




RepliGen

2010 Annual Report



Our goal is to build an integrated biopharmaceutical company by developing and marketing innovative drugs that deliver the benefits of protein therapies in the fields of neurology and gastroenterology. We have a core competency in large-scale protein manufacturing and have out-licensed certain biologics intellectual property which provide ongoing sources of revenue.



Accelerating Biomanufacturing

Entered into a five-year supply agreement with GE Healthcare for recombinant Protein A.

Acquired “plug and play” chromatography technology platform; launched Opus™ pre-packed columns to expand the bioprocessing product offering and increase market access.



Advancing Therapeutics

Completed RG1068 Phase 3 trial for MRI imaging of the pancreas.

Advanced RG2417 Phase 2b trial for bipolar depression.

Filed RG2833 IND for Friedreich’s ataxia; received Orphan Drug Designation.

Licensed spinal muscular atrophy program; identified RG3039 as a clinical candidate.



Protecting Innovation

U.S. patent issued covering the use of uridine (RG2417) to treat the symptoms of bipolar disorder; patent will remain in force until 2025.

U.S. patent issued covering a recently launched recombinant Protein A; patent will remain in force until 2028.



A letter from Walter C. Herlihy, Ph.D.

President and Chief Executive Officer

Over the past year we made substantial progress in advancing our pipeline of therapeutic product candidates. We completed a Phase 3 clinical trial of RG1068 for MRI imaging of the pancreas, and we made significant progress in recruiting patients into our Phase 2b “proof of concept” study of RG2417, a novel therapy for bipolar depression. We expect to report results from both the RG1068 and RG2417 clinical studies by the end of the year. Our product candidate for Friedreich’s ataxia has advanced to an IND filing for Phase 1 studies. We also bolstered our pipeline through in-licensing a potential product for spinal muscular atrophy (SMA) for which toxicology studies are in progress in preparation for clinical trials next year.

Sales of our bioprocessing products were negatively impacted last year by the financial crisis; however, we are now seeing a return to growth for this business. To further expand our market opportunity, we acquired a “plug and play” chromatography platform and launched our first products under the Opus™ brand name. Royalties on Bristol-Myers’ sales of Orenzia grew by 27%, and we recorded \$21.0 million in total revenue and a net loss of \$4.0 million. We ended the year with \$59.1 million in cash and equivalents and no debt.

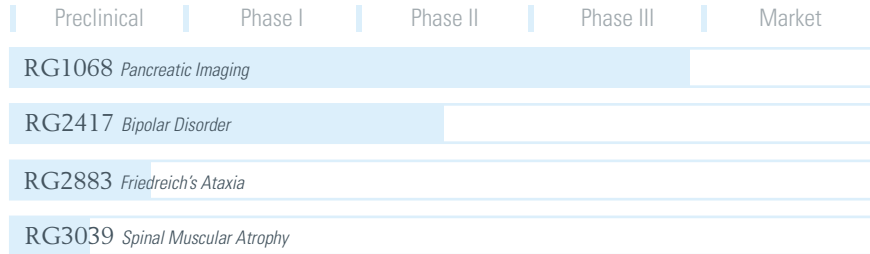
Over the next twelve months, we anticipate completing our pancreatic imaging and bipolar depression trials, advancement of our Friedreich’s ataxia and SMA programs toward clinical trials and significant revenue growth for our bioprocessing business. As in the past, we are continuing to seek acquisitions to bolster both our therapeutic pipeline and our bioprocessing business.

I look forward to updating you on our progress during the year. Thank you for your continued support of Repligen.



Walter C. Herlihy, Ph.D.

August 2, 2010



Development Assets

Innovative Drugs that Deliver the Benefits of Protein Therapies

RG1068—*A GI Hormone for MRI Imaging of the Pancreas*

Until fairly recently, endoscopic retrograde cholangiopancreatography (ERCP) was the primary means for diagnosing and treating patients with suspected pancreatic disease and abnormalities. However, ERCP is a costly, invasive procedure with significant potential for complications including acute pancreatitis, hemorrhage, intestinal perforation and exposure to radiation. It is estimated that more than 50,000 patients suffer serious complications in the U.S. each year following ERCP, and as many as 2,000 patients die.

