REPLIGEN CORP
Form 10-K
June 11, 2009
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 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 March 31, 2009

OR

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

For the transition period from to

Commission file number: 000-14656

REPLIGEN CORPORATION

(Exact name of Registrant as specified in its charter)

Delaware	**04-2729386**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
41 Seyon Street, Building #1, Suite 100, Waltham, Massachusetts	**02453**
(Address of Principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: (781) 250-0111

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.01 Par Value Per Share	**The NASDAQ Stock Market LLC**
Series A Junior Participating Preferred Stock Purchase Rights	

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

Title of Each Class

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ No ¨.

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

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

Large accelerated filer ¨	Accelerated filer x	Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates as of September 30, 2008, the last business day of the registrant s most recently completed second fiscal quarter, was approximately $146,523,828.

The number of shares of outstanding of the registrant s common stock as of June 7, 2009 was 30,741,707.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Company s definitive Proxy Statement in connection with the 2009 annual meeting of Stockholders are incorporated by reference into Part III of this Form 10-K.

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PART I

Item 1. BUSINESS

The following discussion of our business contains forward-looking statements that involve risks and uncertainties. When used in this report, the words intend, anticipate, believe, estimate, plan and expect and similar expressions as they relate to us are included to identify forward-looking statements. Our actual results could differ materially from those anticipated in these forward-looking statements and are a result of certain factors, including those set forth under Risk Factors and elsewhere in this Annual Report on Form 10-K.

Repligen Corporation (Repligen, the Company or we) is developing novel therapeutics primarily for radiology and neuropsychiatry. Our business strategy is to maintain full commercial rights to our product candidates through proof of principle clinical studies after which we may seek corporate partners for further development and marketing or we may decide to market certain products on our own. For the next several years, we expect to fund the development of our proprietary therapeutic product candidates primarily through royalty payments received from Bristol-Myers Squibb Corporation (Bristol) based on their United States sales of Orencia® and the profits from the sales of our Protein A products which are used in the production of many therapeutic monoclonal antibodies. These revenues as well as our existing financial resources will allow us to independently advance our therapeutic product candidates through proof of principle clinical trials while also supporting our business development activities.

We were incorporated in May 1981, under the laws of the State of Delaware. Our principle executive offices are at 41 Seyon Street, Waltham, Massachusetts 02453 and our telephone number is (781) 250-0111.

Currently Marketed Products

We currently sell a line of commercial products based on Protein A, which are used in the production of monoclonal antibodies.

Protein A Products for Antibody Manufacturing

Protein A is widely used in the purification of therapeutic monoclonal antibodies. Most therapeutic monoclonal antibodies are manufactured by the fermentation of mammalian cells that express the monoclonal antibody. The monoclonal antibody is typically produced by a process in which an impure fermentation broth containing the desired monoclonal antibody is passed over a solid support to which Protein A has been chemically attached or immobilized . The immobilized Protein A binds the monoclonal antibody while other impurities are washed away. The monoclonal antibody is then recovered from the support in a substantially purified form.

We manufacture and market several products based on recombinant forms of Protein A. Our primary customers incorporate our Protein A products into their proprietary monoclonal antibody purification products that they sell directly to the biotechnology and pharmaceutical industry. We primarily supply Protein A products to GE Healthcare (GEHC) under a supply agreement which extends through 2010 and to Applied Biosystems, Inc. under a supply agreement that extends until 2011. The majority of our product sales for the last three years have been sales of Protein A products.

Sales of therapeutic monoclonal antibodies have increased from $300 million in 1997 to approximately $34 billion in 2008. This growth is based on the increasing use of therapeutic antibodies, including Enbrel® and Remicade® for rheumatoid arthritis and other inflammatory disorders, and Rituxan® for rheumatoid arthritis and Non-Hodgkin s Lymphoma, among other therapeutic antibodies. There are more than 150 additional monoclonal antibodies in various stages of clinical testing which may lead to additional growth of the antibody market and in turn, increased demand for Protein A.

SecreFlo® for Pancreatic Diagnosis

We discontinued distribution of SecreFlo® in the second quarter of fiscal year 2009 due to the expiration of our agreement with ChiRhoClin, Inc. Previously, we recorded sales of SecreFlo®, a synthetic form of porcine

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(pig-derived) secretin. SecreFlo® is approved by the U.S. Food and Drug Administration (FDA) as an aid in the diagnosis of chronic pancreatitis and gastrinoma (a form of cancer) and as an aid during endoscopic retrograde cholangiopancreatography (ERCP), a gastrointestinal procedure.

Intellectual Property on Monoclonal Antibody and Antibody Fusion Products

Orencia® (CTLA4-Ig) Royalties

CTLA4 is a key regulator of the activity of the immune system. CTLA4 turns off the immune system after it has successfully cleared a bacterial or viral infection by blocking the activation of T-cells, the immune cells responsible for initiating an immune response. CTLA4-Ig s mechanism of action is different from the current therapies for autoimmune disease or organ transplant rejection, thus it may provide a treatment for patients who are refractory to existing therapies. In the 1990 s, our collaborators at the University of Michigan and the U.S. Navy demonstrated in animal models that a fusion protein consisting of fragments of CTLA4 and an antibody (CTLA4-Ig) could be used to treat certain autoimmune diseases. This research finding resulted in the granting of U.S. patent No. 6,685,941 (the 941 Patent) covering the treatment of certain autoimmune disorders including rheumatoid arthritis with CTLA4-Ig.

