LA JOLLA PHARMACEUTICAL CO
Form 424B5
May 07, 2008

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The information in this preliminary prospectus supplement and the accompanying prospectuses is not complete and may be changed. Registration statements relating to these securities have been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectuses are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Filed pursuant to Rule 424(b)(5)
File Nos. 333-101499
333-145009

PRELIMINARY PROSPECTUS SUPPLEMENT SUBJECT TO COMPLETION May 6, 2008
(To Prospectuses dated December 12, 2002 and August 23, 2007)

Units

Consisting of Common Stock and Warrants

We are offering units, with each unit consisting of one share of common stock and a warrant to buy shares of common stock. Each warrant has an exercise price of $ per share, has a term of five years and is exercisable beginning on the date of issue. The shares of common stock and warrants comprising the units are immediately separable and will be issued separately.

Our common stock is listed on the NASDAQ Global Market under the symbol LJPC. The last reported sale price of our common stock on May 5, 2008 was $1.95 per share. We do not intend to list the warrants for trading on any recognized securities exchange.

We have received indications from certain of our principal stockholders of their intent to offer to purchase, either directly or through one or more of their affiliated investment funds, approximately $ million, or %, of the units offered hereby.

Investing in our securities involves a high degree of risk. Before buying any securities, you should read the discussion of material risks of investing in our securities in Risk factors beginning on page S-5 of this prospectus supplement.

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

	Per unit	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$

Proceeds, before expenses, to us	$	$

The above summary of offering proceeds to us does not give effect to any exercise of the warrants being issued in this offering.

The underwriters may also purchase up to an additional units from us at the public offering price, less underwriting discounts and commissions payable by us to cover over-allotments, if any, within 30 days from the date of this prospectus supplement. If the underwriters exercise the option in full, the total underwriting discounts and commissions will be $, and the total proceeds, before expenses, to us will be $.

The underwriters are offering the securities as set forth under Underwriting. Delivery of the units will be made on or about , 2008.

UBS Investment Bank **Canaccord Adams**

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You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectuses. We have not authorized anyone to provide you with different information. We are offering to sell, and seeking offers to buy, shares of our common stock and warrants only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement and the accompanying prospectuses, as well as the information that we have previously filed with the Securities and Exchange Commission and incorporated by reference, is accurate only as of the date of the applicable document, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock or warrants. The descriptions set forth in this prospectus supplement replace and supplement, where inconsistent, the description of the general terms and provisions set forth in the accompanying prospectuses.

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AUGUST 23, 2007 PROSPECTUS

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About this prospectus supplement

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

On December 21, 2005, we completed a one-for-five reverse stock split. The reverse stock split caused every five shares of our outstanding common stock to convert automatically into one share of common stock. All share and share related information set forth in this prospectus supplement and the August 23, 2007 accompanying prospectus is presented on a post-reverse stock split basis. Because we completed this reverse stock split subsequent to the date of the December 12, 2002 accompanying prospectus, all share and share related information set forth in the December 12, 2002 accompanying prospectus remains presented on a pre-reverse stock split basis.

Please read and consider all information contained in this prospectus supplement, the accompanying prospectuses and the documents incorporated by reference in this prospectus supplement and the accompanying prospectuses, including our Annual Report on Form 10-K for the year ended December 31, 2007 filed with the Securities and Exchange Commission on March 17, 2008, together with the additional information described under the section entitled Where you can find more information and incorporation by reference in this prospectus supplement and the section entitled Risk factors in this prospectus supplement before you make an investment decision.

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

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Summary

This is only a summary of the offering. It may not contain all of the information that may be important to you. To fully understand the investment you are contemplating, you should read this prospectus supplement, the accompanying prospectuses and the detailed information incorporated into them by reference before you decide to make an investment. Unless the context otherwise requires, the terms we, us and our refer to La Jolla Pharmaceutical Company, a Delaware corporation and our wholly owned subsidiary.

THE COMPANY

We are a biopharmaceutical company dedicated to improving and preserving human life by developing innovative pharmaceutical products. Our leading product in development, Riquent, is designed to treat lupus renal (kidney) disease by preventing or delaying renal flares. Lupus renal disease is a life-threatening, antibody-mediated disease in which disease-causing antibodies damage the kidneys. Renal flares are periods of extreme, acute kidney inflammation in patients suffering from lupus renal disease. Riquent is currently in a Phase 3 clinical trial under a Special Protocol Assessment and has been granted Fast Track designation by the FDA.