The advancement of magnetic resonance imaging (MRI) technology has resulted in the availability of a less expensive, non-invasive, radiation-free means of evaluating and diagnosing patients with suspected pancreatic diseases and abnormalities. An MRI of the pancreas visualizes water in the pancreatic

ducts as an intrinsic contrast medium. RG1068, the gastrointestinal hormone secretin, stimulates the secretion of pancreatic fluid into the pancreatic ducts, thereby filling the ducts with water which improves the ability to visualize pancreatic abnormalities. RG1068-MRI imaging of the pancreas provides valuable clinical information to physicians for patients who present with abdominal pain and suspected pancreatic pathology especially when a surgical or endoscopic procedure is contemplated. Because RG1068-MRI helps to distinguish between both normal and abnormal anatomy, it aids in avoiding unnecessary and potentially risky ERCP procedures and improves triage and pre-surgical planning. There are more than 400,000 MRIs conducted in the U.S. and Europe each year that could benefit from RG1068, a potential market opportunity of \$100 million.



Bipolar disorder is a chronic complex disease associated with considerable morbidity and mortality and a high rate of suicide. Bipolar disorder affects more than five million adults worldwide.

We are currently analyzing the images from our Phase 3 study of RG1068. The goal of the Phase 3 study is to evaluate the sensitivity and specificity of RG1068 in combination with MRI to improve the detection of structural abnormalities of the pancreatic ducts relative to MRI alone. The ongoing analysis is a “re-read” which was initiated following approval by the FDA and EMA based on the determination that the original analysis by a contract research organization was flawed and therefore inconclusive. We expect to report top-line results in approximately six months which, if positive, may support product registration.

RG2417—A Novel Biological Approach to Treating Bipolar Depression

Bipolar disorder is a chronic complex disease associated with considerable morbidity and mortality and a high rate of suicide. Bipolar disorder affects more than five million adults worldwide and is characterized by “highs” known as mania and “lows” known as depression and is usually diagnosed in early adulthood. It is estimated that in the U.S. bipolar disorder accounts for more than 16 million visits to a physician each year and approximately 150,000 hospitalizations. The National Institute of Mental Health estimates the total costs of bipolar disorder to be \$45 billion each year.

Episodes of depression are the most frequent and long-lived symptom of bipolar disorder and account for the majority

of the disease impairment. While a number of drugs have demonstrated efficacy for the acute mania symptoms, the treatment of bipolar depression remains challenging. Characteristics that distinguish bipolar depression from other forms of depression include a high risk of suicide and psychosis. Antidepressants are ineffective in the treatment of patients with bipolar depression and have been associated with an increased risk of triggering mania. Atypical antipsychotics are used to treat bipolar depression and while effective in some patients, there are troubling side effects, leaving bipolar depression an area of high unmet medical need.

RG2417 is an oral formulation of uridine, a biological compound synthesized by the power plant of the cell known as the mitochondria. Research has established that mitochondrial dysfunction is involved in bipolar disorder establishing the basis for treatment. We are conducting a Phase 2b trial of RG2417, designed to confirm and extend the results of a Phase 2a study in which treatment with RG2417 improved the symptoms of bipolar depression with minimal side effects. The positive effect of treatment was primarily observed in patients with a significant history of disease as determined by the number of episodes of mania and depression experienced during their lifetime. We expect to report top-line results of our study in approximately six months. This novel approach for bipolar depression could result in an important new

The most effective approach to treatment of diseases characterized by inadequate production of a vital protein may be through therapies that replace the deficient protein.

treatment option for patients without the troubling side effects associated with current therapies.

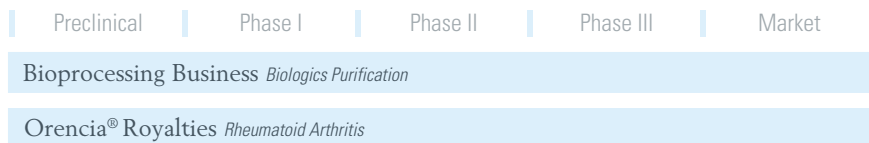
RG2833 and RG3039—Opportunity for protein replacement therapy through activation of gene expression in two orphan diseases

The most effective approach to treatment of diseases characterized by inadequate production of a vital protein may be through therapies that replace the deficient protein. We are developing two pre-clinical compounds that serve as protein replacement therapies for Friedreich's ataxia and spinal muscular atrophy (SMA) through activation of the defective genes that encode the missing proteins. A small increase in the protein available has been shown in animal models and patient cells to have the potential for a significant benefit. Friedreich's ataxia and SMA are devastating neurodegenerative orphan diseases with 15,000–20,000 patients worldwide and for whom there are no treatments.

