Table of Contents

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended **DECEMBER 31, 2002**

OR

[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to_____

Commission file number 0-24274

LA JOLLA PHARMACEUTICAL COMPANY

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**33-0361285**
(State or Other Jurisdiction of Incorporation of Organization)	(I.R.S. Employer Identification No.)

6455 Nancy Ridge Drive, San Diego, CA 92121
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: **(858) 452-6600**

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act: Common Stock, par value $0.01 per share

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes [X] No [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of the Form 10-K or any amendment to this Form 10-K. [ ]

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes [X] No [ ]

The aggregate market value of the common stock of the registrant held by non-affiliates as of June 28, 2002 (the last trading day of the second fiscal quarter) was $264,860,637, based on a closing price of $6.25 on the Nasdaq Stock Market on such date. The number of shares of the registrant's common stock, $.01 par value, outstanding at March 20, 2003 was 42,483,488.

TABLE OF CONTENTS

DOCUMENTS INCORPORATED BY REFERENCE

Part II, Item 5. and Part III of this report incorporate information by reference from the registrant's definitive proxy statement for its annual meeting of stockholders to be held on May 16, 2003, which proxy statement will be filed with the Securities and Exchange Commission no later than 120 days after the close of the fiscal year ended December 31, 2002.

FORWARD-LOOKING STATEMENTS

This report contains forward-looking statements, including without limitation those dealing with La Jolla Pharmaceutical Company's drug development plans and clinical trials. The forward-looking statements in this report involve significant risks and uncertainties, and a number of factors, both foreseen and unforeseen, could cause actual results to differ materially from our current expectations. Forward-looking statements include those which express a plan, belief, expectation, estimation, anticipation, intent, contingency, future development, or similar expression. Although we expect to meet with the regulatory authorities to discuss the results of our Phase III trial of Riquent™, our drug candidate for the treatment of systemic lupus erythematosus ("lupus"), there is no guarantee that a meeting with the regulatory authorities can be held in a timely manner, or at all, or that our meetings with the regulatory authorities will result in us continuing to develop Riquent. Our preliminary analyses of clinical results of Riquent, and LJP 1082, our drug candidate for the treatment of antibody-mediated thrombosis ("thrombosis"), are ongoing and could result in a finding that these drug candidates are not effective in large patient populations, do not provide a meaningful clinical benefit, or may reveal a potential safety issue requiring us to develop new candidates. The clinical results from our recently completed Phase III clinical trial of Riquent are unlikely to be sufficient to obtain regulatory clearance to market Riquent either in the United States or in Europe. We likely will be required to conduct additional clinical studies to demonstrate the safety and efficacy of Riquent before we can seek to obtain marketing approval. There is no guarantee, however, that we will have resources necessary to complete any additional trial, that we will elect to conduct any additional trial, or that any additional trials will sufficiently demonstrate the safety and efficacy of Riquent. Our blood test to measure the binding affinity for Riquent is experimental, has not been validated by independent laboratories, may require regulatory approval, and may be necessary for any approval and commercialization of Riquent. Our other potential drug candidates are at earlier stages of development and involve comparable risks. Analysis of future clinical trials could have negative or inconclusive results. Any positive results observed to date may not be indicative of future results. In any event, the FDA may require additional clinical trials, or may not approve our drugs. Our ability to develop and sell our products in the future may be affected by the intellectual property rights of third parties. Additional risk factors include the uncertainty and timing of: obtaining required regulatory approvals, including delays associated with any approvals we may obtain; the clear need for additional financing; our ability to successfully market any products we may develop; receiving future revenue from product sales or other sources such as collaborative relationships; future profitability; our dependence on patents and other proprietary rights; FDA approval of our manufacturing facilities and processes; the increase in capacity of our manufacturing capabilities for possible commercialization; and our lack of marketing experience. Readers are cautioned to not place undue reliance upon forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect events or circumstances occurring after the date hereof. Interested parties are urged to review the risks described below under the heading "Risk Factors" and elsewhere in this report and in our other reports and registration statements filed with the Securities and Exchange Commission from time to time.

PART I

In this report, all references to "we," "our," and "us" refer to La Jolla Pharmaceutical Company, a Delaware corporation.

Item 1. Business

Overview

La Jolla Pharmaceutical Company was incorporated in Delaware in 1989. We are 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 and antibody-mediated stroke, 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.

Recent Developments

We recently completed a Phase III clinical trial of Riquent™, formerly called LJP 394, our clinical drug candidate for the treatment of lupus renal disease. The results from the Phase III study indicate Riquent appeared to be well tolerated with no apparent differences in the overall incidence of serious adverse events or adverse events between Riquent-treated and placebo-treated patients. However, an initial assessment of the trial data indicates that treatment with Riquent did not increase length of time to renal flare, the primary endpoint, in a statistically significant manner when compared with placebo through the end of the study. There were 298 patients in the intent-to-treat population, 145 on Riquent and 153 on placebo. The intent-to-treat population was comprised of patients with high-affinity antibodies to Riquent. Patients were treated for as long as 92 weeks with a median of 46 weeks.

In the intent-to-treat population, there were fewer renal flares, treatments with HDCC (high-dose corticosteroids and/or cyclophosphamide) and Major SLE (systemic lupus erythematosus or SLE) flares in Riquent-treated patients compared with placebo-treated patients. The estimated median time to renal flare was 123 months in the Riquent-treated group and 89 months in the placebo-treated group. There were 41 renal flares, 17 (12%) in Riquent-treated patients and 24 (16%) in placebo-treated patients. There were 68 treatments with HDCC, 32 (22%) in the Riquent-treated group and 36 (24%) in the placebo-treated group. There were 82 Major SLE flares in the trial, 35 (24%) in patients on Riquent and 47 (31%) in patients on placebo. None of these differences were statistically significant.

There was a statistically significant reduction in antibodies to double-stranded DNA ("dsDNA") in the Riquent-treated group compared with the placebo-treated group ($p<0.001$). Antibodies to dsDNA are believed to result in renal flares and other clinical manifestations of lupus. Riquent was designed to reduce antibodies to dsDNA and this effect has been demonstrated in all clinical studies of Riquent to date.

In the Phase III study, reductions in antibodies to dsDNA strongly correlated with increases in complement C3 levels ($p < 0.001$). Complement C3 levels below normal at baseline (hypocomplementemia) in the Phase III trial strongly correlated with an increased risk of renal flare ($p< 0.001$). Inverse correlations between antibody levels and complement C3 were observed in both the Phase II/III and the Phase III studies

Together, these data confirm the pathogenic nature of these antibodies to dsDNA in lupus patients.

Based on the Phase III trial data analyzed to date, we anticipate that the FDA and European regulatory agencies will likely require us to complete an additional clinical study in order to obtain marketing approval of Riquent. The size, complexity and timing of this study will not be known until after we meet with the agencies to discuss the Phase III results. If the agencies require an additional clinical study, we currently expect to initiate the study before the end of 2003. If any additional study is required, and the study ultimately demonstrates the safety and efficacy of Riquent, marketing approval of Riquent will be delayed for one or more years. To the extent that our development efforts extend beyond the beginning of 2004, we will require additional funding.

Further discussion of the preliminary results of our Phase III trial is contained in this report under the heading “Riquent Clinical Trial History” beginning at page 6.

Antibody-Mediated Diseases

The immune system is the major biological defense mechanism responsible for recognizing and fighting disease. The immune system identifies antigens, such as bacteria, viruses and other disease-causing substances, and seeks to rid the body of these antigens. There are two fundamental types of immune responses: cell-mediated and antibody-mediated. Cell-mediated immunity is primarily responsible for ridding the body of cells that have become infected. Antibody-mediated immunity is primarily responsible for eliminating circulating antigens. These immune responses are controlled by the activities of white blood cells called T cells and B cells. T cells provide cell-mediated immunity and regulate B cells. B cells provide antibody-mediated immunity by producing antibodies that recognize and help to eliminate antigens.

Each B cell produces antibodies against a specific structure on the antigen’s surface called an epitope. The B cell is triggered to produce antibodies when the specific epitope is recognized by and binds to the antibody receptors on the surface of the B cell, and only when the B cell receives an appropriate signal from a T cell. When an epitope binds to the B cell with no corresponding T cell signal, the B cell may become “tolerized” and cease to produce antibodies.

A properly functioning immune system distinguishes between foreign antigens and the body’s healthy tissues. In a malfunctioning immune system, healthy tissue may trigger an immune response that causes B cells to produce disease-causing antibodies, resulting in antibody-mediated autoimmune disease. For example, B cells can produce disease-causing antibodies that are associated with the destruction of the kidneys in lupus and the development of blood clots that can result in stroke, heart attack, deep vein thrombosis and recurrent fetal loss in persons with antibody-mediated thrombosis, also known as Antiphospholipid Syndrome. Other antibody-mediated disorders include the wasting of muscles in myasthenia gravis, organ rejection in xenotransplantation, and Rh hemolytic disease of the newborn.

Many currently available therapies for antibody-mediated diseases have significant shortcomings, including severe side effects and a lack of specificity. Mild forms of antibody-mediated diseases are generally treated with drugs that address only the disease symptoms and fail to suppress disease progression, because such drugs do not control the production of disease-causing antibodies. Severe antibody-mediated diseases like lupus are generally treated with high levels of corticosteroids and immunosuppressive therapy (primarily anti-cancer or chemotherapy drugs and drugs designed to reduce the risk of organ transplant rejection), which broadly suppress the normal function of the entire immune system. These therapies can leave patients susceptible to potentially life-threatening infections that may require hospitalization. Repeated dosing with

corticosteroids may cause other serious conditions, including diabetes, hypertension, cataracts, osteonecrosis and psychosis, and an increased risk of severe infections that may limit the use of this therapy. The use of chemotherapy may lead to acute problems, including weight loss, nausea, an increased risk of severe infections and long-term adverse effects, including sterility and an increased risk of malignancies.

Tolerance Technology®

Our Tolerance Technology program focuses on the discovery and development of proprietary therapeutics, called Toleragens, which target and suppress the production of specific disease-causing antibodies without affecting the protective functions of the immune system. We believe that Toleragens will be able to treat the underlying causes of antibody-mediated diseases, and that our Tolerance Technology may be applied broadly wherever specific antibodies are involved in causing diseases.

Since the 1970s, hundreds of papers have been published by the scientific community describing laboratory studies and a Nobel Prize was awarded for research in tolerance. The underlying science supporting our Tolerance Technology is based on these discoveries as well as on our own patented research.

Toleragens are composed of disease-specific epitopes and a carrier platform, which are proprietary chemical structures that we have developed and synthesized. To mimic the unique epitopes on an antigen's surface, we identify and synthesize epitopes specific to particular antibody-mediated diseases and attach or conjugate these epitopes to the carrier platform, which serves as a vehicle for presenting the epitopes to the antibody receptors on the targeted B cell. When the epitope binds to the antibody receptors on the B cell in the absence of a T cell signal, the B cell may become tolerized and cease to produce disease-causing antibodies.

We design our Toleragens to bind selectively to *disease-causing* B cells without affecting the function of *disease-fighting* B cells. This process involves: collecting and purifying the disease-causing antibodies from patients with the targeted disease; generating and selecting an epitope that strongly binds to the purified antibodies; modifying the epitope's structure to maximize its binding properties while eliminating, if necessary, structures that can activate a patient's T cells (this process is called "optimization"); and linking the optimized epitope to the carrier platform. We believe this process enables us to create Toleragens that will preferentially tolerize and shut down B cells that generate antibodies with the highest binding affinity, and which are believed to be the most harmful.

Business Strategy

Our objective is to become the leading developer of highly specific therapeutics for the treatment of life-threatening antibody-mediated diseases such as lupus, antibody-mediated thrombosis, organ rejection in xenotransplantation, myasthenia gravis, and Rh hemolytic disease of the newborn. Our strategy includes the following key elements:

Complete the analysis of the Phase III data and meet with regulatory agencies. Our primary near-term goal is to complete the analysis of the Phase III data and submit the study results to regulatory agencies in the U.S. and Europe for their review. After which, we expect to meet with these regulatory agencies to review the results of the Phase III trial and with input from the agencies, determine a future development strategy for Riquent. No assurance can be given that we can reach agreements with regulatory agencies regarding the future development of Riquent.

Complete any additional analyses or clinical studies requested by the regulatory agencies. We anticipate that the FDA and European regulatory agencies are likely to require us to complete a second Phase III clinical study in order to obtain marketing approval of Riquent. The size, complexity and timing of this study will not be known until after we meet with the agencies to discuss the Phase III results. If the agencies require an additional clinical study, we expect to initiate the study before the end of 2003. If an additional study is required, and the study demonstrates the safety and efficacy of Riquent as determined by the regulatory agencies, marketing approval of Riquent will be significantly delayed.

Obtain FDA and European regulatory approval of Riquent and initiate commercialization activities. If Riquent is ultimately approved in the U.S., as to which we can provide no assurance, we currently anticipate marketing Riquent ourselves using a small specialty pharmaceutical sales force that can target the rheumatology and nephrology specialists who treat the majority of lupus patients with renal disease. If Riquent is approved in Europe, as to which we can provide no assurance, we currently expect to either market Riquent ourselves or seek a marketing collaboration with a European partner. We believe that the majority of European patients are treated at a limited number of major hospitals, and as is the case in the U.S., that a small specialty pharmaceutical sales force could successfully market Riquent to the physicians at a majority of these sites.

Apply Tolerance Technology to other life-threatening antibody-mediated diseases. We are focusing our development activities on chronic, life-threatening diseases and conditions caused by antibodies, such as antibody-mediated thrombosis, for which there are no existing treatments or for which current therapeutics have significant limitations. We intend to use our Tolerance Technology to design therapeutics that specifically target other antibody-mediated diseases without adversely affecting normal immune system function. Potential development targets include antibody-mediated thrombosis, organ rejection in xenotransplantation, myasthenia gravis, and Rh hemolytic disease of the newborn.

Utilize strategic collaborations to develop and commercialize product candidates. We may seek collaborative relationships with pharmaceutical companies to provide support for some of our early stage research programs, and for the clinical development and commercialization of our drug candidates.

Expand intellectual property position. Currently, we own 98 issued patents and have 92 pending patent applications covering our various technologies and drug candidates, including our Tolerance Technology, our lupus and antibody-mediated thrombosis drug candidates, and our platform and linkage technologies for our Toleragens. We hope to broaden our position with future discoveries and additional patent filings.

Products Under Development

The Lupus Program

Lupus is a life-threatening, antibody-mediated disease in which disease-causing antibodies damage various tissues. According to recent statistics compiled by the Lupus Foundation of America, epidemiological studies and other sources, the number of lupus patients in the United States is estimated to be between 250,000 and 1,000,000, and approximately 16,000 new cases are diagnosed each year. Approximately 9 out of 10 lupus patients are women, who usually develop the disease during their childbearing years. Lupus is characterized by a multitude of symptoms, including chronic kidney inflammation, which can lead to kidney failure, serious episodes of cardiac and central-nervous-system inflammation, as well as extreme fatigue, arthritis and rashes. Approximately 80% of all lupus patients progress to serious symptoms. Approximately 50% of lupus patients have kidney disease.

Antibodies to dsDNA can be detected in approximately 90% of lupus patients who are not receiving immunosuppressive therapy. These antibodies are widely believed to cause kidney disease (nephritis), often resulting in morbidity and mortality in lupus patients. These antibodies are also associated with episodes of potentially life-threatening kidney inflammation — called “renal flares” — that may occur more than once per year and usually require intensive-care hospitalization. Significant kidney destruction occurs during a renal flare. Lupus nephritis can lead to deterioration of kidney function and to end-stage kidney disease, requiring long-term renal dialysis or kidney transplantation to sustain the patient’s life.

Current treatments for lupus patients with kidney disease and other serious symptoms usually include repeated administration of corticosteroids, often at high levels that can have toxic effects when used as a chronic treatment regimen. Many patients with advanced disease are also treated with immunosuppressive therapy, including anti-cancer drugs that have a general suppressive effect on the immune system and may be carcinogenic. This immunosuppressive treatment leaves the patient vulnerable to serious infection and is a significant cause of sickness and death.

We have designed Riquent to suppress the production of antibodies to dsDNA in lupus patients without suppressing the normal function of the immune system. The design of Riquent is based upon scientific evidence of the role of antibodies to dsDNA in lupus. Published studies of lupus patients indicate that a rise in the level of antibodies to dsDNA may be predictive of renal flares in lupus patients with renal involvement, and that suppressing antibodies to dsDNA by treating with corticosteroids prevents relapses in a majority of patients. In a mouse model of lupus nephritis that generates elevated levels of antibodies to dsDNA, administration of Riquent reduced the production of antibodies to dsDNA, reduced the number of antibody-forming cells, reduced kidney disease and extended the life of the animals. We believe that our own and other studies provide evidence that inhibiting antibodies to dsDNA may provide an effective therapy for lupus nephritis.

Some studies of lupus patients indicate that antibodies to dsDNA with the highest binding affinity are associated with the most damage to the kidneys. We believe that Riquent preferentially targets these antibodies.

Riquent Clinical Trial History

Phase I study

Based on our pre-clinical findings, we filed an Investigational New Drug application for Riquent with the FDA in August 1994. In a double-blind, placebo-controlled Phase I clinical trial conducted in December 1994, healthy volunteers received Riquent and displayed no significant drug-related adverse effects and no immune reaction to the drug. Upon completion of our Phase I trial, we began four Phase II clinical trials. Our Phase II clinical trials included a single-dose trial, a repeat dose-escalating trial and two dose-ranging trials.