Lupus renal disease is a chronic illness that can lead to irreversible renal damage, renal failure and the need for dialysis, and is a leading cause of death in lupus patients. Lupus is an antibody-mediated disease caused by autoantibodies, of which antibodies to double-stranded DNA (dsDNA) are an important subgroup. Riquent is designed to prevent or delay renal flares by lowering the levels of circulating antibodies to dsDNA, which are believed to cause lupus renal disease. Current treatments for this autoimmune disorder often address only symptoms of the disease, or nonspecifically suppress the entire immune system, which can result in severe, negative side effects and hospitalization. We believe that Riquent has the potential to treat lupus renal disease without these severe, negative side effects. The Lupus Foundation estimates that there are approximately one million lupus patients in the United States. We believe that 40% to 45% of these lupus patients will develop renal disease.

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

RECENT DEVELOPMENTS

We recently announced positive 12-month interim antibody data from our ongoing double-blind, placebo-controlled, randomized Phase 3 study of Riquent referred to as the Phase 3 ASPEN study (Abetimus Sodium in Patients with a History of Lupus Nephritis). Analyses of 12-month interim antibody data in the first 125 patients randomized in the study indicate that for all patients treated with 900 mg, 300 mg or 100 mg of Riquent per week compared with placebo, there were significantly greater reductions in antibodies to dsDNA ($p < 0.0001$).

The data show a dose-response curve for antibody reduction and also show that the 300 mg and 900 mg doses appear to be near the top of the antibody-related dose-response curve, thus supporting the choice of doses for this study. Antibody levels in the placebo-treated group remained around baseline levels throughout the 12 months. The rate at which antibody levels were maximally reduced appeared to be more rapid in the 900 mg dose group than in the 300 mg or the 100 mg dose groups. Each individual dose group was significantly different from placebo ($p < 0.0001$). An area under the curve (AUC) analysis, which reflects the effect of the drug on antibody levels over time, showed significantly greater antibody-lowering effects for the 300 mg and 900 mg dose groups compared with the placebo

group (decreases of 26.9% for 100 mg, 35.5% for 300 mg and 37.7% for 900 mg, compared with an increase of 7.5% for placebo). The AUC analysis provides additional evidence that the higher doses of Riquent suppressed antibodies further than the 100 mg dose group. The proportion of patients achieving a 50% or greater AUC reduction was 0.0% in the placebo and 100 mg groups, 23% in the 300 mg group, and 30% in the 900 mg group. The 12-month antibody analysis assessed the impact of treatment with

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Riquent or placebo on antibodies to dsDNA. Antibody levels were measured every two weeks for the first 16 weeks of the study and then monthly for the remaining 36 weeks. All demographics and baseline characteristics were comparable across dosing groups.

We also recently announced that our Phase 3 ASPEN study of Riquent appears to be progressing well, in that more than 140 clinical trial sites are active and more than 670 patients have been enrolled. Compliance with weekly visits has been high and the drop-out rate remains low. The Independent Data Monitoring Board (DMB) has completed three reviews of the safety data and has not indicated any safety issues. The study is an event-driven trial designed to be completed when 128 renal flares have occurred. The current overall renal flare rate is lower than the original trial assumption. As a result, in an effort to shorten the time to achieve the required number of renal flares, we will continue enrollment beyond the initially targeted 740 patients and extend the treatment period beyond 12 months until the required number of renal flares is achieved. We now estimate that at least 800 patients will be enrolled in the study. Based on these changes, we expect the trial to complete in the second half of 2009.

The Phase 3 ASPEN study includes two interim efficacy analyses, each with target p values of $p < 0.001$ and a final p value of $p < 0.05$ at the end of the study. We have added a futility analysis to each interim efficacy analysis. The interim efficacy analyses have been moved to occur later in the study when a greater number of renal flares will have been observed. As a result, the first interim efficacy analysis is expected to occur around the fourth quarter of 2008, and the second interim efficacy analysis is expected to occur about midway between the first analysis and the expected end of the study.

These modifications to the trial have been discussed with the FDA, and the trial continues to be conducted under the FDA s Special Protocol Assessment.

On May 1, 2008, we announced preliminary financial results for the three months ended March 31, 2008. We reported that for this period we had a net loss of $13.6 million, or $0.34 per share, and that at March 31, 2008, we had cash, cash equivalents and short-term investments of $25.4 million. Until completion of a review and issuance of financial statements for the three months ended March 31, 2008, any amounts related to this period are subject to change.

