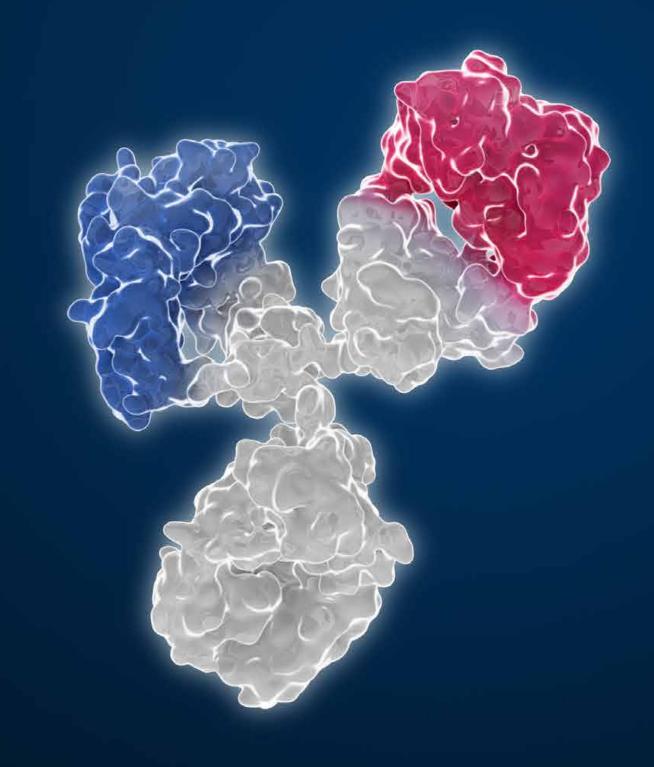


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# REGENERON AT A GLANCE

FDA-approved medicines

MILLION doses of EYLEA® sold globally in 2015

antibodies in clinical trials across multiple therapeutic areas

Ranked #1 or #2 employer in the global biopharmaceutical industry in Science Top Employers Survey 5 years in a row

peer-reviewed publications

organizations through

Most Innovative Company, according to Forbes

Regeneron employees Tộ Ş P Ş P

consented individuals sequenced by the Regeneron Genetics Center

annual reduction in greenhouse gas emissions per employee

# DEAR SHAREHOLDERS,

2015 was a busy and rewarding year for Regeneron as we made major strides in advancing our mission of bringing important new medicines to people with serious diseases, over and over again.

We delivered <u>EYLEA®</u> (aflibercept) <u>Injection</u>, our therapy for serious vision-threatening diseases, to more and more patients, and we launched <u>PRALUENT®</u> (alirocumab) <u>Injection</u>, a first-in-class therapy for uncontrolled <u>LDL</u> cholesterol in certain patients.

In the next few years, we anticipate additional approvals for a number of new therapies. In 2016, we look forward to potentially launching <u>sarilumab</u> for rheumatoid arthritis, pending U.S. Food and Drug Administration (FDA) review of our application. We also expect a potential U.S. regulatory submission for <u>dupilumab</u> in atopic dermatitis, a serious form of eczema, for which we have been granted a Breakthrough Therapy designation by the FDA.

Our <u>pipeline</u> of a dozen clinical-stage antibodies continues to progress, with important programs in eye disease, cancer, infectious disease, pain, cardiovascular disease and inflammation. We also continue to invest in technology and innovation that will position us to bring needed new medicines to patients for many years into the future. Likewise, we have made important infrastructure investments to ensure our long-term success, including adding two new buildings at our headquarters in Tarrytown, New York, and expanding our Industrial Operations facilities in Rensselaer, New York, and Raheen, Ireland.

We have always run Regeneron by the principle of "doing well by doing good." In addition to our work to invent new and needed medicines, we focus on improving our world and operating with the highest standards of integrity.

This year, for the first time, our Annual Report integrates reporting on our <u>citizenship priorities</u> and aspirations, in addition to our financial and business performance.

We invite you to read about our 2015 accomplishments, financial performance and citizenship efforts below and in our 2015 Annual Report on Form 10-K, available on the Investor Relations portion of our website.

Unfortunately, there was also some sadness in 2015. Our longtime friend, mentor, co-founder and Board member, Dr. Alfred G. Gilman, passed away in December. Dr. Gilman was a Nobel Laureate who made lasting contributions to science and medicine. On a personal level, we all benefited greatly from Al's counsel and wry wit over the years, and we will miss him greatly.

We look forward to updating you on our progress as we continue building Regeneron into a leading global biopharmaceutical company.

