2012

ANNUAL REPORT

REGENERON


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# *The Numbers…and Beyond*

During 2008, Regeneron continued to execute on our long-term vision: to discover, develop, and commercialize medicines for the treatment of serious medical conditions. Much of our progress can be charted in numbers: sales of our first marketed product; clinical trials initiated and underway; new molecules discovered and advanced into development; and new employees brought on board to help our company move forward. But some things can't be quantified: the passion of our people for the work they do; the impact of ARCALYST® (rilonacept) Injection for Subcutaneous Use, our first marketed product, on the well-being of patients with Cryopyrin-Associated Periodic Syndromes or CAPS; and the potential of our pipeline to improve health for patients suffering from serious diseases.

From **1** marketed product to **13** programs to **$527** million in cash at year-end 2008, Regeneron's progress can be measured in numbers large and small.

**LEONARD S. SCHLEIFER, M.D., PH.D.**
*President and Chief Executive Officer*

**P. ROY VAGELOS, M.D.**
*Chairman of the Board*

**GEORGE D. YANCOPOULOS, M.D., PH.D.**
*Executive Vice President, Chief Scientific Officer and President, Regeneron Research Laboratories*

## DEAR SHAREHOLDERS,

Reflecting on the past year, one observation stands out: Regeneron is a company that is advancing on all fronts. From discovery through development to manufacturing and commercialization, we have demonstrated our ability to execute our business plan for becoming a fully integrated biopharmaceutical company.

Over the last year:

- We launched our first marketed product, ARCALYST® (rilonacept), an inhibitor of the interleukin-1 cytokine, for Cryopyrin-Associated Periodic Syndromes (CAPS).
- We achieved positive Phase 2 results for rilonacept in drug-induced gout.
- We and sanofi-aventis advanced four Phase 3 studies with aflibercept, our drug candidate targeting Vascular Endothelial Growth Factor (VEGF), in various oncology settings—first-line metastatic hormone-refractory prostate cancer, first-line metastatic pancreatic cancer, second-line non-small cell lung cancer, and second-line metastatic colorectal cancer.
- We and sanofi-aventis started a Phase 2 study of aflibercept in first-line metastatic colorectal cancer.
- We and Bayer HealthCare continued to enroll patients in two Phase 3 studies with VEGF Trap-Eye in wet Age-related Macular Degeneration.
- We and Bayer HealthCare initiated a Phase 2 study of VEGF Trap-Eye in Diabetic Macular Edema.
- We and sanofi-aventis have three *VelocImmune*® antibody product candidates in clinical development and have advanced additional antibodies into preclinical development.
- We greatly expanded our R&D, clinical, and manufacturing capacities.
- We retired our debt and ended 2008 with $527 million in cash and securities.

# 1 Approved Product

With FDA approval of ARCALYST® (rilonacept) as the first and only approved product for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), patients with these rare, hereditary, inflammatory conditions can now live their daily lives with fewer debilitating symptoms.


With the launch of ARCALYST, Regeneron now has the commercial infrastructure and capabilities in place that can be expanded to commercialize larger product opportunities in the United States.

**$11 million in ARCALYST shipments in 2008**

**FROM DISCOVERY THROUGH COMMERCIALIZATION.**

In February 2008, the U.S. Food and Drug Administration (FDA) granted marketing approval for ARCALYST Injection for Subcutaneous Use for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older. This was a watershed event for two important reasons. First, it brings needed relief to CAPS patients who have had no other approved treatment for their debilitating medical condition. During 2008, we transitioned patients who participated in the CAPS pivotal studies from clinical study drug to commercial supplies and shipped approximately **$11 million** of product. Second, FDA clearance demonstrates Regeneron's ability to discover a molecule and take it through clinical development and manufacturing, regulatory review, and commercialization. With the approval of ARCALYST, we can move forward with greater confidence in our ability not only to discover and develop new medicines, but also to manage the process through commercialization.

