

LA JOLLA PHARMACEUTICAL CO

Form 424B5

March 20, 2007

Table of Contents

The information in this prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

**File pursuant to rule 424(b)(5)
Registration No.: 333-101499**

SUBJECT TO COMPLETION, DATED MARCH 20, 2007

PROSPECTUS SUPPLEMENT

(To Prospectus Dated December 12, 2002)

5,000,000 Shares

Common Stock

We are offering 5,000,000 shares of our common stock. Our common stock is traded on the Nasdaq Global Market under the symbol LJPC. On March 16, 2007, the last reported sale price for our Common Stock on the Nasdaq Global Market was \$7.26 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-4.

	Per Share	Total
Public Offering Price	\$	\$
Underwriting Discount	\$	\$
Proceeds, before expenses	\$	\$

We have granted the underwriters the right to purchase up to an additional 750,000 shares of our common stock to cover over-allotments.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. It is illegal for any person to tell you otherwise.

The underwriters expect to deliver the shares against payment on or about _____, 2007.

Needham & Company, LLC

A.G. Edwards

The date of this prospectus supplement is _____, 2007

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

	Page
<u>About This Prospectus Supplement</u>	ii
<u>Summary</u>	S-1
<u>Risk Factors</u>	S-4
<u>Description of Capital Stock</u>	S-15
<u>Dilution</u>	S-17
<u>Use of Proceeds</u>	S-18
<u>Selected Financial Data</u>	S-19
<u>Underwriting</u>	S-20
<u>Legal Matters</u>	S-22
<u>Experts</u>	S-22
<u>Where You Can Find More Information and Incorporation by Reference</u>	S-22
<u>Forward-Looking Statements</u>	S-23

PROSPECTUS

	Page
<u>About This Prospectus</u>	1
<u>The Company</u>	1
<u>Recent Developments</u>	1
<u>Risk Factors</u>	2
<u>Description of Capital Stock</u>	12
<u>Use of Proceeds</u>	14
<u>Plan of Distribution</u>	15
<u>Legal Matters</u>	17
<u>Experts</u>	17
<u>Forward-Looking Statements</u>	17
<u>Where You Can Find More Information</u>	18

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained 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, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock. 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

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.

On December 21, 2005, we completed a one-for-five reverse stock split. The reverse stock split caused every five shares of our outstanding common stock to convert automatically into one share of common stock. All share and share related information set forth in this prospectus supplement is presented on a post-reverse stock split basis. Because we completed this reverse stock split subsequent to the date of the accompanying prospectus, all share and share related information set forth in the accompanying prospectus remains presented on a pre-reverse stock split basis.

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, including our Annual Report on Form 10-K for the year ended December 31, 2006 filed with the Securities and Exchange Commission on March 16, 2007, 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 accompanying 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 and our wholly owned subsidiary.

The Company

We are a biopharmaceutical company focused on developing innovative pharmaceutical products to improve human health by addressing unmet medical needs. Our lead product, Riquent, is designed to treat lupus renal disease by preventing or delaying renal flares. Riquent is currently in a Phase 3 clinical trial under a Special Protocol Assessment and has been granted Fast Track designation by the FDA.

Lupus renal disease is a chronic illness that can lead to irreversible renal damage, renal failure and the need for dialysis, and is a leading cause of death in lupus patients. Lupus is an antibody-mediated disease caused by autoantibodies, of which antibodies to double-stranded DNA (dsDNA) are an important subgroup. Riquent is designed to prevent or delay renal flares by lowering the levels of circulating antibodies to dsDNA, which are believed to cause lupus renal disease. Current treatments for this autoimmune disorder often address only symptoms of the disease, or nonspecifically suppress the normal operation of the immune system, which can result in severe, negative side effects and hospitalization. We believe that Riquent has the potential to treat lupus renal disease without these severe, negative side effects. The Lupus Foundation estimates that there are approximately one million lupus patients in the United States. We believe that 30% to 50% of these lupus patients have renal disease.

We have also developed novel, orally-active, small-molecule SSAO inhibitors for the treatment of autoimmune diseases and acute and chronic inflammatory disorders. Preclinical studies have shown that these inhibitors reduce disease activity in animal models of multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, stroke, systemic inflammation and acute inflammation.

