LA JOLLA PHARMACEUTICAL CO
Form 424B2
September 09, 2015
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The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus do not constitute an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 9, 2015

PROSPECTUS SUPPLEMENT

(To Prospectus dated July 11, 2014)

Shares

Common Stock

We are offering shares of our common stock, $0.0001 par value per share. Our common stock is currently listed on The NASDAQ Capital Market under the symbol LJPC. On September 8, 2015, the last reported sale price of our common stock was $43.90 per share.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-5 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

	PER SHARE	TOTAL
Public Offering Price	$	$

Underwriting Discounts and Commissions [(1)]	$	$
Proceeds to La Jolla Pharmaceutical Company, Before Expenses	$	$

(1) We refer you to Underwriting beginning on page S-20 for additional information regarding underwriter compensation.

Delivery of the shares of common stock is expected to be made on or about , 2015. We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $ and the total proceeds to us, before expenses, will be $.

Book-Running Manager

Jefferies

Prospectus Supplement dated , 2015.

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of the accompanying prospectus entitled Where You Can Find More Information and Incorporation of Certain Information by Reference.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus each form a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. This prospectus supplement provides you with specific information about this offering. The accompanying prospectus, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus and the documents incorporated by reference therein. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein.

In this prospectus supplement, La Jolla, the Company, we, us, and our and similar terms refer to La Jolla Pharmaceutical Company. References to our common stock refer to the common stock of La Jolla Pharmaceutical Company.

All references in this prospectus supplement to our financial statements include, unless the context indicates otherwise, the related notes.

The industry and market data and other statistical information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference are based on management s own estimates, independent publications, government publications, reports by market research firms or other published independent sources, and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING INFORMATION

This prospectus supplement, the accompanying prospectus, and the documents incorporated by reference therein contain forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words believe, expect, anticipate, intend, estimate, project, wil may, plan, intend, assume and other expressions (including their use in the negative) that predict or indicate future events and trends, including our future financial performance, and that do not relate to historical matters.

Such statements include, but are not limited to, statements about: our ability to successfully develop LJPC-501, LJPC-401, LJPC 30s and our other product candidates (collectively our product candidates); the future success of our clinical trials with our product candidates; the timing for the commencement and completion of clinical trials; and our ability to obtain orphan status, break-through status, other regulatory designations or additional patent protection with respect to any of our product candidates. Forward-looking statements are neither historical facts nor assurances of future performance.

These statements are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements.

Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others:

- the risk that our clinical trials with our product candidates may not be successful in evaluating their safety and tolerability or providing preliminary evidence of efficacy;

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- the successful and timely completion of clinical trials;
- our plans and timing with respect to seeking regulatory approvals and uncertainties regarding the regulatory process;
- the availability of funds and resources to pursue our research and development projects, including our clinical trials with our product candidates;
- general economic conditions;
- uncertainties associated with obtaining and enforcing patents;
- the potential commercialization of any of our drug candidates that receive regulatory approval;
- our estimates for future performance; and
- our estimates regarding our capital requirements and our needs for, and ability to obtain, additional financing.

In addition, the factors described under the section captioned Risk Factors in this prospectus, as may be updated from time to time by our future filings under the Securities Exchange Act of 1934, and elsewhere in the documents incorporated by reference in this prospectus, may result in these differences. You should carefully review all of these factors.

We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. The forward-looking statements were based on information, plans and estimates at the date of this prospectus supplement, the accompanying prospectus or the documents incorporated by reference therein, as applicable, and we assume no obligation to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

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PROSPECTUS SUMMARY

The following summary of our business highlights certain of the information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under Where You Can Find More Information and Information Incorporated By Reference in the accompanying prospectus. You should also carefully consider the matters discussed in the section in this prospectus supplement titled Risk Factors and in the accompanying prospectus and in other periodic reports incorporated herein by reference.