AMENDMENT TO RIGHTS PLAN

We have received indications from certain of our principal stockholders Essex Woodlands Health Ventures Fund VI, L.P., Frazier Healthcare V, L.P. and Alejandro Gonzalez of their intent to offer to purchase, either directly or through one or more of their affiliated investment funds, approximately $ million, or %, of the units in this offering. If these stockholders offer to purchase these units, we expect that the underwriters will confirm orders to them in such an amount, and that immediately after the completion of this offering, Essex Woodlands Health Ventures Fund VI, L.P. (and its affiliates), Frazier Healthcare V, L.P. (and its affiliates) and Alejandro Gonzalez (and his affiliates) will beneficially own approximately %, % and %, respectively, of our outstanding common stock, including the shares issuable to these stockholders under the warrants to be sold in this offering.

Under the terms of our rights agreement with American Stock Transfer & Trust Co., dated December 3, 1998, as amended, if Essex Woodlands Health Ventures Fund VI, L.P. (and its affiliates), Frazier Healthcare V, L.P. (and its affiliates) and Alejandro Gonzalez (and his affiliates) purchase units in this offering in the amounts described above, each such stockholder would become an acquiring person under the rights agreement and would trigger the rights issued thereunder. In order to avoid triggering the rights issued under the rights plan in connection with this offering, we expect to amend the rights agreement upon the completion of this offering to allow Essex Woodlands Health Ventures Fund VI, L.P. (and its affiliates), Frazier Healthcare V, L.P. (and its affiliates) and Alejandro Gonzalez (and his affiliates) to beneficially own up to %, % and %, respectively, of our outstanding common stock, in each case, without becoming an acquiring person under the agreement. See Description of capital stock La Jolla

Pharmaceutical Company Rights Plan.

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CORPORATE INFORMATION

We were incorporated in the State of Delaware in 1989. Our principal executive offices are located at 6455 Nancy Ridge Drive, San Diego, California 92121 and our telephone number is (858) 452-6600. Our website is located at *www.ljpc.com*. We have not incorporated by reference into this prospectus supplement the information on our website, and you should not consider our website to be a part of this document. For more complete information please refer to our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

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The offering

Common stock we are offering	shares, plus shares of common stock underlying the warrants offered hereby
Common stock warrants we are offering	Warrants to purchase shares of common stock
Common stock to be outstanding after this offering	shares, or shares if the warrants sold in this offering are exercised in full
Purchases by principal stockholders	We have received indications from certain of our principal stockholders of their intent to offer to purchase, either directly or through one or more of their affiliated investment funds, up to $ million, or %, of the units offered hereby. If these stockholders offer to purchase these units, we expect that the underwriters will confirm orders to them in such an amount.
Use of proceeds after expenses	We estimate that our net proceeds from this offering will be approximately $ million after deducting underwriting discounts and commissions and estimated offering expenses. We intend to use the net proceeds from this offering to fund the development of Riquent and other general corporate purposes, as further described in this prospectus supplement under the heading Use of proceeds.
Risk factors	See the Risk factors section and other information included in this prospectus supplement, the accompanying prospectuses and incorporated by reference for a discussion of factors you should carefully consider before deciding to invest in our securities.
NASDAQ Global Market Symbol	LJPC

The number of shares outstanding after the offering is based on 39,671,491 shares of common stock outstanding as of March 31, 2008 and excludes:

- shares of common stock that are a part of the units that the underwriters have a right to purchase from us to cover over-allotments, if any.
- 4,399,992 shares of common stock that may be issued on the exercise of outstanding warrants at an exercise price of $5.00 per share.
- 5,443,354 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 $7.80 per share.
- Approximately 351,765 shares of common stock reserved for future issuance under our equity incentive and employee stock purchase plans.

Unless otherwise indicated, this prospectus supplement does not assume that any of the warrants issued hereunder will be exercised.

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Risk factors

The shares of our common stock and warrants offered by this prospectus supplement and the accompanying prospectuses are speculative and involve a high degree of risk of loss. Before making an investment, you should carefully read this entire prospectus supplement, the accompanying prospectuses and the information incorporated by reference in them and consider the following risks and speculative factors. Some of these factors have affected our financial condition and operating results in the past or are currently affecting us. All of these factors could affect our future financial condition or operating results. If any of the following risks actually occurs, our business could be very significantly harmed. If that happens, the trading price of our common stock could decline, and you may lose all or part of your investment.