Sincerely,

Leonard Schleifer, MD, PhD

George Yancopoulos, MD, PhD

Roy Vagelos, MD



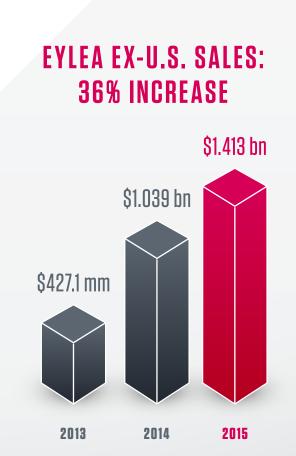
# EYLEA® (AFLIBERCEPT) INJECTION AND RETINAL DISEASE PROGRAMS

Market-leading VEGF-Trap approved in more than 100 countries for the treatment of many blindness-causing retinal conditions, including wet age-related macular degeneration and diabetic macular edema (DME).

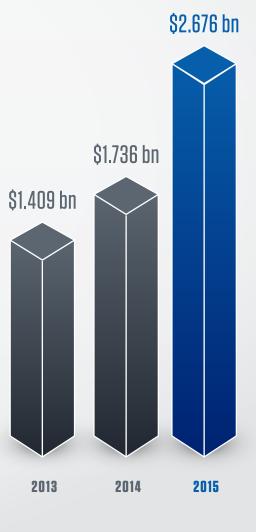
EYLEA net sales in the U.S. increased 54% to \$2.676 billion for the full year of 2015, from \$1.736 billion for the full year 2014. Outside of the U.S., where our collaborator Bayer HealthCare commercializes EYLEA, net sales were \$1.413 billion in 2015, compared to \$1.039 billion in 2014. Regeneron recognized \$467 million from its share of net profit outside the U.S. in 2015, compared to \$301 million in 2014.

This growth was driven in part by the publication in early 2015 of first-year results from an independent National Institutes of Health (NIH)-sponsored comparative effectiveness study in DME. In the study, at one year, EYLEA demonstrated a significantly greater improvement in mean change in best-corrected visual acuity (BCVA) from baseline compared to ranibizumab and bevacizumab, two other VEGF inhibitors used in retinal disease. The rates of most ocular and systemic adverse events were similar across the three study groups.

In 2016, we initiated a Phase 3 study of EYLEA in diabetic retinopathy in patients without DME, a common degenerative eye disease that impacts people with diabetes. We continue to explore EYLEA in combination with other mechanisms, and have two ongoing clinical programs in this area, aflibercept+PDGFR-beta and aflibercept+ANG2, in collaboration with Bayer HealthCare.



### EYLEA U.S. SALES: **54% INCREASE**



# PRALUENT® (ALIROCUMAB) INJECTION

Only monoclonal antibody targeting PCSK9 (proprotein convertase subtilisin/kexin type 9) available in two doses, allowing for tailored therapy based on a patient's LDL-C lowering needs.

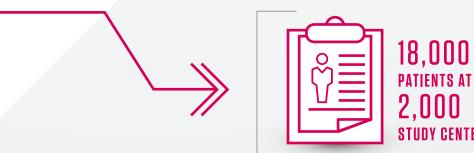
In July 2015, PRALUENT was approved by the FDA as adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C (often referred to as "bad cholesterol"). The effect of PRALUENT on cardiovascular morbidity and mortality has not been determined.

Together with our collaborator Sanofi, the U.S. launch is underway. We have focused on physician education about this new class, as well as achieving patient access and reimbursement coverage from health plans. PRALUENT was also approved in the E.U., and launches are underway across the region.

The ongoing ODYSSEY OUTCOMES clinical trial program, which is evaluating the potential of PRALUENT to prevent heart attacks, stroke and cardiac death, reached full enrollment in 2015, with more than 18,000 patients at more than 2,000 study centers. Interim results are possible in late 2016, and we expect full results in 2017.

