LA JOLLA PHARMACEUTICAL CO
Form 10-K
March 04, 2019
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 1-36282

LA JOLLA PHARMACEUTICAL COMPANY
(Exact name of registrant as specified in its charter)

California	33-0361285
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

4550 Towne Centre Court, San Diego, CA 92121
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: (858) 207-4264
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, Par Value $0.0001 per share	The Nasdaq Capital Market

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Act. Yes o No x

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of the Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company," in Rule 12b-2 of the Exchange Act.

Large accelerated filer	o	Accelerated filer	x
Non-accelerated filer	o	Smaller reporting company	x
		Emerging growth company	o

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

The aggregate market value of voting and non-voting common stock held by non-affiliates of the Company as of June 29, 2018 was approximately $603.7 million, based on the closing price on the Nasdaq Capital Market reported for such date. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 20, 2019, there were 27,076,171 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required to be disclosed in Part III of this report is incorporated by reference from the registrant's definitive Proxy Statement for the 2019 Annual Meeting of Shareholders, which proxy statement is expected to be filed no later than 120 days after the end of the fiscal year covered by this report.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as “intends,” “believes,” “anticipates,” “indicates,” “plans,” “expects,” “suggests,” “may,” “should,” “potential,” “designed to,” “will” and si references. In addition, any statements that refer to expectations, intentions, projections or other characterizations of future events or circumstances are forward-looking statements. These statements relate to future events or the Company’s anticipated future results of operations. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, which may cause actual results to be materially different from these forward-looking statements. The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they were made. Certain of these risks, uncertainties, and other factors are described in greater detail in the Company’s filings with the U.S. Securities and Exchange Commission (SEC), all of which are available free of charge on the SEC’s website www.sec.gov. Actual results may differ materially from those expressed or implied in such statements. These risks include, but are not limited to, risks relating to: our ability to successfully commercialize GIAPREZA™ (angiotensin II); the timing for commencement of preclinical studies and clinical studies; the anticipated timing for completion of such studies and trials, and the anticipated timing for regulatory actions; the success of future development activities for our product candidates; potential indications for which our product candidates may be developed; and the expected duration over which the Company’s cash balances will fund its operations.

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:

- our ability to successfully commercialize, market and achieve market acceptance of GIAPREZA™ (angiotensin II), formerly known as LJPC-501, and other product candidates, including our positioning relative to competing products;
- our ability to grow net sales of GIAPREZA;
- our ability to meet the demand for GIAPREZA in a timely manner;
- the timing and prospects for approval of GIAPREZA by the European Medicines Agency (EMA) or other regulatory authorities;
- potential market sizes for our products, including the market for the treatment of septic or other distributive shock;
- the anticipated treatment of data by the FDA, EMA or other regulatory authorities of La Jolla’s product candidates;
- the cost of producing and selling GIAPREZA;
- unforeseen safety issues from the administration of product and product candidates in patients;
- the timing, costs, conduct and outcome of preclinical studies and clinical studies;
- the expectation for future clinical and regulatory milestones, such as NDA submission and expected timing for commencement and completion of clinical studies;
- the risk that our clinical studies with our product candidates may not be successful in evaluating their safety and tolerability or providing evidence of efficacy;
- the successful and timely completion of clinical studies;
- 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 clinical studies with our product candidates;
- uncertainties associated with obtaining and enforcing patents and the availability of regulatory exclusivity;
- the uncertainty of obtaining raw materials or finished products supplies from third parties (some of which may be single sourced) and other related supply and manufacturing difficulties, interruptions and delays;
- our estimates for future performance including but not limited to net sales and net cash used in operating activities for the full-year 2019;
- our ability to hire and retain our key employees;

- our estimates regarding our capital requirements and our needs for, and ability to obtain, additional financing;

- the expected duration over which the Company's cash balances will fund its operations; and
- those risk factors identified in this Annual Report on Form 10-K under the heading "Risk Factors" and in other filings the Company periodically makes with the SEC.

Forward-looking statements contained in this Annual Report on Form 10-K speak as of the date hereof, and we do not undertake to update any of these forward-looking statements to reflect a change in our views or events or circumstances that occur after the date of this Annual Report on Form 10-K. In addition, please see the "Risk Factors" section of this Annual Report on Form 10-K. These risk factors may be updated from time to time by our future filings under the Exchange Act.

PART I

In this Annual Report on Form 10-K, all references to “we,” “our,” “us,” “La Jolla” and “the Company” refer to La Jolla Pharmaceutical Company, a California corporation, and our subsidiaries, including La Jolla Pharma, LLC, on a consolidated basis.

Item 1. Business.

Overview

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. GIAPREZA™ (angiotensin II), formerly known as LJPC-501, was approved by the U.S. Food and Drug Administration (FDA) on December 21, 2017 as a vasoconstrictor indicated to increase blood pressure in adults with septic or other distributive shock. LJPC-0118 is La Jolla’s investigational product for the treatment of severe malaria. LJPC-401 (synthetic human hepcidin), a clinical-stage investigational product, is being developed for the potential treatment of conditions characterized by iron overload, such as hereditary hemochromatosis, beta thalassemia, sickle cell disease, myelodysplastic syndrome and polycythemia vera.

GIAPREZA™ (angiotensin II)

GIAPREZA™ (angiotensin II), injection for intravenous infusion, was approved by the FDA on December 21, 2017 as a vasoconstrictor indicated to increase blood pressure in adults with septic or other distributive shock. Angiotensin II is a major bioactive component of the renin-angiotensin-aldosterone system (RAAS). The RAAS is one of three central regulators of blood pressure. In March 2018, we announced the commercial availability of GIAPREZA. GIAPREZA is available in 1 mL single-dose vials, each containing 2.5 mg of angiotensin II (as a sterile liquid) through authorized specialty distributors and select wholesalers.

Over 1 million Americans are affected by shock on an annual basis, with 1 in 3 patients being treated for shock in the intensive care unit. Distributive shock is the most common type of shock in the inpatient setting with approximately 800,000 distributive shock cases in the U.S. each year. Of these cases, an estimated 90% are septic shock patients. Approximately 300,000 do not achieve adequate blood pressure response with standard-of-care vasopressor therapy (catecholamines and vasopressin). The inability to achieve or maintain adequate blood pressure results in inadequate blood flow to the body’s organs and tissue and is associated with a mortality rate exceeding most acute conditions requiring hospitalization. In the European Union (EU), the annual incidence of sepsis in adults is estimated to be more than 500,000, with more than 170,000 progressing to septic shock.

The GIAPREZA clinical development program included a Phase 3 study of GIAPREZA in adult patients with septic or other distributive shock who remained hypotensive despite fluid and vasopressor therapy, known as the ATHOS-3 (Angiotensin II for the Treatment of High-Output Shock) Phase 3 study. In ATHOS-3, patients were randomized in a 1:1 fashion to receive either: (i) GIAPREZA plus standard-of-care vasopressors; or (ii) placebo plus standard-of-care vasopressors. ATHOS-3 completed enrollment of 344 patients in the fourth quarter of 2016. In February 2017, we reported positive topline results from ATHOS-3, and, in May 2017, the results of ATHOS-3 were published by The New England Journal of Medicine.