Recent Developments

We recently announced positive interim antibody results from our ongoing double-blind, placebo-controlled randomized Phase 3 trial of Riquent. Analyses of interim antibody data indicate that patients treated with 900 mg or 300 mg per week doses of Riquent had greater reductions in antibodies to dsDNA than patients treated with 100 mg per week or placebo. The results showed a significant dose response when comparing all Riquent-treated patients to placebo-treated patients ($p = 0.0001$), and each Riquent dose group to the placebo dose group ($p = 0.0032$ for 100 mg, $p < 0.0001$ for 300 mg and 900 mg). Following eight weeks of treatment, the median percent reduction in antibodies to dsDNA for Riquent-treated patients compared with placebo-treated patients was 30% (100 mg), 40% (300 mg), and 58% (900 mg). In addition, preliminary assessment of the data indicates that Riquent is being as well tolerated at all doses in the ongoing Phase 3 study as in our previous studies.

Published data from previous clinical trials indicate that patients with sustained reductions in antibodies to dsDNA have a six-fold reduction in the incidence of renal flares. Nearly twice as many patients on 900 mg, as compared to 300 mg, had a consistent 50% reduction in antibodies to dsDNA, but no patients on 100 mg or placebo achieved this level of consistent reduction. A consistent reduction is defined as a patient whose percent antibody reduction exceeded a specified level at weeks 4, 6 and 8.

On February 1, 2007, we announced that we had made continued progress in enrolling patients in our Phase 3 clinical trial of Riquent in that we had enrolled 202 patients in the study and 74 clinical trial sites were open to enroll patients, including newly added sites in Europe and Mexico. In addition, we also announced that following recent discussions with the FDA, we implemented several enhancements to further strengthen our current Phase 3 study, which remains under Special Protocol Assessment. These enhancements include:

Focus on higher doses all new patients entering the study will be randomized in equal numbers to receive weekly doses of either 300 mg or 900 mg of Riquent (the safety of which has been studied) or placebo, with no further patients randomized to the 100 mg dose group.

Increase sample size the study sample size is increased from approximately 600 to approximately 730 patients, which is expected to increase the likelihood of achieving a statistically significant outcome for the individual dose groups when compared with placebo as well as overall.

We expect to further expand the study globally in 2007 and target completing patient enrollment into the study around the end of 2007.

S-1

Table of Contents

Corporate Information

We were incorporated in the State of Delaware in 1989. Our principal executive offices are located at 6455 Nancy Ridge Drive, San Diego, California 92121 and our telephone number is (858) 452-6600. Our website is located at *www.ljpc.com*. We have not incorporated by reference into this prospectus supplement the information on our website, and you should not consider our website to be a part of this document. For more complete information please refer to our Annual Report on Form 10-K for the year ended December 31, 2006, filed with the Securities and Exchange Commission on March 16, 2007.

S-2

Table of Contents

The Offering

Common stock offered by us	5,000,000 shares
Shares outstanding after the offering	37,840,505 shares
Use of proceeds	We estimate that our net proceeds from this offering will be approximately \$33.9 million, assuming an offering price of \$7.26 per share, the last reported sale price of our common stock on the Nasdaq Global Market on March 16, 2007, and 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 other general corporate purposes, 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, the accompanying prospectus and incorporated by reference for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Market symbol	LJPC

The number of shares outstanding after the offering is based on 32,840,505 shares of common stock outstanding as of March 15, 2007 and excludes:

750,000 shares of common stock that the underwriters have a right to purchase from us to cover over-allotments.

4,399,992 shares of common stock that may be issued on the exercise of outstanding warrants at an exercise price of \$5.00 per share.

4,541,925 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 \$9.29 per share.

Approximately 601,092 shares of common stock reserved for future issuance under our equity incentive and employee stock purchase plans.

Table of Contents

RISK FACTORS

The shares of our common stock offered by this prospectus supplement and the accompanying prospectus are speculative and involve a high degree of risk of loss. Before making an investment, you should carefully read this entire prospectus supplement, the prospectus and the information incorporated by reference in them and consider the following risks and speculative factors. 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 very significantly 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 Company and the Industry in Which We Operate

We may not have sufficient financial resources to complete the ongoing Phase 3 clinical benefit trial of Riquent.