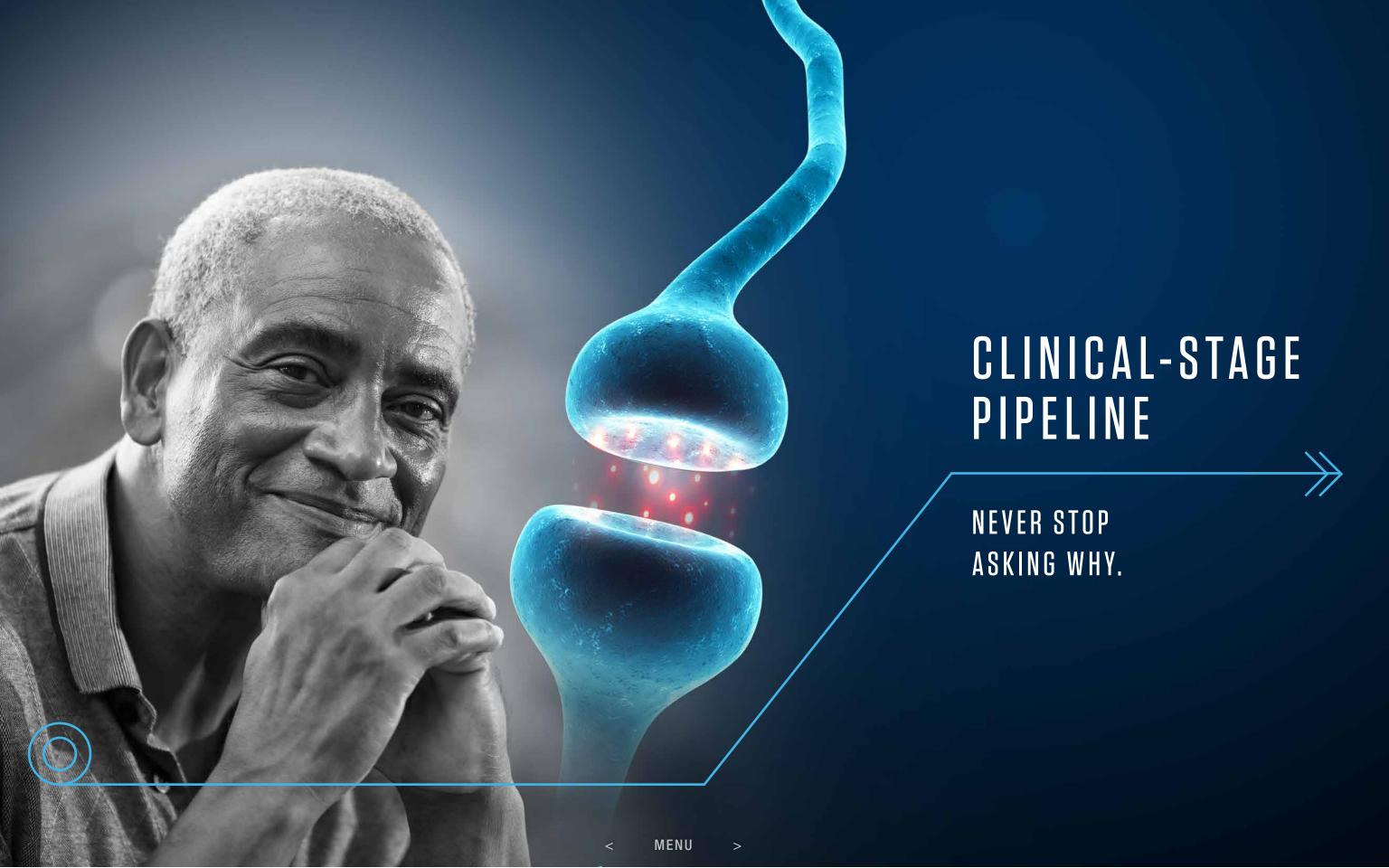


### ODYSSEY OUTCOMES





INTERIM RESULTS POSSIBLE IN 2016 **FULL RESULTS EXPECTED IN** 



# PIPELINE (as of April 2016)

Regeneron has a dozen fully human monoclonal antibodies in clinical development, all of which were developed using our proprietary VelocImmune® technology.

### PHASE 1

### PHASE 2

### PHASE 3

### REGN1979

CD20/CD3 Antibody Cancer

### REGN1908-1909

Allergic disease

### **DUPILUMAB\***

IL-4R Antibody Atopic dermatitis in children, nasal polyps, eosinophilic esophagitis

### SARILUMAB\*

**IL-6R Antibody** Non-infectious uveitis

### TREVOGRUMAB

**GDF8** Antibody Skeletal muscle disorders

### REGN2176-3^

Rinucumab (PDGFR-beta Antibody) + Aflibercept Wet age-related macular degeneration

### **EVINACUMAB**

**Angptl3 Antibody** Lipid disorders

### REGN910-3^

Nesvacumab (Ang2 Antibody) + Aflibercept Ophthalmology

### **REGN2810\***

PD-1 Antibody Cancer

### FASINUMAB\*

**NGF** Antibody Chronic lower back pain

### **ALIROCUMAB\***

PCSK9 Antibody Cardiovascular outcomes

### AFLIBERCEPT^

**VEGF-Trap** Diabetic retinopathy without DME

### SARILUMAB\*

**IL-6R Antibody** Rheumatoid arthritis

### **DUPILUMAB\***

**IL-4R Antibody** Atopic dermatitis in adults, asthma

### REGN2222

**RSV** Antibody Respiratory syncytial virus

### FASINUMAB\*

NGF Antibody Pain due to osteoarthritis

<sup>\*</sup> in collaboration with Sanofi

<sup>^</sup> in collaboration with Bayer HealthCare

<sup>†</sup> in collaboration with Mitsubishi Tanabe

# SARILUMAB

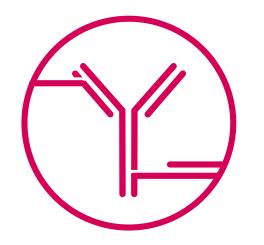
An anti-IL-6 monoclonal antibody under U.S. regulatory review for the treatment of rheumatoid arthritis (RA).

In 2015, we reported positive data from three Phase 3 trials of sarilumab in patients with rheumatoid arthritis. Together with our collaborator, Sanofi, we submitted the U.S. Biologics License Application in November 2015 and were assigned a Prescription Drug User Fee Act (PDUFA) date of October 30, 2016.