Phase II studies

In 1994, the single-dose clinical trial was initiated to evaluate the safety of a single, 100 mg intravenous dose of Riquent in four female lupus patients. We monitored antibody levels, blood chemistry, vital signs and complement (inflammation-promoting proteins) levels for 28 days after dosing. Riquent was well tolerated by all four patients, with no drug-related adverse clinical symptoms and no clinically significant complement level changes. In addition, no clinically significant immune complex formation (inflammation-promoting accumulation of antibodies and antigens) was observed, indicating the absence of an adverse immune response to Riquent. A transient reduction in antibodies to dsDNA levels was also observed. These results

were presented at The Annual Scientific Meeting of the American College of Rheumatology in October 1995.

In 1995, a repeat dose-escalating clinical trial was initiated in which two female patients each received doses of 10, 10, 50, 50, 100 and 100 mg of Riquent at two-week intervals. After the 10-week dosing regimen was completed, the patients were followed for six weeks. Riquent was well tolerated by both patients with no drug-related adverse clinical symptoms, no clinically significant complement changes and no significant immune complex formation. Six weeks after the last dose, the antibodies to dsDNA levels in both patients remained suppressed below baseline levels.

In 1995, we conducted our first double-blind, placebo-controlled dose-ranging trial, in which 58 lupus patients (53 females and five males) with mild lupus symptoms were treated for a four-month period with Riquent or placebo, and then were monitored for two months. Patients were enrolled who were clinically stable and had antibodies to dsDNA levels exceeding those generally found in healthy individuals. The patients were organized into nine treatment groups at three dose levels (1 mg, 10 mg and 50 mg), and three frequencies (once per week, once every two weeks and once every four weeks). Patients were randomized to one of the nine treatment groups so that at each dose and frequency, four to seven patients received Riquent and one patient received a placebo.

Patients in the weekly treatment groups showed a dose-response correlation between increasing doses of Riquent and reductions of levels of antibodies to dsDNA. In patients treated weekly with 10 mg or 50 mg doses of Riquent, antibodies to dsDNA were reduced by statistically significant levels and remained suppressed in certain patients for up to two months after the last dose. In the patient group treated weekly with 50 mg, the reductions in median levels of antibodies to dsDNA were accompanied by increases in median levels of two important inflammation-related complement proteins, C3 and C4, which normally increase with clinical improvement and decrease during active lupus renal disease. These study data suggested that complement levels and antibodies to dsDNA levels were normalizing in parallel in the Riquent-treated group.

Throughout this first dose-ranging trial, the drug was well tolerated with no clinically significant dose-related adverse reactions observed. Three patients experienced lupus renal flares, and three other patients were hospitalized as a result of transient adverse events that the treating clinicians believed were unrelated to the underlying disease or to Riquent. Two of the patients with renal flares withdrew from the study, as did four patients who experienced exacerbations of lupus and one patient who experienced a herpes rash. However, no relationship was observed between the development of an adverse event and the dose or the frequency of administration of Riquent.

In 1999, we completed a second double-blind, placebo-controlled dose-ranging trial, in which 74 lupus patients received weekly injections of 10, 50, or 100 mg of Riquent or placebo for a 12-week period. In patients treated weekly with placebo, 10 mg or 50 mg of Riquent, antibodies to dsDNA increased by 100%, 53% and 10%, respectively, while in patients treated weekly with 100 mg of Riquent, antibodies to dsDNA decreased by 43%, a statistically significant difference from placebo. Seven Riquent-treated patients had serious adverse events, but none were considered related to Riquent treatment.

Phase II/III study

In December 1996, we initiated a double-blind, placebo-controlled multi-center Phase II/III clinical trial of Riquent in which patients received Riquent or placebo and were in the trial for up to 18 months. The purpose of this trial was to evaluate the safety of the drug and its

potential to delay or reduce renal flares, to delay or reduce the need for immunosuppressive or corticosteroids and/or chemotherapy drugs and to improve patients' health-related quality of life. More than 200 patients at more than 50 sites in North America and Europe enrolled in the trial which was conducted by Abbott Laboratories ("Abbott") and us as part of our joint development agreement.

In May 1999, an interim analysis of the Phase II/III clinical trial of Riquent indicated that the trial was unlikely to reach statistical significance for the primary endpoint, time to renal flare, and it was decided to stop the study and evaluate the data. Although both the drug- and placebo-treated groups exhibited serious adverse events, there were no statistically significant differences in the number of events in the two groups, indicating the drug was well tolerated. In September 1999, the joint development agreement for Riquent between Abbott and us was terminated.

In November 1999, we announced encouraging initial results from the analysis of the data from the Phase II/III clinical trial showing a certain group of patients treated with Riquent had fewer renal flares and longer time to treatment with HDCC. These results were based on an analysis of the trial using a new blood test that we developed and that appears to predict which patients will respond to drug treatment. Developed in 1998, the blood test measures the strength of the binding between Riquent and a patient's antibodies. Prior to using the blood test in the Phase II/III trial, we used it retrospectively to evaluate patients samples from the 1995 Phase II dose-ranging trial and found that the blood test predicted which patients would respond to drug treatment as measured by changes in antibody affinity following drug treatment.

In May 2000, we completed our analysis after testing more than 99% of the North American patient samples from the Phase II/III clinical trial. The blood test showed that 89% of the patients had high-affinity antibodies to Riquent (high-affinity patients). The high-affinity patients treated with Riquent experienced significantly longer time to renal flare ($p=0.007$), the primary endpoint of the trial, fewer renal flares ($p=0.008$), longer time to treatments with HDCC ($p=0.002$) and fewer exposures to HDCC ($p=0.001$) when compared to the placebo-treated group.

Also in the Phase II/III study, mean levels of circulating antibodies to dsDNA in patients treated with Riquent were reduced by a statistically significant amount relative to placebo during drug treatment. Levels of an important inflammation-related complement protein, C3, improved when antibodies were reduced. In lupus patients, it is generally observed that complement C3 levels decrease during active renal disease and increase with clinical improvement. The concurrent reduction of antibodies to dsDNA and increase in C3 complement levels is biologically consistent. As noted earlier, this effect had been observed in the 1995 Phase II dose-ranging study of Riquent in 58 lupus patients.

The Phase II/III trial design included periods during which patients received no drug for approximately two months (the "off" periods) and weekly doses of 50 mg over three months (the "on" periods). When patients were on drug, mean levels of antibodies to dsDNA decreased. When patients were off drug, mean levels of antibodies to dsDNA increased. During the first four months of the trial, when patients were treated with 100 mg per week, there were nine renal flares in the placebo-treated group and four in the drug-treated group — approximately a 2:1 ratio in favor of drug treatment. Furthermore, in patients with high-affinity antibodies, during the first four months of the trial, there were eight renal flares in the placebo-treated group and only one renal flare in the drug-treated group ($p=0.035$) — an 8:1 ratio in favor of drug treatment.

The results of this Phase II/III clinical trial were published in *Arthritis & Rheumatism,* Vol. 48, No. 2, February 2003, pp. 442-454 by Alarcon-Segovia, D., et al.

In a predefined group of patients with impaired renal function, there were more renal flares in the patients treated with placebo than in the patients treated with Riquent (p=0.046). In a group of patients with poor renal function and with high-affinity antibodies to Riquent, there were six renal flares in 10 patients treated with placebo and zero renal flares in 11 patients treated with drug (p=0.004).

In January 2001, we announced that approximately 90% of patients in each of three previous clinical trials from whom sera specimens were available had high-affinity antibodies to Riquent, prior to drug treatment. The ratios for the trials were: 89% of the 213 patients in the Phase II/III trial, 94% of the 31 patients in the Phase II trial completed in 1996, and 90% of the 60 patients in the Phase II trial completed in 1999. Patients in the Phase II/III trial had moderate to severe disease and a history of renal flares. Patients in the two Phase II trials had mild to moderate disease. Placebo- and drug-treated groups had similar percentages at baseline in each clinical trial. These data suggest that the percentage of high-affinity patients in a larger population of lupus patients may be 90%, but a larger population of patients would need to be evaluated to confirm this result.

The Phase II/III trial also indicated that 70% of the patients in the study with biopsies had World Health Organization Classifications III (focal) or IV (diffuse) proliferative glomerulonephritis and that 83% of patients in our trial who had a renal flare also had a treatment with HDCC and 48% were also hospitalized during the trial. In patients who entered the trial with impaired renal function and who flared, serum creatinine levels worsened significantly and increased from an average of 1.9 mg/dL at baseline to 5.0 mg/dL at final visit.

Additional data from the Phase II/III trial indicated that treatment with Riquent appeared to be as effective as current immunosuppressive therapy in reducing antibodies to dsDNA. Patients on placebo who were treated with HDCC were compared to patients who received Riquent. Following treatment with HDCC, levels of antibodies to dsDNA in 38 patients receiving placebo were reduced within four weeks by a mean of 25%. In 100 patients treated weekly with 100 mg of Riquent, but not HDCC, antibodies to dsDNA were reduced within four weeks by a mean of 36%. In patients requiring HDCC, mean levels of antibodies to dsDNA decreased 37% in 22 patients receiving Riquent treatment compared with 25% in 38 patients receiving placebo. In patients receiving HDCC, the median dose of corticosteroids was 50 mg per day.

Additional data from the Phase II/III trial indicated that treatment with Riquent improved or sustained health-related quality of life in patients with lupus renal disease following 16 weeks of treatment with Riquent and following renal flares, when compared to placebo. Health-related quality of life is a measure of a patient's sense of mental and physical well-being or how he/she feels and was measured by a standard scoring instrument called the SF-36® Health Survey that categorizes results in eight domains. At the beginning of the study, the mean SF-36 scores for all lupus patients were significantly lower in all domains compared with normal individuals in the U.S. of similar age and sex.

In 190 patients with SF-36 measurements, Riquent-treated patients reported a positive trend in their composite mental component score of 1.3, compared with a worsening of –0.8 for patients treated with placebo, a difference of 2.1. The largest mean change occurred in the role-emotional score where the drug-treated patient score improved by +7.7 points while the placebo-treated patient score decreased by –8.1. This was a relative difference of 15.8 and is of a magnitude that is generally believed to be clinically meaningful. The role-emotional assessment represents the patients' perception of limitations they experience in their daily routine attributed to emotional problems.

In 37 patients with SF-36 measurements before and after a renal flare, Riquent-treated patients experienced an improved or stable health-related quality of life in all domains except one, while placebo-treated patients reported worsening in all domains. For example, the mean change in role-emotional score for Riquent-treated patients improved by +2.1 points, compared with placebo-treated patients where it decreased by –20.6 points, a relative difference of 22.7 points. The changes in role-emotional and the mental component summary scores are of a magnitude that is generally believed to be clinically meaningful.

Results from the Phase II/III lupus study suggested three ways to improve the clinical trial design of a Phase III trial: (i) eliminate "off" periods during which patients are not treated with either drug or placebo; (ii) increase the dosing to 100mg per week throughout the study; and (iii) evaluate the drug in the patients with high-affinity antibodies to Riquent.

Phase III study

Based on the observations from our Phase II/III study and following discussions with the FDA, we initiated a Phase III clinical trial in September 2000 to further evaluate the safety and efficacy of Riquent in the treatment of lupus renal disease. The double-blind, placebo-controlled study was conducted at more than 70 sites in North America and Europe and was designed to evaluate the potential of Riquent to delay and reduce the number of renal flares, and delay and reduce the need for treatment with HDCC and/or chemotherapy drugs in patients with high-affinity antibodies to Riquent. Patients in the study were treated with 100 mg per week of either Riquent or placebo for a period of up to 22 months. The study design also eliminated the two-month "off" periods of the Phase II/III trial during which patients were not dosed.

The prospectively defined analysis groups in the Phase III study were the intent-to-treat population of patients with high affinity antibodies to Riquent and high affinity patients with impaired renal function. Patients with impaired renal function were defined as having a serum creatinine level of 1.5 mg/dL to 3.5 mg/dL at baseline. In general, patients with impaired renal function are at greater risk of progressing to renal flare, kidney failure, and dialysis.

The primary endpoint was time to renal flare. A renal flare was defined as a significant, reproducible increase in serum creatinine, urine protein or blood in the urine. The secondary endpoint was time to treatment with HDCC. HDCC was defined as any dose of cyclophosphamide or an increase in prednisone of 15 mg/day or higher resulting in a final dose greater than 20 mg/day.

Other prospectively defined secondary outcomes included time to Major SLE flare, treatment associated maintenance and/or improvement in health-related quality of life, decreases in antibodies to dsDNA and associated increases in complement C3 levels. A Major SLE flare was defined as the occurrence of any one of the following due to manifestations of active SLE: treatment with HDCC or initiation or increase in treatment with other immunosuppressive agents, including azathioprine, mycophenolate mofetil, methotrexate, cyclosporin and leflunomide; or hospitalization or death. This definition of Major SLE flare was designed to capture serious events where patients were treated for manifestations of active SLE as well as renal disease or where treatment, hospitalization or death could have preceded the occurrence of a documented renal flare.

Complement changes were evaluated by determining the mean change from baseline in the complement protein C3 that indicates overall complement consumption due to active inflammation. Antibody changes were evaluated by determining the mean percent change of antibodies to dsDNA from baseline. Patients' assessments of disease activity and health-related quality of life were measured on a regular basis, including at the time of, and 30 days following, a documented renal flare.

In February 2003, we announced preliminary findings from the Phase III clinical trial evaluating Riquent for the treatment of lupus renal disease. We continue to analyze the results from the trial. The study results indicate that Riquent appeared to be well tolerated with no apparent differences in the overall incidence of serious adverse events or adverse events between Riquent-treated and placebo-treated patients. However, an initial assessment of the trial data indicates that treatment with Riquent did not increase length of time to renal flare, the primary endpoint, in a statistically significant manner when compared with placebo through the end of the study. There were 298 patients in the intent-to-treat population, 145 on Riquent and 153 on placebo. Patients were treated for as long as 92 weeks with a median of 46 weeks.

In the intent-to-treat population, there were fewer renal flares, treatments with HDCC and Major SLE flares in Riquent-treated patients compared with placebo-treated patients. The estimated median time to renal flare was 123 months in the Riquent-treated group and 89 months in the placebo-treated group. There were 41 renal flares, 17 (12%) in Riquent-treated patients and 24 (16%) in placebo-treated patients. There were 68 treatments with HDCC, 32 (22%) in the Riquent-treated group and 36 (24%) in the placebo-treated group. There were 82 Major SLE flares in the trial, 35 (24%) in patients on Riquent and 47 (31%) in patients on placebo. None of these differences were statistically significant.

There was a statistically significant reduction in antibodies to dsDNA in the Riquent-treated group compared with the placebo-treated group ($p<0.001$). Antibodies to dsDNA are believed to result in renal flares and other clinical manifestations of lupus. Riquent was designed to reduce antibodies to dsDNA and this effect has been demonstrated in all clinical studies of Riquent to date.

In this study, reductions in antibodies to dsDNA strongly correlated with increases in complement C3 levels ($p < 0.001$). Complement C3 levels below normal at baseline (hypocomplementemia) strongly correlated with an increased risk of renal flare ($p<0.001$). Inverse correlations between antibody levels and complement C3 were observed in the previous Phase II/III study. Together, these data confirm the pathogenic nature of these antibodies to dsDNA in lupus patients.

A review of the study results for time to renal flare and for the increases in antibody levels showed that the Riquent and placebo groups were separating in favor of Riquent until weeks 46 to 48. In the first 46 weeks, 22 of 24 (90%) renal flares occurred in the study in the placebo patients compared with 10 of 17 (59%) in the Riquent-treated patients. At weeks 44, 46, and 48, the incidence of renal flares was 20:10 ($p = 0.085$), 22:10 ($p = 0.041$) and 22:11 ($p = 0.067$), respectively, in favor of Riquent. At weeks 44, 46 and 48, the incidence of renal and/or Major SLE flares was 43:27 ($p=0.057$), 46:28 ($p=0.033$) and 46:29 ($p=0.061$), respectively, in favor of Riquent.

In a prospectively defined subpopulation with impaired renal function at baseline, defined as a serum creatinine □ 1.5 mg/dl at baseline, there were 43 patients, 20 on Riquent and 23 on placebo. Riquent-treated patients had fewer renal flares, treatments with HDCC, and Major SLE flares compared with patients on placebo, but the number of patients was small and the differences were not statistically significant. There were 8 renal flares, 2 (10%) in patients on Riquent and 6 (26%) in patients on placebo. There were 9 treatments with HDCC, 3 (15%) in

patients on Riquent and 6 (26%) in patients on placebo. There were 11 Major SLE flares, 4 (20%) in patients on Riquent and 7 (30%) in patients on placebo. There were 14 renal flares and/or Major SLE flares, 5 (25%) in patients on Riquent and 9 (39%) in patients on placebo. Similar results in the same group were observed for renal flares in a previous Phase II/III study: no renal flares (0%) were observed in the 11 Riquent-treated high-affinity patients compared with 6/11 (55%) of the placebo–treated high-affinity patients. We believe that a delay in time to, or a decrease in, the incidence of renal flares and/or Major SLE flares in this high-risk population would be considered by experts in the lupus field to be medically meaningful.

In addition, the results from this trial appear to support the use of our high-affinity assay to identify patients who may respond to Riquent and also to confirm the high-affinity analysis approach used in the previous Phase II/III study. As the baseline affinity of patients' antibodies for Riquent increased, the number of renal flares declined in the Riquent-treated group compared with the placebo-treated group.

We plan to complete our analysis of the Phase III data and meet with regulatory agencies. The analysis of data from the health-related quality of life survey and patient self-assessment is ongoing. We will continue to collect data in the ongoing open-label follow-on trial. Based on the observed reduction in antibodies to dsDNA, which we believe confirms LJP's Tolerance Technology® approach, we plan at this time to continue our antibody-mediated thrombosis program and evaluate the use of the technology for other diseases, which will depend on the availability of additional funding.

Several observations may help to explain the results from the recent Phase III study. These observations are preliminary and they will all require review by appropriate regulatory agencies and medical experts.