We will need to successfully complete the ongoing Phase 3 clinical benefit study of Riquent prior to any FDA or any foreign regulatory approvals. We expect that the ongoing Phase 3 clinical benefit trial will involve approximately 730 patients and take two to three years to complete. We expect that the actual costs of completing the ongoing Phase 3 clinical benefit trial of Riquent will exceed our current cash resources, even after giving effect to the proceeds from this offering. If we expend all of the funds that we have raised, including funds from this offering, and do not receive funding from a collaborative agreement with a corporate partner or obtain other financing, we would not have the financial resources to complete the ongoing Phase 3 clinical benefit trial or to continue the development of Riquent, and it would be difficult or impossible for us to continue to operate.

In order to complete our ongoing clinical trial of Riquent, we will need to enroll a sufficient number of patients who meet the trial criteria. If we are unable to successfully complete the trial, our business will be adversely affected and it may be difficult or impossible for us to continue to operate.

We expect that the ongoing Phase 3 clinical benefit trial of Riquent will involve approximately 730 patients, which is significantly more than were involved in our previous Phase 3 trial. In order to complete this trial, we will need to locate and enroll a sufficient number of patients who meet the criteria for the trial. We may have difficulty enrolling patients because, among other matters, there are specific limitations on the medications that a patient may be taking upon entry into the trial. If we are unable to timely enroll a sufficient number of patients, we will not be able to successfully complete the ongoing trial. As a result, it may be difficult or impossible for us to continue to operate.

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

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. In order to sell any product that is 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 foreign 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 is safe and effective. If Riquent is ultimately not found to be safe and effective, we would be unable to obtain regulatory approval to manufacture, market and sell Riquent. Although we have received an approvable letter from the FDA, the analysis of the data from our earlier Phase 3 trial of Riquent showed that the trial

did not reach statistical significance with respect to its primary endpoint, time to renal flare, or with respect to its secondary endpoint, time to treatment with high-dose corticosteroids or cyclophosphamide. In a preliminary assessment of the MAA,

S-4

Table of Contents

the EMEA reviewers indicated that additional clinical data would be needed prior to potential approval. Based on our review of the EMEA assessment, we believe that the ongoing clinical studies of Riquent should provide the necessary data; however, the data will not be available within the timeframe that the EMEA regulations allow for review of the current Riquent application. Therefore, we decided to withdraw the current application, and plan to refile the MAA after the completion of the ongoing clinical trials if they are successful. We can provide no assurances that the FDA or foreign regulatory authorities will ultimately approve Riquent or, if approved, what the indication for Riquent will be.

As currently designed, our ongoing Phase 3 trial contains multiple dosing levels. Even if the Phase 3 clinical trial is successful, the FDA or foreign regulatory authorities may require additional studies to define dosing recommendations before we can obtain approval to market Riquent.

Because substantially all of our resources are currently being devoted to Riquent, our inability to obtain any regulatory approval of Riquent as a result of the current Phase 3 trial would have a severe negative effect on our business, and, in the future, we may not have the financial resources to continue the development of Riquent or any other potential drug candidates.

We are currently devoting nearly all of our resources to the development and approval of Riquent. Accordingly, our efforts with respect to other drug candidates have significantly diminished.

Future development of our small molecules for the treatment of autoimmune diseases and acute and chronic inflammatory disorders depends on our ability to obtain third party financing for this program including through a joint venture, partnership or other collaborative arrangement. As a result, progress with respect to drug candidates other than Riquent, if any, will be significantly delayed and our success and ability to continue to operate depends on whether we obtain regulatory approval to market Riquent.

Current and future clinical trials may be delayed or halted.

Current and future clinical trials of Riquent, trials of drugs related to Riquent, or clinical trials of other drug candidates may be delayed or halted. For example, in 2005, we limited patient enrollment in our ongoing clinical benefit trial in an effort to reduce costs. In addition, our Phase 2/3 clinical trial of Riquent was terminated before planned patient enrollment was completed. Current and future trials may be delayed or halted for various reasons, including:

- supplies of drug product are not sufficient to treat the patients in the studies;
- patients do not enroll in the studies at the rate we expect;
- we do not have sufficient financial resources;
- the products are not effective;
- patients experience negative side effects or other safety concerns are raised during treatment;
- the trials are not conducted in accordance with applicable clinical practices; or
- there is political unrest at foreign clinical sites or natural disasters at any of our sites.

If any current or future trials are delayed or halted, we may incur significant additional expenses, and our potential approval of Riquent may be delayed, which could have a severe negative effect on our business.