In March 2016, the Phase 3 SARIL-RA-MONARCH monotherapy study met its primary endpoint by demonstrating that sarilumab was superior to adalimumab (Humira®) in improving signs and symptoms of active RA at Week 24. The incidence of adverse events, serious adverse events, infections and serious infections was generally similar between groups.



# UNMET NEED IN RHEUMATOID ARTHRITIS REMAINS



# RA IMPACTS MORE THAN 1.3 MILLION AMERICANS<sup>1</sup>

- While significant strides have been made in the treatment of RA, there are continued unmet needs
- A central driver of the destructive effects of RA in the joints is persistently elevated levels of IL-6, a signaling protein in the body.<sup>2-5</sup> At normal levels, IL-6 is responsible for contributing to the healing process after injury or infection.<sup>3,6-7</sup> However, at persistently raised levels, IL-6 triggers inflammation that can destroy bone and cartilage<sup>5,8-12</sup>
- IL-6 may also contribute to the multiple systemic effects of RA, including fatigue, anemia and bone density loss<sup>2</sup>

# DUPILUMAB

A first-in-class investigational monoclonal antibody blocking IL-4 and IL-13, two key cytokines believed to be drivers in allergic inflammation.

Dupilumab is being studied for the treatment of certain allergic conditions, including atopic dermatitis (AD), uncontrolled asthma, nasal polyps and eosinophilic esophagitis.

Dupilumab was granted a Breakthrough Therapy designation by the FDA for the treatment of adults with moderate-to-severe atopic dermatitis who are not adequately controlled with topical prescription therapy and/or for whom these treatments are not appropriate. We expect to submit an application for FDA approval later this year.

In 2016, we reported positive topline results from two large Phase 3 studies in atopic dermatitis and continue to enroll patients in a second pivotal study in asthma. In the atopic dermatitis studies, the overall rate of adverse events was comparable between the dupilumab groups and the placebo groups.



### ATOPIC DERMATITIS: UNMET NEED IN A DEVASTATING AND MISUNDERSTOOD DISEASE

### **APPROXIMATELY** 1.6 MILLION U.S. ADULTS ARE ESTIMATED TO HAVE UNCONTROLLED MODERATE-TO-SEVERE ATOPIC DERMATITIS<sup>13</sup>

- Currently, only topical therapies have been approved by the FDA
- Systemic immuno-suppressants are used off-label, but can have significant side effects

# REGN2222

A fully human monoclonal antibody being investigated for the prevention of serious lower respiratory tract infections associated with Respiratory Syncytial Virus (RSV).

In 2015, we initiated the Phase 3 NURSERY-Pre-term trial that will evaluate the efficacy, safety, pharmacokinetics and immunogenicity of REGN2222 in infants under the age of six months.