In September 2008, we announced the results of a Phase 2 study which evaluated the efficacy and safety of rilonacept in preventing gout flares induced by the initiation of urate-lowering drug therapy, which is commonly used to control gout. In this 83-patient, double-blind, placebo-controlled study, over the first 12 weeks of urate-lowering therapy, the mean number of gout flares per patient in the rilonacept treatment

# 6 Investigational drugs in clinical development

We have drug candidates in all stages of clinical development that target a diverse set of serious conditions, including cancer, eye diseases, inflammatory diseases, and pain.

group was 81 percent lower than in the placebo group. Only 14.6 percent of patients treated with rilonacept experienced a gout flare compared to 45.2 percent of patients treated with placebo. No drug-related serious adverse events were reported in patients receiving rilonacept; injection-site reaction was the most commonly reported adverse event.

We are now enrolling patients in our Phase 3 rilonacept gout program which will include two studies in the prevention of gout flares in patients initiating urate-lowering therapy, one Phase 3 study evaluating rilonacept in the treatment of acute gout flares, and a separate safety study. Regeneron retains worldwide marketing rights to rilonacept.

In gout, uric acid crystals stimulate the production of interleukin-1, which causes an inflammatory response in the joints and surrounding tissues. An estimated one percent of the U.S. population suffers from gout, one of the most painful rheumatic diseases, and 1.4 million people are treated for acute gout attacks each year.

Beyond ARCALYST® (rilonacept), our development pipeline continues to expand and progress. Today we have **6** investigational drugs in clinical development, including three in Phase 3 trials.

**VEGF TRAP-EYE.**
Our VEGF Trap-Eye program showed strong progress during 2008. In September 2008, we and Bayer HealthCare announced the final one-year data from a Phase 2 study evaluating

Regeneron currently has Phase 3 clinical trials underway targeting eye disease, various cancers, and gout. In Phase 3 clinical trials, new treatments are compared to either currently available therapies or placebo to assess effectiveness and safety.

9

## Phase 3 Trials Underway

VEGF Trap-Eye in patients with the neovascular form of Age-related Macular Degeneration (wet AMD). Patients receiving VEGF Trap-Eye experienced improvements in vision and retinal thickness (an anatomic measure of treatment effect) during the 12 weeks of fixed monthly or quarterly dosing. These improvements were generally maintained over the next 40 weeks during which patients received VEGF Trap-Eye on a PRN (as needed) dosing schedule. During the PRN dosing period, patients received, on average, only two additional injections. There were no reported drug-related serious adverse events. The most common adverse events were those typically associated with intravitreal injections.

Currently, we and Bayer HealthCare are enrolling two Phase 3 studies of VEGF Trap-Eye in patients with wet AMD. These trials, involving 1200 patients each, are comparing treatment with VEGF Trap-Eye and Genentech's Lucentis® (ranibizumab), an anti-angiogenic agent approved for use in wet AMD. In 2008, we also initiated a Phase 2 study of VEGF Trap-Eye in patients with Diabetic Macular Edema (DME). Initial data from these studies are expected in 2010. Under our collaboration agreement, Bayer HealthCare has rights to market VEGF Trap-Eye outside the United States, where the companies will share equally in profits from any future sales. We maintain exclusive rights to VEGF Trap-Eye in the United States.

# 3 New antibodies in the clinic from the *VelociSuite*™ of technologies

Regeneron's *VelociSuite* of technologies is further accelerating the development of new product candidates. *VelociGene*® and *VelociMouse*® are designed to aid in the identification of specific genes of therapeutic interest for a particular disease or cell type and validate targets through high-throughput production of mammalian models. *VelocImmune*® increases the speed and efficiency of fully human monoclonal antibody development and is being used to generate antibodies to address clinically relevant targets of therapeutic interest.