We may be required to design and conduct additional trials for Riquent.

We may be required to design and conduct additional studies to further demonstrate the safety and efficacy of Riquent, 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 current or 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

S-5

Table of Contents

foreign regulatory authorities, the identification of new clinical trial endpoints, or the need for additional data regarding safety or efficacy. It is possible that the FDA or foreign regulatory authorities may not ultimately approve Riquent or our other drug candidates for commercial sale in any jurisdiction, even if we believe future clinical results are positive.

We may experience shortages of Riquent for use in our clinical studies.

We may experience shortages of Riquent for use in our clinical studies. We are implementing a commercial scale manufacturing process for Riquent, but we have only manufactured a limited number of lots of Riquent at this commercial scale. In addition, the drug supply needed for our Phase 3 trial as modified will require us to manufacture significant quantities of Riquent in a compressed time frame. If we are unable to manufacture Riquent in accordance with applicable FDA good manufacturing practices at this commercial scale, or if we incur production delays our ability to timely complete clinical trials of Riquent will be negatively affected.

If we encounter delays or difficulties in establishing or maintaining relationships with manufacturing or distribution contractors, our ability to timely complete necessary clinical trials and potentially deliver commercial products 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 may also enter into agreements with contractors to prepare and distribute our drug candidates for use by patients in clinical trials or commercially. If we encounter delays or difficulties in establishing or maintaining relationships with contractors to produce, package or distribute our drug candidates, 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, our ability to timely complete necessary clinical trials and to introduce our products into the market would be negatively affected.

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

We have never operated a commercial manufacturing facility 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 supply the market on a timely and competitive basis. The sales of our products, if any, and our profit margins may also be negatively affected. In addition, substantial capital investment in the expansion and build-out of our manufacturing facilities and/or the engagement of third party contract manufacturers will be required to enable us to manufacture Riquent, if approved, in sufficient commercial quantities. We have limited manufacturing experience, and we may be unable to successfully transition to commercial production.

Our suppliers may not be able to provide us with sufficient quantities of materials that we 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 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;

S-6

Table of Contents

some of our suppliers may be required to pass FDA inspections or validations or to 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 that they provide us may be costly or in short supply; and

there are 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, our ability to produce products for clinical studies and, therefore, to introduce products into the market on a timely and competitive basis, will be impeded. The subsequent sales of our products, if any, and our profit margins may also be negatively affected.

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.

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

We are highly dependent on the principal members of our scientific and management staff, the loss of whose services may delay the achievement of our research and development objectives. Retaining our current key personnel to perform clinical development, manufacturing, regulatory, and business development activities will be critical to our near term success. We expect that recruiting additional qualified personnel to conduct clinical development, manufacturing, regulatory, business development, and marketing and sales activities will be required to successfully further develop Riquent and any additional drug candidates. Because competition for experienced clinical, manufacturing, regulatory, scientific, business development, and 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, manufacture drug, comply with regulatory requirements, enter into collaborative agreements and develop and sell potential 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 on consultants and advisors to assist us in formulating our clinical, manufacturing, regulatory, business development, and 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.

We will need additional funds to support our operations.

Our operations to date have consumed substantial capital resources. Before we can obtain FDA or foreign regulatory approval for Riquent, we will need to successfully complete the ongoing Phase 3 clinical benefit trial and possibly additional trials. Therefore, we expect to expend substantial amounts of capital resources for additional product development and clinical trials of Riquent. 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. Even with the net proceeds of approximately \$62.3 million from our stock and warrant offering in December 2005 and the proceeds from this offering, we will need additional funds to finance our future operations. Our future capital requirements will depend on many factors, including:

the scope and results of our clinical trials;

our ability to manufacture sufficient quantities of drug to support clinical trials;

S-7

Table of Contents

our ability to obtain regulatory approval for Riquent;

the time and costs involved in applying for regulatory approvals;

continued scientific progress in our development programs;

the size and complexity of our development programs;

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 clinical trial, manufacturing, regulatory, and development activities. If we receive regulatory approval for Riquent, or any of our other drug candidates, our manufacturing, marketing and sales activities are likely to substantially increase our expenses and our need for additional working capital. In the future, it is possible that we will not be able to obtain additional funds and thus not have adequate resources to support continuation of our business activities.