The analysis of the primary efficacy endpoint, defined as the percentage of patients achieving a pre-specified target blood pressure response, was highly statistically significant: 23% of the 158 placebo-treated patients had a blood pressure response compared to 70% of the 163 GIAPREZA-treated patients ($p<0.00001$). In addition, there was a

consistent trend toward longer survival over the 28-day study period: 22% reduction in mortality risk through day 28 [hazard ratio=0.78 (0.57-1.07), p=0.12] for GIAPREZA-treated patients.

In this critically ill patient population: 92% of placebo-treated patients compared to 87% of GIAPREZA-treated patients experienced at least one adverse event, and 22% of placebo-treated patients compared to 14% of GIAPREZA-treated patients discontinued treatment due to an adverse event.

Additional analyses from the ATHOS-3 trial have been published:

- In September 2017, an analysis was presented during the 30th European Society of Intensive Care Medicine Annual Congress, entitled “Baseline angiotensin levels and ACE effects in patients with vasodilatory shock treated with

angiotensin II." The pre-specified analysis showed that a relatively low angiotensin II state (as measured by the ratio of angiotensin I to angiotensin II) predicted increased mortality in patients with vasodilatory shock, suggesting that a low angiotensin II state is a negative prognostic indicator of outcomes. Furthermore, the analysis showed a statistically significant treatment effect of GIAPREZA compared to placebo on mortality in these patients with a relatively low angiotensin II state (relative risk reduction of 36%; HR=0.64; 95% CI: 0.41-1.00; p=0.047).

In February 2018, an abstract was presented at the Society of Critical Care Medicine's (SCCM) 47th Critical Care Congress, entitled "Effect of Disease Severity on Survival in Patients Receiving Angiotensin II for Vasodilatory Shock." The abstract, which was published in the January Supplement of Critical Care Medicine, includes results from a pre-specified analysis from the ATHOS-3 Phase 3 study of GIAPREZA in patients with high severity of illness, defined as an APACHE II (Acute Physiology and Chronic Health Evaluation II) score > 30 or baseline MAP < 65 mmHg, despite treatment with high-dose vasopressors. The authors presented data showing a lower 28-day mortality rate in patients with baseline APACHE II scores > 30 in the GIAPREZA group versus the placebo group: 28-day mortality was 51.8% (n = 58) for the GIAPREZA group compared to 70.8% (n = 65) for the placebo group (hazard ratio=0.62 [95% CI: 0.39, 0.98; p=0.037]). In patients with a baseline MAP < 65 mmHg, a trend towards improved 28-day mortality was seen in the GIAPREZA group compared to the placebo group: 28-day mortality was 54.2% (n = 52) for the GIAPREZA group compared to 70.4% (n = 50) for the placebo group (hazard ratio=0.66 [95% CI: 0.40, 1.09; p=0.10]).

- In March 2018, an analysis was presented at the 23rd International Conference on Advances in Critical Care Nephrology AKI & CRRT 2018, entitled "Outcomes in Patients with Acute Kidney Injury Receiving Angiotensin II for Vasodilatory Shock." The manuscript of this analysis, entitled "Outcomes in patients with vasodilatory shock and renal replacement therapy treated with intravenous angiotensin II," was published online in Critical Care Medicine. The presentation and manuscript detail the outcomes of patients with acute kidney injury (AKI) and vasodilatory shock enrolled in the ATHOS-3 study of GIAPREZA. In this post-hoc analysis, the data from 105 AKI patients (GIAPREZA n=45; placebo n=60) requiring renal replacement therapy (RRT) at study drug initiation were analyzed. Survival through day 28 was 53% (95% CI: 38%-67%) for the GIAPREZA group compared to 30% (95% CI: 19%-41%) for the placebo group (p = 0.012). By day 7, 38% (95% CI: 25%-54%) of patients treated with GIAPREZA discontinued RRT compared to 15% (95% CI: 8%-27%) of patients treated with placebo (p = 0.007). Mean arterial pressure (MAP) response at hour 3 was achieved in 53% (95% CI: 38%-68%) of patients treated with GIAPREZA compared to 22% (95% CI: 12%-34%) of patients treated with placebo (p = 0.001).

In June 2018, we announced that the Marketing Authorization Application (MAA) for GIAPREZA was validated by the EMA. Validation of the MAA confirms that the submission is complete and starts the EMA's centralized review process. This followed our announcement in September 2017, in which we reported that the EMA's Committee for Medicinal Products for Human Use (CHMP) issued favorable Scientific Advice regarding the EU regulatory pathway for GIAPREZA. We expect a decision on the GIAPREZA MAA by the EMA in June 2019. If approved, GIAPREZA could be available for marketing in the EU in early 2020.

LJPC-0118

LJPC-0118 is an investigational product for the treatment of severe malaria. The active pharmaceutical ingredient in LJPC-0118 was demonstrated to be superior to quinine in reducing mortality in patients with severe falciparum malaria infection in two randomized, controlled, clinical studies. Severe malaria is a serious and sometimes fatal disease caused by a parasite that commonly infects a certain type of mosquito, which feeds on humans. Symptoms include, but are not limited to: fever, chills, sweating, hypoglycemia and shock. Severe malaria is often complicated by central nervous system infections that may lead to delirium, which may progress to coma. Infections usually occur a few weeks after being bitten. In 2017, an estimated 219 million cases of malaria occurred worldwide, with an estimated 200 million of these cases occurring in the World Health Organization (WHO) African Region, and in 2013, the global annual incidence of severe malaria was estimated to be 2 million cases. In 2017, an estimated 435,000

people died from malaria worldwide.

We plan to file an NDA for LJPC-0118 with the FDA in the fourth quarter of 2019.

LJPC-401

LJPC-401, a clinical-stage investigational product, is our proprietary formulation of synthetic human hepcidin. Hepcidin, an endogenous peptide hormone, is the body's naturally occurring regulator of iron absorption and distribution. In healthy individuals, hepcidin prevents excessive iron accumulation in vital organs, such as the liver and heart, where it can cause significant damage and even result in death. We are developing LJPC-401 for the potential treatment of iron overload, which occurs as a result of primary iron overload diseases such as hereditary hemochromatosis (HH), or secondary iron

overload diseases such as beta thalassemia (BT), sickle cell disease (SCD), myelodysplastic syndrome (MDS) and polycythemia vera.

HH is a disease characterized by a genetic deficiency in hepcidin. HH is the most common genetic disease in Caucasians and causes liver cirrhosis, liver cancer, heart disease and/or failure, diabetes, arthritis and joint pain. There are no FDA approved therapies for HH and the current standard treatment for HH is a blood removal procedure known as phlebotomy. Each phlebotomy procedure, which is usually conducted at a hospital, medical office or blood center, typically involves the removal of approximately one pint of blood. The required frequency of procedures varies by patient but often ranges from one to two times per week for an initial period after diagnosis and once every one to three months for life. Since most of the body's iron is stored in red blood cells, chronic removal of blood can effectively lower iron levels if a phlebotomy regimen is adhered to. However, phlebotomy procedures may cause and may be associated with pain, bruising and scarring at the venous puncture site, joint pain, fatigue and dizziness during and following the procedure and disruption of daily activities. Furthermore, phlebotomy is not appropriate in patients with poor venous access, anemia or heart disease.