There appears to have been changes in medical practice since the completion of the Phase II/III study as evidenced by a difference in prescribing regimens for immunosuppressive drugs. In particular, it appears there were differences in baseline treatments in the patient population in the Phase III study compared with the previous trial. A higher percentage of patients were receiving immunosuppressive treatments at study entry: 73/145 (50%) in the Riquent-treated group versus 63/153 (41%) in the placebo-treated group in the Phase III study, compared with 35/114 (31%) in the Riquent-treated group versus 40/116 (34%) in the placebo-treated group in the Phase II/III trial. The sample size selected for the Phase III study was based on the Phase II/III study.

In addition, the definition of HDCC may not have captured all of the potential events in this study because the definition did not include some of the newer immunosuppressive drugs that are increasingly used instead of cyclophosphamide. While these newer drugs have a better side effect profile than cyclophosphamide, they are still broadly immunosuppressive.

To account for these observed changes in medical practice, a combined analysis of all patients with either a renal flare and/or a Major SLE flare was performed. The definition of Major SLE flare included increases in corticosteroid doses as well as any new or increased dose of immunosuppressive agents, hospitalization or death, provided they were associated with active SLE. In this combined analysis, there were 88 events, 37 (26%) in Riquent-treated patients and 51 (33%) in placebo-treated patients. Thus, changes in medical practice may have resulted in fewer renal flares because patients were being treated before a renal flare could have been observed or documented.

In addition, it appears that "sicker" patients in the Riquent group stayed in the trial longer than "sicker" patients in the placebo group even though a comparable number of patients discontinued in each group before they met a predefined endpoint in the study (a depletion of

susceptible patients). Reviewing a graph of the results showed that the Riquent and placebo lines for time to renal flare and for the changes in antibody levels were separating until weeks 46 to 48. Upon reviewing patient laboratory values, placebo patients remaining in the study past weeks 44 to 48 appeared to have better renal function, as measured by creatinine clearance at baseline, than the placebo group who were in the study for less than 44 to 48 weeks ($p = 0.024$ at week 48). In the placebo-treated group, those who remained in the study after weeks 44 to 48 showed no mean changes in antibodies to dsDNA from baseline.

All patients who completed the Phase III trial are eligible to enroll in our on-going open-label follow-on clinical trial. Patients in the follow-on open-label trial, which is designed to collect longer-term safety data, will receive weekly treatment with Riquent.

We believe that the high affinity antibody blood test we developed identifies lupus patients who are most likely to respond to Riquent treatment. The FDA and other regulatory agencies may require screening of patients for high affinity antibodies by this test prior to treatment with Riquent. We have filed a patent application on this new blood assay.

In September 2000, the FDA granted us orphan drug designation for Riquent for the treatment of lupus kidney disease. The Orphan Drug Act provides for seven years of marketing exclusivity in the U.S. and enables us to obtain research funding, tax credits for certain research expenses, and a waiver of the application user fees.

In November 2001, the European Commission granted orphan medicinal product designation in the European Union for Riquent on the recommendation of the Committee on Orphan Medical Products. Orphan designation in Europe enables us to receive significant fee reductions for scientific advice, marketing authorization and inspections, and provides 10 years of market exclusivity in the European Union.

The Phase III clinical trial, and the development of Riquent in general, involves many risks and uncertainties, and there can be no assurance that any previous clinical results can be replicated in further clinical testing or that Riquent will be effective in inducing and sustaining antibody suppression; will prove to be clinically safe or effective; will receive required regulatory approvals; or will not require further FDA-mandated clinical testing. If the continued development of Riquent is significantly delayed or produces negative or inconclusive results, our business and financial condition will be adversely affected and it may be difficult or impossible for us to survive. Our blood test to measure the binding affinity for Riquent is experimental, has not been validated by independent laboratories, may require regulatory approval, and may be necessary for any approval and commercialization of Riquent.

Antibody-Mediated Thrombosis, Including Stroke, Heart Attack, Deep Vein Thrombosis and Recurrent Fetal Loss

Researchers believe that antibodies called “antiphospholipid” antibodies promote arterial and venous blood clots, which can cause a variety of recurring and potentially life-threatening medical problems. For example, blood clots that lodge in the brain may cause stroke and those that lodge in the legs may cause deep vein thrombosis. There are multiple conditions associated with these antibodies that we collectively refer to as antibody-mediated thrombosis: antibody-mediated stroke, heart attack, deep vein thrombosis, recurrent fetal loss, and complications following cardiovascular surgery. Our program to develop a Toleragen to treat antibody-mediated thrombosis could be helpful in preventing these problems. We estimate that there are up to 2,000,000 patients in the United States and Europe with antibody-mediated thrombosis.

Stroke is a leading cause of death in the United States. In 2002, there were approximately 4,000,000 stroke patients in the United States and approximately 750,000 new episodes will

occur. In 2002, approximately 160,000 people died from stroke. This debilitating condition results from acute neurological injury caused by the blockage or rupture of blood vessels in the brain. Many of the blockages are caused by thromboses, or blood clots, which many clinicians believe may be caused by a number of factors, including antiphospholipid antibodies. It is estimated that these antibodies cause about 10% of the strokes in the United States (thereby affecting about 200,000 to 400,000 patients). Antibody-mediated stroke is thought to occur in younger individuals and with greater frequency than non-antibody-mediated stroke. The cost of treatment to provide hospitalization and home nursing care for a survivor of a serious stroke is approximately $30,000 per year for life.

Antibody-mediated thrombosis is also associated with recurrent fetal loss, a syndrome of repeated miscarriage. Published clinical reports estimate that many women with elevated antiphospholipid antibody levels experience multiple miscarriages, delayed fetal development or premature childbirth. Recent academic research suggests that elevated levels of these antibodies are also found in approximately 10 to 30% of patients with other clotting disorders, including myocardial infarction (heart attack), deep vein thrombosis and cardiac valve lesion, as well as in approximately 30% of lupus patients. In myocardial infarction, recent research suggests the relative risk of a thrombotic event or death is approximately twice as high in people with high antiphospholipid antibodies, and this risk is independent of other risk factors. In deep vein thrombosis, research indicates antiphospholipid antibody-positive patients have recurring deep vein thromboses about twice as often as antiphospholipid antibody-negative patients.

Current treatments for antibody-mediated thrombosis involve the use of chronic, potentially life-long anticoagulant therapy with drugs such as heparin or warfarin to prevent the formation of blood clots. Patients must be carefully monitored to minimize serious bleeding episodes that can occur because of the therapy. If patients are removed from anticoagulant therapy, they are at an increased risk of stroke or another thrombotic episode. Warfarin is not recommended in the treatment of recurrent fetal loss because it is toxic to the developing fetus.

We believe that a Toleragen to treat antibody-mediated thrombosis would be a major step forward in specifically targeting the cause of this clotting disorder, thereby minimizing or avoiding the side effects of current therapies.

Our research supports the finding that specific antibodies in antibody-mediated thrombosis enhance blood-clot formation by interfering with the natural breakdown of a blood component — Factor Va — that accelerates clotting. The true target of these clot-promoting antibodies is not cardiolipin, but a region on a blood protein called beta 2-glycoprotein I (“2 GPI”). To date, our scientists have shown that approximately 90% of patients studied with antibody-mediated thrombosis have antibodies that bind to this region. The identification of a disease target for antibody-mediated thrombosis has allowed us to begin building new drug candidates that bind to these antibodies with high affinity and are designed to tolerize, or shut down, the B cells that produce them.

We have synthesized a family of candidate antibody-mediated thrombosis Toleragens for testing. We have also developed a mouse model of the disease, where the animals produce antibodies to beta 2 GPI and develop a clotting defect similar to that seen in patients with antibody-mediated thrombosis. In this animal model, several candidate molecules have been shown to reduce the production of pathogenic antibodies, a key step in the development of a drug to treat this disorder.

LJP 1082 Clinical Trial History

In July 2000, we selected LJP 1082 as our clinical drug candidate for the treatment of antibody-mediated thrombosis. Based on positive pre-clinical results in mice, rats, and primates,

we chose this candidate for toxicology studies required for the filing of an Investigational New Drug application. In September 2000, at the 9th International Symposium on Antiphospholipid Antibodies in Tours, France, we presented positive results that showed LJP 1082 reduced disease-causing antibodies and the B cells involved in antibody-mediated thrombosis in an animal model of the disease.

In September 2001, we announced that we had filed an Investigational New Drug application with the FDA to begin a Phase I/II clinical trial of LJP 1082. In November 2001, we announced the initiation of the Phase I/II clinical trial. The objective of the study was to evaluate the safety of LJP 1082 and its ability to reduce disease-causing antibody levels in patients with antibody-mediated thrombosis. The Phase I/II trial was a randomized, placebo-controlled dose escalating study designed to evaluate the safety and activity of a single dose of LJP 1082 in a small group of patients. In the Phase I/II trial, five different groups, each consisting of four or five patients, were treated with a single intravenous dose of LJP 1082 of 1, 3, 10, 50 or 200 mg and then monitored for 30 days. One patient in each group received placebo. In order to participate in the trial, patients were required to have elevated levels of antibodies to beta 2 GP1, the target of the antibodies involved in antibody-mediated thrombosis.

In October 2002, we announced preliminary results from the Phase I/II clinical trial. Based on an initial assessment of the trial data, the drug appeared to be well tolerated at the five dose levels used in the study. LJP 1082 had an elimination half-life of at least 12 hours following intravenous administration. Following treatment with a single 50 mg or 200 mg dose, antibodies to LJP 1082 were reduced in some patients. In total, 20 patients with a history of antibody-mediated thrombosis participated in the trial period. Even though there were a small number of patients in the study, there was an apparent dose-dependent response following drug treatment. Patients receiving higher doses of LJP 1082 had larger reductions in antibodies. In the 50 mg and 200 mg treatment groups, there was an apparent correlation between the level of reduction and the affinity of the patient's antibodies for drug.

Standard safety assessments including physical exams, lab values and vital signs, and immunology specific measurements were taken during the 30 days following a single dose of LJP 1082. All adverse events observed were categorized as mild to moderate and were deemed to have no or an unlikely relationship to LJP 1082. The adverse event profiles appeared similar between drug-treated and placebo-treated groups. There were no serious adverse events. We observed no significant increase in circulating immune complexes, changes in complement protein C_3 or activation of patient T cells following drug treatment.

This study is the first of several that may be required to establish appropriate dose regimens and the observed reductions may not be large enough to affect patient health or reduce antibodies to beta 2 GP1 in a majority of patients. Additional analyses are ongoing. Potential drug interference in some of the antibody assays is also being evaluated. This study was not designed to evaluate the ability of LJP 1082 to tolerize B cells that produce antibodies to beta 2 GP1 and additional studies will be needed for this purpose.

Other Antibody-Mediated Diseases

We believe our Tolerance Technology may be applicable to additional diseases and conditions caused by the production of disease-causing antibodies, including xenotransplantation, myasthenia gravis and Rh hemolytic disease occurring in newborns.

Xenotransplantation, the use of animals as a source of donor organs for human transplantation, has become an area of great interest due to the worldwide shortage of human organs available for transplantation. According to the American Society of Transplant Physicians, approximately 100,000 patients in the United States are on waiting lists for organ transplants.

More than 5,000 patients die annually, many of who are too sick to qualify for waiting lists. A typical organ transplant can cost more than $100,000.

Hyper acute rejection, or the immediate destruction of the transplanted animal organ by the recipient's antibodies, is a major barrier to xenotransplantation. Human antibodies recognize and bind to an epitope called alpha galactose found on the tissues of transplanted animal organs. This binding causes massive blood clots that block the blood supply to the transplanted organ, destroying it within minutes.

Myasthenia gravis is a form of muscular paralysis in which neuromuscular receptors are attacked by antibodies, which can lead to a wasting of muscles, progressive loss of strength and life-threatening respiratory arrest. This disease affects an estimated 20,000 people in the United States.

Rh hemolytic disease of the newborn is a life-threatening fetal condition characterized by the hemolysis, or destruction, of fetal red blood cells. This condition occurs in Rh-incompatible pregnancies in which maternal antibodies to Rh cross the placenta, bind to fetal red blood cells and cause their destruction. Each year approximately 500,000 women in the United States have Rh-incompatible pregnancies. We believe that a Toleragen that binds to the appropriate maternal B cells will suppress Rh antibody production, and that once the level of antibodies to Rh(+) red blood cells is reduced, the risk of life-threatening hemolysis will be reduced.

Collaborative Arrangements

As part of our business strategy, we attempt to pursue collaborations with pharmaceutical companies in an effort to access their research, drug development, manufacturing, marketing and financial resources. In December 1996, we entered into a collaborative relationship with Abbott for the worldwide development and commercialization of Riquent. This agreement was terminated in September 1999 following the initial analysis of the Phase II/III lupus trial, and all rights to Riquent were returned to us.

Concurrent with the formation of the collaborative relationship, Abbott made an initial $4.0 million license payment to us and purchased a total of 3,369,604 shares of our common stock in December 1996, September 1997 and October 1998, with gross proceeds of $4.0 million to us on each purchase date. Under the collaborative agreement, Abbott paid us a total of approximately $23.2 million for the research and development costs we incurred in connection with the development of Riquent from 1997 through 1999.

We intend to pursue collaborative arrangements with other pharmaceutical companies to assist in our research programs and the clinical development and commercialization of our drug candidates. There can be no assurance that we will be able to negotiate arrangements with any collaborative partner on acceptable terms, if at all. Once a collaborative relationship is established, there can be no assurance that the collaborative partner will continue funding any particular program or will not pursue alternative technologies or develop alternative drug candidates, either individually or in collaboration with others, including our competitors, as a means for developing treatments for the diseases we have targeted. Furthermore, competing products, either developed by a collaborative partner or to which a collaborative partner has rights, may result in the withdrawal of support by the collaborative partner with respect to all or a portion of our technology.

Failure to establish or maintain collaborative arrangements will require us to fund our own research and development activities, resulting in accelerated expenditure of capital, and will require us to develop our own marketing capabilities for any drug candidate that may receive regulatory approval. The failure of any collaborative partner to continue funding any particular

program of ours, or to commercialize successfully any product, could delay or halt the development or commercialization of any products involved in such program. As a result, failure to establish or maintain collaborative arrangements could hurt our business, financial condition and results of operations.

Manufacturing

We have constructed and are currently operating a production facility that we believe provides sufficient capacity to exceed our anticipated requirements for research, clinical trial, and any initial commercial launch of Riquent. If we were to launch the sale of Riquent, we expect to have the capacity to manufacture approximately 100kgs of Riquent per year. Based on our current projections, we believe this would be enough product to treat approximately 20,000 patients per year. Through internal development programs and external collaborations, we have made several improvements to the manufacturing process for Riquent that have reduced our costs and increased our manufacturing capacity. We have developed proprietary synthesis and conjugation technologies that are being used in the development of our other Toleragen candidates. We intend to further develop these technologies in order to increase our manufacturing efficiencies and apply our knowledge to the development and manufacture of other potential products. There are currently a limited number of suppliers which produce raw materials or the DNA components for Riquent.

While we believe that our current production facility will provide sufficient capacity if we were to launch the sale of Riquent, we believe additional capacity would be required to meet additional potential demand in the marketplace at sometime in the future. Following any launch, we would plan to increase capacity through process improvements and scale-up, use of contract manufacturers, and additional capital investments in the expansion of our facilities. The manufacture of our potential products for clinical trials and the manufacture of any resulting products for commercial purposes are subject to current Good Manufacturing Practices, as defined by the FDA. We have never operated an FDA-approved manufacturing facility, and there can be no assurance that we will obtain the necessary approvals to manufacture our products. We have limited manufacturing experience, and no assurance can be given that we will be able to make the transition to commercial production successfully. We may enter into arrangements with contract manufacturers to expand our own production capacity in order to meet requirements for our products or to attempt to improve our manufacturing efficiency. If we choose to contract for manufacturing services and encounter delays or difficulties in establishing relationships with manufacturers to produce, package and distribute finished products, clinical trials, market introduction and subsequent sales of such products would be adversely affected. Contract manufacturers must also operate in compliance with the FDA's manufacturing requirements. Our potential dependence upon others for the manufacture of our products may adversely affect our profit margins and our ability to develop and deliver such products on a timely and competitive basis.

Marketing and Sales

If we obtain FDA approval in the U.S., we currently anticipate that we would market Riquent ourselves using a small specialty pharmaceutical sales force of 40-50 representatives who can target the rheumatology and nephrology specialists who treat the majority of lupus patients with renal disease. We estimate that the majority of these patients are treated at approximately 300 major centers and that 80-90% of these patients are treated at approximately 1,000 clinical centers. If we obtain approval in Europe, we currently expect to market Riquent ourselves or seek a marketing collaboration with a European partner. We believe that the majority of European patients are treated at 200 to 300 major hospitals and, as is the case in the U.S., that a small specialty pharmaceutical sales force could successfully market Riquent to the majority of these sites.

In order to commercialize Riquent in Europe through a partner, we would need to enter into marketing arrangements with other pharmaceutical or biotechnology companies. These collaborative arrangements may be exclusive or nonexclusive and may provide for marketing rights throughout Europe or only in certain countries. We currently have no arrangements with others for the marketing of any of our drug candidates. There can be no assurance that we will be able to enter into any marketing agreements on favorable terms, if at all, or that any such agreements that we may enter into will result in payments to us. Under any co-promotion or other marketing and sales arrangements that we may enter into with other companies, any revenues that we may receive will be dependent on the efforts of others and there can be no assurance that such efforts will be successful.

To the extent that we choose to attempt to develop our own marketing and sales capability (whether domestic or international), we will compete with other companies that currently have experienced and well-funded marketing and sales operations. Furthermore, there can be no assurance that any collaborative partner or we will be able to establish sales and distribution capabilities without undue delays or expenditures, or gain market acceptance for any of our drug candidates. The ultimate size of the markets for our products is uncertain and difficult to estimate prior to approval. Moreover, we may not earn as much income as we hope due to possible changes in healthcare reimbursement policies by governments and other third party payers.