**AFLIBERCEPT IN ONCOLOGY.**
In collaboration with sanofi-aventis, we have underway four Phase 3 studies of aflibercept (VEGF Trap) in combination with chemotherapy that are targeted to enroll a total of approximately 4000 patients. These studies are being conducted in first-line metastatic pancreatic cancer, first-line metastatic hormone-refractory prostate cancer, second-line non-small cell lung cancer, and second-line metastatic colorectal cancer. All studies are approximately 50 percent enrolled, and we expect initial data from three of the studies in 2010. In addition, a Phase 2 combination study of aflibercept in first-line metastatic colorectal cancer began in the first quarter of 2009.

We are also completing a Phase 2 study of single-agent aflibercept in patients with symptomatic malignant ascites, a condition where fluid accumulates in the abdominal cavity in women with advanced ovarian cancer. We expect initial data later this year.

With a total of **9** Phase 3 clinical trials underway or planned, Regeneron has made great strides in advancing the development of our clinical candidates. The progress we've recorded in our gout, eye, and cancer programs, along with the launch of our first marketed product, add up to a very positive year for our company. But they tell only a part of the Regeneron story. Building on our rich tradition of pioneering research, we have developed a suite of technologies for discovering, developing, and manufacturing fully human monoclonal antibodies. We are using this *VelociSuite* of technologies to generate our future pipeline of drug candidates. In fact, it would not be an overstatement to say that we are building a robust antibody development company within Regeneron, with **3** antibodies already in clinical development.

# $527 million

**in cash and securities at year-end 2008**

Regeneron's cash reserves provide significant operating flexibility as we continue to advance our drug candidates through the development pipeline.

Including the funding from our collaboration agreements, our research and development programs are budgeted for over $500 million in spending in 2009. This leveraged spending has enabled us to build a world-class R&D capability.

**Over**

# $500 million

**in 2009 budgeted R&D spending**

**MONOCLONAL ANTIBODY PROGRAM.** Our *VelociSuite*™ of technologies, including *VelocImmune*®, represents a unique platform for identifying and validating novel drug targets and for generating and manufacturing fully human monoclonal antibodies against these targets. In late 2007, we announced a major collaboration with sanofi-aventis to discover, develop, and commercialize fully human monoclonal antibodies. The sanofi-aventis collaboration provides us with up to $100 million in research funding annually through 2012.

Three human antibodies developed under the sanofi-aventis collaboration are in clinical development: REGN88, an antibody to the interleukin-6 receptor (IL-6R) that is being evaluated in rheumatoid arthritis; REGN421, an antibody to delta-like ligand-4 (Dll4) that is in development to disrupt angiogenesis in patients with cancer; and REGN475, an antibody against nerve growth factor (NGF) that is in development for the treatment of pain. We are on track with our goal to advance an average of two to three new antibodies into clinical development each year.

In September 2008, we also launched our Academic *VelocImmune* Investigators Program (Academic VIP) when we entered into an agreement to provide researchers at Columbia University Medical Center with access to the *VelocImmune* technology platform. In March 2009, we entered into a similar Academic VIP agreement with The University of Texas Southwestern Medical Center at Dallas. Under the agreements, scientists at the universities

# 50,000 Liters

Our biologics manufacturing capacity is being expanded from 22,000 to 50,000 liters at our manufacturing facility in Rensselaer, New York.

will use *VelocImmune*® mice to generate antibodies against their research targets and will conduct research to discover potential human therapeutics based on the antibodies. Regeneron has an exclusive option to license the antibodies for development and commercialization as therapeutic or diagnostic products. We see opportunities to enter into similar arrangements with other academic institutions.

**FINANCIAL STRENGTH.**

Clearly, there is a great deal of positive momentum at Regeneron, and we expect 2009 to be no less productive. Fortunately, we have the resources necessary to continue to move forward at this pace. Financially, we are well positioned. We finished 2008 with **$527 million** of cash and securities and no debt. What's more, our ongoing R&D spending will be largely funded by our collaborators. These collaborations are a strong vote of confidence in the promise of our discovery and development capabilities. They also provide significant investment leverage, enabling us to support an R&D program that we expect will exceed **$500 million** in 2009, including spending by sanofi-aventis and Bayer HealthCare.

