable terms, if at all, whether through issuance of securities, collaborative arrangement, or otherwise. If adequate funds are not available, we may be required to delay, scale back or eliminate one or more of our research and development programs or obtain funds through arrangements with collaborative partners or others that require us to relinquish rights to certain technologies or potential products. We also may be required to merge with another entity to continue our operations. Any one of these outcomes could have a negative impact on our ability to develop products or achieve profitability if our products are brought to market. If, and to the extent, we obtain additional funding through sales of securities, your investment in us will be diluted.

The size of the market for our potential products is uncertain.

We estimate that the number of people who suffer from lupus in the United States and Europe is approximately 1,000,000 and that those with renal impairment, which LJP 394 is designed to treat, is approximately 300,000. With respect to antibody-mediated thrombosis, which LJP 1082 is designed to treat, we estimate that there are approximately 1,000,000 to 2,000,000 patients in the United States and Europe. However, there is limited information available regarding the actual size of these patient populations. In addition, it is uncertain whether the results from previous or current clinical trials of our drug candidates will be observed in broader patient populations, and the number of patients who may benefit from our drug candidates may be significantly smaller than the estimated patient populations. Furthermore, management of patients with renal disease by specialists other than nephrologists and immunologists is likely to reduce our ability to access patients who may benefit from LJP 394.

Our drugs may not achieve market acceptance.

Even if our drug treatment for lupus, LJP 394, or our other drugs candidates receive regulatory approval, patients and physicians may not readily accept our proposed methods of treatment. In order for LJP 394 or our other drug candidates to be commercially successful, we will need to increase the awareness and acceptance of our drugs among physicians, patients and the medical community. LJP 394 is designed to be administered intravenously. It is possible that providers and patients may resist an intravenously administered therapeutic. In addition, if we are unable to manufacture drugs at an acceptable cost, physicians may not readily prescribe our drugs due to cost-benefit considerations when compared to other methods of treatment. If we are unable to achieve market acceptance for our approved products, our revenues and profitability will be negatively affected.

We lack experience in marketing products for commercial sale.

In order to commercialize any drug candidate approved by the FDA, we must either develop marketing and sales programs or enter into marketing arrangements with others. If we cannot do either of these successfully, we will not generate meaningful sales of our products. If we develop our own marketing and sales capabilities, we will be required to employ a sales force, establish and staff a customer service department, and create or identify distribution channels for our drugs. We will compete with other companies that have experienced and well-funded marketing and sales operations. In addition, if we establish our own sales and distribution capabilities, we may experience delays and expenditures and have difficulty in gaining market acceptance for our drug candidates. We currently have no marketing arrangements with others. There can be no guarantee that, if we desire to, we will be able to enter into any marketing agreements on favorable terms, if at all, or that any such agreements will result in payments

Table of Contents

to us. If we enter into co-promotion or other marketing and sales arrangements with other companies, any revenues that we may receive will be dependent on the efforts of others. There can be no guarantee that these efforts will be successful.

Our limited manufacturing capabilities and experience could result in shortages of products for testing and future sale, and our revenues and profit margin could be negatively affected.

Substantial capital investment in the expansion and build-out of our manufacturing facilities will be required to enable us to manufacture LJP 394 in significant commercial quantities. We have limited manufacturing experience, and we may be unable to successfully transition to commercial production. In addition, we have never operated an FDA-approved manufacturing facility, and we will be required to manufacture LJP 394 pursuant to applicable FDA good manufacturing practices. Our inexperience could result in manufacturing delays or interruptions and higher manufacturing costs. This could negatively affect our ability to introduce products into the market on a timely and competitive basis. In addition, the subsequent sales of our products and our profit margins may be negatively affected.

We may enter into arrangements with contract manufacturing companies to expand our own production capacity in order to meet demand for our products, or to attempt to improve manufacturing efficiency. If we choose to contract for manufacturing services and encounter delays or difficulties in establishing relationships with manufacturers to produce, package or distribute our finished products, or the contract manufacturers are unable to meet our needs, the introduction of our products into the market and the subsequent sales of these products would be negatively affected, and our profit margins and our ability to develop and deliver products on a timely and competitive basis may be negatively affected.

Our suppliers may not be able to provide us with sufficient quantities of materials that we may need to manufacture our products.