RISK FACTORS RELATING TO LA JOLLA PHARMACEUTICAL COMPANY AND THE INDUSTRY IN WHICH WE OPERATE

We do not have sufficient financial resources to complete the current Phase 3 ASPEN study of Riquent and may not have sufficient resources to continue to operate unless we are able to raise sufficient additional capital.

We will need to successfully complete the current Phase 3 ASPEN study prior to any FDA or any foreign regulatory approvals. The current Phase 3 ASPEN study is an event-driven trial requiring us to accrue a specified number of renal flares to complete the study. We currently target enrolling at least 800 patients to achieve the required number of renal flares and the trial could take several years to complete. We expect that the actual costs of completing the current Phase 3 ASPEN study will exceed our current cash resources; we expect that the net proceeds from this offering, together with our other cash resources, excluding the value of our currently illiquid auction rate securities, will enable us to continue our operations as currently planned through December 31, 2008. If we expend all of the funds that we have raised and do not receive funding from a collaborative agreement with a corporate partner or obtain other equity or debt financing, we would not have the financial resources to complete the current Phase 3 ASPEN study or to continue the development of Riquent, and we may not be able to continue to operate.

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

Our business is highly cash-intensive and we will need a significant amount of additional cash to continue our operations. There can be no guarantee that additional financing will be available to us on favorable terms, or at all, whether through issuance of additional securities, entry into collaborative arrangements, or otherwise. If adequate funds are not available, we may halt the current Phase 3 ASPEN study, significantly reduce the size of our workforce, sell or license our technologies or obtain funds through other arrangements with collaborative partners or others that require us to relinquish rights to our technologies or potential products. We also may merge with another entity to continue our operations. Any one of these outcomes could have a negative impact on our ability to develop products or achieve profitability if our products are brought to market. If, and to the extent, we obtain additional funding through sales of securities, any previous investment in us will be diluted, and dilution can be particularly substantial when the price of our common stock is low. Moreover, capital markets have experienced a period of instability recently and this instability may make it harder for us to raise capital within the time periods needed or on terms we consider acceptable, if at all. In the current economic environment, our need for additional capital and limited capital resources may force us to accept financing terms that could be significantly more dilutive than if we were raising capital when the capital markets were more stable.

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Negative conditions in the global credit markets may further impair the liquidity of a portion of our investment portfolio.

As of March 31, 2008, our investment securities consist primarily of money market funds and AAA rated asset-backed student loan auction rate securities. As of December 31, 2007, our short-term investments included $28.0 million of AAA rated asset-backed student loan auction rate securities issued primarily by state governments. Subsequent to December 31, 2007, we sold $18.0 million of these asset-backed auction rate securities at par value.

The recent negative conditions in the global credit markets have prevented some investors from liquidating their holdings, including their holdings of student loan auction rate securities. As of March 31, 2008, there was insufficient demand at auction for each of our remaining four AAA rated asset-backed student loan auction rate securities, representing the entire $10.0 million we currently hold in asset-backed auction rate securities. As a result of the insufficient demand, these four securities are currently not liquid and unless a future auction (which occurs approximately every 28 to 91 days) for these investments is successful, we could be required to hold them until they are redeemed by the issuer or to maturity, which ranges between 20-30 years. Based on our current capital resources and projected needs, we will not be able to hold these securities until maturity.

In the event we need to access the funds that are in an illiquid state, we will not be able to do so without a loss of principal, until a future auction on these investments is successful, the securities are redeemed by the issuer or they mature. As of March 31, 2008, management has determined that our student loan auction rate securities are impaired and accordingly we have recorded realized impairment losses of $0.8 million on these investments. The impairment losses on these investments were determined to be other-than-temporary as we may be required to liquidate these auction rate securities in the short term in order to continue our operations. If the credit ratings of the security issuers deteriorate and/or if there is any further decline in market value that is determined to be other-than-temporary, we would be required to further adjust the carrying value of these investments through an impairment charge.

Our independent registered public accounting firm has issued an unqualified opinion with an explanatory paragraph, to the effect that there is substantial doubt about our ability to continue as a going concern.