BT, SCD and MDS are genetic diseases of blood cells that can cause life-threatening anemia and usually require frequent and life-long blood transfusions. These blood transfusions cause excessive iron accumulation in the body, which is toxic to vital organs, such as the liver and heart. In addition, the underlying anemia causes excessive iron accumulation independent of blood transfusions.

In 2015, the EMA Committee for Orphan Medicinal Products (COMP) designated LJPC-401 as an orphan medicinal product for the treatment of beta thalassemia intermedia and major. In 2016, the EMA COMP designated LJPC-401 as an orphan medicinal product for the treatment of SCD.

In September 2016, we reported positive results from a Phase 1 study of LJPC-401 in patients at risk of iron overload suffering from HH, thalassemia and SCD. In this study, single, escalating doses of LJPC-401 were associated with a dose-dependent, statistically significant reduction in serum iron. LJPC-401 was well-tolerated with no dose-limiting toxicities. Injection-site reactions were the most commonly reported adverse event and were all mild or moderate in severity, self-limiting and fully resolved.

In June 2018, two presentations on LJPC-401 were given at the 23rd Congress of the European Hematology Association (EHA). The first was an oral presentation, entitled "A Phase 1, Open-Label Study to Determine the Safety, Tolerability, and Pharmacokinetics of Escalating Doses of LJPC-401 (Synthetic Human Hepcidin) in Patients with Iron Overload." The second was a poster presentation, entitled "A Phase 1, Placebo-Controlled Study to Determine the Safety, Tolerability, and Pharmacokinetics of Escalating Subcutaneous Doses of LJPC-401 (Synthetic Human Hepcidin) in Healthy Adults."

LJPC-401 is currently the subject of two clinical studies, LJ401-HH01 in patients with HH and LJ401-BT01 in patients with BT.

LJ401-HH01

In December 2017, we announced the initiation of LJ401-HH01, a Phase 2 clinical study of LJPC 401 in patients with HH. LJ401-HH01 is a multinational, multicenter, randomized, Phase 2 study that is designed to evaluate the safety and efficacy of LJPC-401 as a treatment for HH. The primary efficacy endpoint of the study is the change in transferrin saturation, a standard measurement of iron levels in the body and one of the two key measurements used to detect iron overload, from baseline to end of treatment. Secondary efficacy endpoints include: (i) the change in serum ferritin, the other key measurement used to detect iron overload, from baseline to end of treatment; and (ii) the requirement for and frequency of phlebotomy procedures used during the study.

We expect to disclose the topline results of LJ401-HH01 in the second half of 2019.

LJ401-BT01

In September 2016, we announced that we reached agreement with the EMA on the design of a pivotal study of LJPC-401 for the treatment of BT patients suffering from iron overload, a major unmet need in an orphan patient population. In December 2017, we announced the initiation of LJ401-BT01, a pivotal, multinational, multicenter, randomized, controlled study that is designed to evaluate the safety and efficacy of LJPC-401 as a treatment for BT patients who, despite chelation therapy, have cardiac iron levels above normal. The primary efficacy endpoint of this study is the change in iron content in the

heart after 6 months, as measured by cardiac magnetic resonance imaging (MRI). If this study is successful, we would anticipate filing an MAA for LJPC-401 in the EU.

We expect to disclose the topline results of LJ401-BT01 in mid-2020.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of commercial or clinical quantities of GIAPREZA or any of our product candidates. We rely on a small number of third-party manufacturers to produce our compounds and expect to continue to do so to meet our commercial needs and the requirements of our product candidates.

We have not had long-term agreements with any third parties and will likely continue to not have long-term arrangements as they relate to our commercial product and clinical and preclinical product candidates. In all of our manufacturing and processing agreements, we require that third-party contract manufacturers produce active pharmaceutical ingredients (API) and finished products in accordance with the FDA's current Good Manufacturing Practices (cGMP) and all other applicable laws and regulations. We maintain confidentiality agreements with potential and existing manufacturers in order to protect our proprietary rights related to our product and product candidates.

With regard to GIAPREZA, we have utilized third parties to manufacture the API, formulate, fill and finish, and perform the analytical release testing of the drug product. We have also completed our commercial scale-up of manufacturing process development and the validation of commercial production runs. The commercial success of GIAPREZA will depend in part on the ability of our contract manufacturers to produce cGMP-compliant API and drug product in commercial quantities and at competitive costs. Further, some of the critical materials and components used in manufacturing GIAPREZA are sourced from single suppliers. An interruption in the supply of key materials could significantly delay our sales or increase our expenses.

We plan to continue to scale up manufacturing through multiple third-party manufacturers as required, with the objectives of realizing important economies of scale and security of supply. These scale-up activities will take time to implement, require additional capital investment, process development, validation and FDA review.

Patents and Proprietary Technologies

Patents and other proprietary rights are important to our business. As part of our strategy to protect our current product and product candidates and to provide a foundation for future products, we have filed a number of patent applications and have licensed rights from third parties for other patent applications related to our product candidates.

As of December 31, 2018, we owned or had the rights to 49 issued patents (21 U.S. and 28 foreign) and 100 pending applications (22 U.S. and 78 foreign). These patents and patent applications owned or licensed by us cover GIAPREZA, LJPC-401 and other product candidates.

	United States			Foreign		
Description	Issued	Pending	Expiration	Issued	Pending	Expiration
GIAPREZA	5	12	2029 - 2038	—	49	2034 - 2037
LJPC-401	3	3	2022 - 2038	7	18	2022 - 2037
Other	13	7	2022 - 2038	21	11	2022 - 2037

In addition to those above, we plan to file additional patent applications that, if issued, would provide further protection for GIAPREZA and LJPC-401. Although we believe the bases for these patents and patent applications are sound, they are untested, and there is no assurance that they will not be successfully challenged. There can be no

assurance that any patent previously issued will be of commercial value, that any patent applications will result in issued patents of commercial value, or that our technology will not be held to infringe patents held by others.

Material Contracts

In December 2014, we entered into a patent license agreement with the George Washington University (GW), which the parties amended and restated on March 1, 2016. Pursuant to the amended and restated license agreement, GW exclusively licensed to us certain intellectual property rights relating to GIAPREZA, including the exclusive rights to certain issued patents

and patent applications covering GIAPREZA. Under the license agreement, we are obligated to use commercially reasonable efforts to develop, commercialize, market and sell GIAPREZA. We have paid a one-time license initiation fee, annual maintenance fees, an amendment fee, additional payments following the achievement of certain development and regulatory milestones, and royalty payments. We may be obligated to make additional milestone payments of up to $0.5 million in the aggregate. Following the commencement of commercial sales of GIAPREZA, we paid tiered royalties in the low- to mid-single digits on products covered by the licensed rights. The patents and patent applications covered by the GW license agreement are expected to expire between 2029 and 2038, and the obligation to pay royalties under this agreement extends through the last-to-expire patent covering GIAPREZA.