We rely on outside suppliers to provide us with specialized chemicals and reagents that we use to manufacture our drugs. In order to manufacture LJP 394, LJP 1082 and our other drug candidates in sufficient quantities for our clinical trials and possible commercialization, our suppliers will be required to provide us with an adequate supply of chemicals and reagents. Our ability to obtain these chemicals and reagents is subject to the following risks:

our suppliers may not be able to increase their own manufacturing capabilities in order to provide us with a sufficient amount of material for our use,

some of our suppliers may be required to obtain FDA or other regulatory approvals of their manufacturing facilities or processes, and they may be delayed or unable to do so,

the materials that our suppliers use to manufacture the chemicals and reagents which they provide us may be costly or in short supply, and

there may be a limited number of suppliers which are able to provide us with the chemicals or reagents that we use to manufacture our drugs.

If we are unable to obtain sufficient quantities of chemicals or reagents, the introduction of our products into the market and the subsequent sales of these products would be negatively affected, and our profit margins and our ability to develop and deliver products on a timely and competitive basis may be negatively affected.

We may not earn as much income as we hope due to possible changes in healthcare reimbursement policies.

The continuing efforts of government and healthcare insurance companies to reduce the costs of healthcare may reduce the amount of income we can generate from our products. For example, in certain foreign markets, pricing and profitability of prescription drugs are subject to government control. In the United States, we expect that there will continue to be a number of federal and state proposals to

Table of Contents

implement similar government controls. In addition, increasing emphasis on managed care in the United States will continue to put pressure on drug manufacturers to reduce prices. Cost control initiatives could reduce the revenue that we receive for any products we may develop and sell in the future.

Our success in developing and marketing our products depends significantly on our ability to obtain patent protection for LJP 394, LJP 1082 and any other developed products. In addition, we will need to successfully preserve our trade secrets and operate without infringing on the rights of others.

We depend on patents and other unpatented intellectual property to prevent others from improperly benefiting from products or technologies that we may have developed. As of December 31, 2001, we owned 96 issued patents and 82 pending patent applications covering various technologies and drug candidates including LJP 394 and LJP 1082. However, there can be no assurance that any additional patents will be issued, that the scope of any patent protection will be sufficient, or that any current or future issued patent will be held valid if subsequently challenged. There is a substantial backlog of biotechnology patent applications at the United States Patent and Trademark Office that may delay the review and issuance of any patents. The patent position of biotechnology firms like ours is highly uncertain and involves complex legal and factual questions, and no consistent policy has emerged regarding the breadth of claims covered in biotechnology patents or the protection afforded by these patents. Currently, we have a number of patent applications pending in the United States relating to our technology, as well as foreign counterparts to some of our United States patent applications. We intend to continue to file applications as believed appropriate for patents covering both our products and processes. There can be no assurance that patents will be issued from any of these applications, or that the scope of any issued patents will protect our technology.

We do not necessarily know if others, including competitors, have patents or patent applications pending that relate to compounds or processes that overlap or compete with our intellectual property. We are aware of one United States patent grant that contains claims covering subject matter that may conflict with some of our key patents and patent applications, and that may affect our ability to manufacture and sell our products. If the United States Patent and Trademark Office or any foreign counterpart issues or has issued patents containing competitive or conflicting claims, and if these claims are valid, the protection provided by our existing patents or any future patents that may be issued could be significantly reduced, and our ability to prevent competitors from developing products or technologies identical or similar to ours could be negatively affected. In addition, there can be no guarantee that we would be able to obtain licenses to these patents on commercially reasonable terms, if at all, or that we would be able to develop or obtain alternative technology. Our failure to obtain a license to a technology or process that may be required to develop or commercialize one or more of our product candidates may have a material adverse effect on our business. In addition, we may have to incur significant expenses in defending or enforcing our patents.

We also rely on unpatented intellectual property such as trade secrets and improvements, know-how, and continuing technological innovation. While we seek to protect these rights, it is possible that:

inventions relevant to our business will be developed by others, including competitors,

our binding confidentiality agreements will be breached, and we will not have adequate remedies for such a breach, or

our trade secrets will otherwise become known or be independently discovered by competitors.

We could incur substantial costs in defending suits brought against us by others for infringement of intellectual property rights or in prosecuting suits that we might bring against others to protect our intellectual property rights.

Table of Contents

Our research and development and operations depend in part on certain key employees. Losing these employees would have a negative effect on our product development and operations.