In December 2005, the FDA approved Bristol s application to market CTLA4-Ig, under the brand name Orencia®, for treatment of rheumatoid arthritis. In January 2006, Repligen and the University of Michigan jointly filed a lawsuit against Bristol in the United States District Court for the Eastern District of Texas for infringement of the 941 Patent. In April 2008, Repligen and the University of Michigan entered into a settlement agreement with Bristol pursuant to which, Bristol made an initial payment of $5 million to Repligen and agreed to pay us royalties on the U.S. net sales of Orencia® for any clinical indication at a rate of 1.8% for the first $500 million of annual sales, 2.0% for the next $500 million and 4.0% of annual sales in excess of $1 billion for each year from January 1, 2008 until December 31, 2013.

The 941 Patent is owned by the University of Michigan and exclusively licensed to Repligen. In consideration of this exclusive license, Repligen agreed to pay the University of Michigan 15% of all royalty income received, after deducting legal expenses. There are no annual or other fees associated with this agreement. Under this agreement, since its inception through fiscal year 2009, Repligen has paid $1.1 million to the University of Michigan.

Erbitux®

Erbitux® is a monoclonal antibody developed by ImClone Systems Incorporated (ImClone) which was approved by the FDA in February 2004 for the treatment of certain forms of colon cancer and in March 2006 for the treatment of head and neck cancer. Erbitux® is manufactured with a cell line which contains certain genetic technologies (DNA enhancers) which increase the productivity of a cell line. A U.S. patent covering the use of DNA enhancers, which expired in May of 2004, was assigned to The Massachusetts Institute of Technology (MIT) and exclusively licensed to Repligen. In May 2004, Repligen and MIT jointly filed a lawsuit against ImClone in U.S. District Court for Massachusetts alleging that ImClone had infringed our patent rights in its production of Erbitux®. In September 2007, Repligen and MIT entered into a settlement agreement under which ImClone was granted a license to the DNA enhancer patent and certain other intellectual property in exchange for a payment of $65,000,000.

Development Stage Products

Secretin for MRI

Secretin is a well-known hormone produced in the small intestine that regulates the function of the pancreas as part of the process of digestion. We are currently evaluating secretin for improvement of MRI imaging of structural abnormalities of the pancreas.

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Several reports published in the literature support the use of secretin with abdominal MRI imaging to improve visualization of pancreaticobiliary structures and to increase diagnostic sensitivity relative to unenhanced abdominal MRI. The use of secretin during MRI harnesses the natural biologic properties of secretin, which signals the release of water-rich fluids into the ducts of the pancreas. Improvement in the detection and delineation of normal and abnormal structures with MRI is attractive for patient care as it can obviate the need for more risky invasive endoscopic procedures.

In June 2006, we initiated a Phase 2 clinical trial to evaluate the use of RG1068, synthetic human secretin, as an agent to improve the detection of structural abnormalities of the pancreatic ducts during MRI imaging of the pancreas. This was a multi-center, baseline controlled, single dose study in which 76 patients with a history of pancreatitis received a secretin-enhanced MRI and an unenhanced MRI of the pancreas.

In May 2007, we announced positive results from this Phase 2 clinical trial to evaluate the use of RG1068 to improve the assessment of pancreatic duct structures by MRI. The study showed an improvement in sensitivity of detection of structural abnormalities of the pancreatic duct of approximately 20% with no loss in specificity. In addition, the study showed highly significant increases in the following three assessments: physician confidence in their ability to identify structural abnormalities, the number of pancreatic duct segments visualized, and improvement in the overall quality of the MRI images. Detailed visual assessment of the pancreatic ducts and identification of structural abnormalities is important in the assessment, diagnosis and treatment of diseases such as acute and chronic pancreatitis.

Our Phase 2 data was reviewed by the FDA and has served as the basis for the design of a pivotal, Phase 3 study. The Phase 3 study was initiated in March 2008 and will seek to recruit approximately 250 patients at 25 clinical sites in the United States and Canada. The primary objective of the Phase 3 study is to demonstrate that secretin improves the ability to detect structural abnormalities of the pancreas by MRI. We believe that a successful Phase 3 study will provide the basis for filing a New Drug Application (NDA) with the FDA for approval to market secretin for this use in the United States. We have received an Orphan Drug designation from the FDA for this use of secretin, which means we will have seven years of marketing exclusivity in the United States following approval of the NDA. We also have received fast track designation from the FDA which means our NDA may receive expedited review by the FDA.

Uridine for Bipolar Depression

Uridine is a biological compound essential for multiple biosynthetic processes including the synthesis of DNA and RNA, the basic hereditary material found in all cells and numerous other factors essential for cell metabolism. Uridine is synthesized by the power plant of the human cell known as the mitochondria. The rationale for uridine therapy in central nervous system (CNS) disorders is supported by pre-clinical and clinical research. Researchers at McLean Hospital previously demonstrated that uridine is active in a well-validated animal model of depression. Literature reports indicate that certain genes that encode for mitochondrial proteins are significantly down-regulated in the brains of bipolar patients. This insight suggests that the symptoms of bipolar disorder may be linked to dysregulation of energy metabolism in the brain.

Bipolar disorder, also known as manic depression, is marked by extreme changes in mood, energy and behavior where a person can alternate between mania (highs) and depression (lows). Bipolar disorder affects more than 2 million adults in the United States. Current drug therapy for bipolar disorder includes the use of lithium and anti-psychotic drugs. However, side effects are frequent and troublesome, and patients do not respond fully, leading to poor patient compliance with therapy and frequent recurrences of mania and depression.