We are expanding and enhancing our physical footprint to accommodate this level of activity. Later this year, we expect to move into two new buildings totaling 230,000 square feet at our existing Tarrytown, New York site. We are more than doubling our biologics manufacturing capacity to **50,000 liters** at our Rensselaer, New York facility. These are important investments in the future of our company.

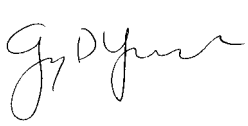
# 1000 Employees

We increased staff by 35 percent in 2008, primarily to expand our antibody discovery and development capabilities and to advance our clinical-stage product candidates. Now nearly 1000 strong, the highly-motivated Regeneron team is committed to the company's mission.

**OUR PEOPLE.**

But our most vital investment will always be in our people. During 2008, we launched a major recruiting effort designed primarily to support the antibody collaboration with sanofi-aventis. Our growing reputation in the medical and research communities has enabled us to attract top talent. By year-end 2009, we expect to grow to more than **1000 employees,** up from 682 at the end of 2007, and 919 at year-end 2008.

We will look to this talented group of professionals to continue the momentum we've achieved in the recent past. Last year's accomplishments moved us closer to our goal of having the pipeline, the discovery platform, the financing, and the people needed to bring breakthrough treatments to patients—and to building a world-class biopharmaceutical company for our shareholders.



During 2008 we asked our employees what it is like to work at Regeneron. From their responses, we distilled and are now featuring in our employee recruiting program these five core attributes of our culture.

# The Regeneron

## Science drives our business and passion drives our science.

We believe great science leads to new and innovative drugs, which can improve people's lives, grow our company, and fund more great science.

## We are a select team.

Regeneron has very high standards for hiring people. If you are talented enough to work here, then you join a team of dedicated people from all walks of life who work together to achieve our goals. Individual effort is rewarded, but true success only comes when we work together as a team.

## You will be challenged. Every day.

No matter your role here, you will be expected to strive for excellence in your field. You will never stop learning and you will continually be sharing your knowledge with others.