On May 10, 2018, the Company closed a $125.0 million royalty financing agreement (the Royalty Agreement) with HealthCare Royalty Partners (HCR). Under the terms of the Royalty Agreement, the Company received $125.0 million in exchange for tiered royalty payments on worldwide net product sales of GIAPREZA. HCR is entitled to receive quarterly royalties on worldwide net product sales of GIAPREZA beginning April 1, 2018. Quarterly payments to HCR under the Royalty Agreement start at a maximum royalty rate, with step-downs based on the achievement of annual net product sales thresholds. Through December 31, 2021, the royalty rate will be a maximum of 10%. Starting January 1, 2022, the maximum royalty rate may increase by 4% if an agreed-upon, cumulative sales threshold has not been met, and, starting January 1, 2024, the maximum royalty rate may increase by an additional 4% if a different agreed-upon, cumulative sales threshold has not been met. The Royalty Agreement is subject to maximum aggregate royalty payments to HCR of 180% of the $125.0 million to be received by the Company, at which time the payment obligations under the Royalty Agreement would expire. In the event of certain material breaches of the Royalty Agreement, HCR would have the right to terminate the Royalty Agreement and demand payment by La Jolla Pharma, LLC of an amount equal to either $125.0 million, minus aggregate royalties paid to HCR, or $225.0 million, minus aggregate royalties paid to HCR, depending on the type of breach. The Royalty Agreement was entered into by the Company’s wholly-owned subsidiary, La Jolla Pharma, LLC, and HCR has no recourse under the Royalty Agreement against La Jolla Pharmaceutical Company or any assets other than GIAPREZA.

Sales and Marketing

Our U.S.-based sales and marketing team consisted of 46 employees as of February 20, 2019. The sales and marketing infrastructure includes marketing, commercial insights, commercial operations and sales training. La Jolla has deployed a hospital market access team, clinical nurse educator team and specialized hospital sales team to focus on a targeted group of hospitals and hospital systems that treat high rates of distributive shock. These teams work to educate critical care physicians, intensive care unit nurses and hospital pharmacists, with the goal that they understand the clinical value of, and adopt, GIAPREZA as part of their clinical pathway for the management of distributive shock.

Customers

GIAPREZA is distributed in the U.S. through a limited number of specialty distributors and select wholesalers who order from us on an as-needed basis and that subsequently resell GIAPREZA to hospitals. Due to the relatively short lead-time required to fill orders for our product, backlog is not material to our business. We have engaged a third-party logistics service provider to act as our logistics and supply-chain manager for the commercial distribution of GIAPREZA.

Competition

The biotechnology and pharmaceutical industries are subject to rapid technological change. Competition from domestic and foreign biotechnology companies, large pharmaceutical and specialty pharmaceutical companies,

generic drug companies and other institutions, is intense and expected to increase. A number of companies are pursuing the development of pharmaceuticals in our targeted areas. However, we are not currently aware of any other angiotensin II drug product in development. We believe that the key competitive factors that will affect the commercial success of GIAPREZA, as well as future product candidates that we may develop, are: efficacy, safety and tolerability profiles; convenience in dosing; and price.

GIAPREZA competes primarily against catecholamines (a generic class of drugs, including dopamine and norepinephrine) and vasopressins, including Vasostrict®, which is marketed by Par Pharmaceuticals. Generic drugs such as catecholamines are significantly less expensive than GIAPREZA, which may limit GIAPREZA's adoption (irrespective of efficacy, safety and tolerability profile). With respect to the competition with Vasostrict, Par Pharmaceuticals is a significantly larger company than La Jolla and has greater resources and experience in successfully commercializing drugs. Additionally, the price of Vasostrict will impact the adoption of GIAPREZA in the hospital setting. If we are unable to successfully compete with these products, our commercial prospects for GIAPREZA will be limited.

Government Regulation

Pharmaceutical Regulation

Pharmaceutical products in the U.S., including GIAPREZA, are subject to extensive government regulation. Likewise, if we seek to market and distribute products abroad, they would also be subject to extensive foreign government regulation.

In the U.S., the FDA regulates pharmaceutical products. FDA regulations govern the testing, research and development activities, manufacturing, quality, storage, advertising, promotion, labeling, sale and distribution of pharmaceutical products. Accordingly, there is a rigorous process for the approval of new drugs and ongoing oversight of marketed products. We are also subject to foreign regulatory requirements governing clinical studies and drug products if products are tested or marketed abroad. The approval process outside the U.S. varies from jurisdiction to jurisdiction and the time required may be longer or shorter than that required for FDA approval.

See Item 1A. Risk Factors of this Annual Report on Form 10-K for a discussion of the factors that could adversely impact our development of commercial products and industry regulation.

Regulation in the U.S.

The FDA testing and approval process requires substantial time, effort and money. We cannot assure you that any of our product candidates will ever obtain approval. The FDA approval process for new drugs includes, without limitation:

- preclinical studies;
- submission in the U.S. of an IND for clinical studies conducted in the U.S.;
- adequate and well-controlled human clinical studies to establish safety and efficacy of the product;
- review and approval of an NDA in the U.S.; and
- inspection of the facilities used in the manufacturing of the drug to assess compliance with the FDA's current cGMP regulations.

The FDA monitors the progress of clinical studies conducted in the U.S. under an IND and may, at its discretion, re-evaluate, alter, suspend or terminate testing based on the data accumulated to that point and the FDA's benefit-risk assessment with regard to the patients enrolled in the trial. The FDA may also withdraw approval for an IND for that drug if deemed warranted. Furthermore, even after regulatory approval is obtained, under certain circumstances, such as later discovery of previously unknown problems, the FDA can withdraw approval or subject the drug to additional restrictions.

Preclinical Testing

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Preclinical studies include laboratory evaluation of the product, as well as animal studies to assess the potential safety and effectiveness of the product. Most of these studies must be performed according to Good Laboratory Practices (GLP), a system of management controls to assure the quality and reliability of data from nonclinical laboratory studies that are intended to support applications for research or marketing permits for FDA-regulated products.

An IND is the request for authorization from the FDA to administer an investigational new drug product to humans. The IND includes information regarding the preclinical studies, the investigational product's chemistry and manufacturing, supporting data and literature, and the clinical investigational plan and protocol(s). Thirty days after an IND is received by the FDA, the IND becomes effective and the proposed clinical trial may begin, unless FDA raises

an objection. If concerns or questions are raised, an IND sponsor and the FDA must resolve any outstanding concerns before clinical studies can proceed.