We are highly dependent on the principal members of our scientific and management staff, the loss of whose services would delay the achievement of our research and development objectives. This is because our key personnel, including Steven Engle, Dr. Matthew Linnik, Dr. Paul Jenn and Dr. Andrew Wiseman, have been involved in the development of LJP 394, LJP 1082 and other drug candidates for several years and have unique knowledge of our drug candidates and of the technology on which they are based. In addition, we will be required to rely on key members of our senior management team, including Bruce Bennett, William Welch, Karen Church, and Dr. Kenneth Heilbrunn, to assist us with our anticipated growth and expansion into areas requiring additional expertise, such as clinical trials, regulatory approvals, manufacturing, marketing and sales. We expect that we will continue to require additional management personnel, and that our existing management personnel will be required to develop additional expertise.

Retaining our current personnel and recruiting additional personnel will be critical to our success.

Retaining our current key personnel and recruiting additional qualified personnel to perform research and development, clinical development, manufacturing, marketing and sales will be critical to our success. Because competition for experienced scientific, clinical, sales, manufacturing, marketing and sales personnel among numerous pharmaceutical and biotechnology companies and research and academic institutions is intense, we may not be able to attract and retain these people. If we cannot attract and retain qualified people, our ability to conduct necessary clinical trials and to develop and sell our products may be negatively affected because, for instance, the trials may not be conducted properly, or the manufacturing or sales of our products may be delayed. In addition, we rely upon consultants and advisors to assist us in formulating our research and development, clinical, regulatory, manufacturing, marketing and sales strategies. All of our consultants and advisors have outside employment and may have commitments or consulting or advisory contracts with other entities that may affect their ability to contribute to our business.

Our freedom to operate our business or profit fully from sales of our products may be limited if we enter into collaborative agreements.

We may seek to collaborate with pharmaceutical companies to gain access to their research, drug development, manufacturing, marketing, sales and financial resources. However, we may not be able to negotiate arrangements with any collaborative partners on favorable terms, if at all. Any collaborative relationships that we enter into may include restrictions on our freedom to operate our business or may limit the sales of our products. If a collaborative arrangement is established, the collaborative partner may discontinue funding any particular program or may, either alone or with others, pursue alternative technologies or develop alternative drug candidates for the diseases we are targeting. Competing products, developed by a collaborative partner or to which a collaborative partner has rights, may result in the collaborative partner withdrawing support as to all or a portion of our technology.

Without collaborative arrangements, we must fund our own research, development, manufacturing, marketing and sales activities which would accelerate the depletion of our cash and require us to develop our own manufacturing, marketing and sales capabilities. Therefore, if we are unable to establish and maintain collaborative arrangements and if other sources of cash are not available, we could experience a material adverse effect on our ability to develop products and, if developed, to manufacture, market and sell them successfully.

Because a number of companies compete with us, many of which have greater resources than we do, and because we face rapid changes in technology in our industry, we cannot be certain that our products will be accepted in the marketplace or capture market share.

Competition from domestic and foreign biotechnology companies, large pharmaceutical companies and other institutions is intense and is expected to increase. A number of companies and institutions are

Table of Contents

pursuing the development of pharmaceuticals in our targeted areas, many of which are very large, and have financial, technical, sales and distribution and other resources substantially greater than ours. The greater resources of these competitors could enable them to develop competing products more quickly than we are able to, and to market any competing product more quickly or effectively so as to make it extremely difficult for us to develop a share of the market for our products. These competitors also include companies that are conducting clinical trials and pre-clinical studies for the treatment of lupus and thrombosis. Our competitors may develop or obtain regulatory approval for products more rapidly than we do. Also, the biotechnology and pharmaceutical industries are subject to rapid changes in technology. Our competitors may develop and market technologies and products that are more effective or less costly than those being developed by us, or that would render our technology and proposed products obsolete or noncompetitive.

An interruption in the operation of our sole manufacturing facility could disrupt our operations.

We have only one drug manufacturing facility. A significant interruption in the operation of this facility, whether as a result of a natural disaster or other causes, could significantly impair our ability to manufacture drugs for our clinical trials or possible commercialization.

The use of LJP 394, LJP 1082 and other potential products in clinical trials, as well as the sale of any approved products, may expose us to lawsuits resulting from the use of these products.