In March 2006, we initiated a Phase 2a clinical trial of RG2417, an oral formulation of uridine, in patients with bipolar depression. This was a multi-center, dose escalating study in 82 patients which compared daily, oral dosing with either RG2417 or a placebo for six weeks. Patients were evaluated weekly for the safety and effectiveness of RG2417 on the symptoms of bipolar depression. The study showed a statistically significant improvement in the symptoms of depression over the six week course of treatment in the patients treated with

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RG2417 compared to placebo. In addition, the patients treated with RG2417 showed a greater improvement in a global assessment of their overall symptoms of bipolar disorder compared to placebo-treated patients. RG2417 was well tolerated by patients with a safety profile similar to those treated with a placebo. In November 2008, we initiated a Phase 2b trial to confirm the effects of uridine on bipolar depression as a monotherapy. The Phase 2b study involves 150 patients enrolled at 25 sites in the United States.

Histone Deacetylase Inhibitors for Friedreich s Ataxia

Friedreich s ataxia is a progressive disability that typically emerges between the ages of 5 and 15 and often leads to severe disability, incapacitation or loss of life in early adulthood. Friedreich s ataxia is caused by a single gene defect that results in inadequate production of the protein frataxin. The protein frataxin appears to be essential for the proper functioning of the mitochondria, the power plant of both neural and muscle cells. Low levels of frataxin leads to degeneration of both the nerves controlling muscle movements in the arms and legs and the nerve tissue in the spinal cord. Approximately one in every 50,000 people in the United States has Friedreich s ataxia.

In April 2007, we entered into an exclusive commercial license (the Scripps License Agreement) with The Scripps Research Institute (Scripps) for intellectual property covering compounds which may have utility in treating Friedreich s ataxia. Research in cells derived from patients, as well as in mice indicates that the licensed compounds increase production of the protein frataxin, which suggests potential utility of these compounds in slowing or stopping progression of the disease. There is currently no treatment for Friedreich s ataxia.

We have chemically synthesized several libraries of compounds related to the initial compounds licensed from Scripps. Some of these compounds have higher potency or improved specificity in laboratory assays. These compounds are currently being evaluated in a variety of animal models for safety and efficacy to determine if one may be a suitable candidate for clinical trials. Preliminary data also suggest that these compounds may be useful in treating other disorders such as Spinal Muscular Atrophy and Huntington s disease.

Sales and Marketing

We sell our Protein A products primarily through value-added resellers including GEHC and Applied Biosystems, Inc., as well as through distributors in certain foreign markets. Prior to its discontinuation in the second quarter of fiscal year 2009, we marketed SecreFlo® directly to hospital-based gastroenterologists in the United States.

Significant Customers and Geographic Reporting

Customers for our Protein A products include chromatography companies, diagnostics companies, biopharmaceutical companies and laboratory researchers. In April 2008, we settled our litigation with Bristol regarding their sales of Orencia® for which we now receive a royalty. For fiscal year 2009, royalty revenue from Bristol represented 46% of total revenues, and our largest Protein A customer accounted for 36% of total revenues. During fiscal years 2008 and 2007, two Protein A customers accounted for more than 70% of our total revenue in each year.

In fiscal years 2009, 2008 and 2007, total revenues from sales to customers in the United States were approximately 59%, 32% and 47%, respectively. During the same fiscal periods, total revenues generated though sales to customers in Sweden were 37%, 61% and 49%, respectively.

Employees

As of May 31, 2009, we had 69 employees. Of those employees, 51 were engaged in research, development and manufacturing and 18 were in administrative and marketing functions. Twenty of our employees hold doctorates or other advanced degrees. Each of our employees has signed a confidentiality agreement. None of our employees are covered by collective bargaining agreements.

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Patents, Licenses and Proprietary Rights

Our policy is to seek patent protection for our therapeutic product candidates. We pursue patent protection in the United States and file corresponding patent applications in relevant foreign jurisdictions. We believe that patents are an important element in the protection of our competitive and proprietary position, but other elements, including trade secrets, orphan drug status and know-how, are also important. We own or have exclusive rights to a number of U.S. patents and corresponding foreign equivalents. The terms of such patents expire at various times between 2009 and 2021. In addition, we have rights to more than 20 U.S. pending patent applications and corresponding foreign applications. The invalidation of key patents owned or licensed by us or the failure of patents to issue on pending patent applications could create increased competition, with potential adverse effects on our business prospects. For each of our license agreements where we license the rights to patents or patent applications, the license will terminate on the day that the last to expire patent covered by each such license agreement expires.

We also rely upon trade secret protection for our confidential and proprietary information. Our policy is to require each of our employees, consultants, business partners and significant scientific collaborators to execute confidentiality agreements upon the commencement of an employment, consulting or business relationship with us. These agreements generally provide that all confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees and consultants, the agreements generally provide that all inventions conceived by the individual in the course of rendering services to Repligen shall be our exclusive property.

CTLA4-Ig

The 941 patent was issued in February 2004, covering the use of CTLA4-Ig to treat specific autoimmune disorders including rheumatoid arthritis and multiple sclerosis. The patent is assigned to the University of Michigan and the U.S. Navy and is exclusively licensed to Repligen. In April 2008, Repligen granted Bristol-Myers Squibb an exclusive sublicense to this patent (see Legal Proceedings).