Clinical Studies

Clinical trials involve the administration of the product candidate that is the subject of the trial to volunteers or patients under the supervision of a qualified principal investigator and in accordance with a clinical trial protocol, which sets forth details, such as the study objectives and the safety and effectiveness criteria to be evaluated. Each clinical trial must be reviewed and approved by an independent institutional review board (IRB) in the U.S. or ethics committee in the European Union (EU) at each institution at which the study will be conducted. The IRB or ethics committee will consider, among other things, ethical factors, safety of human subjects and the possible liability of the institution arising from the conduct of the

proposed clinical trial. In addition, clinical studies in the U.S. must be performed according to current good clinical practices (cGCPs), which are enumerated in FDA regulations and are intended to protect the rights of patients and to define the roles of trial sponsors, administrators and monitors. Some studies include oversight by an independent group of experts, known as a data safety monitoring board, which provides authorization for whether a study may move forward based on certain data from the study and may stop the clinical trial if it determines that there is an unacceptable safety risk for subjects or on other grounds.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials in the U.S. typically are conducted in sequential phases: Phases 1, 2, 3 and 4. The phases may overlap. The FDA may require that we suspend clinical studies at any time on various grounds, including if the FDA makes a finding that the subjects participating in the trial are being exposed to an unacceptable health risk.

In Phase 1 clinical studies, the investigational product is usually tested on a small number of healthy volunteers to determine safety, any adverse effects, proper dosage, absorption, metabolism, distribution, excretion and other drug effects. Phase 1b clinical studies may also evaluate efficacy with respect to trial participants.

In Phase 2 clinical studies, the investigational product is usually tested on a limited number of patients (generally up to several hundred) to preliminarily evaluate the efficacy of the drug for specific, targeted indications, determine dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks. Multiple Phase 2 clinical studies may be conducted to obtain information prior to beginning Phase 3 clinical studies and support proof of concept.

In Phase 3 clinical studies, the investigational product is administered to an expanded patient population to support efficacy claims, provide evidence of clinical efficacy and to further test for safety, generally at multiple clinical sites.

In Phase 4 clinical studies or other post-approval commitments, additional studies and patient follow-up are conducted to gain experience from the treatment of patients in the intended therapeutic indication. FDA may require a commitment to conduct post-approval Phase 4 studies as a condition of approval. Additional studies and follow-up may be conducted to document a clinical benefit where drugs are approved under accelerated approval regulations and based on surrogate endpoints. In clinical studies, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. Failure to timely conduct Phase 4 clinical studies and follow-up could result in withdrawal of approval for products approved under accelerated approval regulations.

We cannot assure you that any of our current or future clinical studies will result in approval to market our product candidates.

Clinical Data Review and Approval in the U.S.

The data from the clinical studies, together with preclinical data and other supporting information that establishes a product candidate's safety, are submitted to the FDA in the form of an NDA, or NDA supplement (for approval of a new indication if the product candidate is already approved for another indication). Under applicable laws and FDA

regulations, FDA reviews the NDA within 60 days of receipt of the NDA to determine whether the application will be accepted for filing based on FDA's threshold determination that the NDA is sufficiently complete to permit substantive review. If deemed complete, the FDA will "file" the NDA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. Along with the preclinical and clinical data, the FDA will evaluate the proposed product labeling and other information in the cGMP. In addition, the FDA may convene a scientific advisory committee, comprised of clinicians and other experts, to review and provide a non-binding recommendation as to whether the application should be approved.

The FDA has established internal substantive review goals of 10 months for most NDAs. The FDA also has special programs, including Fast Track, Breakthrough Therapy, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval based on surrogate endpoints. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track designation is designed to facilitate the development, and expedite the review of drugs that are intended to treat serious diseases

and address an unmet medical need. Breakthrough Therapy designation may be granted for a drug that is intended to treat a serious condition and if preliminary evidence indicates that the drug may demonstrate substantial clinical improvement over available therapies. Both Fast Track and Breakthrough Therapy designations may be requested at the time of IND submission, and the FDA will respond within 60 calendar days of receipt of the request. Priority review, which is requested at the time of an NDA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists, an initial review within six months as compared to a standard review time of 10 months. Although Fast Track, Breakthrough Therapy, and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with sponsors of Fast Track and Breakthrough Therapy drugs, and the FDA aims to expedite review of drugs granted priority review. Accelerated approval provides an earlier approval of drugs to treat serious diseases and that address an unmet medical need based on a surrogate or intermediate endpoint that is reasonably likely to predict clinical benefit. Under these special programs, the FDA is not legally required to complete its review within an expedited time period, and performance goals may change over time. Furthermore, the FDA may later decide that a drug no longer qualifies for review under one or more of these programs.

The 21st Century Cures Act of 2016 amended section 506 of the U.S. Federal Food, Drug, and Cosmetic Act to provide for the expedited development and review of regenerative medicine therapies, which are defined as cell therapies, therapeutic tissue engineering products, human cell and tissue products, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations. A regenerative medicine therapy is eligible for “regenerative medicine advanced therapy” (RMAT) designation if it is intended to treat, modify, reverse or cure a serious condition, and the preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition. RMAT designation gives the applicant the benefits of fast track and Breakthrough Therapy designations, including early interactions with the FDA to discuss potential surrogate or intermediate endpoints to support accelerated approval, and FDA may grant priority review. In a guidance document, dated February 2019, the FDA stated that the preliminary clinical evidence required to support the RMAT designation should be generated on the product intended for clinical development but that the types of evidence required would be determined on a case-by-case basis, but could include evidence such as data from historical controls, studies conducted outside the United States, and retrospective studies.

If the FDA approves the NDA, it will issue an approval letter authorizing the commercial marketing of the drug with prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. In many cases, the outcome of the review, even if generally favorable, is not an actual approval, but a “complete response” that generally outlines the deficiencies in the submission, which may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA’s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter.

Satisfaction of FDA requirements or similar requirements of state, local, and foreign regulatory agencies typically take several years and requires the expenditure of substantial financial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit or prevent regulatory approval at any stage of the process. Accordingly, the actual time and expense required to bring a product to market may vary substantially. We cannot assure you that we will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Data obtained from clinical activities is not always conclusive and may be susceptible to

varying interpretations, which could delay, limit or prevent regulatory approval. Success in early stage clinical studies does not ensure success in later stage clinical studies. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages, or have conditions placed on it that restrict the commercial applications, advertising, promotion or distribution of these products.

Once issued, the FDA may withdraw product approval or request product recalls if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the safety or effectiveness of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. The FDA may also request or require additional Phase 4 clinical studies after a product is approved. The results of Phase 4 clinical studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA's voluntary adverse drug reaction reporting system.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements on us and our third-party manufacturers. We cannot be certain that we, or our present or future suppliers, will be able to comply with the cGMP regulations and other FDA regulatory requirements.

In addition, both before and after approval is sought, we are required to comply with a number of FDA requirements. For example, we are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain limitations and other requirements concerning advertising and promotion for our products. In addition, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with continuing cGMP. In addition, discovery of problems, such as safety problems, may result in changes in labeling or restrictions on a product manufacturer or NDA holder, including removal of the product from the market.

The FDA closely regulates the marketing and promotion of drugs and drugs may only be marketed in a manner consistent with their FDA-approved labeling. Approval may be subject to post-marketing surveillance and other record-keeping and reporting obligations, and involve ongoing requirements. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing.