Our Company

La Jolla Pharmaceutical Company is a biopharmaceutical company focused on the discovery, development and commercialization of innovative therapies intended to significantly improve outcomes in patients suffering from life-threatening diseases. We have several product candidates in development. LJPC-501 is our proprietary formulation of angiotensin II for the potential treatment of catecholamine-resistant hypotension. LJPC-401 is our novel formulation of hepcidin for the potential treatment of conditions characterized by iron overload, such as hereditary hemochromatosis and beta thalassemia. LJPC-30Sa and LJPC-30Sb are our next-generation gentamicin derivatives for the potential treatment of serious bacterial infections and rare genetic disorders, such as cystic fibrosis and Duchenne muscular dystrophy.

Our common stock is currently listed on The NASDAQ Capital Market under the symbol LJPC.

Program Overview

LJPC-501

Catecholamine-Resistant Hypotension

LJPC-501, our lead product candidate, is our proprietary formulation of angiotensin II. Angiotensin II, the major bioactive component of the renin-angiotensin system, serves as one of the body s central regulators of blood pressure. We are developing LJPC-501 for the treatment of catecholamine-resistant hypotension, or CRH, which is an acute, life-threatening condition in which blood pressure drops to dangerously low levels in patients who respond poorly to current treatments. Angiotensin II has been shown to raise blood pressure in a randomized, placebo-controlled clinical trial in CRH, which was recently published in the journal Critical Care, as well as in animal models of hypotension. Preclinical pharmacology studies that we have conducted have demonstrated that catecholamine resistance may be in part a result of reduced endogenous production of angiotensin II. In October 2014, we presented positive data from a preclinical study of LJPC-501 for the treatment of CRH.

We initiated a Phase 3 clinical trial with LJPC-501 for the treatment of CRH, called the ATHOS (Angiotensin II for the Treatment of High-Output Shock) 3 trial, in March 2015. In February 2015, we reached agreement with the U.S. Food and Drug Administration, or FDA, on a Special Protocol Assessment, or SPA, for this multicenter, randomized, double-blind, placebo-controlled, Phase 3 clinical trial. In accordance with the SPA, the primary efficacy endpoint for the ATHOS 3 registration trial is increase in blood pressure at three hours. The ATHOS 3 trial is designed to enroll approximately 315 patients. Patients are to be randomized in a 1:1 fashion to receive either: (i) LJPC-501 plus standard-of-care vasopressors; or (ii) placebo plus standard-of-care vasopressors. Randomized patients are to receive their assigned treatment via continuous IV infusion for up to seven days. The primary efficacy endpoint in the study is

to compare the change in mean arterial pressure in patients with CRH who receive an IV infusion of LJPC-501 plus standard-of-care vasopressors to those that receive placebo plus standard-of-care vasopressors. Secondary endpoints include comparison of changes in Cardiovascular Sequential Organ Failure Assessment scores, and the safety and tolerability of LJPC-501 in patients with CRH. Results from ATHOS 3 are expected by the end of 2016.

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Hepatorenal Syndrome

We are also developing LJPC-501 for hepatorenal syndrome, or HRS. HRS is a life-threatening form of progressive renal failure in patients with liver cirrhosis or fulminant liver failure. In these patients, the diseased liver secretes vasodilator substances (e.g., nitric oxide and prostaglandins) into the bloodstream that cause under-filling of blood vessels. This low blood pressure state causes a reduction in blood flow to the kidneys. As a means to restore systemic blood pressure, the kidneys induce both sodium and water retention, which contribute to ascites, a major complication associated with HRS. Studies have shown that LJPC-501 may improve renal function in patients with conditions similar to HRS. We are currently enrolling patients in a Phase 1/2 clinical trial of LJPC-501 in HRS.

LJPC-401

LJPC-401 is our novel formulation of hepcidin. Hepcidin is a naturally occurring regulator of iron absorption and distribution. By regulating the absorption and distribution of iron, hepcidin prevents excessive iron accumulation in tissues, such as the liver and heart, where it can cause significant damage and even result in death.