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

Our business is highly cash-intensive and we will need a significant amount of additional cash to continue our operations. There can be no guarantee that additional financing will be available to us on favorable terms, or at all, whether through issuance of additional securities, entry into collaborative arrangements, or otherwise. If adequate funds are not available, we may delay, scale back or halt the ongoing Phase 3 clinical benefit trial of Riquent, reduce the size of our workforce, sell or license our technologies or obtain funds through other arrangements with collaborative partners or others that require us to relinquish rights to our technologies or potential products. We also may 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, any investment in us will be diluted, and dilution can be particularly substantial when the price of our common stock is low.

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 need to collaborate with other pharmaceutical companies to gain access to their financial, research, drug development, manufacturing, or marketing and sales 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 our revenues from potential 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 clinical development, manufacturing, and marketing and sales activities, which accelerates the depletion of our cash and requires us to develop our own manufacturing and 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 will experience a severe adverse effect on our ability to develop products and, if developed and approved, to manufacture, market and sell them successfully.

S-8

Table of Contents

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 Riquent or any of our other 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.

Even if we receive regulatory approval for our product candidates, we will be subject to ongoing regulatory obligations and review, including validation of our manufacturing facilities and processes.

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 cGMPs. 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 significant 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.

Although a successful pre-approval inspection was conducted by the FDA in July 2004, we have never operated a commercial manufacturing facility and we have not yet completed the validation of our manufacturing processes. If we are unable to maintain validated conditions at our manufacturing facilities or fail to successfully validate our manufacturing processes to the satisfaction of the regulatory authorities, they will not approve Riquent for commercial use.

Our drugs may not achieve market acceptance.

Even if Riquent or our other drug candidates receive regulatory approval, patients and physicians may not readily or quickly 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. In our current Phase 3 clinical trial, Riquent is 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 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 or foreign regulatory authorities, 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

S-9

Table of Contents

operations. In addition, if we establish our own sales and distribution capabilities, we will incur material expenses and may experience delays or 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 revenue 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 revenue that we can generate from sales of future products, if any. 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. Moreover, even if Riquent were approved we cannot predict what the dosage requirements or degree of efficacy would be and therefore whether or not healthcare reimbursement policies would enable a sales price that allows us to be profitable.

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 \$299.8 million as of December 31, 2006. We expect to incur substantial losses each year for at least the next several years as we conduct clinical trials of our drug candidates, seek regulatory approval and continue our clinical development, manufacturing, and regulatory activities. In addition, assuming we ultimately receive approval from the FDA or foreign regulatory authorities for Riquent or our other drug candidates, we will be required to establish commercial manufacturing capabilities and marketing and sales 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.

Our success in developing and marketing our drug candidates depends significantly on our ability to obtain patent protection for Riquent 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. We currently own 111 issued patents and 65 pending patent applications in the United States and in foreign countries. These patents and patent applications cover various technologies and drug candidates, including Riquent. There can be no assurance, however, that any additional patents will be issued, that the scope of any patent protection will be sufficient to protect us or our technology, 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. We intend to continue to file patent applications as believed appropriate for patents covering both our products and processes. There can be no assurance that patents

Table of Contents

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 or which may affect our freedom to operate. We are aware of certain families of patents and patent applications that contain claims covering subject matter that may affect our ability to develop, manufacture and sell our products in the future. We have conducted investigations into these patent families to determine what impact, if any, the patent families could have on our continued development, manufacture and, if approved by the FDA, sale of our drug candidates, including Riquent. Based on our investigations to date, we currently do not believe that these patent families are likely to impede the advancement of our drug candidates, including Riquent.

However, there can be no assurance that upon our further investigation, these patent families or other patents will not ultimately be found to impact the advancement of our drug candidates, including Riquent. 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 drug candidates may have a material adverse effect on our business. In addition, we may have to incur significant expenses and management time 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:

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

our confidentiality agreements will be breached, and we may not have, or be successful in obtaining, 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 and devote substantial management time in defending suits that others might bring against us 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. The FDA has not determined that we have proven Riquent to be safe and effective in humans, and the technology on which it is based has been used only in our pre-clinical tests and clinical trials. Clinical trials of Riquent may be viewed as a test of our entire approach to developing therapies for antibody-mediated diseases. If Riquent does not work as intended, or if the data from our clinical trials indicates that Riquent is not safe and effective, the applicability of our technology for successfully 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.