Patents and Proprietary Technologies

We file patent applications in the United States and in foreign countries for the protection of our proprietary technologies and drug candidates as we deem appropriate. We currently own 98 issued patents and have 92 pending patent applications and 1 allowed application covering various technologies and drug candidates, including our Tolerance Technology, our lupus and antibody-mediated thrombosis drug candidates (Toleragens), and our carrier platform and linkage technologies for our Toleragens. Our issued patents include:

- four issued United States patents, one issued Australian patent, one granted Portuguese patent, one granted Norwegian patent, one granted European patent (which has been unbundled as 13 European national patents), two granted Canadian patents, one granted Finnish patent and one granted Irish patent concerning our lupus Toleragens (expiring in 2010, 2011, 2013, 2014, 2007, 2013, 2011, 2011, 2011, 2011, 2011 and 2011, respectively);

- two issued United States patents, one issued Australian patent, one granted European patent (which has been unbundled as 15 European national patents), one granted Japanese patent, one granted Canadian patent, one granted South Korean patent and one granted Irish patent concerning our Tolerance Technology (expiring in 2011, 2011, 2008, 2012, 2012, 2012, 2012, and 2012, respectively);

- seven issued United States patents, five issued Australian patents, one granted European patent (which has been unbundled as 15 European national patents), two issued Japanese patents, one granted Hong Kong patent, one granted Portuguese patent and one granted South Korean patent concerning carrier platform and linkage technologies for our Toleragens (expiring in 2012, 2014, 2015, 2015, 2015, 2016, 2019, 2014, 2014, 2012, 2012, 2017, 2012, 2012, 2012, 2012 2014, and 2014, respectively); and

- two issued United States patents and one issued Australian patent concerning our antibody-mediated thrombosis drug candidates (expiring in 2016, 2015 and 2016, respectively).

We have received a Notice of Allowance from the Canadian Patent Office for a patent application for our Tolerance Technology.

Competition

The biotechnology and pharmaceutical industries are subject to rapid technological change. Competition from domestic and foreign biotechnology companies, large pharmaceutical companies and other institutions is intense and expected to increase. A number of companies are pursuing the development of pharmaceuticals in our targeted areas. These include companies that are conducting clinical trials and pre-clinical studies for the treatment of lupus, thrombosis and other antibody-mediated diseases.

In addition, there are many academic institutions, both public and private, engaged in activities relating to the research and development of therapeutics for autoimmune, inflammatory and other diseases. Most of these companies and institutions have substantially greater facilities, resources, research and development capabilities, regulatory compliance expertise, and manufacturing and marketing capabilities than we do. In addition, other technologies may in the future be the basis of competitive products. There can be no assurance that our competitors will not develop or obtain regulatory approval for products more rapidly than we can, or develop and market technologies and products that are more effective than those being developed by us or that would render our technology and proposed products obsolete or noncompetitive.

We believe that our ability to compete successfully will depend upon our ability to attract and retain experienced scientists, develop patented or proprietary technologies and products, obtain regulatory approvals, manufacture and market products either alone or through third parties, and secure additional capital resources to fund anticipated net losses for at least the next several years. We expect that competition among products approved for marketing will be based in large part upon product safety, efficacy, reliability, availability, price and patent position.

Government Regulation

Our research and development activities and the future manufacturing and marketing of any products we develop are subject to significant regulation by numerous government authorities in the United States and other countries. In the United States, the Federal Food, Drug and Cosmetic Act and the Public Health Service Act govern the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising and promotion of any products we may develop. In addition to FDA regulations, we are subject to other federal, state and local regulations, such as the Occupational Safety and Health Act and the Environmental Protection Act, as well as regulations governing the handling, use and disposal of radioactive and other hazardous materials used in our research activities. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources. In addition, this regulatory framework is subject to changes that may adversely affect approval, delay an application or require additional expenditures.

The steps required before a pharmaceutical compound may be marketed in the United States include pre-clinical laboratory and animal testing; submission to the FDA of an Investigational New Drug application, which must become effective before clinical trials may commence; adequate and well-controlled clinical trials to establish the safety and efficacy of the drug; submission to the FDA of a New Drug application; and FDA approval of the New Drug application prior to any commercial sale or shipment of the drug. In addition to obtaining FDA

approval for each product, each domestic drug-manufacturing establishment must be registered with, and approved by, the FDA. Drug product manufacturing establishments located in California also must be licensed by the State of California in compliance with separate regulatory requirements.

Pre-clinical testing includes laboratory evaluation of product chemistry and animal studies to assess the safety and efficacy of the product and its formulation. The results of pre-clinical testing are submitted to the FDA as part of an Investigational New Drug application and, unless the FDA objects, the Investigational New Drug application becomes effective 30 days following its receipt by the FDA.

Clinical trials involve administration of the drug to healthy volunteers or to patients diagnosed with the condition for which the drug is being tested under the supervision of a qualified clinical investigator. Clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor safety, and the efficacy criteria to be evaluated. Each protocol is submitted to the FDA as part of the Investigational New Drug application. Each clinical trial is conducted under the auspices of an independent Institutional Review Board. The Board considers, among other matters, ethical factors, the safety of human subjects and the possible liability of the clinical institution.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the phase in which the drug is initially introduced into healthy human subjects, the drug is tested for adverse effects, dosage tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase II trials involve the testing of a limited patient population in order to characterize the actions of the drug in targeted indications, to determine drug tolerance and optimal dosage, and to identify possible adverse side effects and safety risks. When a compound is found to be effective and to have an acceptable safety profile in Phase II clinical trials, Phase III clinical trials are undertaken to further evaluate and confirm clinical efficacy and safety within an expanded patient population at multiple clinical trial sites. The FDA reviews the clinical plans and monitors the results of the trials and may discontinue the trials at any time if significant safety issues arise.

The results of pre-clinical testing and clinical trials are submitted to the FDA in the form of a New Drug application or Product License application for marketing approval. The testing and approval process is likely to require substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all. The approval process is affected by a number of factors, including the severity of the disease, the availability of alternative treatments and the risks, and benefits demonstrated in clinical trials.

Additional pre-clinical testing or clinical trials may be requested during the FDA review period and may delay any marketing approval. After FDA approval for the initial indications, further clinical trials may be necessary to gain approval for the use of the product for additional indications. The FDA mandates that adverse effects be reported to the FDA and may also require post-marketing testing to monitor for adverse effects, which can involve significant expense.

Among the conditions for FDA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to the FDA's current Good Manufacturing Practices requirements. Domestic manufacturing facilities are subject to biannual FDA inspections and foreign manufacturing facilities are subject to periodic inspections by the FDA or foreign regulatory authorities.

We are also subject to numerous and varying foreign regulatory requirements governing the design and conduct of clinical trials and marketing approval for pharmaceutical products to be marketed outside of the United States. The approval process varies among countries and can

involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. The foreign regulatory approval process includes all of the risks associated with obtaining FDA approval, and approval by the FDA does not ensure approval by the health authorities of any other country.

Employees

As of March 18, 2003 we employ 156 full-time employees (including 21 people who have a Ph.D. and two people who have an M.D.), 96 of whom are involved full-time in research, development and manufacturing activities. All of our management has had prior experience with pharmaceutical, biotechnology or medical product companies. We believe that we have been successful in attracting skilled and experienced personnel, but competition for personnel is intense and there can be no assurance that we will be able to attract and retain the individuals needed. None of our employees is covered by collective bargaining agreements and management considers relations with our employees to be good.

Executive Officers of the Registrant

Our executive officers and key employees and their ages are set forth below.

Name	Age	Title
Steven B. Engle	48	Chairman of the Board and Chief Executive Officer
David Duncan, Jr.	54	Chief Financial Officer
Matthew D. Linnik, Ph.D.	43	Chief Scientific Officer, Executive Vice President of Research and Assistant Secretary
Kenneth R. Heilbrunn, M.D.	45	Vice President of Clinical Development
William J. Welch	41	Vice President of Sales and Marketing
Paul C. Jenn, Ph.D.	52	Vice President of Product Development
Bruce K. Bennett, Jr.	51	Vice President of Manufacturing
Karen K. Church, R.A.C	57	Vice President of Regulatory Affairs
Theodora Reilly	53	Vice President of Human Resources
Andrew Wiseman, Ph.D.	54	Senior Director of Business Development and Investor Relations
Gail A. Sloan, CPA	40	Senior Director of Finance, Controller and Secretary

Steven B. Engle, Chairman of the Board and Chief Executive Officer, joined the Company in 1993 as Executive Vice President and Chief Operating Officer. He assumed the offices of President, Director and Secretary in 1994, became Chief Executive Officer in 1995, and Chairman of the Board in 1997. From 1991 to 1993, Mr. Engle served as Vice President of Marketing at Cygnus Inc., a publicly held company that develops drug-delivery systems for

therapeutic drugs, including Nicotrol®, a smoking cessation transdermal patch. From 1987 to 1991, he was Chief Executive Officer of Quantum Management Company, a privately held management consulting firm serving the pharmaceutical and other industries. From 1984 to 1987, he was Vice President of Marketing and Divisional General Manager for Micro Power Systems, Inc., a privately held company that manufactures high technology products, including medical devices, which was acquired by Exar Corporation. From 1979 to 1984, he was a management consultant at Strategic Decisions Group and SRI International where he advised pharmaceutical, high technology and other companies. Mr. Engle is a member of the Board of the Lupus Foundation of America and is a former Chairman of BIOCOM, a regional trade association for the biotechnology and medical devices industries. Mr. Engle holds an M.S.E.E. and a B.S.E.E. with a focus in biomedical engineering from the University of Texas.

David Duncan, Jr., Chief Financial Officer, joined the Company in October 2002. Prior to joining the Company, Mr. Duncan served as Vice President of Finance and Chief Financial Officer of Medinox, Inc., a privately held pharmaceutical company, from December 2000 through October 2002. From August 1998 through October 2000, Mr. Duncan served as Vice President of Finance and Chief Financial Officer of Tanox, Inc., a publicly held biotechnology company and from 1994 to March 1998 he served as Chief Financial Officer at Neuromedical Systems, Inc., a privately held medical device company which filed a voluntary petition for bankruptcy under Chapter 11 of the U.S. bankruptcy code on March 26, 1999. From 1988 to 1994, Mr. Duncan served as Chief Financial Officer at Telios Pharmaceuticals, Inc., a publicly held pharmaceutical company, and from 1983 to 1988, he served as the Controller at Hybritech Incorporated, a publicly held medical diagnostic company. Mr. Duncan received an M.B.A. from Indiana University.

Matthew D. Linnik, Ph.D., Chief Scientific Officer, and Executive Vice President of Research, joined the Company in 1998 as Director of Research and Development, was promoted to Vice President of Research in February 1999, to Executive Vice President of Research in June 1999 and to Chief Scientific Officer and Executive Vice President of Research in 2002. Prior to joining the Company, from 1989 to 1998, Dr. Linnik served as Senior Pharmacologist, Scientist, Research Scientist and Project Leader for Hoechst Marion Roussel, formerly Marion Merrell Dow and Marion Laboratories, a publicly held pharmaceutical company. From 1996 to 1998, he also served as Adjunct Associate Professor of Neurosurgery at the University of Cincinnati School of Medicine. From 1986 to 1988, he served as Postdoctoral Fellow, then Instructor, in the Departments of Neurology and Neurosurgery at Massachusetts General Hospital and Harvard Medical School. Dr. Linnik holds a B.A. in Physiology from Southern Illinois University and a Ph.D. in Physiology and Pharmacology from Southern Illinois University School of Medicine.

Kenneth R. Heilbrunn, M.D., Vice President of Clinical Development, joined the Company in June 2002. Prior to joining the Company, from 1998 to 2002, he progressed to Vice President of Clinical Research at Advanced Tissue Sciences, a publicly held tissue engineering company, where he was responsible for the multicenter Phase III clinical trial leading to the FDA approval of Dermagraft®, a bioengineered human tissue. From 1997 to 1998, Dr. Heilbrunn served as Vice President of Medical Affairs at Hepatix, a privately held manufacturer of organic-hybrid technologies engaged in the development bioengineered liver technology. From 1994 to 1996, he served as Staff Vice President of Medical Affairs at C.R. Bard, a publicly held manufacturer of healthcare products. From 1989 to 1994, he served as Medical Affairs Director for Cardiovascular and Pulmonary Drugs at Ciba-Geigy Pharmaceuticals Division, a manufacturer of health-care products, where he participated in the launch of the nicotine patch, Habitrol®, and the antihypertensive drug, Lotensin®. From 1986 to 1989, Dr. Heilbrunn served as Staff Internist and Director of the Critical Care unit at the 31st Tactical Air Force Hospital. Dr. Heilbrunn completed his residency in internal medicine at Baystate Medical Center in Springfield,

Massachusetts after receiving his M.D. from New York Medical College and his B.A. from Brown University.

William J. Welch, Vice President of Sales and Marketing, joined the Company in 1998 as Vice President of Business Development. He rejoined the Company in 2001 as Vice President of Marketing and was promoted to his current position in 2002. Prior to rejoining the Company, Mr. Welch was Vice President of Global Marketing at Dade Behring, a privately held global diagnostic company. From 1993 until 1998, Mr. Welch worked for Abbott Laboratories, a publicly held global healthcare company, as General Manager of Abbott Ambulatory Infusion Systems, Senior Marketing Manager of Abbott Renal Care and as Manager of Strategic Planning, Corporate Planning and Development. From 1991 to 1993, Mr. Welch was Director of Business Development for In-Process Technology, a privately held company that manufactured processing systems for the pharmaceutical industry. From 1989 to 1991, Mr. Welch was Senior Associate for D'Accord Inc., a global investment banking company. Mr. Welch holds a B.S. in Chemical Engineering from the University of California, Berkeley and an M.B.A. from Harvard University.

Paul C. Jenn, Ph.D., Vice President of Product Development, joined the Company in 1994 as Associate Director of Production and Process Development. Dr. Jenn was promoted to Director of Operations in 1999, Senior Director of Operations in 2000, Vice President of Operations in 2001, and Vice President of Product Development in 2002. Prior to joining the Company, from 1992 to 1994, Dr. Jenn was Director of Peptide Manufacturing at Telios Pharmaceuticals, Inc., a publicly held pharmaceutical company, and held several other positions. From 1988 to 1992, he served as Senior Research Associate at Mallinckrodt Specialty Chemicals, a publicly held specialty chemical company. From 1984 to 1988, Dr. Jenn served as a Research Scientist at International Minerals and Chemical Corp., a public chemical company. From 1982 to 1984, he performed his post-doctoral research at the Lawrence Berkeley Laboratory at the University of California at Berkley. Dr. Jenn holds a B.S. in Chemistry from Fu-Jen Catholic University, Taipei, Taiwan and a Ph.D. in Chemistry from State University of New York at Buffalo.

Bruce K. Bennett, Jr., Vice President of Manufacturing, joined the Company in January 2002. Prior to joining the Company, from 2000 to 2001, Mr. Bennett was Vice President of Operations at Provasis Therapeutics, Inc., a privately held medical device company. From 1997 to 2000, he served as Vice President of Operations, Regulatory Affairs/Quality Assurance and Commercial Development at VIA Medical Corporation, a privately held medical device company. From 1995 to 1996, he was Vice President of Manufacturing at Mulay Plastic, Inc., a privately held injection molding company. From 1992 to 1995, Mr. Bennett served as Vice President of Operations at Cygnus Therapeutic Systems, Inc., a publicly held company that develops drug-delivery systems for therapeutic drugs. From 1989 to 1992, he was Vice President of Manufacturing at Progress Lighting, a privately held manufacturer of decorative lighting fixtures. From 1987 to 1989, he was Vice President of Manufacturing at Sulzer Intermedics, Inc., a publicly held medical device company. From 1986 to 1987, Mr. Bennett served as Director of Manufacturing at Kendall Respiratory Care, Inc., a medical device division of Kendall— a subsidiary of Colgate-Palmolive Company. From 1979 to 1986, he was Operations Director at Kendall McGaw Laboratories, a medical device division of Kendall, and held several other positions. Mr. Bennett holds a B.S. in Industrial Technology from the California State University, Long Beach and an M.B.A. from Pepperdine University.

Karen K. Church, R.A.C., Vice President of Regulatory Affairs, joined the Company in October 2002. Prior to joining the Company, from 2000 to 2002, Ms. Church was Vice President of Regulatory Affairs and Quality Assurance at Ancile Pharmaceuticals, a privately held specialty pharmaceutical company. From 1999 to 2000, she served as Senior Director and Consultant for Regulatory Affairs at Neurocrine Biosciences, a publicly held pharmaceutical company. From 1997 to 1998, she was Vice President of Regulatory Affairs at Advanced Bioresearch Associates, a regulatory consulting firm and clinical research organization. From 1995 to 1997, Ms. Church

was Vice President of Regulatory Affairs, Clinical Research, Quality Assurance and Quality Control at InSite Vision, a publicly held ophthalmic product development company. From 1988 to 1995, she held the positions of Divisional Vice President of Regulatory Affairs and Research Quality Assurance, as well as Executive Director, Senior Director and Director of Regulatory Affairs at Gensia, Inc., (now Sicor, Inc., a publicly held multinational pharmaceutical company). From 1980 to 1988, Ms. Church was Associate Director of Drug Regulatory Affairs at Hoffmann-La Roche, Inc., a U.S. prescription drug unit of the Roche Group, a publicly held international health care company. From 1973 to 1980, she served as Senior Regulatory Product Manager of Pharmaceutical Products Regulatory Operations at Abbott Laboratories, a publicly held pharmaceutical company. From 1970 to 1973, Ms. Church was Senior Editor of the Department of Regulatory Affairs at Astra Pharmaceutical Products, Inc., (now Astra Zeneca Pharmaceuticals, LP, a publicly held pharmaceutical company). Ms. Church holds a B.S. from the University of Wyoming and her R.A.C. from the Regulatory Affairs Professionals Society.