Uridine

In November 2000 and December 2000, Repligen entered into two license agreements (the UCSD Uridine License Agreements) with the University of California, San Diego (UCSD) for certain patent applications pertaining to the use of uridine and uridine derivatives for the treatment of mitochondrial disease and purine autism. In April 2004, a U.S. patent was issued to Repligen and UCSD, which claims methods of treating certain developmental disorders, including certain forms of autism, with uridine compositions which expires in October 2020. In January 2009, the Company elected to terminate the UCSD license agreements as they were no longer deemed necessary for our current product development activities.

In March 2009, we entered into an exclusive license agreement for the worldwide rights to the use of uridine in the treatment of patients with bipolar disorder from McLean Hospital. The use of uridine in the treatment of patients with bipolar disorder is currently the subject of a patent application and upon issue, the patent will remain in force until 2025 prior to any regulatory extensions. Under the terms of the license agreement, McLean received an upfront payment, and is eligible to receive payments upon certain product development milestones and royalties upon successful commercialization of uridine for bipolar disorder.

Protein A

We own a U.S. patent covering recombinant Protein A, which expires in September 2009, as well as significant know-how in the manufacture of high-purity Protein A. We also own certain other U.S. patent rights covering modified forms of Protein A, that were non-exclusively licensed to Amersham Biosciences (now GEHC) in 1998 as part of a ten-year agreement, which was amended and extended in 2005 through 2010, covering the supply of Protein A to GEHC.

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Research and Development

For the past three years, we have devoted substantial resources to the research and development of therapeutic product candidates and our commercial products and product candidates discussed herein. We spent $12,772,000 in fiscal 2009, $7,241,000 in fiscal 2008, and $5,924,000 in fiscal 2007 on company-sponsored research and development activities.

Competition

Our Protein A products compete on the basis of quality, performance, cost effectiveness, and application suitability with numerous established technologies. Additional products using new technologies that may be competitive with our products may also be introduced. Many of the companies selling or developing competitive products have financial, manufacturing and distribution resources significantly greater than ours.

The field of drug development is characterized by rapid technological change. New developments are expected to continue at a rapid pace in both industry and academia. There are many companies, both public and private, including large pharmaceutical companies, chemical companies and specialized biotechnology companies, engaged in developing products competitive with products that we have under development. Many of these companies have greater capital, human resources, research and development, manufacturing and marketing experience than we do. They may succeed in developing products that are more effective or less costly than any that we may develop. These competitors may also prove to be more successful than we are in production and marketing. In addition, academic, government and industry-based research groups compete intensely with us in recruiting qualified research personnel, in submitting patent filings for protection of intellectual property rights and in establishing corporate strategic alliances. We cannot be certain that research, discoveries and commercial developments by others will not render any of our programs or potential products noncompetitive.

Manufacturing

Protein A for Antibody Manufacturing

We manufacture Protein A products from recombinant strains of bacteria. We manufacture Protein A for GEHC under a supply agreement which extends through 2010. In addition, we have a long term supply agreement with Applied Biosystems, Inc. that provides that Repligen will be the preferred provider of recombinant Protein A to Applied Biosystems until 2011. We utilize our own facility and third parties to carry out certain fermentation and recovery operations, while the purification, immobilization, packaging and quality control testing of our Protein A products are conducted at our facilities. We maintain an active quality assurance effort to support the regulatory requirements of our customers and achieved ISO 9001 certification in fiscal 2009. We purchase raw materials from more than one commercially established company and believe that the necessary raw materials are currently commercially available in sufficient quantities necessary to meet market demand.

Therapeutic Product Candidates

We currently rely, and will continue to rely, for at least the next few years, upon contract manufacturers for both the procurement of raw materials and the production of our product candidates for use in our clinical trials. Our product candidates will need to be manufactured in a facility and by processes that comply with the FDA s good manufacturing practices and other similar regulations. It may take a substantial period of time to begin manufacturing our products in compliance with such regulations. If we are unable to establish and maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components that meet our planned time and cost parameters, the development and timing of our clinical trials may be adversely affected.

We purchase raw materials from more than one commercially established company. Our necessary raw materials are currently commercially available in quantities that far exceed the scale required to complete all of our current and future planned clinical trials.

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Government Regulation

The development of drug candidates is subject to regulation in the United States by the FDA and abroad by foreign equivalents. Product development and approval within the FDA regulatory framework usually takes a significant number of years and involves the expenditure of substantial capital resources. Timelines for development are uncertain.

Before clinical testing in the United States of any drug candidate may begin, FDA requirements for preclinical efficacy and safety must be completed. Required toxicity testing typically involves characterization of the drug candidate in several animal species. Safety and efficacy data are submitted to the FDA as part of an Investigational New Drug Application (IND) and are reviewed by the FDA prior to the commencement of human clinical trials.

Clinical trials involve the administration of the drug to human volunteers or patients under the supervision of a qualified investigator, usually a physician, with an FDA-approved protocol. Human clinical trials are typically conducted in three sequential phases:

Phase 1 clinical trials represent the initial administration of the investigational drug to a small group of human subjects to test for safety (adverse effects), dose tolerance, absorption, biodistribution, metabolism, excretion and clinical pharmacology and, if possible, to gain early evidence regarding efficacy.

Phase 2 clinical trials typically involve a small sample of the actual intended patient population and seek to assess the efficacy of the drug for specific targeted indications, to determine dose tolerance and the optimal dose range, and to gather additional information relating to safety and potential adverse effects.

Once an investigational drug is found to have some efficacy and an acceptable safety profile in the targeted patient population, Phase 3 clinical trials are initiated to establish further clinical safety and efficacy of the investigational drug in a broader sample of the general patient population at multiple study sites in order to determine the overall risk-benefit ratio of the drug and to provide an adequate basis for product approval. The Phase 3 clinical development program consists of expanded, large-scale studies of patients with the target disease or disorder to obtain definitive statistical evidence of the efficacy and safety of the proposed product.