Table of Contents

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 these companies 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. Our competitors may develop or obtain regulatory approval for products more rapidly than we do. If the FDA were to approve a drug that is significantly similar in structure to Riquent for the same indication that Riquent is designed to treat, and such drug received marketing exclusivity under the Orphan Drug Act, the FDA may be prevented from approving Riquent. 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 we are developing, or that would render our technology and proposed products obsolete or noncompetitive.

We may not be able to take advantage of the orphan drug designation for Riquent.

In September 2000, the FDA granted us orphan drug designation for Riquent for the treatment of lupus nephritis. The Orphan Drug Act potentially enables us to obtain research funding and tax credits for certain research expenses. In addition, the Orphan Drug Act allows for seven years of exclusive marketing rights to a specific drug for a specific orphan indication. Exclusivity is conferred upon receipt of marketing approval from the FDA to the first sponsor who obtains such approval for a designated drug. The marketing exclusivity prevents FDA approval during the seven-year period of the same drug, as defined in the FDA regulations, from another company for the same orphan indication. Whether we will be able to take advantage of some of the benefits afforded by the orphan drug designation will ultimately be determined by the FDA only after further review of our NDA.

The use of Riquent or 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 or other potential products may expose us to legal liability and 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. However, product liability insurance is becoming increasingly expensive. In addition, in the event of any commercialization of any of our products, we will likely need to obtain additional insurance, which will increase our insurance expenses. 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 and manufacturing activities, we use radioactive and other materials that could be

S-12

Table of Contents

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

The ownership of our common stock is concentrated.

As of March 15, 2007, our three largest stockholders beneficially owned approximately 46% of our outstanding shares of common stock. Investors who purchase our common stock may be subject to certain risks due to the concentrated ownership of our common stock. For example, the sale by any of our large stockholders of a significant portion of that stockholder's holdings could have a material adverse effect on the market price of our common stock. In addition, two of these stockholders have the ability, either alone or jointly, to appoint four members of our board of directors. Accordingly, these two stockholders, either directly or indirectly, have the ability to significantly influence the outcome of all matters submitted to a vote of our stockholders.

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:

- our clinical trial results;
- actions or decisions by the FDA and other comparable agencies;
- 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 us or our stockholders;
- developments concerning potential agreements with collaborators;
- comments by securities analysts and general market conditions; and
- government regulation, including any legislation that may impact the price of any commercial products that we may seek to sell.

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.

Future sales of our stock by our stockholders could negatively affect the market price of our stock.

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. As of March 15, 2007, there were:

Approximately 32,829,736 shares of common stock that have been issued in registered offerings or were otherwise freely tradable in the public markets.

Approximately 10,769 shares of common stock eligible for resale in the public market pursuant to SEC Rule 144.

S-13

Table of Contents

4,399,992 shares of common stock underlying warrants which have been registered for resale under a Registration Statement on Form S-3.

4,541,925 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 \$9.29 per share.

Approximately 601,092 shares of common stock reserved for future issuance pursuant to awards granted under our equity incentive and employee stock purchase plans, which shares are covered by effective registration statements under the Securities Act of 1933, as amended (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. As of March 15, 2007, there was \$53,937,500 of our common stock available for future issuance.

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 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.

Failure to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and stock price.

Section 404 of the Sarbanes-Oxley Act requires us to evaluate annually the effectiveness of our internal controls over financial reporting as of the end of each fiscal year beginning in 2004 and to include a management report assessing the effectiveness of our internal control over financial reporting in all annual reports beginning with the annual report on Form 10-K for the fiscal year ended December 31, 2004. Section 404 also requires our independent registered public accounting firm to attest to, and report on, management's assessment of our internal control over financial reporting. We evaluated our internal control over financial reporting as of December 31, 2006 in order to comply with Section 404 and concluded that our disclosure controls and procedures were effective as of such date. In addition, our independent registered public accounting firm reported on our assertion with respect to the effectiveness of our internal control over financial reporting as of December 31, 2006. If we fail to maintain the adequacy of our internal controls, as such standards are modified, supplemented or amended from time to time, we cannot provide any assurances that we will be able to conclude in the future that we have effective internal control over financial reporting in accordance with Section 404. If we fail to achieve and maintain a system of effective internal control over financial reporting, it could have a material adverse effect on our business and stock price.