The failure to comply with FDA’s requirements can result in adverse publicity, warning letters, corrective advertising, restrictions on marketing or manufacturing, refusals to review pending product applications, refusals to permit the import or export of products, seizures, injunctions, and civil and criminal penalties.

Clinical Trial Conduct and Product Approval Regulation in Non-U.S. Jurisdictions

In addition to regulations in the U.S., we may be subject to a variety of foreign regulations governing clinical studies and commercial sales and distribution of our products. Our clinical studies conducted in the EU must be done under a clinical trial application (CTA), which must be supported by an Investigational Medicinal Product Dossier (IMPD), and the oversight of an ethics committee. If we market our products in foreign countries, we also will be subject to foreign regulatory requirements governing marketing approval for pharmaceutical products. The requirements governing the conduct of clinical studies, product approval, pricing and reimbursement vary widely from country to country. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained before manufacturing or marketing the product in those countries. The approval process varies from country to country and the time required for such approvals may differ substantially from that required for FDA approval. This foreign regulatory approval process involves all of the risks associated with FDA marketing approval discussed above. There is no assurance that any future FDA approval of any of our product candidates will result in similar foreign approvals or vice versa. The process for clinical studies in the EU is similar, and trials are heavily scrutinized by the designated ethics committee. In addition, foreign regulations may include applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals and entities.

Section 505(b)(2) Applications

Some of our product candidates may be eligible for submission of applications for approval under the FDA's Section 505(b)(2) approval process, which provides an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and allows approval of NDAs that rely, at least in part, on studies that were not conducted by or for the applicant and to which the applicant has not obtained a right of reference. Such studies can be provided by published literature, or the FDA can rely on previous findings of safety and efficacy for a previously approved drug. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical studies or clinical studies of the new product. Section 505(b)(2) applications may be submitted for drug products that represent a modification (e.g., a new indication or new dosage form) of an eligible approved drug. In such cases, the additional information in 505(b)(2) applications necessary to support the change from the previously approved drug is frequently provided by new studies submitted by the applicant. Because a Section 505(b)(2) application relies in part on previous studies or previous FDA findings of safety and effectiveness, preparing 505(b)(2) applications is generally less costly and time-consuming than preparing an NDA based entirely on new data and information from a full set of clinical studies. The FDA may approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the

Section 505(b)(2) applicant. The law governing Section 505(b)(2) or FDA's current policies may change in such a way as to adversely affect our applications for approval that seek to utilize the Section 505(b)(2) approach. Such changes could result in additional costs associated with additional studies or clinical studies and delays.

The FDA provides that reviews and/or approvals of applications submitted under Section 505(b)(2) will be delayed in various circumstances. For example, the holder of the NDA for the listed drug may be entitled to a period of market exclusivity during which the FDA will not approve, and may not even review, a Section 505(b)(2) application from other sponsors. If the listed drug is claimed by one or more patents that the NDA holder has listed with the FDA, the Section 505(b)(2) applicant must submit a certification with respect to each such patent. If the 505(b)(2) applicant certifies that a listed patent is invalid, unenforceable or not infringed by the product that is the subject of the Section 505(b)(2) application, it must notify the patent holder and the NDA holder. If, within 45 days of providing this notice, the NDA holder sues the 505(b)(2) applicant for patent infringement, the FDA will not approve the Section 505(b)(2) application until the earlier of 30 months, a court decision favorable to the Section 505(b)(2) applicant, settlement of the lawsuit or expiration of the patent. The regulations governing marketing exclusivity and patent protection are complex, and it is often unclear how they will be applied in particular circumstances.

Drug Enforcement Agency Regulation

Our research and development processes involve the controlled use of hazardous materials, including chemicals. Some of these hazardous materials are considered to be controlled substances and subject to regulation by the U.S. Drug Enforcement Agency (DEA). Controlled substances are those drugs that appear on 1 of 5 schedules promulgated and administered by the DEA under the Controlled Substances Act (CSA). The CSA governs, among other things, the distribution, recordkeeping, handling, security and disposal of controlled substances. We must be registered by the DEA in order to engage in these activities, and are subject to periodic and ongoing inspections by the DEA and similar state drug enforcement authorities to assess ongoing compliance with the DEA's regulations. Any failure to comply with these regulations could lead to a variety of sanctions, including the revocation, or a denial of renewal, of the DEA registration, injunctions or civil or criminal penalties.

Third-Party Payor Coverage and Reimbursement

Commercial success of GIAPREZA, and any of our other product candidates that are approved or commercialized for any indication will depend, in part, on the availability of coverage and reimbursement from third-party payors at the federal, state and private levels. Government payor programs, including Medicare and Medicaid, private healthcare insurance companies and managed care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The U.S. Congress and state legislatures, from time to time, propose and adopt initiatives aimed at cost containment. Ongoing federal and state government initiatives directed at lowering the total cost of healthcare will likely continue to focus on healthcare reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems.

Examples of how limits on drug coverage and reimbursement in the U.S. may cause reduced payments for drugs in the future include:

- changing Medicare reimbursement methodologies;
- fluctuating decisions on which drugs to include in formularies;
- revising drug rebate calculations under the Medicaid program or requiring that new or additional rebates be provided to Medicare, Medicaid, other federal or state healthcare programs; and
- reforming drug importation laws.

Some third-party payors also require pre-approval of coverage for new drug therapies before they will reimburse healthcare providers that use such therapies. While we cannot predict whether any proposed cost-containment

measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and to operate profitably.

Reimbursement systems in international markets vary significantly by country and, within some countries, by region. Reimbursement approvals must be obtained on a country-by-country basis. In many foreign markets, including markets in which we hope to sell our products, the pricing of prescription pharmaceuticals is subject to government pricing control. In these markets, once marketing approval is received, pricing negotiations could take significant additional time. As in the U.S., the lack of satisfactory reimbursement or inadequate government pricing of any of our products would limit widespread use and lower potential product revenues.

Anti-Kickback, Fraud and Abuse and False Claims Regulation

On commercial launch of a product in the U.S., we will be subject to healthcare fraud and abuse regulation and enforcement by both the federal government and the states in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Arrangements with third-party payors and customers may expose us to applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval.

Regulations under applicable federal and state healthcare laws and regulations include the federal healthcare programs' Anti-Kickback Law, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral or purchase of any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced-price items and services. Many states have similar laws that apply to their state healthcare programs as well as private payors. In addition, the False Claims Act (FCA) imposes liability on persons who, among other things, present or cause to be presented false or fraudulent claims for payment by a federal healthcare program. The FCA has been used to prosecute persons submitting claims for payment that are inaccurate or fraudulent, that are for services not provided as claimed, or for services that are not medically necessary. Actions under the FCA may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the FCA can result in significant monetary penalties and treble damages. The federal government is using the FCA, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices.

The risk of being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Moreover, recent healthcare reform legislation has strengthened many of these laws. For example, the Patient Protection and Affordable Care Act (PPACA), among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, PPACA provides that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes.