Our independent registered public accounting firm has issued an unqualified opinion with an explanatory paragraph, to the effect that there is substantial doubt about our ability to continue as a going concern. This unqualified opinion with an explanatory paragraph could have a material adverse effect on our business, financial condition, results of operations and cash flows. See Liquidity and Capital Resources, Management s Discussion and Analysis of Financial Condition and Results of Operations and note 1 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2007, which is incorporated by reference into this prospectus supplement.

We have no committed sources of capital and do not know whether additional financing will be available when needed on terms that are acceptable, if at all. Our current lack of resources is exacerbated by our inability to liquidate holdings of certain student loan auction rate securities. The addition of this going concern statement from our independent registered public accounting firm may discourage some investors from purchasing our stock or providing alternative capital financing. The failure to satisfy our capital requirements will adversely affect our business, financial condition, results of operations and prospects.

Unless we raise additional funds, including through the sale of equity securities and through one or more collaborative arrangements, we will need to halt the Phase 3 ASPEN study and significantly reduce our workforce and our operating expenses. If we do not take these actions, we will not have sufficient funds to continue operations. Even if we take these actions, they may be insufficient, particularly if our costs are higher than projected or unforeseen expenses arise. Halting our Phase 3

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ASPEN study or significantly reducing our workforce or operating expenses will adversely affect our business and prospects.

In order to complete our current Phase 3 ASPEN study, we will need to accrue a sufficient number of renal flares by enrolling a sufficient number of patients who meet the trial criteria. If we are unable to successfully complete the trial, our business will be adversely affected and it may be difficult or impossible for us to continue to operate.

The current Phase 3 ASPEN study is an event-driven trial requiring us to accrue a specified number of renal flares to complete the study. We currently target enrolling at least 800 patients to achieve the required number of renal flares. We may need to enroll more patients in order to reach the required number of renal flares. We may have difficulty enrolling patients because, among other matters, there are specific limitations on the medications that a patient may be taking upon entry into the trial and intense competition for available lupus patients. If we are unable to accrue a sufficient number of renal flares or to timely enroll a sufficient number of patients, we will not be able to successfully complete the current Phase 3 ASPEN study. As a result, it may be difficult or impossible for us to continue to operate.

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

Our drug candidates are subject to extensive government regulations related to development, clinical trials, manufacturing and commercialization. In order to sell any product that is under development, we must first receive regulatory approval. To obtain regulatory approval, we must conduct clinical trials and toxicology studies that demonstrate that our drug candidates are safe and effective. The process of obtaining FDA and foreign regulatory approvals is costly, time consuming, uncertain and subject to unanticipated delays.

The FDA and foreign regulatory authorities have substantial discretion in the approval process and may not agree that we have demonstrated that Riquent is safe and effective. If Riquent is ultimately not found to be safe and effective, we would be unable to obtain regulatory approval to manufacture, market and sell Riquent. Although we have received an approvable letter from the FDA, the analysis of the data from our previous Phase 3 trial of Riquent showed that the trial did not reach statistical significance with respect to its primary endpoint, time to renal flare, or with respect to its secondary endpoint, time to treatment with high-dose corticosteroids or cyclophosphamide. In a preliminary assessment of the MAA submitted in March 2006, the EMEA reviewers indicated that additional clinical data would be needed prior to potential approval. Based on our review of the EMEA assessment, we believe that the current Phase 3 ASPEN study should provide the necessary data; however, since the data would not be available within the timeframe that the EMEA regulations allow for review of the Riquent application we submitted, we withdrew the application. We plan to refile the MAA after the completion of the current Phase 3 ASPEN study, if it is successful. We can provide no assurances that the FDA or foreign regulatory authorities will ultimately approve Riquent or, if approved, what the indication for Riquent will be.

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

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

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

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

Current and future clinical trials may be delayed or halted.

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

Ø we do not have sufficient financial resources;

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

Ø patients do not enroll in the studies at the rate we expect;

Ø the observed renal flare rate is lower than we expect;

Ø the products are not effective;

Ø patients experience negative side effects or other safety concerns are raised during treatment;

Ø the trials are not conducted in accordance with applicable clinical practices; or

Ø there is political unrest at foreign clinical sites; or

Ø there are natural disasters at any of our clinical sites.

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

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

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

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

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

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If we encounter delays or difficulties in establishing or maintaining relationships with manufacturing or distribution contractors, our ability to timely complete necessary clinical trials and potentially deliver commercial products may be negatively affected.