Theodora Reilly, Vice President of Human Resources, joined the Company in 1998 as Director of Human Resources and was promoted to Vice President of Human Resources in 2001. Prior to joining the Company, from 1997 to 1998, Ms. Reilly was Director of Human Resources at ThermoLase Corporation, a public subsidiary of Thermo Electron Corporation, which developed laser-based systems for laser-based skin resurfacing. From 1994 to 1997, Ms. Reilly served as Director of Human Resources at Solectek Corporation, a privately held high tech manufacturer of wireless interconnectivity products. Ms. Reilly received a B.S. in Psychology from the Christian Bible College and Seminary located in Independence, Missouri.

Andrew Wiseman, **Ph.D.**, Senior Director of Business Development, joined the Company in May 1989 as Director of Business Development and was one of the Company's original founders. Dr. Wiseman has also served as head of investor relations since 1994. From 1983 to 1989, Dr. Wiseman held several positions with Quidel Corporation, a publicly held manufacturer of diagnostic tests, including Manager of Business Development, Project Manager in Diagnostic Research and Development, and Senior Research Scientist. Dr. Wiseman was an Assistant Professor at the Medical Biology Institute and an Assistant Member at the Scripps Clinic and Research Foundation. He received a B.S. in Zoology and a Ph.D. in Genetics from Duke University.

Gail A. Sloan, **CPA,** Senior Director of Finance, Controller and Secretary, joined the Company in 1996 as Assistant Controller and was promoted to Controller in 1997 and Senior Director of Finance in 2002. Prior to joining the Company, from 1993 to 1996, Ms. Sloan served as Assistant Controller at Affymax Research Institute, a publicly held drug-discovery research company and a part of the Glaxo Wellcome Group. From 1985 to 1993, she progressed to the position of Audit Manager with Ernst & Young, LLP. Ms. Sloan holds a B.S. in Business Administration from California Polytechnic State University at San Luis Obispo and is a Certified Public Accountant.

Available Information

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed with or furnished to the Securities and Exchange Commission pursuant to Section 13(a) or 15(d) of the Exchange Act of 1934, as amended, are available free of charge through our web site at www.ljpc.com as soon as reasonably practicable after we electronically file or furnish the reports with or to the Securities and Exchange Commission.

RISK FACTORS

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

If the continued development of Riquent is significantly delayed because of the results of our recently completed Phase III clinical trial, our business and financial condition will be adversely affected and it may be difficult or impossible for us to survive.

We recently completed our Phase III clinical trial of Riquent. An initial assessment of the trial data indicates that treatment with Riquent did not increase length of time to renal flare, the primary endpoint, in a statistically significant manner when compared with placebo. As a result, we are unlikely to obtain regulatory clearance to market Riquent either in the United States or in Europe based on the data from the trial. After completing our analysis of the Phase III data and meeting with the regulatory agencies, we likely will be required to conduct at least one additional clinical trial of Riquent before we can seek to obtain marketing approval. The uncertainty regarding the future development of Riquent caused by the Phase III trial results will likely negatively affect our ability to raise necessary additional funding. If the continued development of Riquent is significantly delayed for any reason, and if we are unable to timely raise additional funding, we may not have the financial resources to continue research and development of Riquent, LJP 1082 or any other potential drug candidates, and it may be difficult or impossible for us to survive.

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 Riquent and LJP 1082 are promising, they may not be found to be safe or effective in future clinical trials and studies and results from previous trials and studies may not be observed in future trials and studies.

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

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

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. The process of obtaining FDA and other regulatory approvals is costly, time consuming, uncertain and subject to unanticipated delays. The FDA and foreign regulatory authorities have substantial discretion in the approval process. The FDA and foreign regulatory authorities may not agree that we have demonstrated that Riquent or LJP 1082 are safe and effective after we complete our clinical trials. The FDA

may refuse to approve an application for approval of a drug candidate if it believes that applicable regulatory criteria are not satisfied.

Even if the results of future 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, including the recently concluded Phase III trial of Riquent, a possible failure to conduct clinical trials in complete adherence to FDA good clinical practice standards and similar standards of foreign regulatory authorities, the identification of new clinical trial endpoints, or the need for additional data regarding the safety or efficacy of our drug candidates. 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 Riquent, LJP 1082 or our other drug candidates for commercial sale in any jurisdiction, even if future 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.

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

We 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 currently plan to continue to expend substantial amounts of capital resources for research, product development, pre-clinical testing and clinical trials of drug candidates. If we ultimately receive favorable clinical results and regulatory approval for our drug candidates, we may also devote substantial additional 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 effective marketing and sales programs.

We expect to incur substantial losses each year for at least the next several years as we continue our planned research, clinical development, manufacturing and marketing activities. If we ultimately receive regulatory approval for Riquent, LJP 1082 or our other drug candidates, our manufacturing, marketing and sales activities are likely to substantially increase our expenses and our need for working capital. We anticipate that our existing cash, investments and interest earned thereon will be sufficient to fund our operations as currently planned, which includes an additional clinical trial of Riquent, into the first quarter of 2004. This estimate also assumes that we do not undertake significant commercialization activities for Riquent. However, the amounts expended by us may vary significantly, and it is possible that our cash requirements will exceed current projections and that we will therefore need additional financing sooner than currently expected. In the future, it is possible that we will not have adequate resources to support continuation of our business activities.

We 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, and dilution can be particularly substantial when the price of our common stock is low.

If we are to obtain regulatory approval of Riquent, the FDA must also approve our manufacturing facilities and processes.

In addition to demonstrating the safety and efficacy of Riquent in clinical trials, we must also obtain FDA approval of our manufacturing facilities in order to obtain FDA approval for the commercial use of Riquent. As part of the approval process, we must 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 Riquent for commercial use even if future clinical trials are successful.

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

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

additional regulatory approval. If additional regulatory approval of the testing laboratory is required, the approval and possible commercialization of Riquent may be delayed even if future clinical trials are successful.

The technology underlying our products is uncertain and unproven.

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

Future clinical trials may be delayed or halted.

Future clinical trials of Riquent or LJP 1082, trials of drugs related to these drugs, or clinical trials of other drug candidates may be delayed or halted. During the development of Riquent, our Phase 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,
- 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 $153.6 million as of December 31, 2002. We expect to incur substantial losses each year for at least the next several years as we continue our planned research, clinical development, manufacturing and marketing activities, including the production of Riquent for an open-label follow-on study, additional clinical trials of Riquent and the production of LJP 1082 for clinical and toxicology studies. In addition, assuming we ultimately receive favorable clinical results and FDA approval for Riquent, LJP 1082 or our other drug candidates, we will be required to develop commercial manufacturing capabilities and sales and marketing programs which may result in substantial additional losses. To achieve profitability we must, among other matters, complete the development of our products, obtain all necessary regulatory approvals and establish commercial manufacturing, marketing and sales capabilities. The amount of losses and the time required by us to reach sustained profitability are highly uncertain and we may never achieve profitability. We do not expect to generate revenues from the

sale of Riquent, if approved, or our other products, if any, for several years, and we may never generate product revenues.

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

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

Our drugs may not achieve market acceptance.

Even if Riquent or our other drugs candidates receive regulatory approval, patients and physicians may not readily accept our proposed methods of treatment. In order for Riquent or our other drug candidates to be commercially successful, we will need to increase the awareness and acceptance of our drugs among physicians, patients and the medical community. Riquent 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 potential for profitability will be negatively affected.

We lack experience in marketing products for commercial sale.

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

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 Riquent, if approved, in significant commercial quantities. We have limited manufacturing experience, and we may be unable to successfully transition to commercial production. In addition, we have never operated an FDA-approved 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 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 Riquent, LJP 1082 and our other drug candidates in sufficient quantities for our clinical trials and possible commercialization, our suppliers will be required to provide us with an adequate supply of chemicals and reagents. Our ability to obtain these chemicals and reagents is subject to the following risks:

- our suppliers may not be able to increase their own manufacturing capabilities in order to provide us with a sufficient amount of material for our use,
- some of our suppliers may be required to 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 that are able to provide us with the chemicals or reagents that we use to manufacture our drugs.

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

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 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 Riquent, LJP 1082 and any other developed products. In addition, we will need to successfully preserve our trade secrets and operate without infringing on the rights of others.

We depend on patents and other unpatented intellectual property to prevent others from improperly benefiting from products or technologies that we may have developed. As of December 31, 2002, we owned 98 issued patents and 92 pending patent applications covering various technologies and drug candidates including Riquent and LJP 1082. However, there can be no assurance that any additional patents will be issued, that the scope of any patent protection will be sufficient, or that any current or future issued patent will be held valid if subsequently challenged. There is a substantial backlog of biotechnology patent applications at the United States Patent and Trademark Office that may delay the review and issuance of any patents. The patent position of biotechnology firms like ours is highly uncertain and involves complex legal and factual questions, and no consistent policy has emerged regarding the breadth of claims covered in biotechnology patents or the protection afforded by these patents. Currently, we have a number of patent applications pending in the United States relating to our technology, as well as foreign counterparts to some of our United States patent applications. We intend to continue to file applications as believed appropriate for patents covering both our products and processes. There can be no assurance that patents will be issued from any of these applications, or that the scope of any issued patents will protect our technology.

We do not necessarily know if others, including competitors, have patents or patent applications pending that relate to compounds or processes that overlap or compete with our intellectual property. We are aware of one 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:

- others, including competitors, will develop inventions relevant to our business,
- our binding confidentiality agreements will be breached, and we will not have adequate remedies for such a breach, or
- our trade secrets will otherwise become known or be independently discovered by competitors.

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 Riquent, LJP 1082 and other drug candidates for several years and have unique knowledge of our drug candidates and of the technology on which they are based. In addition, we will be required to rely on other key members of our senior management team, including Bruce Bennett, William Welch, Karen Church, and Dr. Kenneth Heilbrunn, to assist us with growth and expansion into areas requiring additional expertise, such as clinical trials, regulatory approvals, manufacturing, marketing and sales. We expect that we will continue to require additional management personnel, and that our existing management personnel will be required to develop additional expertise.

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

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

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

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

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

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

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

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

The use and possible sale of Riquent, LJP 1082 and other potential products may expose us to legal liability and generate negative publicity if we are subject to claims that our products harmed people. These claims might be made directly by patients, pharmaceutical companies, or others. We currently maintain $10.0 million of product liability insurance for claims arising from the use of our products in clinical trials. 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, in sufficient amounts, or with broad enough coverage to protect us against possible losses. Furthermore, it is possible that our financial resources would be insufficient to satisfy potential product liability or other claims. A successful product liability claim or series of claims brought against us could negatively impact our business and financial condition.

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

Due to the nature of our manufacturing processes, we are subject to stringent federal, state and local laws governing the use, handling and disposal of certain materials and wastes. We may have to incur significant costs to comply with environmental regulations if and when our manufacturing increases to commercial volumes. Current or future environmental laws may significantly affect our operations because, for instance, our production process may be required to be altered, thereby increasing our production costs. In our research activities, we use radioactive and other materials that could be hazardous to human health, safety or the environment. These materials and various wastes resulting from their use are stored at our facility

pending ultimate use and disposal. The risk of accidental injury or contamination from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any resulting damages, and any such liability could exceed our resources. Although we maintain general liability insurance, we do not specifically insure against environmental liabilities.

II. Risk Factors Related Specifically To Our Stock

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

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

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

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

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

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

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

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

- Approximately 42,411,140 shares of common stock that have been issued in registered offerings or are otherwise freely tradable in the public markets.
- Approximately 72,348 shares of common stock are currently eligible for resale in the public market pursuant to SEC Rule 144.
- As of March 20, 2003, there are an aggregate of 6,399,506 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 $4.97 per share.
- We have in effect registration statements under the Securities Act of 1933, as amended (the "Securities Act"), registering approximately 8,100,000 shares of common stock reserved under our incentive stock option and employee stock purchase plans. Approximately 144,900 shares of common stock that may be issued on the exercise of outstanding stock options will be available for public resale under SEC Rule 144 pursuant to Rule 701 under the Securities Act.
- Pursuant to a registration statement on Form S-3 filed on December 10, 2002, we may issue up to an additional $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, which may have the effect of delaying or preventing changes in our management. For example, one anti-takeover device provides for a board of directors that is separated into three classes, with their terms in office staggered over three year periods. This has the effect of delaying a change in control of our board of directors without the cooperation of the incumbent board. In addition, our bylaws require stockholders to give us written notice of any proposal or director nomination within a specified period of time prior to the annual stockholder meeting, establish certain qualifications for a person to be elected or appointed to the board of directors during the pendency of certain business combination transactions, and do not allow stockholders to call a special meeting of stockholders.

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

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

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

Item 2. Properties.

We lease two adjacent buildings in San Diego, California covering a total of approximately 54,000 square feet. One building contains our research and development labs and clinical manufacturing facilities and the other contains our corporate offices and warehouse. Both building leases expire in July 2004. Each lease includes an option to extend the term of the lease for an additional five years and each is subject to an escalation clause that provides for annual rent increases. We also lease approximately 1,500 square feet of laboratory space in San Diego, California, for research and development purposes. This lease, which was extended in February 2003, expires in August 2003. We believe that these facilities will be adequate to meet our needs for the near term. Over the longer term, management believes additional space can be secured at commercially reasonable rates.

Item 3. Legal Proceedings.

We are currently not a party to any legal proceedings.

Item 4. Submission of Matters to a Vote of Security Holders.

No matters were submitted to a vote of security holders during the three-month period ended December 31, 2002.

PART II

Item 5. Market For Registrant's Common Equity and Related Stockholder Matters.

Information About Our Common Stock

Our common stock trades on the Nasdaq National Market under the symbol "LJPC." Set forth below are the high and low sales prices for our common stock for each full quarterly period within the two most recent fiscal years.

	Prices	
	High	Low
Year Ended December 31, 2002		
First Quarter	9.42	5.42
Second Quarter	7.58	3.85
Third Quarter	6.13	4.05
Fourth Quarter	7.05	3.40
Year Ended December 31, 2001		
First Quarter	8.25	4.44
Second Quarter	10.75	4.94
Third Quarter	9.50	3.40
Fourth Quarter	9.18	3.88

We have never paid dividends on our common stock and we do not anticipate paying dividends in the foreseeable future. The number of record holders of our common stock as of March 20, 2003 was 343.

Information About Our Equity Compensation Plans

Information regarding the securities authorized for issuance under our equity compensation plans required by Item 5 is incorporated by reference from our definitive proxy statement for the 2003 annual meeting of stockholders, which will be filed with the Securities and Exchange Commission no later than 120 days after the end of the fiscal year ended December 31, 2002.

Item 6. Selected Financial Data.

The following Selected Financial Data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in Item 7 below and the financial statements of the Company and related notes thereto beginning at page F-1 of this report.

	Years Ended December 31,				
	1998	1999	2000	2001	2002
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenue from collaborative agreements – related party	$ 8,600	$ 4,690	$ —	$ —	$ —
Expenses:					
Research and development	14,627	11,686	12,933	23,228	37,696
General and administrative	3,076	2,944	2,706	4,268	6,944
Loss from operations	(9,103)	(9,940)	(15,639)	(27,496)	(44,640)
Interest expense	(6)	(20)	(6)	(30)	(51)
Interest income	1,232	811	1,846	2,843	1,373
Net loss	$ (7,877)	$ (9,149)	$(13,799)	$(24,683)	$(43,318)
Basic and diluted net loss per share	$ (0.42)	$ (0.45)	$ (0.53)	$ (0.71)	$ (1.03)
Shares used in computing basic and diluted net loss per share	18,649	20,135	26,138	34,604	42,046
Balance Sheet Data:					
Working capital	$19,911	$10,661	$ 37,215	$ 44,387	$ 46,490
Total assets	$25,815	$14,043	$ 43,016	$ 51,686	$ 61,864
Noncurrent portion of obligations under capital leases and notes payable	$ —	$ 44	$ —	$ —	$ 1,111
Stockholders' equity	$21,859	$12,793	$ 39,742	$ 48,545	$ 53,799

Quarterly Results of Operations

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2002 and 2001 (in thousands except per share data):

	Quarters Ended			
	Mar. 31,	Jun. 30,	Sept. 30,	Dec. 31,
2002				
Expenses:				
Research and development	$ 7,244	$ 9,661	$ 9,448	$ 11,343
General and administrative	1,413	1,788	1,656	2,087
Loss from operations	(8,657)	(11,449)	(11,104)	(13,430)
Interest expense	(6)	(9)	(7)	(29)
Interest income	548	100	425	300
Net loss	$ (8,115)	$(11,358)	$(10,686)	$(13,159)
Basic and diluted net loss per share	$ (0.20)	$ (0.27)	$ (0.25)	$ (0.31)
Shares used in computing basic and diluted net loss per share	40,979	42,356	42,402	42,427
2001				
Expenses:				
Research and development	$ 6,465	$ 5,949	$ 4,939	$ 5,875
General and administrative	884	1,024	1,042	1,318
Loss from operations	(7,349)	(6,973)	(5,981)	(7,193)
Interest expense	—	(13)	(10)	(7)
Interest income	800	880	645	518
Net loss	$ (6,549)	$ (6,106)	$ (5,346)	$ (6,682)
Basic and diluted net loss per share	$ (0.20)	$ (0.17)	$ (0.15)	$ (0.19)
Shares used in computing basic and diluted net loss per share	32,689	35,150	35,224	35,255

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Recent Developments

In February 2003, we completed a Phase III clinical trial of Riquent, our clinical drug candidate for the treatment of lupus renal disease. The results from the Phase III study indicate Riquent appeared to be well tolerated with no apparent differences in the overall incidence of serious adverse events or adverse events between Riquent-treated and placebo-treated patients. However, an initial assessment of the trial data indicates that treatment with Riquent did not increase length of time to renal flare, the primary endpoint, in a statistically significant manner when compared with placebo through the end of the study. There was a statistically significant reduction in antibodies to dsDNA in the Riquent-treated group compared with the placebo-treated group.