The continuing interpretation and application of these laws could have a material adverse impact on our business and our ability to compete should we commence marketing a product.

Federal and State Sunshine Laws

We must comply with federal "sunshine" laws that require transparency regarding financial arrangements with healthcare providers. This would include the reporting and disclosure requirements imposed by the PPACA on drug manufacturers regarding any "payment or transfer of value" made or distributed to physicians and teaching hospitals. Failure to submit required information can result in civil monetary penalties. A number of states have laws that require the implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices, and/or require pharmaceutical companies to track and report payments, gifts and other benefits provided to physicians and other healthcare professionals and entities.

Foreign Corrupt Practices Act

We are subject to the Foreign Corrupt Practices Act of 1997 (FCPA). The FCPA and other similar anti-bribery laws in other jurisdictions, such as the U.K. Bribery Act, generally prohibit companies and their intermediaries from providing money or anything of value to officials of foreign governments, foreign political parties, or international organizations with the intent to obtain or retain business or seek a business advantage. Recently, there has been a substantial increase in anti-bribery law enforcement activity by U.S. regulators, with more frequent and aggressive investigations and enforcement proceedings by both the Department of Justice and the SEC. A determination that our operations or activities are not, or were not, in compliance with U.S. or foreign laws or regulations could result in the imposition of substantial fines, interruptions of business, loss of supplier, vendor or other third-party relationships, termination of necessary licenses and permits, and other legal or equitable sanctions. Other internal or government investigations or legal or regulatory proceedings, including lawsuits brought by private litigants, may also follow as a consequence.

Patient Privacy and Data Security

We are required to comply, as applicable, with numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, and to govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who may prescribe products we may sell in the future and from whom we may obtain patient health information are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology and Clinical Health Act (HITECH), and its implementing regulations. We are not a HIPAA covered entity, do not currently intend to become one, and we do not operate as a business associate to any covered entities. Therefore, these privacy and security requirements do not apply to us. However, we could be subject to civil and criminal penalties if we knowingly obtain individually identifiable health information from a covered entity in a manner that is not authorized or permitted by HIPAA or for aiding and abetting the violation of HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business, and any failure to comply could result in harm to our reputation and potential fines and penalties.

In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In May 2018, the EU Data Protection Directive was replaced with the recently adopted European General Data Protection Regulation (GDPR) which contains new provisions specifically directed at the processing of health information, higher sanctions and extraterritoriality measures intended to bring non-EU companies under the regulation. We currently conduct clinical studies in the EU are subject to such requirements. We anticipate that over time we may expand our business operations to include additional operations in the EU. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

Environmental, Health and Safety Laws

Our operations and those of our third-party manufacturers are subject to complex and increasingly stringent environmental, health and safety laws and regulations. Further, in the future, we may open manufacturing facilities that would likely be subject to environmental and health and safety authorities in the relevant jurisdictions. These authorities typically administer laws which regulate, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. Violations of these laws could subject us to strict liability, fines, or liability to third parties.

Other Laws

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the U.S., including laws relating to the oversight activities of the SEC and the regulations of the Nasdaq Capital Market, on which our shares are traded. We are also subject to various laws, regulations and recommendations relating to safe working conditions, laboratory practices and the experimental use of animals.

Employees

As of February 20, 2019, we employed 169 regular, full-time employees, 96 of whom are engaged in research and clinical development activities, and 73 of whom are in sales and marketing, finance, information technology, human resources and administration. None of our employees are covered by collective bargaining agreements.

Corporate and Other Information

The Company was incorporated in Delaware in 1989 and reincorporated in California in 2012. Our principal office is located at 4550 Towne Centre Court, San Diego, CA 92121 and our telephone number is (858) 207-4264. Our common stock trades on the Nasdaq Capital Market under the symbol “LJPC.” Our website address is www.ljpc.com. Information contained on or accessible through our website is not a part of this Annual Report on Form 10-K, and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We file electronically with the U.S. Securities and Exchange Commission (SEC) our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. We make available on our website at www.ljpc.com, free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

Item 1A. Risk Factors.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below and the other information before deciding to invest in our common stock. The risks described below are not the only ones facing our Company. Additional risks not presently known to us or that we currently consider immaterial may also adversely affect our business. We have attempted to identify below the major factors that could cause differences between actual and planned or expected results, but we cannot assure you that we have identified all of those factors.

If any of the following risks actually happen, our business, financial condition and operating results could be materially adversely affected. In this case, the trading price of our common stock could decline, and you could lose all or part of your investment.

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

We are substantially dependent on the commercial success of GIAPREZA™ (angiotensin II).

The near-term success of our business is largely dependent on our ability to successfully commercialize GIAPREZA™ (angiotensin II), our only commercial product. Although members of our management team have prior experience launching new products, GIAPREZA is the first product we have launched.

Even if our sales organization performs as expected, the revenue that we may receive from sales of GIAPREZA may be less than anticipated due to factors that are outside of our control. These factors that may impact revenue include:

- the perception of physicians and other members of the healthcare community of the safety and efficacy and cost-competitiveness relative to that of competing products;
- our ability to maintain successful sales, marketing and educational programs for certain physicians and other healthcare providers;
- our ability to raise patient and physician awareness;
- the cost-effectiveness of our product;
- acceptance by institutional formulary committees;
- patient and physician satisfaction with our product;
- the size of the potential market for our product;
- our ability to obtain adequate reimbursement from government and third-party payors;
- unfavorable publicity concerning our product or similar products;
- the introduction, availability and acceptance of competing treatments;
- adverse event information relating to our product or similar classes of drugs;
- product liability litigation alleging injuries relating to the product or similar classes of drugs;
- our ability to maintain and defend our patents for GIAPREZA;
- our ability to have GIAPREZA manufactured at a commercial production level successfully and on a timely basis;
- the availability of raw materials;
- our ability to access third parties to manufacture and distribute our product on acceptable terms or at all;
- regulatory developments related to the manufacture or continued use of our product;

- any pediatric investigation plan requirements and the results thereof;

- any post-approval study requirements and the results thereof;
- the extent and effectiveness of sales and marketing and distribution support for our product;
- our competitors' activities, including decisions as to the timing of competing product launches, generic entrants, pricing and discounting; and
- any other material adverse developments with respect to the potential commercialization of our product.

Our business will be adversely affected if, due to these or other factors, our commercialization of GIAPREZA does not achieve the acceptance and demand necessary to sustain revenue growth. If we are unable to successfully commercialize GIAPREZA, our business and results of operations will suffer.

If we are unable to maintain effective sales, marketing and distribution capabilities to sell and market GIAPREZA or any other products we may develop, our product sales may be hindered.

In order to successfully commercialize GIAPREZA, we must increase our sales, marketing, distribution and other non-technical capabilities. The development of a sales organization to market GIAPREZA, or any other product we may develop, is expensive and time-consuming, and we cannot be certain that we will be able to successfully develop this capacity or that this function will execute as expected. If we are unable to establish adequate sales, marketing and distribution capabilities, we may not be able to generate product revenue and our business and results of operations will suffer.