The use and possible sale of LJP 394, LJP 1082 and other potential products may expose us to legal liability and generate negative publicity if we are subject to claims that people were harmed by our products. These claims might be made directly by patients, pharmaceutical companies, or others. We currently maintain \$10.0 million of product liability insurance for claims arising from the use of our products in clinical trials. However, coverage is becoming increasingly expensive, and there can be no guarantee that we will be able to maintain insurance or that insurance can be acquired at a reasonable cost or in sufficient amounts to protect us against possible losses. Furthermore, it is possible that our financial resources would be insufficient to satisfy potential product liability claims. A successful product liability claim or series of claims brought against us could negatively impact our business and financial condition.

We face environmental liabilities related to certain hazardous materials used in our operations.

Due to the nature of our manufacturing processes, we are subject to stringent federal, state and local laws governing the use, handling and disposal of certain materials and wastes. We may have to incur significant costs to comply with environmental regulations if and when our manufacturing increases to commercial volumes. Our operations may be significantly affected by current or future environmental laws because, for instance, our production process may be required to be altered, thereby increasing our production costs. In our research activities, we use radioactive and other materials that could be hazardous to human health, safety or the environment. These materials and various wastes resulting from their use are stored at our facility pending ultimate use and disposal. The risk of accidental injury or contamination from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any resulting damages, and any such liability could exceed our resources. Although we maintain general liability insurance, we do not specifically insure against environmental liabilities.

II. Risk Factors Related Specifically to Our Stock

Our common stock price is volatile and may decline even if our business is doing well.

The market price of our common stock has been and is likely to continue to be highly volatile. Market prices for securities of biotechnology and pharmaceutical companies, including ours, have historically been highly volatile, and the market has from time to time experienced significant price and

Table of Contents

volume fluctuations that are unrelated to the operating performance of particular companies. The following factors, among others, can have a significant effect on the market price of our securities:

- our clinical trial results,
- announcements of technological innovations or new therapeutic products by us or others,
- developments in patent or other proprietary rights,
- public concern as to the safety of drugs discovered or developed by us or others,
- future sales of significant amounts of our common stock by existing stockholders,
- developments concerning potential agreements with collaborators,
- comments by securities analysts and general market conditions, and
- government regulation.

The realization of any of the risks described in these Risk Factors could have a negative effect on the market price of our common stock.

In the future, our stock may be removed from listing on the Nasdaq quotation system and may not qualify for listing on any stock exchange, in which case it may be difficult to find a market in our stock.

If our stock is no longer traded on a national trading market, it may be more difficult for you to sell shares that you own, and the price of the stock may be negatively affected. Currently, our securities are traded on the Nasdaq National Market. Nasdaq has several continued listing requirements, including a minimum trading price. Previously, we have received notice from Nasdaq that our stock price fell below this minimum trading price. Although we have since come back into compliance with this Nasdaq requirement, it is possible that we will fall out of compliance with this and/or other Nasdaq continued listing criteria at some point in the future. Failure to comply with any one of several Nasdaq requirements may cause our stock to be removed from listing on Nasdaq. Should this happen, we may not be able to secure listing on other exchanges or quotation systems. This would have a negative effect on the price and liquidity of our stock.

Future sales of our stock by existing stockholders could negatively affect the market price of our stock and make it more difficult for us to sell stock in the future.

Sales of our common stock in the public market, or the perception that such sales could occur, could result in a drop in the market price of our securities and make it more difficult for us to complete future equity financings on acceptable terms, if at all. We have outstanding the following shares of common stock:

Approximately 42,354,328 shares of common stock that have been issued in registered offerings or are otherwise freely tradable in the public markets.

Approximately 72,473 shares of common stock currently eligible for resale in the public market pursuant to SEC Rule 144.

As of November 20, 2002, there are an aggregate of 5,673,355 shares of common stock that may be issued on the exercise of outstanding stock options granted under our various stock option plans at a weighted average exercise price of \$4.82 per share.

We have in effect registration statements under the Securities Act registering approximately 8,100,000 shares of common stock reserved under our incentive stock option and employee stock purchase plans. Approximately 147,600 shares of common stock that may be issued on the exercise of outstanding stock options will be available for public resale under SEC Rule 144 pursuant to Rule 701 under the Securities Act.

Table of Contents

Pursuant to the registration statement of which this prospectus forms a part, we may issue up to \$125,000,000 aggregate amount of common stock.