UNMET NEED IN A **VULNERABLE POPULATION** 

MEDICAL ATTENTION FOR RSV14

## **FASINUMAB**

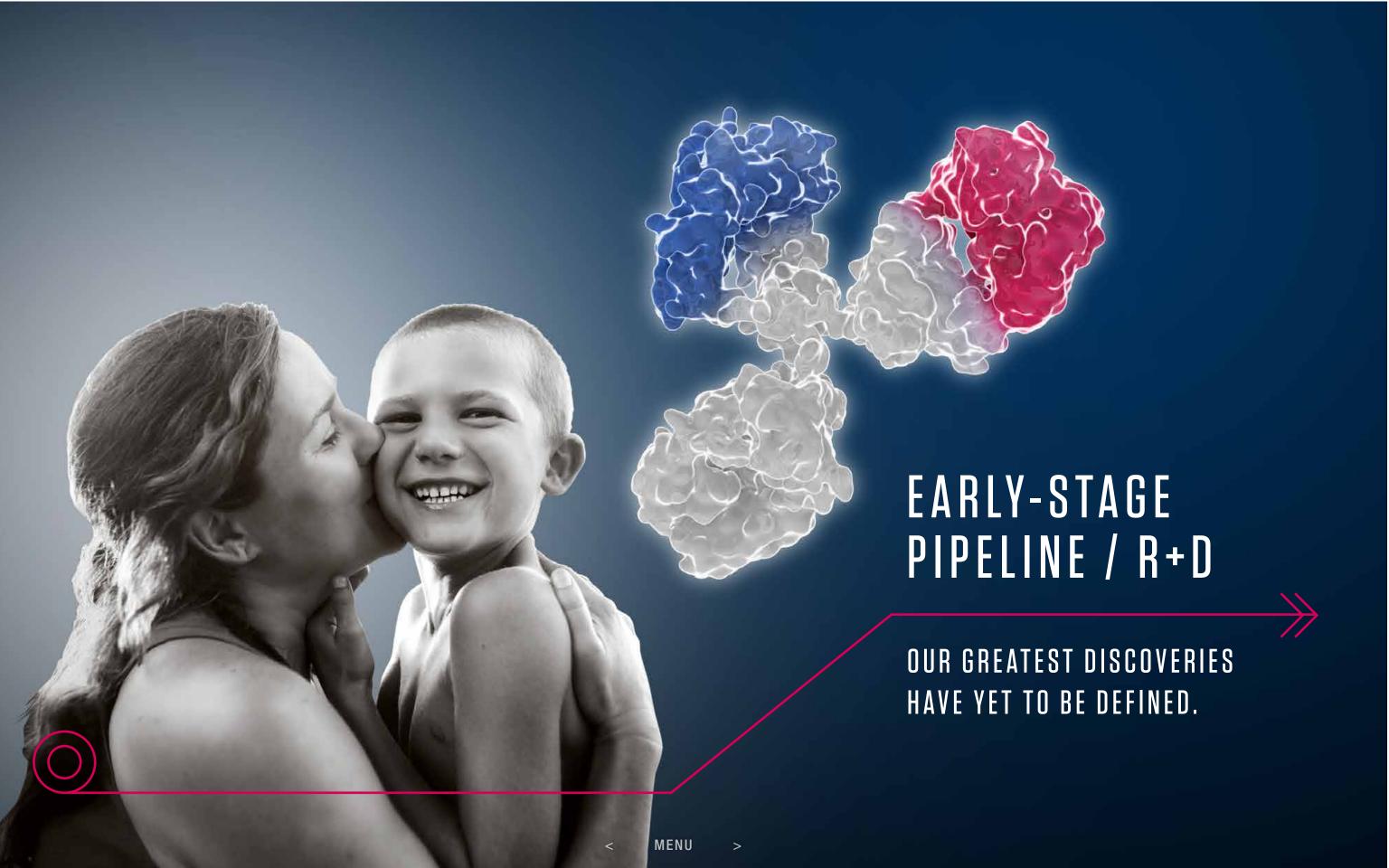
An antibody targeting nerve growth factor being evaluated for the potential to offer a novel, non-opioid approach to addressing chronic pain.

Two clinical trials of fasinumab for pain due to osteoarthritis and chronic back pain were initiated in 2016. In 2015, we entered into a collaboration with Mitsubishi Tanabe Pharma Corporation to develop and commercialize fasinumab in Japan, Korea and nine other Asian countries (excluding China).

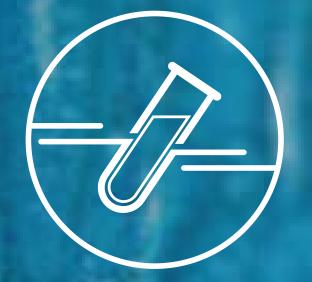


UNMET NEED IN CHRONIC PAIN

CHRONIC OR SEVERE PAIN<sup>15</sup>



# IMMUNO-ONCOLOGY



# RAPID RESPONSE + INFECTIOUS DISEASE



Building on our existing Sanofi antibody collaboration, we launched a new \$2.2B global immuno-oncology collaboration with Sanofi.

This new undertaking will provide important new resources to advance our portfolio in this rapidly developing field, which seeks to harness the body's immune system to fight cancer.

We continued to explore multiple approaches in immuno-oncology, including bispecific antibodies, checkpoint inhibitors and antibody drug conjugates. We have two antibodies, a CD20/CD3 bispecific antibody and a PD-1 inhibitor, in clinical studies with data expected in 2016. A number of additional immuno-oncology antibodies are expected to enter the clinic this year and next.

Regeneron's Rapid Response capabilities leverage our core VelociSuite® technologies to significantly compress the time required for discovery and preclinical validation of potential treatments for emerging infectious diseases.