Anti-takeover devices may prevent changes in our board of directors and 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 of such preferred stock could have voting, dividend, liquidation and other rights superior to those of holders of our common stock.

S-14

Table of Contents

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-22. On the date of this prospectus supplement, our authorized capital stock consists of 225,000,000 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 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

S-15

Table of Contents

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 subsequently amended to eliminate the concept of continuing directors in response to a clarification of Delaware law and to permit certain stockholders to acquire more than 15% of our outstanding common stock without triggering the rights agreement by amending 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 December 31, 2006 was \$39.9 million, or approximately \$1.22 per share, based on 32,692,676 shares outstanding as of December 31, 2006. 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 December 31, 2006, other than to give effect to the sale of 5,000,000 shares of common stock offered by us at an assumed public offering price of \$7.26 per share, the last reported sale price of our common stock on the Nasdaq Global Market on March 16, 2007, and after deducting the underwriting discount and estimated offering expenses payable by us, our net tangible book value would have been \$73.8 million, or approximately \$1.96 per share based on 37,692,676 shares outstanding. This represents an immediate increase in net tangible book value of \$0.74 per share to existing stockholders and an immediate dilution in net tangible book value of \$5.30 per share to new investors.

Assumed public offering price per share	\$ 7.26
Net tangible book value per share as of December 31, 2006	\$ 1.22
Increase per share attributable to new investors	\$ 0.74
As adjusted net tangible book value per share after the offering	\$ 1.96
Dilution in net tangible book value per share to new investors	\$ 5.30

This table excludes 4,302,379 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2006 at a weighted average exercise price of \$9.83 per share (1,859,139 were exercisable as of December 31, 2006 and the balance becomes 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.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of our common stock will be approximately \$33.9 million, assuming an offering price of \$7.26 per share, the last reported sale price of our common stock on the Nasdaq Global Market on March 16, 2007, and after deducting the underwriting discount and estimated offering expenses. We intend to use the net proceeds we receive to fund the ongoing clinical trials of Riquent, including the production of drug for the clinical trials, 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 results of our clinical trials, the progress of our research and development efforts and 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.

S-18

Table of Contents

SELECTED FINANCIAL DATA
(in thousands, except per share data)

The consolidated statements of operations and balance sheet data as of and for the years ended December 31, 2004, 2005 and 2006 are derived from our audited consolidated financial statements and related notes which are incorporated by reference into this prospectus supplement. The historical results presented are not necessarily indicative of results to be expected from any future period. The following selected financial data should be read in conjunction with, and is qualified by reference to, Risk Factors included in this prospectus supplement and Management's Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and related notes which are incorporated by reference into this prospectus supplement.

	Fiscal Year Ended		
	December 31, 2004	December 31, 2005	December 31, 2006
Consolidated Statements of Operations Data:			
Expenses:			
Research and development	\$ 33,169	\$ 22,598	\$ 32,938
General and administrative	7,568	5,405	9,287
Loss from operations	(40,737)	(28,003)	(42,225)
Interest expense	(190)	(116)	(46)
Interest income	383	756	2,826
Net loss	\$ (40,544)	\$ (27,363)	\$ (39,445)
Basic and diluted net loss per share	\$ (3.40)	\$ (1.77)	\$ (1.21)
Shares used in computing basic and diluted net loss per share	11,941	15,446	32,588
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	\$ 23,065	\$ 72,877	\$ 42,909
Working capital	\$ 17,539	\$ 70,124	\$ 37,673
Total assets	\$ 33,026	\$ 80,928	\$ 49,525
Noncurrent portion of obligations under capital leases and notes payable	\$ 716	\$ 142	\$ 196
Stockholders' equity	\$ 26,001	\$ 77,130	\$ 43,089

Table of Contents

UNDERWRITING

Needham & Company, LLC is acting as sole bookrunning manager of the offering, and, together with A.G. Edwards & Sons, Inc., are acting as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement, each underwriter named below has agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name.

Underwriter	Number of Shares
Needham & Company, LLC	
A.G. Edwards & Sons, Inc.	
Total	

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares if they purchase any of the shares. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters propose to offer some of the shares directly to the public at the public offering price set forth on the cover page of this prospectus supplement. If all of the shares are not sold at the initial offering price, the representatives may change the public offering price and the other selling terms.