We cannot estimate the number of shares of common stock that may actually be resold in the public market because this will depend on the market price for our common stock, the individual circumstances of the sellers and other factors. We also have a number of institutional stockholders that own significant blocks of our common stock. If these stockholders sell significant portions of their holdings in a relatively short time, for liquidity or other reasons, the market price of our common stock could drop significantly.

Anti-takeover devices may prevent changes in our management.

We have in place several anti-takeover devices, including a stockholder rights plan, that may have the effect of delaying or preventing changes in our management. For example, one anti-takeover device provides for a board of directors that is separated into three classes, with their terms in office staggered over three year periods. This has the effect of delaying a change in control of our board of directors without the cooperation of the incumbent board. In addition, our bylaws require stockholders to give us written notice of any proposal or director nomination within a specified period of time prior to the annual stockholder meeting, establish certain qualifications for a person to be elected or appointed to the board of directors during the pendency of certain business combination transactions, and do not allow stockholders to call a special meeting of stockholders.

We may also issue shares of preferred stock without further stockholder approval and upon terms that our board of directors may determine in the future. The issuance of preferred stock could have the effect of making it more difficult for a third party to acquire a majority of our outstanding stock, and the holders of such preferred stock could have voting, dividend, liquidation and other rights superior to those of holders of our common stock.

We do not pay dividends and this may negatively affect the price of our stock.

We have not paid any cash dividends since our inception and do not anticipate paying any cash dividends in the foreseeable future. The future price of our common stock may be depressed by the fact that we have not paid dividends.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock sets forth general terms and provisions of our common stock to which a prospectus supplement may relate. The following summary of our amended and restated certificate of incorporation and amended and restated bylaws does not describe the certificate and bylaws entirely. We urge you to read our certificate and bylaws which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. See *Where You Can Find More Information* on page 15. On the date of this prospectus, our authorized capital stock consists of 100,000,000 shares of common stock, \$0.01 par value per share, and 8,000,000 shares of preferred stock, \$0.01 par value per share.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote per share on all matters to be voted upon by our stockholders. The vote of the holders of a majority of the stock represented at a meeting at which a quorum is present is generally required to take stockholder action, unless a greater vote is required by law or specifically required by our certificate of incorporation or bylaws. Special stockholder meetings may be called only by the board of directors, the chairman of the board or the president. Our certificate provides that our stockholders may not act by written consent. In addition, our bylaws include an advance notice procedure with regard to the nomination, other than by or at the direction of the board of directors, of candidates for election as directors and with regard to matters to be brought before an annual meeting or special meeting of stockholders.

Table of Contents

Dividends and Other Rights. Holders of our common stock are entitled to receive, as when and if declared by the board of directors from time to time, such dividends and other distributions in cash, stock or property from our assets or funds legally available for such purposes subject to any dividend preferences that may be attributable to preferred stock that may be authorized. In the event of our liquidation, dissolution or winding up, after all liabilities and the holders of each series of preferred stock, if any, have been paid in full, the holders of our common stock are entitled to share ratably in all remaining assets available for distribution. Our common stock has no preemptive, subscription, redemption or conversion rights. There are no sinking fund provisions applicable to our common stock.

Classified Board of Directors. Our certificate of incorporation and bylaws provide for a classified board of directors. Our board is classified into three classes, each as nearly equal in number as possible. At each annual meeting, the successors to the class of directors whose term expire at that meeting are elected for a term of office to expire at the third succeeding annual meeting after their election or until their successors have been duly elected and qualified. Delaware law provides that, unless the certificate of incorporation provides otherwise, directors serving on a classified board of directors may be removed only for cause. Our certificate of incorporation does not provide otherwise. Therefore, our directors may only be removed for cause. The affirmative vote of the holders of 75% or more of the total voting power of all outstanding shares of voting stock would be required to amend our certificate or bylaws to remove the classified board provisions.

Rights Plan. Each outstanding share of our common stock is accompanied by a right to purchase our preferred stock, our common stock or the common stock of a successor company pursuant to the terms of a rights agreement. Please refer to the discussion entitled "La Jolla Pharmaceutical Company Rights Plan" below.

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of the corporation's voting stock. Delaware law, the existence of our Rights Agreement, and the provisions of our certificate and bylaws may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent. American Stock Transfer & Trust Company is the Transfer Agent and Registrar for the shares of our common stock.