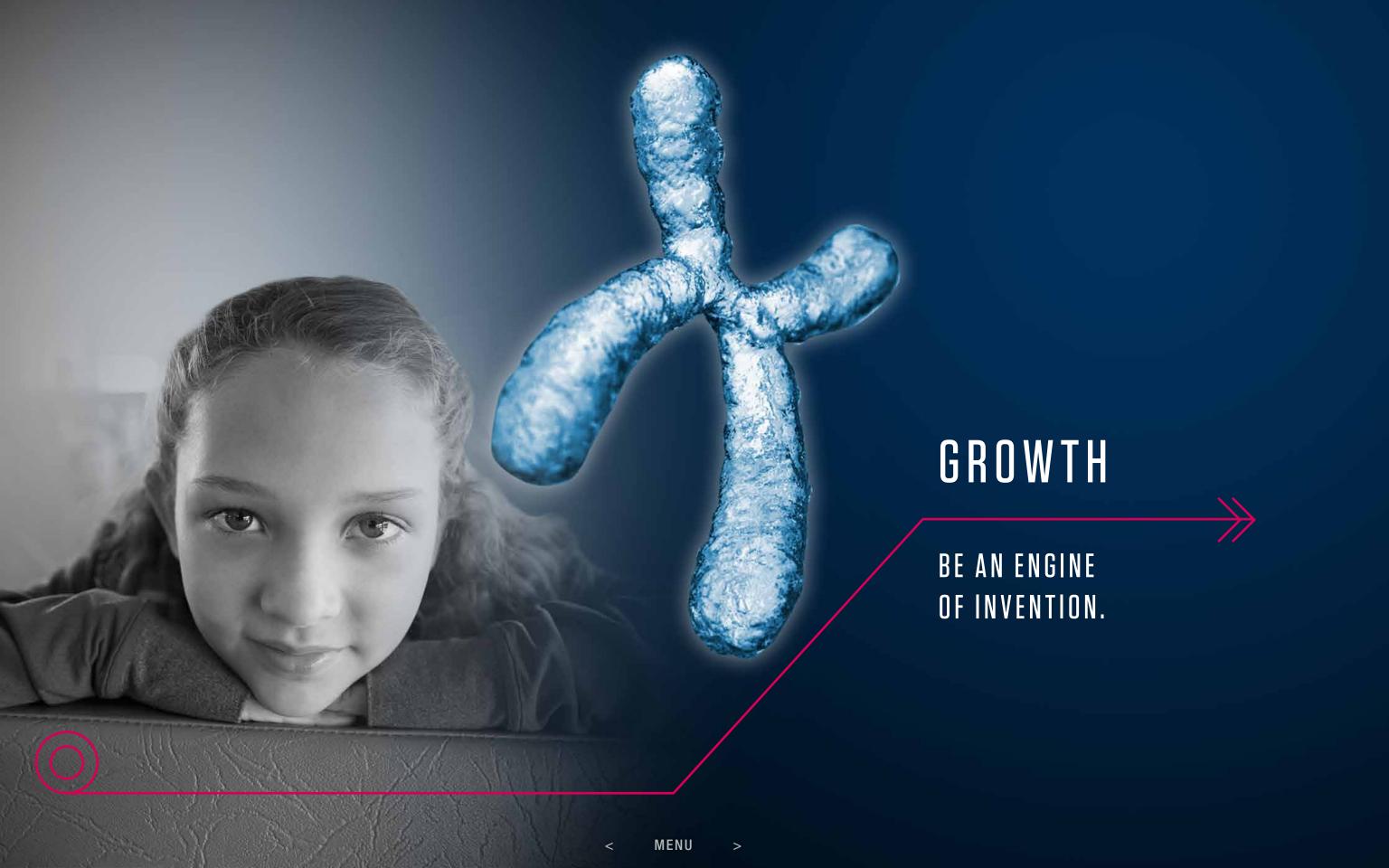
In 2015, we identified and validated a novel therapeutic cocktail of three antibodies targeting the Ebola virus, and reached an agreement with the Biomedical Advanced Research and Development Authority (BARDA) of the U.S. Department of Health and Human Services to develop, test and manufacture this potential treatment. A Phase 1 study in healthy volunteers is planned for the first half of 2016. We similarly identified and validated an antibody against MERS (Middle East Respiratory Virus) and are working to advance this program, as well as pursuing antibody therapies for other devastating viral diseases such as Zika and Dengue.

# REGENERON GENETICS CENTER

In its second full year, the Regeneron Genetics Center (RGC) continued to grow rapidly in terms of scope, scale and speed.

The RGC was created to elucidate, on a large scale, genetic factors that cause or influence a range of human diseases. The team has sequenced over 100,000 exomes to date, and is now delivering new target opportunities and validating existing targets in our preclinical and clinical programs. We continued to bring world-class collaborators from industry, academia and leading health-systems on board, and published the RGC's first peer-reviewed publication in the New England Journal of Medicine.

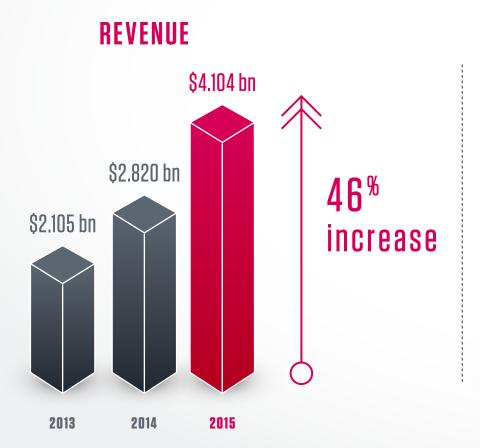




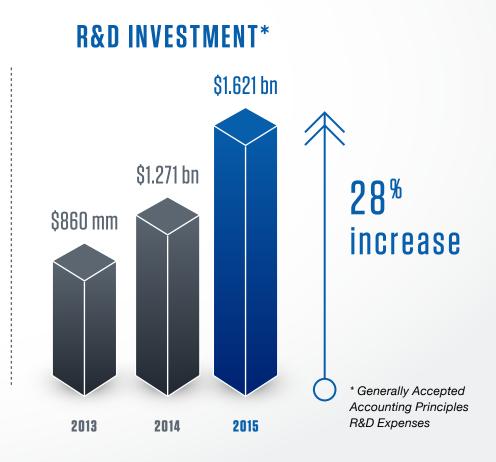
# GROWTH

### In 2015, we grew in many aspects of our business.

We continued construction of our world-class, 400,000-square-foot manufacturing facility in Limerick, Ireland, which will significantly expand our biologic supply capabilities for commercial products. We opened new buildings in our Rensselaer Industrial Operations headquarters and our Tarrytown R&D laboratories and corporate headquarters. And we welcomed our 4,000th Regeneron employee, all while remaining focused on sustaining the innovative culture that makes us unique.