We are developing LJPC-401 for the treatment of conditions characterized by iron overload, such as hereditary hemochromatosis and beta thalassemia. Hereditary hemochromatosis, or HH, is a disease characterized by a deficiency in hepcidin that results in excessive iron accumulation. HH is the most common genetic disease in Caucasians and causes liver cirrhosis, liver cancer, heart disease and/or failure, dementia and diabetes.

LJPC-401 has been shown to be effective in reducing serum iron in preclinical testing. We filed an Investigational New Drug Application, or IND, with the FDA and expect to release preliminary results from a Phase 1 study by the end of 2015.

LJPC-30Sa and LJPC-30Sb

LJPC-30Sa and LJPC-30Sb are our next-generation gentamicin derivatives. Despite kidney toxicity, gentamicin has become one of the most commonly prescribed hospital antibiotics due to its broad spectrum of antimicrobial efficacy. Gentamicin consists primarily of a mixture of four distinct but closely related chemical entities that may contribute differentially to the product s toxicity profile.

LJPC-30Sa and LJPC-30Sb are purified components of the currently marketed gentamicin product that retain the biologic activity of gentamicin, yet appear to lack the traditional kidney toxicity associated with it. We are developing LJPC-30Sa and LJPC-30Sb not only for the potential treatment of serious bacterial infections but also for the potential treatment of rare genetic disorders, such as cystic fibrosis and Duchenne muscular dystrophy.

We believe that gentamicin s ability to induce a lack of fidelity in gene transcription, intrinsic to its antimicrobial mechanism of action, can also be leveraged in the correction of certain human genetic mutations that lead to rare genetic disorders, such as cystic fibrosis and Duchenne muscular dystrophy. In spite of favorable short-term clinical proof-of-efficacy data in cystic fibrosis, development of gentamicin as a chronic treatment for these genetic diseases has been limited by its toxicity profile.

Following a pre-IND meeting with the FDA, we have received guidance that we may proceed with a proposed Phase 1 clinical trial following the submission of an IND.

Patents and Proprietary Technologies

We own two U.S. patent applications and two international applications covering methods of use for LJPC-501. Our license with the George Washington University provides rights in two U.S. applications and an international application directed to methods of using LJPC-501. These applications, if issued as patents, will have expiration dates from 2029 to 2035.

Our license from Inserm in France provides rights in a portfolio of patents and applications covering methods of use of LJPC-401. This portfolio includes one issued U.S. patent, two pending U.S. applications, issued

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patents in Canada, China, Europe, and Japan, and pending applications in Europe, China, and Japan. The issued U.S. patent will expire in May 2022.

We have licensed rights in one U.S. provisional patent application and one issued U.S. patent and one pending U.S. non-provisional patent application from Indiana University Research and Technology Corporation. The licensed rights cover methods of using LJPC-30Sa and LJPC-30Sb. The issued patent and any patents issuing from the pending U.S. non-provisional patent application will expire in 2027, if not extended, and any patents that may issue based on the provisional application are expected to expire no earlier than 2036.

In addition to the above, we plan to file additional patent applications that, if issued, would provide further protection for LJPC-501, LJPC-401 and LJPC-30S.

Recent Developments

In May 2015, we announced a reprioritization of our product development programs that resulted in the discontinuation of the development of our polysaccharide-based galectin-3 inhibitors, GCS-100 and LJPC-1010. This reprioritization has allowed us to reallocate resources to our other development candidates that are more in line with our strategic focus.

Corporate Information

Our executive offices are located at 10182 Telesis Court, 6th Floor, San Diego, California 92121 and our telephone number is (858) 207-4264. Additional information regarding our company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. See Where You Can Find More Information on page 9 of the accompanying prospectus and Incorporation of Certain Information by Reference beginning on page 10 of the accompanying prospectus.