We are continuing to analyze the results of our Phase III clinical trial of Riquent and currently expect to complete our analysis by the end of April 2002. We plan to discuss these results with the regulatory agencies. After this discussion we will elect how to proceed with any further development of Riquent. There can be no guarantee that a meeting with the regulatory agencies can be held in a timely manner, or at all, or that our meetings with them will result in our being able to continue to develop Riquent in an economically viable manner. If for any reason our development efforts as to Riquent are terminated, it would have a material, adverse effect on our business and future prospects.

Since our inception in May 1989, we have devoted substantially all of our resources to the research and development of technology and potential drugs to treat antibody-mediated diseases. We have never generated any revenue from product sales and have relied upon private and public investors, revenue from collaborative agreements, equipment financings and interest income on invested cash balances for our working capital. Depending on the results of the data analysis from the clinical trial of Riquent and our meeting with the regulatory agencies, our research and development expenses may increase significantly in the future if we continue our clinical trial and manufacturing activities of Riquent, increase our development activities of LJP 1082 and intensify our efforts to develop additional drug candidates. Our activities to date are not as broad in depth or scope as the activities we may undertake in the future, and our historical operations and the financial information included in this report are not necessarily indicative of our future operating results or financial condition.

We expect losses to fluctuate from quarter to quarter as a result of the timing of expenses incurred and revenues from any potential collaborative arrangements we may enter into. Some of these fluctuations may be significant. As of December 31, 2002, our accumulated deficit was approximately $153.6 million.

Our business is subject to significant risks including, but not limited to, the risks inherent in research and development efforts, including clinical trials, uncertainties associated with both obtaining and enforcing patents and with the potential enforcement of the patent rights of others, the lengthy, expensive and uncertain process of seeking regulatory approvals, uncertainties regarding government reforms and of product pricing and reimbursement levels, technological change and competition, manufacturing uncertainties, our lack of marketing experience and the uncertainty of receiving future revenue from product sales or other sources such as collaborative relationships, the uncertainty of future profitability and the need for additional financing. Even if our product candidates appear promising at an early stage of development, they may not reach the market for numerous reasons, including the possibilities that the products will be ineffective or unsafe during clinical trials, will fail to receive necessary regulatory approvals, will be difficult to

manufacture on a large scale, will be uneconomical to market or will be precluded from commercialization by the proprietary rights of third parties or competing products.

Critical Accounting Policies and Estimates

The discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We evaluate our estimates on an ongoing basis, including those related to patent costs and income taxes. We base our estimates on historical experience and on other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect the significant judgments and estimates used in the preparation of our consolidated financial statements (see note 1 to our financial statements).

Valuation of Short-Term Investments. We primarily invest our excess cash in U.S. government securities and debt instruments of financial institutions and corporations with strong credit ratings. We have established guidelines relative to diversification and maturities that maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends and interest rates. In determining if and when a decline in market value below amortized cost is other-than-temporary, we, together with our external portfolio managers, evaluate the market conditions, offering prices, trends of earnings, price multiples, and other key measures for our investments in debt instruments. When a decline in value is deemed to be other-than-temporary, we recognize an impairment loss in the period operating results to the extent of the decline. To date, we have not had any impairment losses related to our short-term investments.

Patent Costs. We capitalize the costs incurred to file our patent applications. These costs are amortized using the straight-line method over the lesser of the remaining useful life of the related technology or the remaining patent life, commencing on the date the patent is issued. At December 31, 2002, capitalized costs related to issued patents totaled $0.9 million (net of accumulated amortization) and $1.2 million related to unissued patents. Our results of operations could be materially impacted when we begin amortizing the costs related to unissued patents. In addition, we expense all costs related to abandoned patent applications. If we elect to abandon any of our currently issued or unissued patents, the related expense could be material to our results of operations for the period of the abandonment.

Results of Operations

Years Ended December 31, 2002, 2001 and 2000

Revenue. We earned no revenue for the years ended December 31, 2002, 2001, and 2000.

Research and Development Expense. Our research and development expense increased to $37.7 million for the year ended December 31, 2002 from $23.2 million in 2001 and $12.9 million in 2000. The increase in research and development expense in 2002 from 2001 and 2000 was primarily due to the cost of the recently completed Phase III clinical trial for Riquent which

was initiated in September 2000, the cost of the Phase I/II clinical trial for LJP 1082 which was initiated in November 2001 and completed in October 2002, and the cost of the on-going open-label follow-on clinical trial for Riquent which was initiated in July 2002.

Research and development expense of $37.7 million for the year ended December 31, 2002 consisted of $29.1 million for lupus research and development related expense, $6.4 million for thrombosis research and development related expense and $2.2 million for other research and development related expense. Total lupus related research and development expense consisted primarily of investigator fees, clinical research organization fees, expenses related to the open-label follow-on clinical trial, salaries and other costs related to research, manufacturing and clinical personnel, clinical lab fees, raw materials for the production of Riquent for clinical trials and advertising fees for the enrollment of the Phase III clinical trial for lupus. Total thrombosis related research and development expense consisted primarily of salaries for research and development personnel, raw materials for the production of LJP 1082 for clinical trials, investigator fees and contract clinical research associate fees for the Phase I/II clinical trial for antibody-mediated thrombosis. Total other research and development expense consisted primarily of salaries for research and development personnel, depreciation expense and research supplies.

Our research and development expense may increase significantly in the future if we initiate commercialization activities for Riquent, increase our development activities of LJP 1082 or intensify our development of additional drug candidates.

General and Administrative Expense. Our general and administrative expense of $6.9 million for the year ended December 31, 2002 increased from $4.3 million in 2001 and from $2.7 million in 2000. The increase in general and administrative expense in 2002 as compared to 2001 and 2000 was due to an increase in headcount and administrative infrastructure to support increased clinical trial, manufacturing and research and development activities. General and administrative expense may increase in the future to support possible increases in commercialization, clinical trial, manufacturing and research and development activities.

Interest Income and Expense. Our interest income decreased to $1.4 million for the year ended December 31, 2002 from $2.8 million in 2001 and $1.8 million in 2001. The decrease in interest income in 2002 was due to lower average interest rates on our investments as compared to 2001 and 2000. This decrease was partially offset by higher average balances of cash and short-term investments as a result of receiving net proceeds of $48.3 million from the sale of common stock in January 2002. Interest expense increased to $51,000 for the year ended December 31, 2002 from $30,000 in 2001 and $6,000 in 2000. The higher interest expense in 2002 as compared to 2001 and 2000 was due to new notes payable obligations entered into in 2002 to finance equipment purchases.

Net Operating Loss Carryforwards. At December 31, 2002, we had available net operating loss carryforwards and research tax credit carryforwards of approximately $146.7 million and $46.1 million, respectively, for federal income tax purposes, which will begin to expire in 2004 unless utilized.

Liquidity and Capital Resources

From inception through December 31, 2002, we have incurred a cumulative net loss of approximately $153.6 million and have financed our operations through private and public offerings of securities, revenues from collaborative agreements, equipment financings and interest income on invested cash balances. As of December 31, 2002, we had raised $206.5 million in net proceeds since inception from sales of equity securities.

At December 31, 2002, we had $52.7 million in cash, cash equivalents and short-term investments, as compared to $47.0 million at December 31, 2001. Our working capital at December 31, 2002 was $46.5 million, as compared to $44.4 million at December 31, 2001. The increase in cash, cash equivalents and short-term investments resulted from net proceeds of $48.3 million we received from the sale of 7,000,000 shares of our common stock to private investors in January 2002. We invest our cash in corporate and United States government-backed debt instruments. We classified all of our cash investments as available-for-sale securities as of December 31, 2002, as we expect to sell them in order to support our current operations regardless of their maturity date. As of December 31, 2002, available-for-sale securities of $16.9 million have stated maturity dates of one year or less and $34.8 million have maturity dates after one year.

As of December 31, 2002, we had acquired an aggregate of $11.5 million in property and equipment, of which $0.2 million and $1.4 million of equipment is financed under capital lease and notes payable obligations, respectively. In addition, we lease our office and laboratory facilities and certain equipment under operating leases. We currently have no material commitments for the acquisition of property and equipment. However, we may increase our investment in property and equipment if we expand our research and development and manufacturing facilities and capabilities.

The following table summarizes our contractual obligations at December 31, 2002, and the effect such obligations are expected to have on our liquidity and cash flows in future periods:

	Payments Due by Period			
	Less than 1 Year	Years 2-3	Years 4-5	More than 5 Years
Long-term debt	$ 580	$ 1,111	$ 101	$ —
Capital lease obligations	67	—	—	—
Operating lease obligations	1,229	734	5	—
Total	$ 1,876	$ 1,845	$ 106	$ —

We intend to use our financial resources to fund our research and development efforts, to fund possible further clinical trials, manufacturing and commercialization activities of Riquent, and for working capital and other general corporate purposes. The amounts actually expended for each purpose may vary significantly depending on numerous factors, including the analysis of the Phase III clinical data, the outcome of meetings with regulatory authorities, results of future clinical trials, the timing of any regulatory applications and approvals, and technological developments. Expenditures also will depend on any establishment and progress of collaborative arrangements and contract research as well as the availability of other funding or financings. There can be no assurance that future funds will be available on acceptable terms, if at all.

We anticipate that our existing cash and cash investments and interest earned thereon, will be sufficient to fund our operations as currently planned, which includes an additional trial for Riquent, into the first quarter of 2004. This estimation also assumes that we do not undertake significant commercialization activities for Riquent during 2003. Our future capital requirements will depend on many factors, including continued scientific progress in our research and development programs, the size and complexity of these programs, the scope and results of clinical trials, the analysis of data from the Phase III clinical trial for lupus and Phase I/II clinical trial for thrombosis, the outcome of meetings with regulatory authorities, the time and costs involved in applying for any 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 relationships, and the cost of possible

manufacturing and commercialization activities. We expect to incur significant net operating losses each year for at least the next several years as we continue our current research and development efforts, including possible additional clinical trials, manufacturing and commercialization activities of Riquent, and incur general and administrative expenses to support these efforts. It is possible that our cash requirements will exceed current projections and that we will therefore need additional financing sooner than currently expected.

We have no current means of generating cash flow from operations. Our lead drug candidate, Riquent, will not generate revenues, if at all, until it has been proven safe and effective, has received regulatory approval and has been successfully commercialized. This process, if completed, could take several years. Our other drug candidates are much less developed than Riquent. There can be no assurance that our product development efforts with respect to Riquent or any other drug candidate will be successfully completed, that required regulatory approvals will be obtained or that any product, if introduced, will be successfully marketed or achieve commercial acceptance. Accordingly, we must continue to rely upon outside sources of financing to meet our capital needs for the foreseeable future.

We will continue to seek capital through any appropriate means, including issuance of our securities and establishment of additional collaborative arrangements. However, there can be no assurance that additional financing will be available on acceptable terms, if at all, and our negotiating position in capital-raising efforts may worsen as we continue to use existing resources or if the development of Riquent is delayed or terminated. There is also no assurance that we will be able to enter into further collaborative relationships.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk.

We invest our excess cash in interest-bearing investment-grade securities that we hold for the duration of the term of the respective instrument. We do not utilize derivative financial instruments, derivative commodity instruments or other market-risk-sensitive instruments, positions or transactions in any material fashion. Accordingly, we believe that, while the investment-grade securities we hold are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices or other market changes that affect market-risk-sensitive instruments.

Item 8. Financial Statements and Supplementary Data.

The financial statements and supplementary data required by this item can be found above under the caption “Quarterly Results of Operations” on page 39 and at the end of this report beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

PART III

Item 10. Directors and Executive Officers of the Registrant.

Except for information concerning our executive officers which is included under the caption “Executive Officers of the Registrant” beginning on page 22 of this report, the information required by Item 10 is incorporated by reference from our definitive proxy statement for the 2003 annual meeting of stockholders, which will be filed with the Securities and Exchange Commission no later than 120 days after the close of the fiscal year ended December 31, 2002.

Item 11. Executive Compensation.

The information required by Item 11 is incorporated by reference from our definitive proxy statement for the 2003 annual meeting of stockholders, which will be filed with the Securities and Exchange Commission no later than 120 days after the close of the fiscal year ended December 31, 2002.

Item 12. Security Ownership of Certain Beneficial Owners and Management.

The information required by Item 12 is incorporated by reference from our definitive proxy statement for the 2003 annual meeting of stockholders, which will be filed with the Securities and Exchange Commission no later than 120 days after the close of the fiscal year ended December 31, 2002.

Item 13. Certain Relationships and Related Transactions.

None.

Item 14. Controls and Procedures.

Within 90 days prior to the date of this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer (CEO) and our Chief Financial Officer (CFO), of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-14. Because our current CFO assumed his position on October 21, 2002, the evaluation also included, to the extent necessary, the analysis of our Senior Director of Finance and Controller. Based upon that evaluation, the CEO and CFO concluded that our disclosure controls and procedures are effective in timely alerting them to material information relating to the Company required to be included in our periodic SEC filings. In January 2003, we installed SAP software for our financial and materials management systems. Other than this, there have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to the date we carried out our evaluation.

PART IV

Item 15. Exhibits, Financial Statement Schedules, and Reports on Form 8-K.

(a) Documents filed as part of this report.

1. Financial Statements.

The following financial statements of La Jolla Pharmaceutical Company are included in Item 8:

2. Financial Statement Schedules.

The schedules are omitted because they are not required, or are not applicable, or the required information is shown in the financial statements or notes thereto.

3. Exhibits.

See table below.

Exhibit Number	Description
3.1	Amended and Restated Bylaws of the Company (1)
3.2	Amended and Restated Certificate of Incorporation of the Company (2)
4.1	Rights Agreement dated as of December 3, 1998 between the Company and American Stock Transfer & Trust Company (3)
4.2	Certificate of Designation, Preferences and Rights of Series A Junior Participating Preferred Stock of the Company (4)
4.3	Amendment to Rights Agreement, effective as of July 21, 2001, between the Company and American Stock Transfer & Trust Company (5)
10.1	Stock Option Agreement dated February 4, 1993 entitling Joseph Stemler to purchase 35,000 shares of Common Stock (6) *
10.2	Steven B. Engle Employment Agreement (6)*
10.3	Amendment No. 1 to Steven B. Engle Employment Agreement (7)*
10.4	Amendment No. 2 to Steven B. Engle Employment Agreement (1)*
10.5	Form of Directors and Officers Indemnification Agreement (6)
10.6	Option and Collaborative Research Agreement, dated June 10, 1991, regarding certain compounds for potential treatment of muscular dystrophies or myasthenia gravis between the Company and CepTor Corporation (6)
10.7	Form of Employee Invention and Confidential Information Agreement (6)
10.8	Industrial Real Estate Lease (6)
10.9	La Jolla Pharmaceutical Company 1989 Incentive Stock Option Plan and 1989 Nonstatutory Stock Option Plan (6) *
10.10	Form of Stock Option Agreement under the 1989 Nonstatutory Stock Option Plan (6)*
10.11	La Jolla Pharmaceutical Company 1994 Stock Incentive Plan (Amended and Restated as of May 22, 2002) (8)*
10.12	La Jolla Pharmaceutical Company 1995 Employee Stock Purchase Plan (Amended and Restated as of May 22, 2002) (8)*
10.13	Letter of Agreement, dated June 7, 1993, between the Company and Vector Securities International regarding Vector's engagement as financial advisor to the Company with respect to potential corporate strategic alliances (6)
10.14	Second Amendment to Lease, dated June 30, 1994, by and between the Company and BRE Properties, Inc. (9)
10.15	Third Amendment to Lease, dated January 26, 1995, by and between the Company and BRE Properties, Inc. (10)
10.16	Master Lease Agreement, dated September 13, 1995, by and between the Company and Comdisco Electronics Group (11)
10.17	Agreement, dated September 22, 1995, between the Company and Joseph Stemler regarding option vesting (12) *
10.18	Building Lease Agreement, effective November 1, 1996, by and between the Company and WCB II-S BRD Limited Partnership (13)
10.19	Master Lease Agreement, dated December 20, 1996, by and between the Company and Transamerica Business Credit Corporation (14)
10.20	License and Supply Agreement, dated December 23, 1996, by and between the Company and Abbott Laboratories (14) (15)

10.21	Stock Purchase Agreement, dated December 23, 1996, by and between the Company and Abbott Laboratories (14)
10.22	Waiver of Contractual Restrictions dated February 6, 2001 (16)
10.23	Master Lease Agreement No. 2, dated June 23, 1998, by and between the Company and Transamerica Business Credit Corporation (17)
10.24	Supplement to employment offer letter for Matthew Linnik, Ph.D. (18)*
10.25	Supplement to employment offer letter for William J. Welch (19)*
10.26	Supplement to employment offer letter for Theodora Reilly (19)*
10.27	Supplement to employment offer letter for Paul Jenn, Ph.D. (19)*
10.28	Supplement to employment offer letter for Bruce K. Bennett, Jr. (20)*
10.29	Supplement to employment offer letter for Kenneth R. Heilbrunn (8)*
10.30	Supplement to employment offer letter for Karen K. Church (21)*
10.31	Supplement to employment offer letter for David Duncan, Jr. (21)*
10.32	Master Security Agreement, effective September 6, 2002, between the Company and General Electric Capital Corporation (21)
10.33	Promissory Note, dated as of September 26, 2002, between the Company and General Electric Capital Corporation (21)
10.34	Amendment to Promissory Note, effective as of September 27, 2002, between the Company and General Electric Capital Corporation (21)
23.1	Consent of Ernst & Young LLP, Independent Auditors
99.1	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

* This exhibit is a management contract or compensatory plan or arrangement.