All data obtained from a comprehensive development program are submitted in an NDA to the FDA and the corresponding agencies in other countries for review and approval. The NDA includes information pertaining to clinical studies and the manufacture of the new drug. Review of an NDA by the FDA can be a time-consuming process and the FDA may request that we submit additional data or carry out additional studies.

Available Information

We maintain a website with the address www.repligen.com. We are not including the information contained on our website as a part of, or incorporating it by reference into, this annual report on Form 10-K. We make available free of charge through our website our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and amendments to these reports, as soon as reasonably practicable after we electronically file such materials with, or furnish such materials to, the Securities and Exchange Commission. Our Code of Business Conduct and Ethics is also available free of charge through our website.

In addition, the public may read and copy any materials that we file with the Securities and Exchange Commission at the Securities and Exchange Commission s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the Securities and Exchange Commission at 1-800-SEC-0330. Also, our filings with the Securities and Exchange Commission may be accessed through the Securities and Exchange Commission s Electronic Data Gathering, Analysis and Retrieval (EDGAR) system at www.sec.gov.

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Item 1A. RISK FACTORS

Investors should carefully consider the risk factors described below before making an investment decision.

If any of the events described in the following risk factors occur, our business, financial condition or results of operations could be materially harmed. In that case the trading price of our common stock could decline, and investors may lose all or part of their investment. Additional risks and uncertainties that we are unaware of or that we currently deem immaterial may also become important factors that affect Repligen.

This annual report on Form 10-K contains forward looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward looking statements as a result of certain factors, including the risks faced by us described below and elsewhere in this annual report on Form 10-K.

We are dependent on others to develop, conduct clinical trials for, manufacture, market and sell our principal products.

We conduct some of our development activities, and conduct most of our commercialization activities, through collaborations. These collaborations include academic researchers as well as contracts with vendors. Our collaborations are heavily dependent on the efforts and activities of our collaborative partners. Our existing and any future collaborations may not be technically or commercially successful. For example, if any of our collaborative partners were to breach or terminate an agreement with us, reduce its funding or otherwise fail to conduct the collaboration successfully, we may need to devote additional internal resources to the program that is the subject of the collaboration, scale back or terminate the program or seek an alternative partner, any of which could lead to delays in development and/or commercialization of our products.

We depend on, and expect to continue to depend on, a limited number of customers for a high percentage of our revenues.

As a result, the loss of, or a significant reduction in orders from, any of these customers would significantly reduce our revenues and harm our results of operations. If a large customer purchases fewer of our products, defers orders or fails to place additional orders with us, our revenue could decline, and our operating results may not meet market expectations. In addition, if those customers order our products, but fail to pay on time or at all, our liquidity and operating results could be materially and adversely affected.

Our research activities may not identify a clinical candidate with appropriate efficacy, safety and pharmacology to support clinical trials in humans.

In order to conduct phase 1 clinical trials in humans, we must first demonstrate suitable efficacy, safety and pharmacology characteristics of any potential drug candidates. If we are unsuccessful in these efforts, we may be forced to identify alternative drug candidates at substantial cost, or possibly abandon certain pre-clinical research activities.

If our clinical trials are not successful, we will not be able to develop and commercialize related products.

In order to obtain regulatory approvals for the commercial sale of our future therapeutic products, we and our collaborative partners will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of the products. We have limited experience in conducting clinical trials.

The submission of an Investigational New Drug (IND) may not result in FDA authorization to commence clinical trials. If clinical trials begin, we or our collaborative partners may not complete testing successfully within any specific time period, if at all, with respect to any of our products. Furthermore, we, our collaborative partners, or the FDA, may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to unacceptable health risks. Clinical trials, if completed, may not show any potential product to be safe or effective. Thus, the FDA and other regulatory authorities may not approve any of our potential products for any indication.

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The rate of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, and the existence of competitive clinical trials. Delays in planned patient enrollment may result in increased costs and delays in completion of clinical trials.

We may not obtain regulatory approvals; the approval process is costly and lengthy.

We must obtain regulatory approval for our ongoing development activities and before marketing or selling any of our future therapeutic products. We may not receive regulatory approvals to conduct clinical trials of our products or to manufacture or market our products. In addition, regulatory agencies may not grant such approvals on a timely basis or may revoke previously granted approvals.

The process of obtaining FDA and other required regulatory approvals is lengthy and expensive. The time required for FDA and other clearances or approvals is uncertain and typically takes a number of years, depending on the complexity and novelty of the product. Our analysis of data obtained from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Any delay in obtaining or failure to obtain required clearance or approvals could materially adversely affect our ability to generate revenues from the affected product. We have only limited experience in filing and prosecuting applications necessary to gain regulatory approvals.

We are also subject to numerous foreign regulatory requirements governing the design and conduct of the clinical trials and the manufacturing and marketing of our future products. The approval procedure varies among countries. The time required to obtain foreign approvals often differs from that required to obtain FDA approvals. Moreover, approval by the FDA does not ensure approval by regulatory authorities in other countries (or vice versa).

All of the foregoing regulatory risks also are applicable to development, manufacturing and marketing undertaken by our collaborative partners or other third parties.

Even if we obtain marketing approval, our therapeutic products will be subject to ongoing regulatory review, which will be expensive and may affect our ability to successfully commercialize our products.