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THE OFFERING

Common Stock we are Offering	shares
Common Stock to be Outstanding after this Offering	shares
Option to Purchase Additional Shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to additional shares.
Use of Proceeds	We intend to use the net proceeds of this offering for general corporate purposes, funding our ongoing and future clinical trials and for general and administrative expenses, and for potential future acquisitions and other strategic purposes. See Use of Proceeds on page S-18 of this prospectus supplement.
Risk Factors	See Risk Factors beginning on page S-5 of this prospectus supplement for a discussion of factors you should read and consider carefully before investing in our common stock.
NASDAQ Capital Market symbol	LJPC

If the underwriters option to purchase additional shares is exercised in full, we will issue and sell an additional shares of our common stock and will have shares outstanding after the offering.

The number of shares of common stock shown above to be outstanding after this offering is based on the 15,250,840 shares outstanding as of June 30, 2015 and excludes:

- 1,278,435 shares of our common stock subject to options outstanding as of June 30, 2015 having a weighted average exercise price of $14.76 per share;
- 171,089 shares of our common stock that have been reserved for issuance in connection with future grants under the La Jolla 2013 Equity Incentive as of June 30, 2015;
- 6,754,128 shares of our common stock that have been reserved for issuance upon the conversion of 3,917 shares of our Series C-1[2] Convertible Preferred Stock (the Series C-1[2] Preferred Stock) issued and outstanding as of June 30, 2015; and

- 782,032 shares of our common stock that have been reserved for issuance upon the conversion of 2,737 shares of our Series F Convertible Preferred Stock (the Series F Preferred Stock) issued and outstanding as of June 30, 2015.

During the six months ended June 30, 2015, a total of 60.762 shares of Series F Preferred Stock were converted into a total of 17,360 shares of common stock.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriters option to purchase additional shares.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned Risk Factors contained in our Annual Report on Form 10-K for the year ended December 31, 2014, which is incorporated by reference in the accompanying prospectus in its entirety, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

This prospectus supplement, the accompanying prospectus and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus supplement are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of such documents. We disclaim any intent to update any forward-looking statements.

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

We have only limited assets and will need to raise additional capital before we can expect to become profitable.

As of June 30, 2015, we had no revenue sources, an accumulated deficit of $506.2 million and available cash and cash equivalents of approximately $36.0 million. To fund future operations to the point where we are able to generate positive cash flow from the sales or out-licensing of our drug candidates, we will need to raise significant additional capital. The amount and timing of future funding requirements will depend on many factors, including the timing and results of our ongoing development efforts, the potential expansion of our current development programs, potential new development programs and related general and administrative support, as well as the overall condition of capital markets, including capital markets for development-stage biopharmaceutical companies. We anticipate that we will seek to fund our operations through public and private equity and debt financings or other sources, such as potential collaboration agreements. We cannot assure you that anticipated additional financing will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through equity securities offerings, there can be no assurance that we will be able to do so in the future. If we are unable to raise additional capital to fund our clinical development and other business activities, we could be forced to abandon one or more programs and curtail or cease our operations.

We have never generated any revenue from product sales and may never be profitable.

We have no products approved for commercialization and have never generated any revenue from product sales. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- completing research and nonclinical and clinical development of our product candidates;

- obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;

- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;

- obtaining market acceptance of our product candidates as viable treatment options;

- addressing any competing technological and market developments;

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- identifying, assessing, acquiring or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable.

The technology underlying our compounds is uncertain and unproven.

The development efforts for LJPC-501, LJPC-401 and LJPC-30s are based on unproven technologies and therapeutic approaches that have not been widely tested or used. To date, no products that use the technology underlying these drug candidates have been approved or commercialized. Application of our technology to treat life-threatening diseases is in early stages. Preclinical studies and future clinical trials of these product candidates may be viewed as a test of our entire approach to developing therapies for patients suffering from life-threatening diseases. If our product candidates do not work as intended, or if the data from our future clinical trials indicate that our product candidates are not safe and effective, the applicability of our technology for successfully treating life-threatening 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 technologies will result in any commercially successful products.