## "That's the way we've always done it" is the wrong answer.

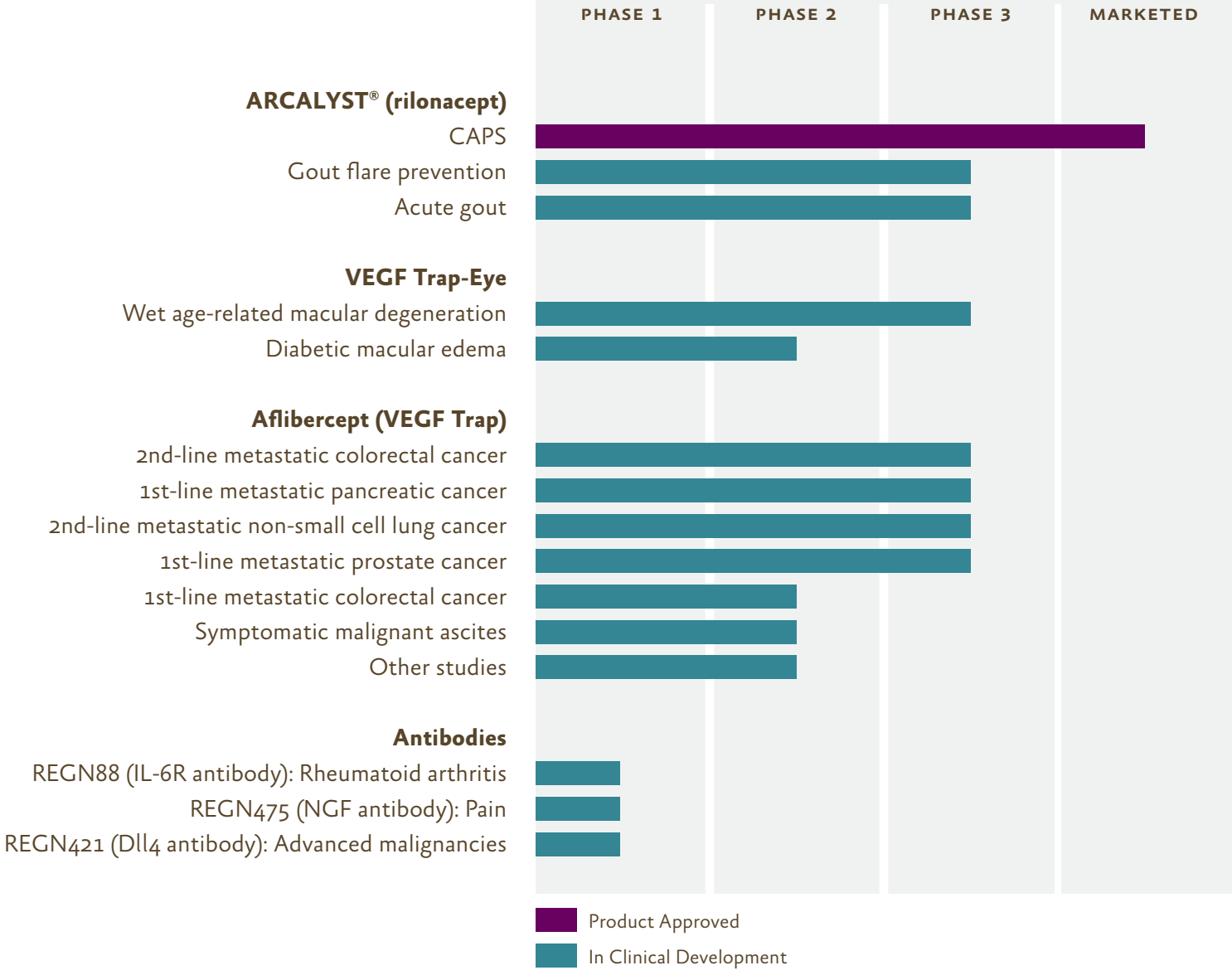
We will not settle for the way things have always been done. At Regeneron, we are willing to see the world in our own way, and we're always looking for new and better ways to do things.

## We won't let bureaucracy block good ideas.

Successful companies require organization and processes to function effectively. We have them too, but we work hard to ensure that unnecessary bureaucracy does not stand in the way of conducting great science and developing successful drugs.

# 13 *Clinical Programs*


With drug candidates in all stages of clinical development, Regeneron has the expertise, infrastructure, resources, and corporate collaborations needed to move these candidates through the development process.


PHASE 1
PHASE 2
PHASE 3
MARKETED
ARCALYST® (rilonacept)
CAPS
Gout flare prevention
Acute gout
VEGF Trap-Eye
Wet age-related macular degeneration
Diabetic macular edema
Aflibercept (VEGF Trap)
2nd-line metastatic colorectal cancer
1st-line metastatic pancreatic cancer
2nd-line metastatic non-small cell lung cancer
1st-line metastatic prostate cancer
1st-line metastatic colorectal cancer
Symptomatic malignant ascites
Other studies
Antibodies
REGN88 (IL-6R antibody): Rheumatoid arthritis
REGN475 (NGF antibody): Pain
REGN421 (Dll4 antibody): Advanced malignancies
Product Approved
In Clinical Development

# CORPORATE INFORMATION

### COMMON STOCK AND RELATED MATTERS

Our Common Stock is quoted on The NASDAQ Global Select Market under the symbol "REGN." Our Class A Stock, par value $.001 per share, is not publicly quoted or traded.

The following table sets forth, for the periods indicated, the range of high and low sales prices for the Common Stock as reported by The NASDAQ Global Select Market.

| 2007 | HIGH | LOW |
|---|---|---|
| First Quarter | $22.84 | $17.87 |
| Second Quarter | 28.74 | 17.55 |
| Third Quarter | 21.78 | 13.55 |
| Fourth Quarter | 24.90 | 16.77 |
| **2008** | | |
| First Quarter | $25.25 | $15.61 |
| Second Quarter | 21.68 | 13.75 |
| Third Quarter | 24.00 | 13.29 |
| Fourth Quarter | 22.82 | 12.62 |

As of April 14, 2009, there were 476 shareholders of record of our Common Stock and 42 shareholders of record of our Class A Stock. The closing bid price for the Common Stock on that date was $13.26.

