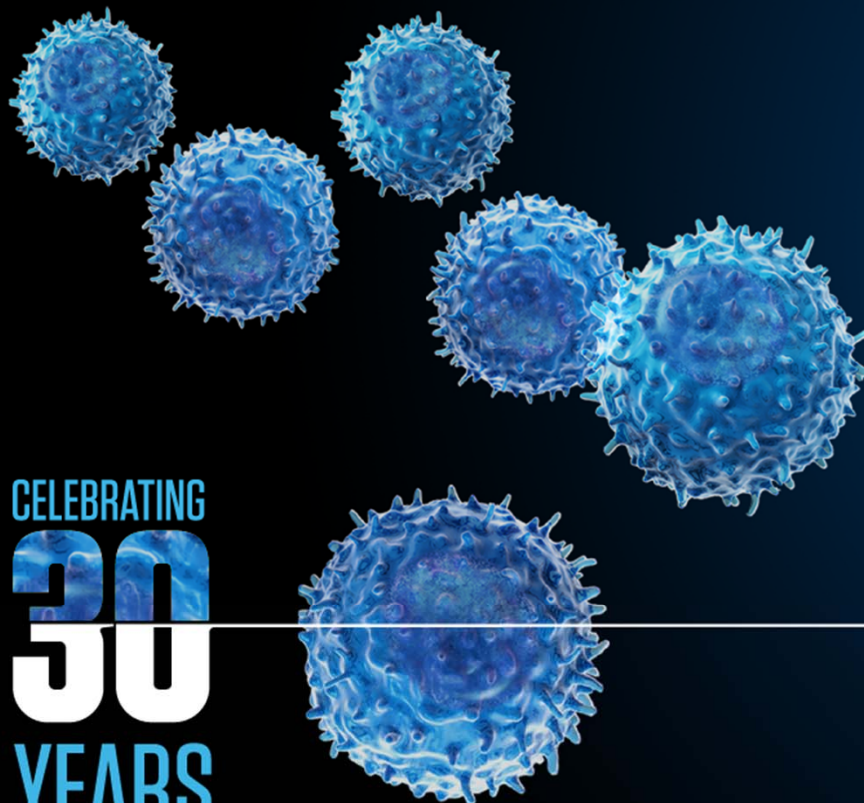


**REGENERON**  
SCIENCE TO MEDICINE®



CELEBRATING  
**30**  
YEARS  
1988-2018

# CORPORATE PRESENTATION



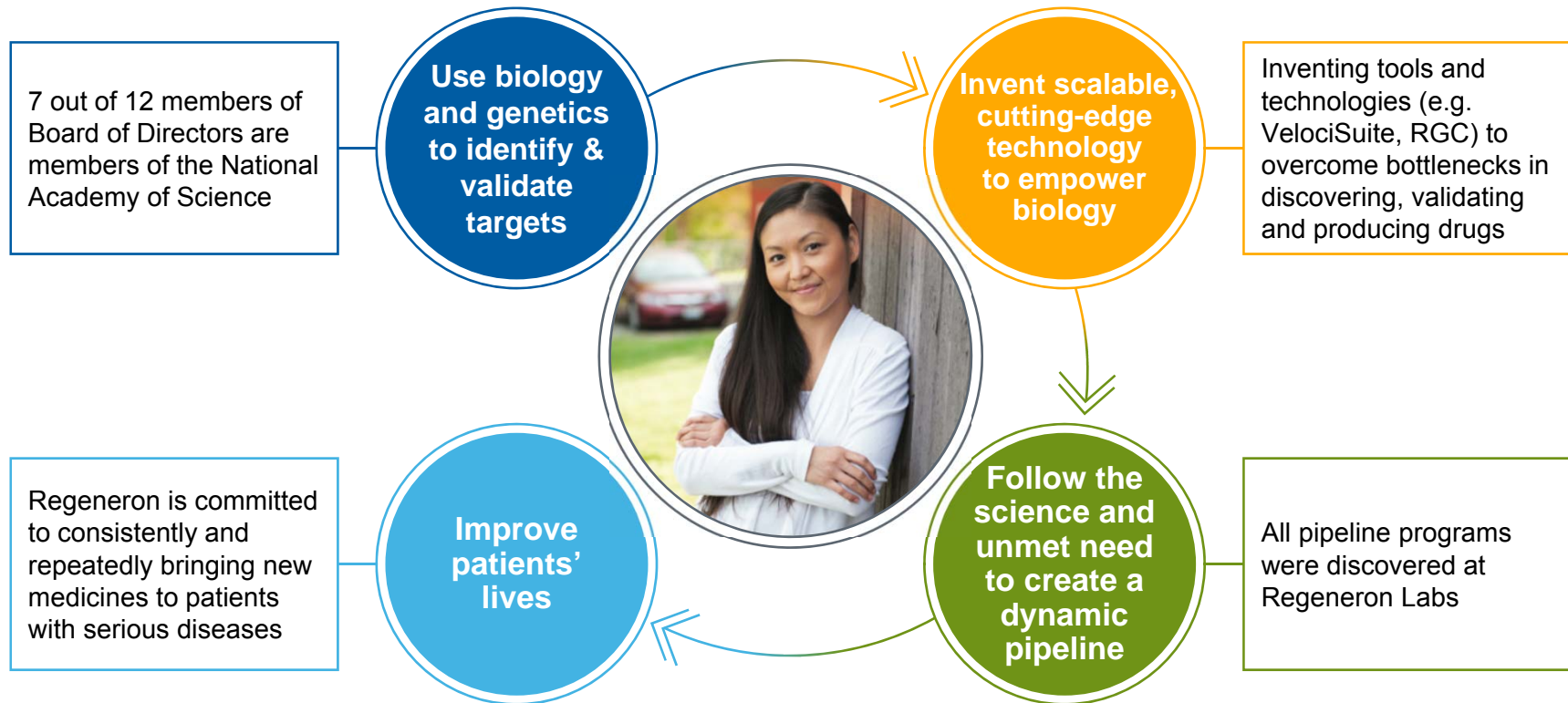
September 2018

# NOTE REGARDING FORWARD-LOOKING STATEMENTS AND NON-GAAP FINANCIAL MEASURES

This presentation includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("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 Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation EYLEA® (afibercept) Injection, Praluent® (alirocumab) Injection, Dupixent® (dupilumab) Injection, Kevzara® (sarilumab) Injection, cemiplimab, fasinumab, Regeneron's earlier-stage product candidates, and the use of human genetics in Regeneron's research programs; the extent to which the results from Regeneron's research programs or preclinical testing may lead to advancement of product candidates to clinical trials or therapeutic applications; 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 Regeneron's product candidates in clinical trials; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, including without limitation EYLEA, Praluent, Dupixent, Kevzara, cemiplimab, and fasinumab; risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation proceedings relating to Praluent, the ultimate outcome of any such litigation proceeding, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition; the likelihood and timing of achieving any of the anticipated milestones described in this presentation; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as EYLEA, Praluent, Dupixent, and Kevzara), research and clinical programs, and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's products and product candidates; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties to perform filling, finishing, packaging, labelling, distribution, and other steps related to Regeneron's 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; the ability of Regeneron to meet any of its sales or other financial projections or guidance and changes to the assumptions underlying those projections or guidance; and the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated without any further product success. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the fiscal year ended December 31, 2017 and its Form 10-Q for the quarterly period ended June 30, 2018 including in each case 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. Regeneron does 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.

This presentation uses non-GAAP unreimbursed R&D and non-GAAP SG&A, which are financial measures that are not calculated in accordance with U.S. Generally Accepted Accounting Principles ("GAAP"). These non-GAAP financial measures are computed by excluding certain non-cash and other items from the related GAAP financial measure. Non-GAAP adjustments also include the income tax effect of reconciling items. The Company makes such adjustments for items the Company does not view as useful in evaluating its operating performance. For example, adjustments may be made for items that fluctuate from period to period based on factors that are not within the Company's control, such as the Company's stock price on the dates share-based grants are issued. Management uses these and other non-GAAP measures for planning, budgeting, forecasting, assessing historical performance, and making financial and operational decisions, and also provides forecasts to investors on this basis. Additionally, such non-GAAP measures provide investors with an enhanced understanding of the financial performance of the Company's core business operations. However, there are limitations in the use of these and other non-GAAP financial measures as they exclude certain expenses that are recurring in nature. Furthermore, the Company's non-GAAP financial measures may not be comparable with non-GAAP information provided by other companies. Any non-GAAP financial measure presented by Regeneron should be considered supplemental to, and not a substitute for, measures of financial performance prepared in accordance with GAAP.