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

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 our drug candidates are safe and effective. If our drug candidates are ultimately not found

to be safe and effective, we would be unable to obtain regulatory approval to manufacture, market and sell them. We can provide no assurances that the FDA or foreign regulatory authorities will approve our drug candidates or, if approved, what the scope of the approved indication might be.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies may not be predictive of future study results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of nonclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates that have shown promising results in early-stage clinical trials may still suffer significant setbacks in subsequent clinical trials.

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For example, the safety or efficacy results generated to date in our clinical trials do not ensure that later clinical trials will demonstrate similar results. There is a high failure rate for drugs proceeding through clinical trials, and product candidates in later stages of clinical trials may fail to show the desired safety and efficacy, despite having progressed through nonclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our drug candidates.

Future clinical trials that we may undertake may be delayed or halted.

Any clinical trials of our drug candidates that we may conduct in the future may be delayed or halted for various reasons, including:

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

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

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have agreements with third-party contract research organizations, or CROs, to monitor and manage data for our preclinical and clinical programs. We rely heavily on these parties for execution of our preclinical and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our

studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fails to comply with applicable cGCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the cGCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP regulations, and will require a large number of test subjects. Our or our CROs failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated

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and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we may incur significant additional expenses, and our potential approval of our drug candidates may be delayed, which could have a severe negative effect on our business.

If the third-party manufacturers upon which we rely fail to produce our drug candidates that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the trials, regulatory submissions, required approvals or commercialization of our drug candidates.

We do not manufacture our drug candidates nor do we plan to develop any capacity to do so. We contract with third-party manufacturers to manufacture all of our drug candidates. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, which include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. The third-party manufacturers we contract with may not perform as agreed or may terminate their agreements with us.

In addition to product approval, any facilities in which our drug candidates are manufactured or tested for their ability to meet required specifications must be inspected by and approved by the FDA and/or the EMA before a commercial product can be manufactured. Failure of such a facility to be approved could delay the approval of one or more of our drug candidates.

Any of these factors could cause us to delay or suspend any future clinical trials, regulatory submissions, required approvals or commercialization of one or more of our drug candidates, entail higher costs and result in our being unable to effectively commercialize products.

Our success in developing and marketing our drug candidates depends significantly on our ability to obtain patent protection and operate without infringing on the rights of others.

We depend on patents and other intellectual property to prevent others from improperly benefiting from products or technologies that we developed or acquired. Our patents and patent applications cover various technologies and drug candidates. 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. Additionally, recent U.S. Supreme Court and Federal Circuit opinions further limit the scope of patentable inventions in the life sciences space and have added increased uncertainty around the validity of certain issued patents and the successful prosecution of certain pending patent applications. We intend to continue to file patent applications as we believe is appropriate to obtain patents covering both our products and processes. There can be no assurance, however, that any additional patents will be issued, that the scope of any patent that has issued or may issue will be sufficient to protect our technology, or that any current or future issued patent will be held not invalid if subsequently challenged. There is a substantial backlog of biotechnology patent applications at the United States Patent and Trademark Office, or USPTO, which may delay the review and issuance of any patents.

Others, including our competitors, could have patents or patent applications pending that relate to compounds or processes that overlap or compete with our intellectual property or which may affect our freedom to operate.

There can be no assurance that third-party patents will not ultimately be found to impact the advancement of our drug candidates. For example, we are aware that the USPTO has issued a patent to a third party with claims that may cover

one of our product candidates. While we intend to challenge the issuance and validity of this patent, we may not be successful. If the USPTO or any foreign counterpart issues or has issued any other 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

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technology or process that may be required to develop or commercialize one or more of our drug candidates may have a material adverse effect on our business.

We do not have complete patent protection for our product candidates as the active pharmaceutical ingredients in our product candidates are known compounds that are not themselves covered by composition of matter patents, and thus may only be protected by formulation or method-of-use patents (to the extent that such patents are granted and are enforceable) and/or regulatory exclusivity (to the extent available). Therefore, it is possible that a competitor could develop the same or similar technology if we fail to obtain protection of this type. We may have to incur significant expense and management time in defending or enforcing our patents. If we cannot obtain and maintain effective patent rights and/or regulatory exclusivity for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first-to-file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

If our product candidates infringe the rights of others, we could be subject to expensive litigation or be required to obtain licenses from others to develop or market them.