We have never paid cash dividends and do not anticipate paying any in the foreseeable future.

### CORPORATE OFFICE

777 Old Saw Mill River Road
Tarrytown, NY 10591-6707
(914) 345-7400

### SEC FORM 10-K

A copy of our annual report to the Securities and Exchange Commission on Form 10-K is available without charge from the Regeneron Investor Relations Department.

### ANNUAL MEETING

The Annual Meeting will be held on Friday, June 12, 2009 at 10:30 a.m. at the Westchester Marriott Hotel, 670 White Plains Road, Tarrytown, NY 10591.

### SHAREHOLDERS' INQUIRIES

Inquiries relating to stock transfer or lost certificates and notices of changes of address should be directed to our Transfer Agent, American Stock Transfer & Trust Co., 59 Maiden Lane, Plaza Level, New York, NY 10038, (800) 937-5449. General information regarding the Company, recent press releases, and SEC filings are available on our web site at www.regeneron.com, or can be obtained by contacting our Investor Relations Department at (914) 345-7741.

### TRANSFER AGENT AND REGISTRAR

American Stock Transfer & Trust Co.
59 Maiden Lane
Plaza Level
New York, NY 10038

### INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

PricewaterhouseCoopers LLP

# *Financial Information*

# CORPORATE DIRECTORY

## DIRECTORS

P. Roy Vagelos, M.D.
Chairman of the Board
Retired Chairman of the Board
and Chief Executive Officer,
Merck & Co., Inc.

Leonard S. Schleifer, M.D., Ph.D.
President and Chief Executive Officer

Charles A. Baker
Retired Chairman of the Board,
President and Chief Executive Officer,
The Liposome Company, Inc.

Michael S. Brown, M.D.
Regental Professor and Director,
Jonsson Center for Molecular Genetics
The University of Texas
Southwestern Medical Center at Dallas

Alfred G. Gilman, M.D., Ph.D.
Executive Vice President
for Academic Affairs and Provost
Dean, University of Texas
Southwestern Medical School
Regental Professor of Pharmacology
The University of Texas
Southwestern Medical Center at Dallas

Joseph L. Goldstein, M.D.
Regental Professor and Chairman,
Department of Molecular Genetics
The University of Texas
Southwestern Medical Center at Dallas

Arthur F. Ryan
Retired Chairman of the Board
and Chief Executive Officer,
Prudential Financial, Inc.

Eric M. Shooter, Ph.D.
Professor Emeritus,
Department of Neurobiology,
Stanford University School of Medicine

George L. Sing
Chief Executive Officer, Stemnion, Inc.
Managing Director, Lancet Capital

George D. Yancopoulos, M.D., Ph.D.
Executive Vice President,
Chief Scientific Officer and President,
Regeneron Research Laboratories

## SENIOR MANAGEMENT TEAM

Leonard S. Schleifer, M.D., Ph.D.
President and Chief Executive Officer

George D. Yancopoulos, M.D., Ph.D.
Executive Vice President,
Chief Scientific Officer and President,
Regeneron Research Laboratories

Murray A. Goldberg
Senior Vice President,
Finance and Administration,
Chief Financial Officer, Treasurer
and Assistant Secretary

Stuart A. Kolinski
Senior Vice President,
General Counsel and Secretary

Peter Powchik, M.D.
Senior Vice President,
Clinical Development

Neil Stahl, Ph.D.
Senior Vice President,
Research and Developmental Sciences

Robert J. Terifay
Senior Vice President,
Commercial

Daniel Van Plew
Senior Vice President
and General Manager,
Industrial Operations and Product Supply

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