If we fail to comply with our reporting and payment obligations under U.S. governmental pricing and contracting programs, we could be subject to additional reimbursement requirements, penalties and fines, which could have a material adverse effect on our business, financial condition, and results of operations.

The Medicare program and certain government pricing programs, including the Medicaid drug rebate program, the Public Health Services' 340B drug pricing program, and the pricing program under the Veterans Health Care Act of 1992 impact the reimbursement we may receive from sales of GIAPREZA, or any other products that are approved for marketing. Pricing and rebate calculations vary among programs. The calculations are complex and are often subject to interpretation by manufacturers, governmental or regulatory agencies, and the courts. We are required to submit a number of different pricing calculations to government agencies on a quarterly basis. Failure to comply with our reporting and payment obligations under U.S. governmental pricing and contracting programs may result in additional payments, penalties and fines due to government agencies, which may have a material adverse effect on our business, financial condition and results of operations.

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

As of December 31, 2018, we had GIAPREZA sales as our sole revenue source and available cash and cash equivalents of $172.6 million. To fund future operations to the point where we are able to generate positive cash flow from GIAPREZA and our product candidates, we will need to raise significant additional capital. The amount and timing of future funding requirements will depend on many factors, including the success of our commercialization efforts for GIAPREZA, 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. We anticipate that we will seek to fund our operations through equity, debt, royalty-based financings or other sources, such as potential collaboration agreements. We cannot provide assurance that additional financing will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through equity 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, commercialization efforts, and other business activities, we could be forced to abandon one or more programs and curtail or cease our operations.

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

We have a single product approved for commercialization and have generated approximately $10.1 million in total GIAPREZA sales since the commercial launch of the product. Our ability to continue to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully continue the commercialization of GIAPREZA and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, our product candidates in development. Our ability to generate revenue from product sales depends heavily on our success in many areas, including but not limited to:

- successfully commercializing GIAPREZA, including increasing physician awareness and adoption of the product and managing our pricing and overall commercial strategy so that hospitals are willing to purchase the product;
- successfully completing research and nonclinical and clinical development of our product candidates;

- obtaining regulatory and marketing approvals for GIAPREZA outside of the United States, as well as our ability to obtain marketing approvals for other product candidates for which we complete clinical studies;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- 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.

We anticipate incurring significant costs associated with continued commercializing GIAPREZA and development of our product candidates. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform additional clinical, nonclinical or other types of studies in addition to those that we currently anticipate. For GIAPREZA and other product candidates that may be approved, our revenue will be dependent, in part, on 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 be unable to generate significant revenue from sales of approved products.

Results from our clinical studies may not be sufficient to obtain regulatory approvals to market our product candidates in the U.S. or other countries on a timely basis, if at all.

Product candidates are subject to extensive government regulations related to development, clinical studies, 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 studies and toxicology studies that demonstrate that our product candidates are safe and effective. The process of obtaining FDA and foreign regulatory approvals is costly, time-consuming, uncertain and subject to unanticipated delays.

Even where we have obtained regulatory approval for a product in one jurisdiction, such as FDA approval of GIAPREZA in the United States, there can be no assurance that we will be able to obtain regulatory approval for that same product in other jurisdictions. Regulatory authorities such as the FDA and EMA have substantial discretion in the approval process and may not agree that we have demonstrated that our product candidates are safe and effective. If our product 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, EMA or other foreign regulatory authorities will approve our product 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 studies of our product candidates may not be predictive of the results of later-stage clinical studies. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent clinical studies. For example, the safety or efficacy results generated to date in our clinical studies do not ensure that later clinical studies will demonstrate similar results. There is a high failure rate for drugs proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy, despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the

biopharmaceutical industry have suffered significant setbacks in advanced clinical studies 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 studies we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our product candidates.

Clinical trials that we may undertake may be delayed or halted.

Any clinical studies of our product 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 product 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 studies. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, our studies may not be completed in a timely fashion or in a manner that generates acceptable data, and we may not be able to obtain regulatory approval for or commercialize our product candidates.

We have agreements with third-party contract research organizations (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 studies, 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 (cGCPs), which are regulations and guidelines enforced by the FDA, EMA and other 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 fail to comply with applicable cGCP regulations, the clinical data generated in our clinical studies may be deemed unreliable and the FDA, EMA and other foreign regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that, on inspection, such regulatory authorities will determine that any of our clinical studies comply with the cGCP regulations. In addition, our clinical studies must be conducted with product produced under 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 studies, 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 studies may be extended, delayed or terminated 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 product candidates may be delayed, which could have a severe negative effect on our business.

If the third-party manufacturers on which we rely fail to produce the materials that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face commercial supply

shortages, delays in the trials, regulatory submissions, required approvals or commercialization of our product and product candidates.

We do not manufacture GIAPREZA or any of our product candidates, nor do we plan to develop any capacity to do so. Instead, we contract with third-party manufacturers to manufacture and supply GIAPREZA and all of our product 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. Although we believe that we could identify and qualify alternate suppliers if necessary, the steps needed for a pharmaceutical manufacturer to implement a validated manufacturing process can be time-consuming and costly. As a result, and because we currently have only a single manufacturer for GIAPREZA, termination of this manufacturing relationship or a disruption in their manufacturing facilities could adversely affect the available commercial supply of GIAPREZA. Further, certain critical materials used in manufacturing GIAPREZA have historically been sourced from single suppliers. An interruption in the supply of a key material could also significantly impact our ability to meet the demand for GIAPREZA.

Any facilities in which our product or product 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 commercial sale or approval of one or more of our products or product candidates.

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

Our success in developing and marketing our product and product 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 sell, develop or acquire. Our patents and patent applications cover various technologies, product and product 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 U.S. Patent and Trademark Office (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 sales of GIAPREZA or the advancement 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 technology or process that may be required to develop or commercialize one or more of our product candidates may have a material

adverse effect on our business.

We do not have complete patent protection for GIAPREZA or our other product candidates, as the active pharmaceutical ingredients in GIAPREZA and our other 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 U.S. 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 U.S. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. 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 U.S. prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the U.S., the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act (Leahy-Smith Act), enacted on September 16, 2011, the U.S. 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 products 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 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
- 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 occur, 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 GIAPREZA and certain 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 and product candidates, there may be times when patents relating to our products or product candidates are controlled by our licensors, such as with GIAPREZA, where patent prosecution is controlled by our licensor, the George Washington University. If any of our licensing partners fail to appropriately prosecute and maintain patent protection for patents covering any licensed patents, 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 certain product candidates, we may face greater commercial competition and our revenue will be reduced.

Regulatory authorities in some jurisdictions, including the U.S. and EU may designate drugs for relatively small patient populations as orphan drugs. Our business strategy for certain of our product and product 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 U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. 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 5 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 patient population that we believe may be eligible for orphan status, it is possible that the FDA 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 studies 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 and product candidates may cause undesirable side effects or have other properties that could delay or prevent their market acceptance or 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 or product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies and commercial sales 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 or product candidates for any or all targeted indications.

The drug-related side effects could affect commercial sales, 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 crea