Even if we or our collaborative partners receive regulatory approval of a product, such approval may be subject to limitations on the indicated uses for which the product may be marketed, which may limit the size of the market for the product or contain requirements for costly post-marketing follow-up studies. The manufacturers of our products for which we or our collaborative partners have obtained marketing approval will be subject to continued review and periodic inspections by the FDA and other regulatory authorities. The subsequent discovery of previously unknown problems with the product, clinical trial subjects, or with a manufacturer or facility may result in restrictions on the product or manufacturer, including withdrawal of the product from the market.

If we or our collaborative partners fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

If we are unable to obtain, maintain and enforce patents or regulatory exclusivity (orphan drug or new chemical entity exclusivity) for our products, we may not be able to succeed commercially.

We endeavor to obtain and maintain patent and trade secret protection for our products and processes when available in order to protect them from unauthorized use and to produce a financial return consistent with the significant time and expense required to bring our products to market. Our success will depend, in part, on our ability to:

- obtain and maintain patent protection for our products and manufacturing processes;

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preserve our trade secrets;

operate without infringing the proprietary rights of third parties; and

secure licenses from others on acceptable terms.

We cannot be sure that any patent applications relating to our products that we will file in the future or that any currently pending applications will issue on a timely basis, if ever. Since patent applications in the United States filed prior to November 2000 are maintained in secrecy until patents issue and since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions covered by each of our pending patent applications or that we were the first to file patent applications for such inventions. Even if patents are issued, the degree of protection afforded by such patents will depend upon the:

scope of the patent claims;

validity and enforceability of the claims obtained in such patents; and

our willingness and financial ability to enforce and/or defend them.

The patent position of biotechnology and pharmaceutical firms is often highly uncertain and usually involves complex legal and scientific questions. Moreover, no consistent policy has emerged in the United States nor in many other countries regarding the breadth of claims allowed in biotechnology patents. Patents which may be granted to us in certain foreign countries may be subject to opposition proceedings brought by third parties or result in suits by us, which may be costly and result in adverse consequences for us.

In some cases, litigation or other proceedings may be necessary to assert claims of infringement, to enforce patents issued to us or our licensors, to protect trade secrets, know-how or other intellectual property rights we own or to determine the scope and validity of the proprietary rights of third parties. Such litigation could result in substantial cost to us and diversion of our resources. An adverse outcome in any such litigation or proceeding could have a material adverse effect on our business, financial condition and results of operations.

If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may be required to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention, which would result in substantial costs to us.

With our U.S. patent covering recombinant Protein A expiring in September 2009, we may face increased competition which could harm our results of operations, financial condition, cash flow and future prospects.

Other companies could begin manufacturing and selling recombinant Protein A in the U.S. and may directly compete with us once our U.S. patent covering recombinant Protein A expires in September 2009. This may induce us to sell Protein A at lower prices and may erode our market share which could adversely affect our results of operations, financial condition, cash flow and future prospects.

Our freedom to develop our product candidates may be challenged by others and we may have to engage in litigation to determine the scope and validity of competitors' patents and proprietary rights, which, if we do not prevail, could harm our business, results of operations, financial condition, cash flow and future prospects.

There has been substantial litigation and other proceedings regarding the complex patent and other intellectual property rights in the pharmaceutical and biotechnology industries. We have been a party to, and in the future may become a party to, patent litigation or other proceedings regarding intellectual property rights.

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Other types of situations in which we may become involved in patent litigation or other intellectual property proceedings include:

- We may initiate litigation or other proceedings against third parties to seek to invalidate the patents held by such third parties or to obtain a judgment that our products or services do not infringe such third parties patents.
- We may initiate litigation or other proceedings against third parties to seek to enforce our patents against infringement.
- If our competitors file patent applications that claim technology also claimed by us, we may participate in interference or opposition proceedings to determine the priority of invention.
- If third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights, we will need to defend against such claims.

The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If a patent litigation or other intellectual property proceeding is resolved unfavorably to us, we or our collaborative partners may be enjoined from manufacturing or selling our products and services without a license from the other party and be held liable for significant damages. The failure to obtain any required license on commercially acceptable terms or at all may harm our business, results of operations, financial condition, cash flow and future prospects.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time, attention and resources.

For more information about the legal proceedings in which we were involved but which have been settled, please see Legal Proceedings.

We may become involved in litigation or other proceedings with collaborative partners, which may be time consuming, costly and could result in delays in our development and commercialization efforts.

We conduct some of our development activities, and conduct most of our commercialization activities, through collaborations with collaborative partners. Therefore, any disputes with such partners that lead to litigation or similar proceedings may result in us incurring legal expenses, as well as facing potential legal liability. Such disputes, litigation or other proceedings are also time consuming and may cause delays in our development and commercialization efforts.

We have limited sales and marketing experience and capabilities.

We have limited sales, marketing and distribution experience and capabilities. We may, in some instances, rely significantly on sales, marketing and distribution arrangements with our collaborative partners and other third parties. In these instances, our future revenues will be materially dependent upon the success of the efforts of these third parties.

If in the future we determine to perform sales, marketing and distribution functions ourselves, we would face a number of additional risks, including:

- we may not be able to attract and build a significant marketing staff or sales force;
- the cost of establishing a marketing staff or sales force may not be justifiable in light of any product revenues; and

our direct sales and marketing efforts may not be successful.

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We have limited manufacturing capabilities and will be dependent on third party manufacturers.

We have limited manufacturing experience and no commercial or pilot scale manufacturing facilities for the production of pharmaceuticals. In order to continue to develop pharmaceutical products, apply for regulatory approvals and, ultimately, commercialize any products, we may need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities.