(1) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended September 30, 2000 and incorporated by reference herein.

(2) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended September 30, 1999 and incorporated by reference herein.

(3) Previously filed with the Company's Registration Statement on Form 8-A (No. 000-24274) as filed with the Securities and Exchange Commission on December 4, 1998.

(4) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 1999 and incorporated by reference herein.

(5) Previously filed with the Company's report on Form 8-K filed on January 26, 2001 and incorporated by reference herein. The changes effected by the Amendment are also reflected in the Amendment to Application for Registration on Form 8-A/A filed on January 26, 2001.

(6) Previously filed with the Company's Registration Statement on Form S-1 (No. 33-76480) as declared effective by the Securities and Exchange Commission on June 3, 1994.

(7) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 1997 and incorporated by reference herein.

(8) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2002 and incorporated by reference herein.

(9) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 1994 and incorporated by reference herein.

(10) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended March 31, 1995 and incorporated by reference herein.

(11) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended September 30, 1995 and incorporated by reference herein.

(12) Previously filed with the Company's annual report on Form 10-K for the fiscal year ended December 31, 1995 and incorporated by reference herein.

(13) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended September 30, 1996 and incorporated by reference herein.

(14) Previously filed with the Company's annual report on Form 10-K for the fiscal year ended December 31, 1996 and incorporated by reference herein.

(15) Portions of the Exhibit 10.20 have been omitted and filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment under Rule 24b-2 of the Securities Exchange Act of 1934.

(16) Previously filed with the Company's annual report on Form 10-K for the fiscal year ended December 31, 2000 and incorporated by reference herein.

(17) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 1998 and incorporated by reference herein.

(18) Previously filed with the Company's annual report on Form 10-K for the fiscal year ended December 31, 1999 and incorporated by reference herein.

(19) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2001 and incorporated by reference herein.

(20) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended March 31, 2002 and incorporated by reference herein.

(21) Previously filed with the Company's quarterly report on Form 10-Q for the quarter ended September 30, 2002 and incorporated by reference herein.

(b) Reports on Form 8-K.

On November 26, 2002, we filed a current report on Form 8-K to report that officers and directors of La Jolla Pharmaceutical Company had entered into trading plans in accordance with Securities and Exchange Commission Rule 10b5-1. On December 18, 2002, we filed a current report on Form 8-K to report that we had completed our Phase III clinical trial of Riquent.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

LA JOLLA PHARMACEUTICAL COMPANY

By: /s/ Steven B. Engle

March 27, 2003

Steven B. Engle
Chairman of the Board and
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Steven B. Engle Steven B. Engle	Chairman of the Board and Chief Executive Officer (Principal Executive Officer and Director)	March 27, 2003
/s/ David Duncan, Jr. David Duncan, Jr.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 27, 2003
/s/ Thomas H. Adams Thomas H. Adams, Ph.D.	Director	March 27, 2003
/s/ William E. Engbers William E. Engbers	Director	March 27, 2003
/s/ Robert A. Fildes Robert A Fildes, Ph.D.	Director	March 27, 2003
/s/ Stephen M. Martin Stephen M. Martin	Director	March 27, 2003
/s/ William R. Ringo William R. Ringo	Director	March 27, 2003
/s/ W. Leigh Thompson W. Leigh Thompson, M.D., Ph.D.	Director	March 27, 2003

Certifications

I, Steven B. Engle, certify that:

1. I have reviewed this annual report on Form 10-K of La Jolla Pharmaceutical Company;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statement made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:

    a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

    b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

    c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

    a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and

    b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and

6. The registrant's other certifying officers and I have indicated in this annual report whether there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 27, 2003

/s/ Steven B. Engle

Steven B. Engle
Chairman and Chief Executive Officer

Certifications

I, David Duncan, Jr., certify that:

1. I have reviewed this annual report on Form 10-K of La Jolla Pharmaceutical Company;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statement made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officers and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:

    a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

    b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

    c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

    a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and

    b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and

6. The registrant's other certifying officers and I have indicated in this annual report whether there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 27, 2003

/s/ David Duncan, Jr.

David Duncan, Jr.
Chief Financial Officer

Report of Independent Auditors

The Board of Directors and Stockholders
La Jolla Pharmaceutical Company

We have audited the accompanying balance sheets of La Jolla Pharmaceutical Company as of December 31, 2002 and 2001, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2002. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of La Jolla Pharmaceutical Company at December 31, 2002 and 2001, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2002, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

ERNST & YOUNG LLP

San Diego, California
February 14, 2003

La Jolla Pharmaceutical Company

Balance Sheets

(In thousands, except share and per share data)

	December 31,	
	2002	2001
Assets		
Current assets:		
Cash and cash equivalents	$ 5,610	$ 9,932
Short-term investments	47,115	37,028
Other current assets	719	568
Total current assets	53,444	47,528
Property and equipment, net	6,034	1,921
Patent costs and other assets, net	2,386	2,237
	$ 61,864	$ 51,686
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,846	$ 743
Accrued clinical expenses	2,454	703
Accrued pre-marketing expenses	191	536
Accrued expenses	637	541
Accrued payroll and related expenses	1,332	451
Obligations under capital leases	60	167
Current portion of obligations under notes payable	434	—
Total current liabilities	6,954	3,141
Noncurrent portion of notes payable	1,111	—
Commitments:		
Stockholders' equity:		
Preferred stock, $.01 par value; 8,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock, $.01 par value; 100,000,000 shares authorized, 42,461,326 and 35,281,753 shares issued and outstanding at December 31, 2002 and 2001, respectively	425	353
Additional paid-in capital	206,905	158,223
Other comprehensive income	36	218
Accumulated deficit	(153,567)	(110,249)
Total stockholders' equity	53,799	48,545
	$ 61,864	$ 51,686

See accompanying notes.

La Jolla Pharmaceutical Company

Statements of Operations

(In thousands, except per share data)

	Years Ended December 31,		
	2002	2001	2000
Expenses:			
Research and development	$ 37,696	$ 23,228	$ 12,933
General and administrative	6,944	4,268	2,706
Total expenses	44,640	27,496	15,639
Loss from operations	(44,640)	(27,496)	(15,639)
Interest expense	(51)	(30)	(6)
Interest income	1,373	2,843	1,846
Net loss	$(43,318)	$(24,683)	$(13,799)
Basic and diluted net loss per share	$ (1.03)	$ (0.71)	$ (0.53)
Shares used in computing basic and diluted net loss per share	42,046	34,604	26,138

See accompanying notes.

La Jolla Pharmaceutical Company

Statements of Stockholders' Equity
(In thousands)
For the Years Ended December 31, 2000, 2001 and 2002

	Common stock		Additional paid-in capital	Accumulated deficit	Other comprehensive income (loss)	Total stockholders' equity
	Shares	Amount				
Balance at December 31, 1999	20,204	$ 202	$ 84,358	$ (71,767)	$ —	$ 12,793
Issuance of common stock, net	8,840	88	40,156	—	—	40,244
Issuance of common stock under Employee Stock Purchase Plan	186	2	189	—	—	191
Exercise of stock options	159	2	196	—	—	198
Exercise of warrants	4	—	10	—	—	10
Net loss	—	—	—	(13,799)	—	(13,799)
Net unrealized gains on available-for-sale securities	—	—	—	—	105	105
Comprehensive loss						(13,694)
Balance at December 31, 2000	29,393	294	124,909	(85,566)	105	39,742
Issuance of common stock, net	5,700	57	33,037	—	—	33,094
Issuance of common stock under Employee Stock Purchase Plan	145	2	226	—	—	228
Exercise of stock options	44	—	51	—	—	51
Net loss	—	—	—	(24,683)	—	(24,683)
Net unrealized gains on available-for-sale securities	—	—	—	—	113	113
Comprehensive loss						(24,570)
Balance at December 31, 2001	35,282	353	158,223	(110,249)	218	48,545
Issuance of common stock, net	7,000	70	48,230	—	—	48,300
Issuance of common stock under Employee Stock Purchase Plan	77	1	284	—	—	285
Exercise of stock options	102	1	168	—	—	169
Net loss	—	—	—	(43,318)	—	(43,318)
Net unrealized losses on available-for-sale securities	—	—	—	—	(182)	(182)
Comprehensive loss						(43,500)
Balance at December 31, 2002	42,461	$ 425	$206,905	$ (153,567)	$ 36	$ 53,799

See accompanying notes.

La Jolla Pharmaceutical Company

Statements of Cash Flows
(In thousands)

	Years Ended December 31,		
	2002	2001	2000
Operating activities			
Net loss	$(43,318)	$(24,683)	$(13,799)
Adjustments to reconcile net loss to net cash used for operating activities:			
Depreciation and amortization	1,391	684	381
Write-off of property and equipment	—	96	—
Accretion of interest income	426	117	(634)
Changes in operating assets and liabilities:			
Other current assets	(151)	22	(126)
Accrued clinical expenses	1,751	(1,211)	1,914
Accrued pre-marketing expenses	(345)	536	—
Accounts payable and accrued expenses	1,199	256	283
Accrued payroll and related expenses	881	163	26
Net cash used for operating activities	(38,166)	(24,020)	(11,955)
Investing activities			
Purchases of short-term investments	(71,333)	(33,886)	(40,716)
Sales of short-term investments	29,942	3,488	13,439
Maturities of short-term investments	30,696	25,204	3,172
Additions to property and equipment	(5,143)	(1,341)	(541)
Proceeds from sale of property and equipment	—	—	97
Increase in patent costs and other assets	(348)	(554)	(288)
Net cash used for investing activities	(16,186)	(7,089)	(24,837)
Financing activities			
Net proceeds from issuance of common stock	48,754	33,373	40,643
Proceeds from issuance of notes payable	1,656	—	—
Payments on notes payable	(111)	—	—
Payments on obligations under capital leases	(269)	(393)	(199)
Net cash provided by financing activities	50,030	32,980	40,444
(Decrease) increase in cash and cash equivalents	(4,322)	1,871	3,652
Cash and cash equivalents at beginning of period	9,932	8,061	4,409
Cash and cash equivalents at end of period	$ 5,610	$ 9,932	$ 8,061
Supplemental disclosure of cash flow information:			
Interest paid	$ 51	$ 30	$ 6
Supplemental schedule of noncash investing and financing activities:			
Capital lease obligations incurred for property and equipment	$ 162	$ 516	$ —
Other comprehensive (loss) income on investments	$ (182)	$ 113	$ 105

See accompanying notes.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies

Organization and Business Activity

La Jolla Pharmaceutical Company (the "Company") is a biopharmaceutical company focused on the research and development of highly specific therapeutics for the treatment of certain life-threatening antibody-mediated diseases. These diseases, including autoimmune conditions such as systemic lupus erythematosus ("lupus") and antibody-mediated stroke, are caused by abnormal B cell production of antibodies that attack healthy tissues in the body. Current therapies for these autoimmune disorders target the symptoms of the disease or nonspecifically suppress the normal operation of the immune system, frequently resulting in severe, adverse side effects and hospitalization. The Company's drug candidates, called Toleragens®, are designed to treat the underlying cause of many antibody-mediated diseases without these severe side effects. The Company's clinical drug candidates are known as Riquent™, previously referred to as LJP 394, a drug for the treatment of lupus, and LJP 1082, a drug for the treatment of antibody-mediated thrombosis. The Company completed its Phase III clinical trial for Riquent™ in December 2002 and the drug is currently in an on-going open-label follow-on clinical trial which is designed to collect longer-term safety data. The Company completed its initial Phase I/II clinical trial for LJP 1082 in October 2002.

The Company actively seeks additional financing to fund its research and development efforts and to commercialize its technologies. There is no assurance such financing will be available to the Company when needed or that such financing would be available under favorable terms.

The Company believes that patents and other proprietary rights are important to its business. The Company's policy is to file patent applications to protect its technology, inventions and improvements to its inventions that are considered important to the development of its business. The patent positions of biotechnology firms, including the Company, are uncertain and involve complex legal and factual questions for which important legal principles are largely unresolved. 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.

Basis of Presentation

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. This basis of accounting contemplates the recovery of the Company's assets and the satisfaction of liabilities in the normal course of business. The Company has incurred operating losses since its inception and has an accumulated deficit of $153.6 million at December 31, 2002. The Company believes its available cash, cash equivalents and short-term investments and interest earned thereon, will be sufficient to fund its operations as currently planned, which includes an additional trial for Riquent, into the first quarter of 2004. This estimation also assumes that the Company does not undertake significant commercialization activities for Riquent during 2003. Prior to the commercialization of any of its products, substantial capital resources will be required to fund continuing operations related to the Company's research and development, manufacturing, clinical testing and business development activities. The Company believes there may be a number of alternatives available to meet the continuing capital requirements of its operations, such as collaborative agreements and public or private financings. There

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

can be no assurance that any of these financings will be consummated in the necessary time frames needed for continuing operations or on terms favorable to the Company. If adequate funds in the future are not available, the Company will be required to significantly curtail its operating plans and may have to sell or license out significant portions of the Company's technology or potential products.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and disclosures made in the accompanying notes to the financial statements. Actual results could differ materially from those estimates.

Reclassification

Certain amounts in the 2001 financial statements have been reclassified to conform to the 2002 presentation.

Cash, Cash Equivalents and Short-Term Investments

Cash and cash equivalents consist of cash and highly liquid investments which include money market funds and debt securities with maturities from purchase date of three months or less and are stated at market. Short-term investments mainly consist of debt securities with maturities from purchase date of greater than three months. In accordance with Financial Accounting Standards Board ("FASB") Statement of Financial Accounting Standards ("SFAS") No. 115, *Accounting for Certain Investments in Debt and Equity Securities,* management has classified the Company's cash equivalents and short-term investments as available-for-sale securities in the accompanying financial statements. Available-for-sale securities are stated at fair market value, with unrealized gains and losses reported in other comprehensive income (loss). Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in interest income and have been immaterial for each of the years presented. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

Fair Value of Financial Instruments

Financial instruments, including cash and cash equivalents, accounts payable and accrued expenses, are carried at cost, which management believes approximates fair value because of the short-term maturity of these instruments. Short-term investments are carried at fair value. None of the Company's debt instruments that are outstanding at December 31, 2002 have readily ascertainable market values; however, the carrying values are considered to approximate their fair values.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

Concentration of Risk

Cash, cash equivalents and short-term investments are financial instruments which potentially subject the Company to concentrations of credit risk. The Company deposits its cash in financial institutions. At times, such deposits may be in excess of insured limits. The Company invests its excess cash in United States Government-backed securities, money market funds and debt instruments of financial institutions and corporations with strong credit ratings. The Company has established guidelines relative to the diversification of its cash investments and their maturities in an effort to maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates. To date, the Company has not experienced any impairment losses on its cash, cash equivalents and short-term investments.

Impairment of Long-Lived Assets and Assets to Be Disposed Of

In accordance with Statement of Financial Accounting Stardards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, if indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through the undiscounted future operating cash flows. If impairment is indicated, the Company measures the amount of such impairment by comparing the carrying value of the asset to the fair value of the asset and records the impairment as a reduction in the carrying value of the related asset and a charge to operating results. While the Company's current and historical operating and cash flow losses are indicators of impairment, the Company believes the future cash flows to be received from the long-lived assets will exceed the assets' carrying value, and accordingly the Company has not recognized any impairment losses through December 31, 2002.

Property and Equipment

Property and equipment is stated at cost and depreciated using the straight-line method over the estimated useful lives of the assets (primarily five years). Leasehold improvements and equipment under capital leases are stated at cost and amortized on a straight-line basis over the shorter of the estimated useful life or the lease term.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

Property and equipment is comprised of the following (in thousands):

	December 31, 2002	2001
Laboratory equipment	$ 5,383	$ 3,649
Computer equipment	1,472	779
Furniture and fixtures	404	238
Leasehold improvements	2,125	1,295
Construction in progress	2,154	283
	11,538	6,244
Less: Accumulated depreciation and amortization	(5,504)	(4,323)
	$ 6,034	$ 1,921

Depreciation and amortization expense for the periods ending December 31, 2002, 2001 and 2000 was $1,192,000, $620,000 and $322,000, respectively.

Patents

The Company has filed numerous patent applications with the United States Patent and Trademark Office and in foreign countries. Legal costs and expenses incurred in connection with pending patent applications have been deferred. Costs related to successful patent applications are amortized using the straight-line method over the lesser of the remaining useful life of the related technology or the remaining patent life, commencing on the date the patent is issued. Total cost and accumulated amortization were $2,518,000 and $399,000 at December 31, 2002 and $2,313,000 and $288,000 at December 31, 2001, respectively. Deferred costs related to patent applications are charged to operations at the time a determination is made not to pursue such applications.

Stock-Based Compensation

As allowed under Statement of Financial Accounting Standard No. 123, *Accounting and Disclosure of Stock-Based Compensation* (“SFAS 123”), the Company has elected to continue to account for stock option grants in accordance with Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (“APB 25”), and related interpretations. In March 2000, FASB issued Interpretation No. 44, *Accounting for Certain Transactions Involving Stock Compensation*, which clarifies certain isssues in the application of APB 25. Pursuant to APB 25, compensation expense for employee or director stock options represents the difference between the exercise price and the fair value of the common stock on the date of grant. This compensation expense is amortized to expense in accordance with FASB Interpretation No. 28, *Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans*, over the vesting period of the options. The Company generally grants stock options for a fixed number of shares to employees and directors with an exercise price equal to the fair value of the shares at the date of grant and therefore, under APB 25, recognized no compensation expense for such stock option grants.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

Pro forma information regarding net loss and net loss per share is required by SFAS 123, which also requires that the information be determined as if the Company has accounted for its employee stock plans granted after December 31, 1994 under the fair value method of that statement. The fair value was estimated at the date of grant using a Black-Scholes option pricing model with the following weighted-average assumptions for 2002, 2001 and 2000, respectively: risk-free interest rate of 3.0%, 4.4 % and 5.6%; volatility factor of the expected market price of the Company's common stock of 1.056, 1.109 and 1.113; a weighted-average expected life of 4.9 years, 4.8 years and 4.5 years and a dividend yield of 0% for all three years presented.