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

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

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

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

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

- Ø 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;
- Ø some of our suppliers may be required to pass FDA inspections or validations or to obtain other regulatory approvals of their manufacturing facilities or processes, and they may be delayed or unable to do so;
- Ø the materials that our suppliers use to manufacture the chemicals and reagents that they provide us may be costly or in short supply; and
- Ø there are a limited number of suppliers that are able to provide us with the chemicals or reagents that we use to manufacture our drugs.

If we are unable to obtain sufficient quantities of chemicals or reagents, our ability to produce products for clinical studies and, therefore, to introduce products into the market on a timely and competitive basis, will be impeded. The

subsequent sales of our products, if any, and our profit margins may also be negatively affected.

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

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

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

We are highly dependent on the principal members of our clinical development, manufacturing and management staff, the loss of whose services may delay the achievement of our research and development objectives. Retaining our current key personnel to perform clinical development, manufacturing, regulatory, and business development activities will be critical to our near term success. We expect that recruiting additional qualified personnel to conduct clinical development, manufacturing, regulatory, and marketing and sales activities will be required to successfully further develop Riquent and any additional drug candidates. Because competition for experienced clinical, manufacturing, regulatory, business development and marketing and sales personnel among numerous pharmaceutical and biotechnology companies and research and academic institutions is intense, we may not be able to attract and retain these people. If we cannot attract and retain qualified people, our ability to conduct necessary clinical trials, manufacture drug, comply with regulatory requirements, enter into collaborative agreements and develop and sell potential products may be negatively affected because, for instance, the trials may not be conducted properly, or the manufacturing or sales of our products may be delayed. In addition, we rely on consultants and advisors to assist us in formulating our clinical, manufacturing, regulatory, business development, and marketing and sales strategies. All of our consultants and advisors have outside employment and may have commitments or consulting or advisory contracts with other entities that may limit their ability to contribute to our business.

We will need additional funds to support our operations.

Our operations to date have consumed substantial capital resources. Before we can obtain FDA or foreign regulatory approval for Riquent, we will need to successfully complete the current Phase 3 ASPEN study and possibly additional trials. Therefore, we expect to expend substantial amounts of capital resources for additional product development and clinical trials of Riquent. We may also devote substantial additional capital resources to establish commercial-scale manufacturing capabilities and to market and sell potential products. These expenses may be incurred prior to or after any regulatory approvals that we may receive. Even with the net proceeds of approximately $ million from this offering, we will need additional funds to finance our future operations. Our future capital requirements will depend on many factors, including:

Ø the scope and results of our clinical trials;

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

Ø our ability to obtain regulatory approval for Riquent;

Ø the time and costs involved in applying for regulatory approvals;

Ø continued scientific progress in our development programs;

Ø the size and complexity of our development programs;

Ø 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.

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We expect to incur substantial losses each year for at least the next several years as we continue our planned clinical trial, manufacturing, regulatory, and development activities. If we receive regulatory approval for Riquent, or any of our other drug candidates, our manufacturing, marketing and sales activities are likely to substantially increase our expenses and our need for additional working capital. In the future, it is possible that we will not be able to obtain additional funds and thus not have adequate resources to support continuation of our business activities.

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

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

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

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

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

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

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

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

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 potentially more than 1,000,000 and those with renal impairment, which Riquent is designed to treat, is approximately 300,000. However, there is limited and differing 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 Riquent will be observed in broader patient populations, and the number of patients who may benefit from Riquent may be significantly smaller than the estimated patient populations. Furthermore, management of patients with renal disease by specialists other than nephrologists and rheumatologists 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 drug candidates receive regulatory approval, patients and physicians may not readily or quickly accept our proposed methods of treatment. In order for Riquent or our other drug candidates to be commercially successful, we will need to increase the awareness and acceptance of our drug candidates among physicians, patients and the medical community. Riquent is designed to be administered weekly by intravenous injection. It is possible that providers and patients may resist an intravenously administered therapeutic. It is also possible that physician treatment practices may change and that the use of other drugs, either newly approved or currently on the market for other conditions, may become widely utilized by clinicians for the treatment of patients with lupus and reduce the potential use of Riquent in this patient population. In addition, if we are unable to manufacture drugs at an acceptable cost, physicians may not readily prescribe drugs that we may manufacture due to cost-benefit considerations when compared to other methods of treatment. If we are unable to achieve market acceptance for approved products, our revenues and potential for profitability will be negatively affected.

We lack exp