We currently rely upon third parties to produce material for preclinical and clinical testing purposes and expect to continue to do so in the future. We also expect to rely upon third parties, including our collaborative partners, to produce materials required for the commercial production of certain of our products if we succeed in obtaining necessary regulatory approvals. We believe that there is no proprietary aspect to the manufacture of our products. However, there are only a limited number of manufacturers that operate under the FDA s regulations for good manufacturing practices which are capable of and/or approved to manufacture our products. Timing for the initiation of new manufacturers is uncertain, and, if we are unable to arrange for third party manufacturing of our products on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them. We currently rely upon third parties for fermentation relating to certain Protein A products.

We believe that there is no proprietary aspect to the manufacture of our commercial products. However, timing for the initiation of new manufacturers is uncertain, and, if we are unable to arrange for third party manufacturing of our products on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our products or market them. To the extent that we enter into manufacturing arrangements with third parties, we are dependent upon these third parties to perform their obligations in a timely manner. If such third party suppliers fail to perform their obligations, we may be adversely affected in a number of ways, including:

- we may not be able to meet commercial demands for our products;
- we may not be able to initiate or continue clinical trials of products that are under development;
- we may be delayed in completing our clinical trials of products under development; and
- we may be delayed in submitting applications for regulatory approvals for our products.

The manufacture of products by us and our collaborative partners and suppliers is subject to regulation by the FDA and comparable agencies in foreign countries. Delay in complying or failure to comply with such manufacturing requirements could materially adversely affect the marketing of our products.

If we are unable to continue to hire and retain skilled personnel, then we will have trouble developing and marketing our products.

Our success depends largely upon the continued service of our management and scientific staff and our ability to attract, retain and motivate highly skilled technical, scientific, management, regulatory compliance and marketing personnel. Potential employees with an expertise in the field of molecular biology, biochemistry, regulatory affairs and/or clinical development of new drug and biopharmaceutical manufacturing are not generally available in the market and are difficult to attract and retain. We also face significant competition for such personnel from other companies, research and academic institutions, government and other organizations who have superior funding and resources to be able to attract such personnel. The loss of key personnel or our inability to hire and retain personnel who have technical, scientific or regulatory compliance backgrounds could materially adversely affect our product development efforts and our business.

The market may not be receptive to our products upon their introduction.

The commercial success of our therapeutic products that are approved for marketing will depend upon their acceptance by the medical community and third party payors as being clinically useful, cost effective and safe. All of the products that we are developing are based upon new technologies or therapeutic approaches. As a result, it is hard to predict market acceptance of our products.

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Other factors that we believe will materially affect market acceptance of our products and services include:

- the timing of receipt of marketing approvals and the countries in which such approvals are obtained;
- the safety, efficacy and ease of administration of our products;
- the success of physician education programs;
- the availability of government and third party payor reimbursement of our products; and
- competition from products which may offer better safety, efficacy or lower cost.

We compete with pharmaceutical and biotechnology companies who are capable of developing new approaches that could make our products and technology obsolete.

The market for therapeutic and commercial products is intensely competitive, rapidly evolving and subject to rapid technological change. Pharmaceutical and biotechnology companies may have substantially greater financial, manufacturing, marketing, and research and development resources than we have. New approaches by these competitors may make our products and technologies obsolete or noncompetitive.

We have incurred substantial losses, we may to continue to incur operating losses and we will not be successful until we reverse this trend.

Although the company had significant net income in fiscal years 2008 and 2009 as a result of the ImClone and Bristol settlements, we have historically incurred operating losses since our founding in 1981. We expect to incur operating losses for the foreseeable future.

While we generate revenue from product sales and began receiving royalty payments in fiscal year 2009 from Bristol for the net sales of their Orencia® product in the United States, this revenue may not be sufficient to cover the costs of our clinical trials and drug development programs. We plan to continue to invest in key research and development activities. As a result, we will need to generate significant revenues in order to achieve profitability. We cannot be certain whether or when this will occur because of the significant uncertainties that affect our business.

Royalty revenue from Bristol-Myers Squibb Company for sales of Orencia® could fail to materialize.

Our royalty agreement with Bristol provides for us to receive payments from Bristol based on their net sales of their Orencia® product in the United States. We have no control over Bristol s sales and marketing practices for Orencia® and Bristol has no obligation to use commercially reasonable efforts to sell Orencia®. Bristol s sales could be significantly impacted by regulatory and market influences beyond our control, resulting in low or even no royalty revenue for us.

If we do not obtain additional capital for our drug development programs, we may be unable to develop or discover new drugs.

We may need additional long-term financing to develop our drug development programs through the clinical trial process as required by the FDA and to develop our commercial products business. We also may need additional long-term financing to support future operations and capital expenditures, including capital for additional personnel and facilities. If we spend more money than currently expected for our drug development programs and our commercial products business, we may need to raise additional capital by selling debt or equity securities, by entering into strategic relationships or through other arrangements. We may be unable to raise any additional amounts on reasonable terms or when they are needed due to the volatile nature of the biotechnology marketplace. If we are unable to raise this additional capital, we may have to delay or postpone critical clinical studies or abandon other development programs.

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Our stock price could be volatile, which could cause you to lose part or all of your investment.

The market price of our common stock, like that of the common stock of many other development stage biotechnology companies, is highly volatile. In addition, the stock market has experienced extreme price and volume fluctuations. This volatility has significantly affected the market prices of securities of many biotechnology and pharmaceutical companies for reasons frequently unrelated to or disproportionate to the operating performance of the specific companies. These broad market fluctuations may adversely affect the market price of our common stock.