Friedreich's ataxia is an inherited neurodegenerative disease caused by a single gene defect that results in inadequate production of the protein frataxin resulting in a progressive degeneration of the nerves controlling muscle movements in the arms and legs. Symptoms typically emerge at a young age and progress to severe disability or loss of life in early adulthood. Preclinical studies have shown that RG2833 crosses the blood brain barrier, activates the defective gene

and increases production of frataxin protein indicating that RG2833 may increase frataxin in patients and arrest disease progression. We have filed an RG2833 IND, and hope to initiate a Phase 1 normal volunteer study this year. RG2833 has been developed in collaboration with The Scripps Research Institute and international scientific thought leaders, and partially funded by the Muscular Dystrophy Association, the Friedreich's Ataxia Research Alliance, GoFar and the National Ataxia Foundation.

Spinal muscular atrophy (SMA) is an inherited neurodegenerative disease caused by a defect in the SMN1 gene resulting in low levels of SMN protein. Inadequate production of SMN protein leads to progressive damage to the motor neurons, loss of muscle function and in many patients, early death. Symptoms of SMA are often evident in infancy and typically progress to severe physical disability or loss of life. RG3039 has been shown to increase production of SMN in patient cells and to extend survival in an animal model of SMA. We licensed the rights to RG3039 from Families of Spinal Muscular Atrophy who invested approximately \$15 million to discover and conduct the initial development. RG3039 has been designated a clinical candidate, and we are conducting toxicology studies to evaluate its appropriateness for clinical testing.



Commercial Assets

Expanding and Diversifying the Bioprocessing Business

For over twenty years, we have been a leading supplier to the biopharmaceutical industry of Protein A products used in the manufacturing of therapeutic and diagnostic monoclonal antibodies. Monoclonal antibodies are the largest class of biologic drugs and include important new therapies for rheumatoid arthritis, osteoporosis and cancer. This year we entered into a five-year supply agreement with GE Healthcare, extending the more than 10-year relationship that we have had as their supplier of recombinant Protein A. In addition, we have developed and launched a new recombinant Protein A product and subsequently received a U.S. patent this year covering the product, which will remain in force until 2028.

We are seeking to leverage our expertise in protein manufacturing through developing and commercializing new products that improve efficiency in biopharmaceutical manufacturing.

This year we acquired a technology platform for the production of pre-packed, “plug and play” chromatography columns. This patented technology enables economical production of chromatography columns in a format that is ready for use in the production of a broad range of biopharmaceuticals including monoclonal antibodies, vaccines and recombinant proteins. We will continue to grow our bioprocessing product line through internal product development initiatives and acquisition of new products and technologies.

Sales of our bioprocessing products and royalties that we receive from licensing of a U.S. patent to Bristol-Myers Squibb covering their drug Orencia® resulted in total revenue for the year of \$21 million, which allowed us to continue to advance our therapeutic pipeline and bioprocessing business and maintain our cash reserves for future acquisitions.



RepliGen

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RepliGen

2010 Financial Information on Form 10-K

Corporate Information

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Harvard Medical School

Earl Webb Henry, M.D.
Chief Medical Officer
inVentiv Clinical Solutions

Walter C. Herlihy, Ph.D.
President and Chief Executive Officer
Repligen Corporation

Alexander Rich, M.D., Chairman
Sedgwick Professor of Biophysics
Department of Biology
Massachusetts Institute of Technology

Thomas F. Ryan, Jr.
Retired/Private Investor

Corporate Officers

Walter C. Herlihy, Ph.D.
President and Chief Executive Officer

William J. Kelly
Chief Financial Officer

James R. Rusche, Ph.D.
Sr. Vice President,
Research and Development

Daniel P. Witt, Ph.D.
Vice President, Operations

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The Transfer Agent is responsible for handling shareholder questions regarding lost certificates, address changes and changes of ownership or name in which shares are held.

General Counsel

Goodwin Procter LLP
Exchange Place
53 State Street
Boston, MA 02109

Independent Accountants

Ernst & Young, LLP
200 Clarendon Street
Boston, MA 02116

Annual Meeting

The Annual Meeting of Stockholders will be held on Thursday, September 9, 2010, at 10:00 AM at Repligen's corporate offices:

41 Seyon Street
Building #1, Suite 100
Waltham, MA 02453

Market for Repligen Corporation Stock
NASDAQ Global Market
Common Stock: RGEN

Investor Information

Copies of our annual reports on Form 10-K, proxy statements, quarterly reports on Form 10-Q and current reports on Form 8-K are available to stockholders upon request without charge. Please visit our website at www.repligen.com or send requests to:

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Disclaimer

This annual report contains "forward-looking statements" within the meaning of the federal securities laws. See discussion under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this report for matters to be considered in this regard.

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