Preferred Stock

Our board of directors has the authority, without further action by stockholders, to issue up to 8,000,000 shares of preferred stock in one or more series and to fix the powers, designations, rights, preferences, privileges, qualifications, and restrictions thereof, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preferences and sinking fund terms, any or all of which may be greater than the rights of our common stock. Our board of directors, without further stockholder approval, can issue preferred stock with voting, conversion, and other rights that could adversely affect the voting power and other rights of the holders of common stock. The issuance of preferred stock in certain circumstances may have the effect of delaying, deferring or preventing a change in control of La Jolla Pharmaceutical, may discourage bids for our common stock at a premium over the market price of the common stock, and may adversely affect the market price of our common stock. As of the date of this prospectus, there are no shares of our preferred stock outstanding.

We have filed a certificate of designation with the Secretary of State of the State of Delaware which designates 100,000 shares of preferred stock as Series A Junior Participating Preferred Stock in connection

Table of Contents

with our stockholder rights plan, as described below. We refer to our Series A Junior Participating Preferred Stock as our Series A Preferred Shares. Except to the extent that a right to purchase our Series A Preferred Shares accompanies each share of our common stock, no shares of our preferred stock are covered by this prospectus.

La Jolla Pharmaceutical Company Rights Plan

On November 19, 1998, our board of directors authorized and declared a dividend of one right for each share of our common stock. On December 3, 1998, we entered into a Rights Agreement with American Stock Transfer & Trust Company, as Rights Agent, and filed a Certificate of Designation with the State of Delaware regarding our Series A Preferred Shares. The Company paid the rights dividend to the holders of record of common stock as of the close of business on December 18, 1998. Common stock certificates issued after December 18, 1998, and prior to the Distribution Date (as defined in the Rights Agreement), contain a notation incorporating the Rights Agreement by reference. Currently, there are no separate rights certificates. Each right is attached to each share of our common stock and trades automatically with the common stock. Rights will not be separable from common stock or exercisable, unless specified events described in the Rights Agreement occur. Upon the occurrence of the events described in the Rights Agreement, the rights will separate from the common stock and may thereafter become exercisable to purchase additional securities. The Rights Agreement, as amended, can be found in the documents that are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. See [Where You Can Find More Information](#) on page 15.

USE OF PROCEEDS

We intend to use the net proceeds we receive from the sale of the securities offered by this prospectus to fund the continued research and development of our potential products, including the funding of our current and future trials of LJP 394 and LJP 1082 and any related regulatory submissions, to expand and validate our existing facilities, processes and infrastructures, for other general corporate purposes, or for any other purposes that may be described in an accompanying prospectus supplement.

We will retain broad discretion over the use of the net proceeds from any sale of our common stock offered hereby. The amounts and timing of expenditures may vary significantly depending on several factors, including the progress of our research and development efforts, the results of our clinical trials, the time and costs of obtaining regulatory approvals, our future capital expenditures, our need to develop commercial marketing and sales capabilities, and our ability to generate revenues in the future.

PLAN OF DISTRIBUTION

The securities that may be offered pursuant to this prospectus and any prospectus supplement may be offered by us to one or more underwriters for public offering and sale by them, to investors directly (through a specific bidding or auction process, or otherwise) or through agents. Any such underwriter or agent involved in the offer and sale of such securities will be named in the applicable prospectus supplement. Sales of such securities may be effected from time to time in one or more types of transactions, which may include block transactions, on the Nasdaq National Market or other securities exchange, in the over-the-counter market, in negotiated transactions, through put or call options transactions relating to the securities, through short sales of the securities, or a combination of such methods of sale. Such transactions may or may not involve brokers or dealers.

Underwriters may offer and sell the securities at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The consideration may be cash or another form negotiated by the parties.

In connection with the sale of the securities, underwriters may receive compensation from us in the form of underwriting discounts, concessions or commissions and may also receive commissions from purchasers of the securities for whom they may act as agent. Underwriters may sell the securities to or

Table of Contents

through dealers who may receive compensation from the underwriters in the form of discounts, concessions or commissions or commissions from the purchasers for whom they may act as agents.

Direct sales of securities may be made on a national securities exchange or otherwise.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, 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 of 1933, as amended. Underwriters, dealers, agents and remarketing firms described below may be entitled, under agreements entered into with us, to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act of 1933, as amended.