# COMMITTED TO A BETTER FUTURE

In addition to our work to invent new and needed medicines, we are focused on improving our world and operating with the highest standards of integrity. We are proud not only of what we do, but how we do it.

These four pillars help us articulate how we view our responsibility and commitment to society:







# FOSTERING THE FUTURE OF SCIENTIFIC INNOVATION

We believe our STEM (Science, Technology, Engineering and Math) education is a top priority; we are focused on ensuring a strong pipeline of STEM talent for many years to come.

Spanning from elementary school to postdoctoral fellowships, our STEM programs spark interest in science and enhance knowledge, scientific research and careers in biotechnology.

### ATTRACT, SUPPORT AND REWARD

the best and brightest minds in science research

Our immersive internship program offers college and graduate students a uniquely collaborative work environment to gain hands-on, real-world experience. We are also a founding supporter and title sponsor of the Westchester Science and Engineering Fair (affiliated with the International Science and Engineering Fair, or ISEF) high school science research competition, and award the Regeneron Prize to graduate and postdoctoral students every year.

### INCREASE THE EFFECTIVENESS

of teachers in STEM

Created in partnership with the STEM Leadership Center, our teaching fellowship gives New York state-certified middle and high school science teachers the tools they need to deliver higher-quality instruction.

### BRIDGE STEM SKILLS GAPS AND CAREER AWARENESS

among students historically underrepresented in the sciences

Our Sci2Med Academy initiative with Yonkers Partners in Education is an after-school program for high school juniors that broadens knowledge of science and awareness of careers in biotechnology. Students have the opportunity to learn about biotechnology and drug discovery, hear from Regeneron researchers and tour the labs.



Number of REGN Interns:





# CULTIVATING SUSTAINABLE COMMUNITIES

We proudly support the communities where we work and live, and that includes a company-wide commitment to environmental sustainability.

### **Community Service**

Regeneron in the Community (RIC), our company volunteer program, unites our people through days of service, company-sponsored activities and employee-led projects. RIC inspires action, fosters collaboration and motivates our people to self-organize around service projects that reflect their individual passions.

organizations volunteer through RIC hours at

additional organizations supported through the Matching Gifts Program

of employees feel good about the ways we contribute to the community

Great Places to Work Employee Survey

### **Environmental Sustainability**

We want to grow our business while reducing our environmental impact. We proactively seek environmentally responsible ways to better operate our business now and in the future, and we focus on environmental stewardship throughout our value chain.



### CARBON'

Reduced our carbon footprint per employee by 14%, moving toward our expanded 2018 goal of 30%



### WASTE

44% of our waste avoids the landfill. moving toward our 2018 goal of 90%

In 2013, we set five-year targets in four key areas to help inform our choices and actions, all with the aim of reducing our environmental footprint as we grow.



Reduced our consumption per employee by 5%, moving toward our 2018 goal of 10%



### HAZARDOUS CHEMICAL WASTE

51% reduction per lab employee, just short of our 2018 goal of 60%

\*Carbon and Electricity are reported based on the Carbon Disclosure Project reporting year; 2013 noted above corresponds to June 2013 – May 2014 reporting year.



# SUPPORTING PATIENT COMMUNITIES

Our employees are focused on putting science, technology and innovation to work to make a difference in patients' lives.

This effort starts in the labs, moves into the clinic and continues with our commitment to ensuring patients can access the therapies they need.

Comprehensive patient programs, like <u>MyPraluent</u>™ and <u>EYLEA4U</u>SM, provide support for patients throughout their treatment journey by offering insurance eligibility support, financial assistance and free medicine to eligible patients. Additional services include access to educational information and clinical support for physicians, nurses and pharmacists.

Regeneron does not influence or control the operations of independent co-pay assistance foundations and cannot guarantee assistance will be provided.

We also aim to support community needs through unique programs and active engagement with the advocacy organizations that represent the patients we serve.



Regeneron is a national Eye-Care Services Sponsor for ITNAmerica/Rides in Sight. ITNAmerica is the first, national non-profit transportation network committed to providing safe, low-cost, community-based transportation options for seniors and those with vision loss to help them maintain their independence.



### **Advocacy Partnerships**

Our company was built on the fundamental goal of helping patients, and we regularly engage with advocacy organizations to help empower patients. For example, we partnered with the Arthritis Foundation to create patient advocacy summits and patient ambassador programs, all with the goal of catalyzing national and local advocacy efforts.