We and our officers and directors and certain stockholders have agreed that, for a period of 90 days from the date of the underwriting agreement, we and they will not, without the prior written consent of Needham & Company, LLC, dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for our common stock, subject to certain exceptions. The exceptions permit our officers and directors to transfer shares of common stock as bona fide gifts, pursuant to previously established 10b5-1 trading plans and as approved by Needham & Company, LLC. Needham & Company, LLC in its sole discretion may release any of the securities subject to these lock-up agreements at any time without notice.

The common stock is quoted on the Nasdaq Global Market under the symbol LJPC.

We have granted the underwriters an option to buy up to 750,000 additional shares of our common stock. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with this offering. The underwriter has 30 days from the date of the prospectus supplement to exercise this option.

The following table shows the per share and total underwriting discounts and commissions we will pay to the underwriters, assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional 750,000 shares.

	No Exercise	Full Exercise
Per share	\$	\$

Total \$ \$

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, syndicate covering transactions and stabilizing transactions. Short sales involve syndicate sales of common stock in excess of the number of shares to be purchased by the underwriters in the offering, which creates a syndicate short position. The underwriters must close out any short sale by purchasing shares in the open market. Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. Stabilizing transactions consist of bids for or purchases of shares in the open market while the offering is in progress.

S-20

Table of Contents

The underwriters also may impose a penalty bid. Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when an underwriter repurchases shares originally sold by that syndicate member in order to cover syndicate short positions or make stabilizing purchases.

Any of these activities may have the effect of preventing or retarding a decline in the market price of the common stock. They may also cause the price of the common stock to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market or in the over-the-counter market, or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

In addition, in connection with this offering, some of the underwriters (and selling group members) may engage in passive market making transactions in the common stock on the Nasdaq Global Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when that limit is reached. Passive market making may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. If the underwriters commence passive market making transactions, they may discontinue them at any time.

We estimate that the total expenses of the offering, excluding the underwriting discount and commissions, will be approximately \$0.3 million.

The underwriters may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business.

This prospectus supplement and the accompanying prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters. The representatives may agree to allocate a number of shares to the underwriters for sale to their online brokerage account holders. The representatives will allocate shares to underwriters that may make Internet distributions on the same basis as other allocations. In addition, shares may be sold by the underwriters to securities dealers who resell shares to online brokerage account holders.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933 and liabilities resulting from any breach by us of the underwriting agreement, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Table of Contents

LEGAL MATTERS

Goodwin Procter LLP of Boston, Massachusetts 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 underwriters by Choate, Hall & Stewart LLP of Boston, Massachusetts.

EXPERTS

The financial statements of La Jolla Pharmaceutical Company appearing in La Jolla Pharmaceutical Company's Annual Report on Form 10-K for the year ended December 31, 2006, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein and incorporated herein by reference. Such 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, or the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, N.E., 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>.

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:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2006;

Our Current Reports on Form 8-K filed with the SEC on February 1, 2007, February 9, 2007, March 8, 2007 and March 20, 2007; and

The description of our capital stock contained in our Registration Statements on Form 8-A, filed on June 2, 1994 and on December 4, 1998, and the post-effective amendments thereto, filed on January 26, 2001, December 12, 2005 and March 1, 2006.

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 and accompanying 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 supplement is accurate as of any date other than the date on the front of this prospectus supplement.

S-22

Table of Contents

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. The forward-looking statements made 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. We undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events. These forward-looking 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. 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, as well as regulatory approvals, which can result in loss of profitability and long delays in getting products to market, and other factors discussed in Risk Factors and elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference.

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	12
USE OF PROCEEDS	14
PLAN OF DISTRIBUTION	15
LEGAL MATTERS	17
EXPERTS	17
FORWARD-LOOKING STATEMENTS	17
WHERE YOU CAN FIND MORE INFORMATION	18

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. However, the amounts expended by us may vary significantly, and it is possible that our cash requirements will exceed current

Table of Contents

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 to us. If we

enter into co-promotion or other marketing and sales arrangements with other companies, any

Table of Contents

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 implement similar government controls. In addition, increasing emphasis on managed care in the United

Table of Contents

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.

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

Table of Contents

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 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

Table of Contents

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 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,

Table of Contents

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.

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

Table of Contents

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.

Table of Contents

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 18. 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.

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,

Table of Contents

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 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 18.

Table of Contents

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.

Table of Contents

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 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

Table of Contents

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.

Table of Contents

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>.

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