Certain of the underwriters, dealers, agents and remarketing firms and their associates may engage in transactions with, and perform services for, us in the ordinary course of business.

We may directly solicit offers to purchase the securities and we may make sales of securities directly to institutional investors or others. These persons may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, with respect to any resales of the securities. To the extent required, the prospectus supplement will describe the terms of any such sales, include the terms of any bidding or auction process, if used.

Under the securities laws of some states, the securities offered by the prospectus may be sold in those states only through registered or licensed brokers or dealers.

It is possible that one or more underwriters may make a market in our common stock, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for our common stock.

Offered securities may also be offered and sold, if so indicated in the applicable prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreements, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters, as that term is defined in the Securities Act of 1933, as amended, in connection with the securities marketed by them.

If we so indicate in the prospectus supplement, we may authorize agents, underwriters or dealers to solicit offers from certain purchasers to purchase securities from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the applicable prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

Certain persons participating in the offering may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Over-allotment 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. 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. The persons engaging in these activities may discontinue any of these activities at any time.

Table of Contents

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP has rendered an opinion with respect to the validity of the securities being offered by this prospectus. If counsel for any underwriters passes on legal matters in connection with an offering of the securities described in this prospectus, we will name that counsel in the prospectus supplement relating to that offering.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2001, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

FORWARD-LOOKING STATEMENTS

We have made forward-looking statements in this prospectus that are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements include information concerning our possible or assumed future results of operations and statements preceded by, followed by, or that include the words believes, expects, anticipates, intends, plans, estimates, or similar expressions.

Forward-looking statements involve risks, uncertainties and assumptions. Actual results may differ materially from those expressed in these forward-looking statements. You are cautioned not to put undue reliance on any forward-looking statements. Except as may be required by law, we do not have any intention or obligation to update forward-looking statements after we distribute this prospectus. These statements appear in a number of places in this prospectus and include statements regarding our intentions, plans, strategies, beliefs or current expectations and those of our directors or our officers with respect to, among other matters:

the results of our clinical trials;

our financial prospects;

our financing plans;

trends affecting our financial condition or operating results;

our strategies for growth, operations, and product development and commercialization; and

conditions or trends in or factors affecting the biotech industry.

You should understand that a number of factors could cause our results to differ materially from those expressed in the forward-looking statements. The information incorporated by reference or provided in this prospectus identifies important factors that could cause such differences. Those factors include, among others, the high cost and uncertainty of technology and drug development, which can result in loss of profitability and long delays in getting products to market.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (the SEC). You may read and copy any document we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may also obtain copies from the SEC's public reference room by mail at prescribed rates. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference room. Our SEC filings are also available to the public from the SEC's web site at <http://www.sec.gov>. Information about La Jolla Pharmaceutical Company is also available to the public from our website at <http://www.ljpc.com>.

Table of Contents

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933, as amended. This prospectus does not contain all of the information set forth in the registration statement. You should read the registration statement for further information about us and the securities. You may inspect the registration statement and its exhibits without charge at the office of the SEC at 450 Fifth Street, N.W., Washington, D.C. 20549, and you may obtain copies from the SEC at prescribed rates.

The SEC allows us to incorporate by reference the information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, except for any information that is superseded by information that is included directly in this prospectus. The information we file with the SEC in the future will update and supersede this information. We incorporate by reference the documents listed below and any future filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, until we sell all of the securities offered by this prospectus:

1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 2001;
2. Our Proxy Statement filed on April 11, 2002 for our 2002 Annual Meeting of Stockholders;
3. Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2002, June 30, 2002 and September 30, 2002;
4. Our Current Report on Form 8-K, filed on November 26, 2002;
5. The description of our common stock contained in our Registration Statements on Form 8-A, filed on June 2, 1994, December 4, 1998 and January 26, 2001; and
6. All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of the offering of the shares offered by this prospectus.

You may request a copy of any or all of the information incorporated by reference in this prospectus at no cost by writing or telephoning us at the following address or telephone number:

Corporate Secretary

La Jolla Pharmaceutical Company
6455 Nancy Ridge Drive
San Diego, California 92121
(858) 452-6600

You should rely only on the information contained in this prospectus. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this prospectus.

Table of Contents

8,695,653 Shares

La Jolla Pharmaceutical Company

Common Stock

PROSPECTUS SUPPLEMENT

PACIFIC GROWTH EQUITIES, LLC

February 19, 2004