# NURTURING OUR HIGH-ENGAGEMENT, HIGH-INTEGRITY CULTURE

We empower our people to thrive personally and professionally, work together to create positive change, and promote an ethical culture of diversity and inclusion.

Most Innovative Company, according to Forbes

100 Best Companies to Work For, Fortune

**5 YKS** 

Ranked #1 or #2 employer in the global biopharmaceutical industry in *Science* Top Employers Survey 5 years in a row

of employees say "I'm proud to tell others I work here" - Great Places to Work Employee Survey

We work hard to nurture our highly ethical culture through:

### **Opportunities for Growth**

We encourage and assist our employees in their quests to continue learning throughout their careers.

#### **Culture of Collaboration**

We thrive on diverse ideas and individuals who aren't afraid to challenge convention, and we believe our next great discovery could spring from any level of the organization.

### **Integrity at Work**

We pride ourselves on doing the right thing and have rigorous policies in place to ensure that our colleagues, vendors and business partners are acting in accordance with all applicable laws, rules and regulations.

# FORWARD-LOOKING STATEMENTS

This Annual Report includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("we," "us," "our," "Regeneron," or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of our products, product candidates, and research and clinical programs now underway or planned, including without limitation EYLEA® (aflibercept) Injection, PRALUENT® (alirocumab) Injection, sarilumab, dupilumab, fasinumab, REGN 2222, and the immuno-oncology program; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of our product candidates in clinical trials; the likelihood and timing of possible regulatory approval and commercial launch of our late-stage product candidates and new indications for marketed products, including without limitation EYLEA®, PRALUENT®, sarilumab, dupilumab, fasinumab, and REGN 2222; ongoing regulatory obligations and oversight impacting our marketed products (such as EYLEA® and PRALUENT®), research and clinical programs, and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict our ability to continue to develop or commercialize our products and product candidates; competing drugs and product candidates that may be superior to our products and product candidates; uncertainty of market acceptance and commercial success of our products and product candidates; our ability to manufacture and manage supply chains for multiple products and product candidates; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; unanticipated expenses; the costs of developing, producing, and selling products; our ability to meet any of its sales or other financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including our agreements with Sanofi and Bayer HealthCare LLC, to be canceled or terminated without any further product success; and risks associated with third-party intellectual property and pending or future litigation relating thereto. A more complete description of these and other material risks can be found in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 (filed with the Securities and Exchange Commission on February 11, 2016), including in the section thereof captioned "Item 1A. Risk Factors." Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. We do not undertake any obligation to update publicly any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.



# CORPORATE INFORMATION

#### **Common Stock and Related Matters**

Our Common Stock is traded on The NASDAQ Global Select Market under the symbol "REGN." Our Class A Stock 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.

2014	<u>HIGH</u>	LOW	<u>2015</u>	<u>HIGH</u>	LOW
First Quarter	\$352.49	\$262.97	First Quarter	\$495.50	\$393.00
Second Quarter	\$320.00	\$269.50	Second Quarter	\$544.00	\$433.47
Third Quarter	\$369.31	\$285.06	Third Quarter	\$605.93	\$435.52
Fourth Quarter	\$437.64	\$320.06	Fourth Quarter	\$592.59	\$488.10

As of April 14, 2016, there were 211 shareholders of record of our Common Stock and 23 shareholders of record of our Class A Stock. The closing sales price for the Common Stock on that date was \$406.83.

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

#### SEC Form 10-K

A copy of our 2015 Annual Report on Form 10-K filed with the Securities and Exchange Commission (which accompanies and forms part of this 2015 Annual Report to Shareholders) is available without charge from the Regeneron Investor Relations Department.

#### 2016 Annual Shareholder Meeting

The 2016 Annual Shareholder Meeting will be held on Friday, June 10, 2016, at 10:30 a.m. at the Westchester Marriott Hotel, 670 White Plains Road, Tarrytown, New York 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., 6201 15th Avenue, Brooklyn, New York 11219, (800) 937-5449, www.amstock.com/main. General information regarding the Company, recent press releases, and SEC filings are available on our website at www.regeneron.com, or can be obtained by contacting our Investor Relations Department at (914) 847-7741.

#### **Corporate Office**

777 Old Saw Mill River Road Tarrytown, New York 10591-6707 (914) 847-7400

### **Transfer Agent and Registrar**

American Stock Transfer & Trust Co. 6201 15th Avenue Brooklyn, New York 11219

### **Independent Registered Public Accounting Firm**

PricewaterhouseCoopers LLP

REGENERON®, Science to Medicine®, and the following are registered trademarks of Regeneron Pharmaceuticals, Inc.: ARCALYST®, EYLEA®, VelociGene®, and VelocImmune<sup>®</sup>. PRALUENT<sup>®</sup> is a registered trademark of Sanofi.



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