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the options' vesting period. The Company's pro forma information follows (in thousands except for net loss per share information):

	Years Ended December 31,		
	2002	2001	2000
Pro forma net loss	$(48,472)	$(27,919)	$(15,423)
Pro forma basic and diluted net loss per share	$ (1.15)	$ (0.81)	$ (0.59)

The effects of applying SFAS 123 for either recognizing compensation expense or providing pro forma disclosures are not likely to be representative of the effects on reported net loss for future years.

Options or stock awards issued to non-employees have been determined in accordance with SFAS 123 and EITF 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.* Deferred charges for options granted to non-employees are periodically remeasured as the options vest. In October 2002, the Company granted a non-qualified stock option to purchase 5,000 shares of common stock to a consultant at an exercise price equal to fair market value of the stock at the date of grant. The Company recognized approximately $3,000 in compensation expense for this stock option grant for the year ended December 31, 2002.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

Net Loss Per Share

Basic and diluted net loss per share is computed using the weighted-average number of common shares outstanding during the periods in accordance with Statement of Financial Accounting Standard No. 128, *Earnings per Share.* As the Company has incurred a net loss for all three years presented, stock options and warrants are not included in the computation of net loss per share since their effect is anti-dilutive.

Comprehensive Loss

In accordance with Statement of Financial Accounting Standard No. 130, *Reporting Comprehensive Income (Loss),* unrealized gains and losses on available-for-sale securities are included in other comprehensive income (loss). The Company's comprehensive net loss totaled $43,500,000 and $24,570,000 for the years ended December 31, 2002 and 2001, respectively.

Segment Information

In accordance with Statement of Financial Accounting Standard No. 131, *Segment Information,* the Company has determined that it operates in one business segment.

Recently Issued Accounting Standards

In June 2002, FASB issued Statement of Financial Accounting Standard No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* ("SFAS 146"). SFAS 146 nullifies Emerging Issues Task Force Issue No. 94-3, *Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (including Certain Costs Incurred in a Restructuring)* ("EITF 94-3"). SFAS 146 requires that a liability for a cost associated with an exit or disposal activity be recognized when the liability is incurred, whereas EITF 94-3 has recognized the liability at the commitment date to an exit plan. SFAS 146 is effective for exit or disposal activities initiated after December 31, 2002. The adoption of this statement is not expected to have a material impact on the financial position or results of operations of the Company.

In December 2002, the FASB issued SFAS No. 148, Accounting for Stock-Based Compensation-Transition and Disclosure - An Amendment of FASB Statement No. 123. SFAS No. 148 amends SFAS No. 123 to provide alternative methods of voluntarily transitioning to the fair value based method of accounting for stock-based employee compensation. SFAS No. 148 also amends the disclosure requirements of SFAS No. 123 to require prominent disclosure in both the annual and interim financial statements about the method used to account for stock-based employee compensation and the effect of the method on reported results. SFAS 148 does not permit the use of the original SFAS 123 prospective method of transition for changes to the fair value based method made in fiscal years beginning after December 15, 2003. The Company has not yet completed the final evaluation of transitioning options presented by SFAS 148. However, during 2003, we expect to reach a determination of whether and, if so, when to change our existing accounting for stock-based compensation to the fair value method in accordance with the transition alternatives of SFAS 148.

La Jolla Pharmaceutical Company

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies (continued)

In November 2002, the Emerging Issues Task Force (EITF) reached a consensus on Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables." EITF Issue No. 00-21 provides guidance on how to account for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets. The Company will be required to adopt this provision for revenue arrangements entered into on or after June 15, 2003. Management is currently evaluating the effect that the adoption of EITF 00-21 may have on the Company's results of operations and financial condition.

2. Cash Equivalents and Short-term Investments

The following is a summary of available-for-sale securities (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
December 31, 2002				
Money market accounts	$ 6,529	$ —	$ —	$ 6,529
United States corporate debt securities	17,148	43	20	17,171
Government-asset-backed securities	23,019	—	—	23,019
United States Treasury securities and obligations of the United States government agencies	5,010	13	—	5,023
	$51,706	$ 56	$ 20	$51,742
December 31, 2001				
Money market accounts	$ 204	$ —	$ —	$ 204
United States corporate debt securities	34,931	225	60	35,096
Government-asset-backed securities	9,375	53	—	9,428
United States Treasury securities and obligations of the United States government agencies	1,016	—	—	1,016
	$45,526	$ 278	$ 60	$45,744

The net adjustment to unrealized holding gains (losses) on available-for-sale securites included in comprehensive income (loss) totaled ($182,000) and $113,000 in 2002 and 2001, respectively. Included in cash and cash equivalents at December 31, 2002 and 2001 were $4,628,000 and $8,716,000, respectively, of securities classified as available-for-sale as we expect to sell them in order to support our current operations regardless of their maturity date. As of December 31, 2002, available-for-sale securities of $16,905,000 mature in one year or less and $34,837,000 are due after one year.

La Jolla Pharmaceutical Company

Notes to Financial Statements

3. Commitments

Leases

In July 1992, the Company entered into a non-cancelable operating lease for the rental of its office and research and development facilities, which lease expires in July 2004. The lease is subject to an escalation clause that provides for annual increases based on the Consumer Price Index. The lease also contains an option to extend the lease term for an additional five years and a one-time cancellation option with the payment of certain penalties.

In October 1996, the Company entered into an additional non-cancelable operating lease for additional office space. In November 2001, the Company extended the term of this lease to July 2004. The lease contains a provision for scheduled annual rent increases and an option to extend the lease term for an additional five years.

In September 2002, the Company entered into an additional non-canelable operating lease for additional research space. In February 2003, the Company extended the term of this lease to August 2003.

Annual future minimum lease payments as of December 31, 2002, are as follows (in thousands):

Years ended December 31,	Operating Leases	Capital Leases
2003	$ 1,229	$ 67
2004	666	—
2005	68	—
2006	5	—
2007	—	—
Total	$ 1,968	67
Less amount representing interest		(7)
Present value of net minimum lease payments		60
Less current portion		(60)
Noncurrent portion of capital lease obligations		$ —

Rent expense under all operating leases totaled $1,718,000, $2,330,000, and $2,776,000 for the years ended December 31, 2002, 2001 and 2000, respectively. Equipment acquired under capital leases included in property and equipment totaled $65,000 and $168,000 (net of accumulated amortization of $99,000 and $348,000) at December 31, 2002 and 2001, respectively. Amortization expense associated with these assets is included in depreciation and amortization expense for each of the three years in the period ended December 31, 2002.

La Jolla Pharmaceutical Company

Notes to Financial Statements

4. Long-Term Debt

The Company entered into a note payable for $958,000 in September 2002 and one for $698,000 in December 2002 to finance certain purchases of property and equipment. Both notes are secured by the financed property and equipment, bear interest at 9.45% and 9.70% per annum, respectively, and are payable in monthly installments of principal and interest of approximately $28,000 for the first 36 months and $17,000 for the remaining six months for the first note and approximately $20,000 for the first 36 months and $13,000 for the remaining six months for the second note.

Annual future minimum notes payable payments as of December 31, 2002, are as follows (in thousands):

Years ended December 31,	Notes Payable
2003	$ 580
2004	580
2005	531
2006	101
2007	—
Total	1,792
Less amount representing interest	(247)
Present value of net minimum notes payable payments	1,545
Less current portion	(434)
Noncurrent portion of notes payable	$1,111

5. Stockholders' Equity

Preferred Stock

As of December 31, 2002, the Company is authorized to issue 8,000,000 shares of preferred stock with a par value of $0.01 per share, in one or more series.

The Board of Directors designated 75,000 shares of preferred stock as nonredeemable Series A Junior Participating Preferred Stock ("Series A Preferred Stock") when adopting the Company's Stockholders Rights Plan. In the event of liquidation, each share of Series A Preferred Stock is entitled to receive a preferential liquidation payment of $1,000 per share plus the amount of accrued unpaid dividends. The Series A Preferred Stock is subject to certain anti-dilution adjustments, and the holder of each share is entitled to 1,000 votes, subject to adjustments. Cumulative quarterly dividends of the greater of $0.25 or, subject to certain adjustments, 1,000 times any dividend declared on shares of common stock, are payable when, as and if declared by the Board of Directors, from funds legally available for this purpose.

Stock Option Plans

In May 1989, the Company adopted the 1989 Stock Option Plan and the 1989 Nonstatutory Stock Option Plan (the "1989 Plan"), under which 904,000 shares of common stock have been authorized for issuance upon exercise of options granted by the Company. The 1989 Plan expired in 1999.

La Jolla Pharmaceutical Company

Notes to Financial Statements

5. Stockholders' Equity (continued)

In June 1994, the Company adopted the 1994 Stock Incentive Plan (the "1994 Plan"), under which 7,100,000 shares of common stock have been authorized for issuance upon exercise of options granted by the Company. The 1994 Plan provides for the grant of incentive and non-qualified stock options, as well as other stock-based awards, to employees, directors, consultants and advisors of the Company with various vesting periods as determined by the compensation committee, as well as automatic fixed grants to non-employee directors of the Company.

A summary of the Company's stock option activity and related data follows:

		Outstanding Options	
	Options Available For Grant	Number of Shares	Weighted-Average Exercise Price
Balance at December 31, 1999	413,590	2,259,851	$ 2.49
Additional shares authorized	1,000,000	—	—
Expired	(7,988)	—	$ 1.00
Granted	(1,081,544)	1,081,544	$ 5.28
Exercised	—	(159,170)	$ 1.34
Cancelled	66,688	(66,688)	$ 4.48
Balance at December 31, 2000	390,746	3,115,537	$ 3.47
Additional shares authorized	1,700,000	—	—
Expired	(2,260)	—	$ 1.00
Granted	(1,522,600)	1,522,600	$ 6.80
Exercised	—	(43,550)	$ 1.35
Cancelled	63,427	(63,427)	$ 6.61
Balance at December 31, 2001	629,313	4,531,160	$ 4.57
Additional shares authorized	1,900,000	—	—
Granted	(2,067,700)	2,067,700	$ 5.70
Exercised	—	(102,132)	$ 1.62
Cancelled	84,672	(84,672)	$ 6.70
Balance at December 31, 2002	546,285	6,412,056	$ 4.95

La Jolla Pharmaceutical Company

Notes to Financial Statements

5. Stockholders' Equity (continued)

	Years Ended December 31,					
	2002		2001		2000	
	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price	Options	Weighted-Average Exercise Price
Exercisable at end of year	3,605,876	$ 4.08	2,770,587	$ 3.20	2,121,134	$ 2.62
Weighted-average fair value of options granted during the year	$ 4.41		$ 5.42		$ 4.18	

Exercise prices and weighted-average remaining contractual lives for the options outstanding as of December 31, 2002 follow:

Options Outstanding	Range of Exercise Prices	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Options Exercisable	Weighted-Average Exercise Price
806,968	$ 0.34 - $1.00	5.71	$ 0.56	806,968	$ 0.56
868,124	$ 1.28 - $3.69	6.30	$ 3.22	859,671	$ 3.22
977,650	$ 3.75 - $5.03	6.11	$ 4.41	731,290	$ 4.40
820,367	$ 5.08 - $5.25	8.76	$ 5.12	176,581	$ 5.15
995,450	$ 5.28 - $5.90	9.47	$ 5.85	110,722	$ 5.67
559,980	$ 6.00 - $7.03	8.02	$ 6.93	358,755	$ 6.97
601,819	$ 7.05 - $7.10	9.06	$ 7.08	177,431	$ 7.09
781,698	$ 7.12 - $12.06	8.40	$ 7.73	384,458	$ 7.71
6,412,056	$ 0.34 - $12.06	7.67	$ 4.95	3,605,876	$ 4.08

At December 31, 2002, the Company has reserved 6,958,341 shares of common stock for future issuance upon exercise of options granted or to be granted under the 1989 and 1994 Plans.

La Jolla Pharmaceutical Company

Notes to Financial Statements

5. Stockholders' Equity (continued)

Employee Stock Purchase Plan

Effective August 1, 1995, the Company adopted the 1995 Employee Stock Purchase Plan, as amended (the "Purchase Plan"). Under the amended Purchase Plan, a total of 1,000,000 shares of common stock are reserved for sale to employees, as defined. Employees may purchase common stock under the Purchase Plan every three months (up to but not exceeding 10% of each employee's earnings) over the offering period at 85% of the fair market value of the common stock at certain specified dates. The offering period may not exceed 24 months. For the year ended December 31, 2002, 77,441 shares of common stock had been issued under the Purchase Plan (145,125 shares for the year ended December 31, 2001). To date, 598,214 shares of common stock have been issued under the Purchase Plan and 401,786 shares of common stock are available for issuance.

	Years Ended December 31,		
	2002	2001	2000
Weighted-average fair value of employee stock purchase plan purchases	$ 4.21	$ 2.84	$ 2.70

Stockholder Rights Plan

The Company has adopted a Stockholder Rights Plan (the "Rights Plan") which was amended in July 2000. The Rights Plan provides for a dividend of one right (a "Right") to purchase fractions of shares of the Company's Series A Preferred Stock for each share of the Company's common stock. Under certain conditions involving an acquisition by any person or group of 15% or more of the common stock (or in the case of State of Wisconsin Investment Board, 20% or more), the Rights permit the holders (other than the 15% holder, or, in the case of State of Wisconsin Investment Board, 20% holder) to purchase the Company's common stock at a 50% discount upon payment of an exercise price of $30 per Right. In addition, in the event of certain business combinations, the Rights permit the purchase of the common stock of an acquirer at a 50% discount. Under certain conditions, the Rights may be redeemed by the Board of Directors in whole, but not in part, at a price of $.001 per Right. The Rights have no voting privileges and are attached to and automatically trade with the Company's common stock. The Rights expire on December 2, 2008.

6. 401(k) Plan

The Company has established a 401(k) defined contribution retirement plan (the "401(k) Plan"), which was amended in May 1999 to cover all employees. The 401(k) Plan provides for voluntary employee contributions up to 20% of annual compensation (as defined). The Company does not match employee contributions or otherwise contribute to the 401(k) Plan.

La Jolla Pharmaceutical Company

Notes to Financial Statements

7. Income Taxes

At December 31, 2002, the Company had federal and California income tax net operating loss carryforwards of approximately $146,684,000 and $46,123,000, respectively. The difference between the federal and California tax loss carryforwards is primarily attributable to the capitalization of research and development expenses for California income tax purposes and the 50% to 55% percent limitation on California loss carryforwards. The Company also had federal and California research tax credit carryforwards of approximately $7,292,000 and $4,130,000, respectively. The federal net operating loss and tax credit carryforwards will begin to expire in 2004 unless previously utilized. California net operating loss will begin to expire in 2004, unless previously utilized.

Pursuant to Sections 382 and 383 of the Internal Revenue Code, annual use of the Company's net operating loss and credit carryforwards may be limited if a cumulative change in ownership of more than 50% occurs within a three-year period.

Significant components of the Company's deferred tax assets are shown below (in thousands):

	December 31, 2002	2001
Deferred tax assets:		
Net operating loss carryforwards	$ 53,992	$ 38,434
Research and development credits	9,976	7,926
Capitalized research and development	4,486	4,010
Total deferred tax assets	68,454	50,370
Deferred tax liability	—	(825)
	68,454	49,545
Valuation allowance for deferred tax assets	(68,454)	(49,545)
Net deferred tax assets	$ —	$ —

A valuation allowance of $68,454,000 has been recognized to offset the deferred tax assets as realization of such assets is uncertain.

Table of Contents

Exhibit Index

Exhibit Number	Description
23.1	Consent of Ernst & Young LLP, Independent Auditors
99.1	Certification pursuant to 18 U.S.C. section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

EXHIBIT 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-89980) pertaining to the 1994 Stock Incentive Plan and the 1995 Employee Stock Purchase Plan and in the Registration Statements on Form S-3 (Nos. 333-101499, 333-31142, 333-43066, 333-55370 and 333-81432) of La Jolla Pharmaceutical Company of our report dated February 14, 2003, with respect to the financial statements of La Jolla Pharmaceutical Company included in its Annual Report (Form 10-K) for the year ended December 31, 2002.

/s/ Ernst & Young LLP

ERNST & YOUNG LLP

San Diego, California
March 26, 2003

EXHIBIT 99.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Each of the undersigned, in his capacity as an officer of La Jolla Pharmaceutical Company (the "Registrant"), hereby certifies, for purposes of 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- the annual report of the Registrant on Form 10-K for the year ended December 31, 2002 ("the Report"), which accompanies this certification, fully complies with the requirements of Section 13(a) or 15(d) of the Securities and Exchange Act of 1934; and

- the information contained in the Report fairly presents, in all material respects, the financial condition of the Registrant at the end of such year and the results of operations of the Registrant of such year.

Date: March 27, 2003

/s/ Steven B. Engle

Steven B. Engle
Chairman and Chief Executive Officer

/s/ David Duncan, Jr.

David Duncan, Jr.
Chief Financial Officer

Note: A signed original of this written statement required by Section 906 has been provided to La Jolla Pharmaceutical Company and will be retained by La Jolla Pharmaceutical Company and furnished to the Securities and Exchange Commission or its staff upon request.