Anti-takeover provisions may deter a third party from acquiring us, limiting our stockholders ability to profit from such a transaction.

Our Board of Directors has the authority to issue up to 5,000,000 shares of preferred stock, of which 40,000 have been reserved for issuance in connection with our stockholder rights plan, and to determine the price, rights, preferences and privileges of those shares without any further vote or action by our stockholders. We also adopted a poison pill stockholder rights plan that will dilute the stock ownership of acquirers of our common stock upon the occurrence of certain events. This stockholder rights plan could have the effect of making it more difficult for a third party to acquire a majority of our outstanding voting stock.

We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits us from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person becomes an interested stockholder, unless the business combination is approved in a prescribed manner. This provision could have the effect of delaying or preventing a change of control of the Company. Section 203 and the stockholder rights plan may have the effect of deterring hostile takeovers or delaying or preventing changes in our management, including transactions in which stockholders might otherwise receive a premium for their shares over then current market prices.

Item 1B. UNRESOLVED STAFF COMMENTS

None.

Item 2. PROPERTIES

We lease approximately 25,000 square feet of space located in Waltham, Massachusetts which we use for our corporate headquarters, manufacturing, research and development, marketing and administrative operations. This lease expires in 2011. We also lease approximately 10,000 square feet of space in a second facility also in Waltham to provide for expanded manufacturing and administrative operations. This lease expires in 2012. During fiscal 2009, we incurred aggregate rental costs for our facility of approximately $631,000.

Item 3. LEGAL PROCEEDINGS

ImClone Systems

In May 2004, Repligen and the Massachusetts Institute of Technology (MIT) filed an action in the United States District Court for the District of Massachusetts against ImClone Systems, Incorporated (ImClone) for infringement of U.S. Patent No. 4,663,281 (the 281 patent) based on ImClone s manufacture and sale of Erbitux®. The 281 patent, which covers the use of certain genetic elements that increase protein production in a mammalian cell, is assigned to MIT and exclusively licensed to Repligen.

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On September 10, 2007, the Company and MIT entered into a settlement agreement (the ImClone Settlement) with ImClone relating to the lawsuit against ImClone for infringement of the 281 patent. Pursuant to the ImClone Settlement, ImClone made a payment of $65 million to Repligen and MIT that resulted in net proceeds to Repligen of $40.17 million, as follows:

Gross proceeds from ImClone Settlement agreement	$ 65,000,000
Less: Amounts paid to MIT	(11,000,000)
Less: Legal fees and other costs	(13,830,000)
Net gain on litigation settlement	$ 40,170,000

The ImClone Settlement served as the basis for the Company and MIT to dismiss the lawsuit against ImClone and for the Company to grant ImClone a non-exclusive sublicense to the 281 patent and certain other intellectual property. There are no further obligations to the Company with respect to the sublicenses. The net gain on the litigation settlement was recorded as a separate component of operating expenses in the Company s statement of operations in fiscal 2008.

Bristol-Myers Squibb Company

In January 2006, Repligen and the University of Michigan jointly filed a complaint against Bristol in the United States District Court for the Eastern District of Texas for infringement of U.S. Patent No. 6,685,941 (the 941 patent) for the commercial sale of Orencia®. The 941 patent, entitled Methods of Treating Autoimmune Disease via CTLA4-Ig, covers methods of using CTLA4-Ig to treat rheumatoid arthritis, as well as other therapeutic methods. Repligen has exclusive rights to this patent from its owners, the University of Michigan and the U.S. Navy. In February 2006, Bristol answered the complaint and counterclaimed seeking a declaratory judgment that the 941 patent is invalid and unenforceable and that Bristol does not infringe the patent.

On April 7, 2008, Repligen and the University of Michigan entered into a settlement agreement (the Bristol Settlement) with Bristol relating to the lawsuit against Bristol for infringement of the 941 patent. Pursuant to the Bristol Settlement, Bristol made an initial payment of $5 million to Repligen. The settlement further provides for Bristol to pay royalties on the United States net sales of Orencia® for any clinical indication at a rate of 1.8% for the first $500 million of annual net sales, 2.0% for the next $500 million of annual net sales and 4% of annual net sales in excess of $1 billion for each year from January 1, 2008 until December 31, 2013. Pursuant to the Bristol Settlement agreement, the Company has recognized $13.4 million in royalty revenue in fiscal 2009, including a $5 million initial payment, $1.3 million for sales of Orencia® from January 1, 2008 through December 31, 2008, as well as $7.1 million for sales in fiscal year 2009 (see Note 2). The Bristol Settlement served as the basis for Repligen and the University of Michigan to dismiss the lawsuit against Bristol and for Repligen and the University of Michigan to grant to Bristol an exclusive license to the 941 patent and certain other intellectual property.

Repligen must also remit to the University of Michigan 15% of all royalty revenue received from Bristol, after first deducting certain legal and other costs incurred related to the settlement. The Company has incurred approximately $6.1 million in such legal costs, which when deducted from the $13.4 million in royalty revenue earned to date, results in a net amount due to the University of Michigan of $1.1 million. This operating expense has been included on our Statements of Operations under the line item Cost of royalty and other revenue .

Other

From time to time, we may be subject to other legal proceedings and claims in the ordinary course of business. We are not currently aware of any such proceedings or claims that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

No matters were submitted to a vote of the security holders of the Company through the solicitation of proxies or otherwise, during the last quarter of the fiscal year ended March 31, 2009.

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PART II

Item 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information