Our competitors or others may have patent rights that they choose to assert against us or our licensees, suppliers, customers or potential collaborators. Moreover, we may not know about patents or patent applications that our products would infringe. For example, because patent applications do not publish for at least 18 months, if at all, and can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our product candidates would infringe. In addition, if third parties file patent applications or obtain patents claiming technology also claimed by us or our licensors in issued patents or pending applications, we may have to participate in interference proceedings in the USPTO to determine priority of invention. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our foreign patent applications.

If a third party claims that we infringe its proprietary rights, any of the following may occur:

- we may become involved in time-consuming and expensive litigation, even if the claim is without merit;
- we may become liable for substantial damages for past infringement if a court decides that our technology infringes a competitor s patent;
- a court may prohibit us from selling or licensing our product without a license from the patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross licenses to our patents; and

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- we may have to redesign our product candidates or technology so that they do not infringe patent rights of others, which may not be possible or commercially feasible.

If any of these events occurs, our business and prospects will suffer and the market price of our common stock will likely decline substantially.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when patents relating to our product candidates are controlled by our licensors. If any of our future licensing partners fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be materially adversely affected and we may not be able to prevent competitors from making, using, selling and importing competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

In addition to patent protection, we will need to successfully preserve our trade secrets. If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets.

If we fail to obtain orphan or other regulatory exclusivity for our product candidates, we may face greater commercial competition and our revenue will be reduced.

Regulatory authorities in some jurisdictions, including the United States and the European Union, or EU, may designate drugs for relatively small patient populations as orphan drugs. Our business strategy for certain of our drug candidates includes seeking orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no

reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA s Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the EU. If orphan drug status is granted, we may be eligible for a period of commercial exclusivity, which would afford us additional protection from generic competition, beyond that protection that may be afforded by patents. Even if a particular disease has a small

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patient population that we believe may be eligible for orphan status, it is possible that the FDA and/or EMA may not grant orphan status. If we do not obtain orphan drug exclusivity for our drug products and biologic products, particularly for any products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity and our revenue could be reduced.

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

Competition from domestic and foreign biotechnology companies, large pharmaceutical companies and other institutions is intense and is expected to increase. A number of companies and institutions are pursuing the development of pharmaceuticals in our targeted areas. Many of these companies are very large, and have financial, technical, sales and distribution and other resources substantially greater than ours. The greater resources of these competitors could enable them to develop or market competing products more quickly or effectively, making 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 preclinical studies in the field of cancer therapeutics. 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 we are developing or that would render our technology and proposed products obsolete or noncompetitive.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our studies could reveal a high and unacceptable severity and prevalence of undesirable side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

The drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, or result in potential product liability claims. We carry product liability insurance in the amount of $10.0 million in the aggregate. We believe our product liability insurance coverage is sufficient in light of our clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management s attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;

- regulatory authorities may require additional warnings on the label;

- we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;

- we could be sued and held liable for harm caused to patients; and

- our reputation may suffer.

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Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate and could significantly harm our business, results of operations, and prospects.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, biologic license application, or BLA, or market authorization application, or MAA. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product s approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;

- impose civil or criminal penalties;

- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers facilities; or
- seize or detain products, or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory

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sanctions are applied or if regulatory approval is withdrawn, the value of our Company and our operating results will be adversely affected.

We may not be successful in our efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to identify, license, discover, develop or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- our product candidates may not succeed in preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

If the market opportunities for our product candidates are smaller than we believe, our revenue may be adversely affected, and our business may suffer.

Our estimates of the potential market opportunity for each of our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of these assumptions proves to be inaccurate, then the actual market for our product candidates could be smaller than our estimates of our potential market opportunity. If the actual market for our product candidates is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

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The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients and third-party payors accepting our product candidates as medically useful, cost-effective and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any of our product candidates, i