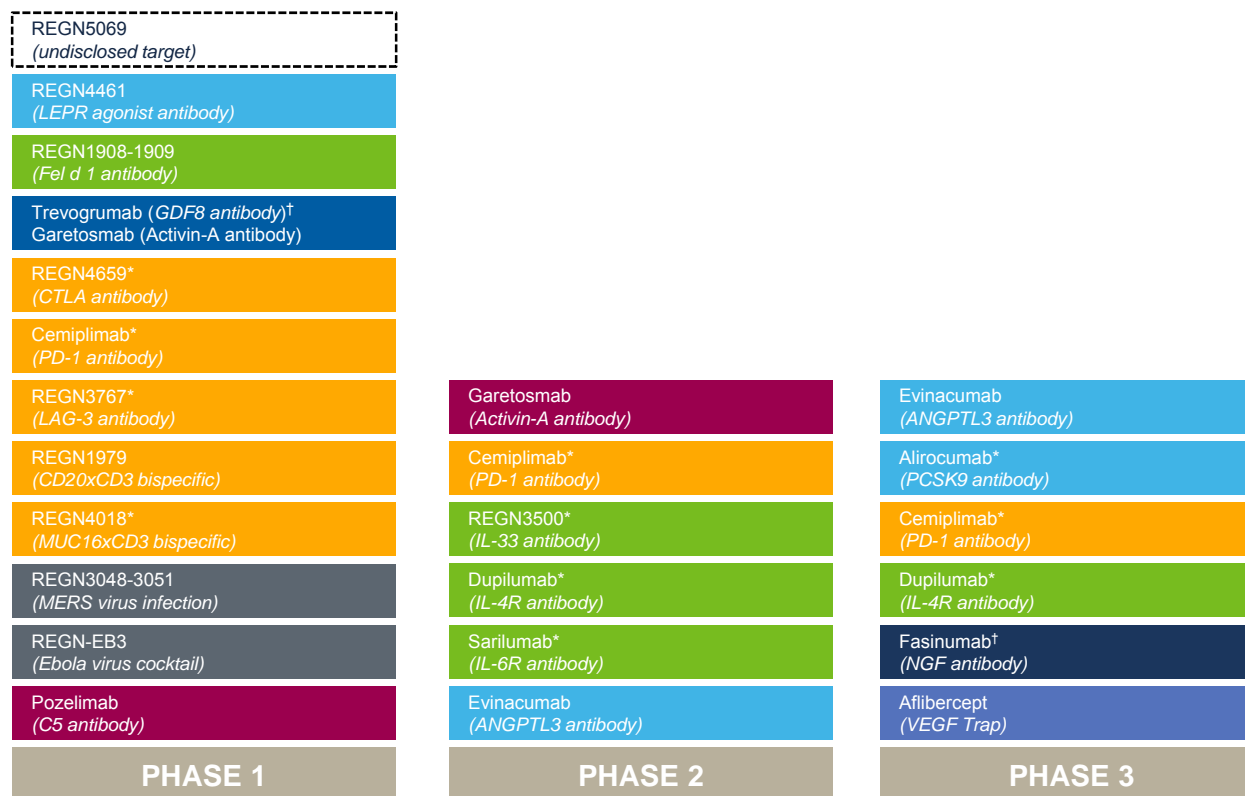
# COMBINING SCIENCE AND TECHNOLOGY TO IMPROVE PATIENTS' LIVES



# ROBUST PIPELINE ACROSS MANY THERAPEUTIC AREAS

- Skeletal Diseases
- Oncology/IO
- Immunology & Inflammation
- Infectious Diseases
- Cardiovascular & Metabolic
- Pain
- Ophthalmology
- Rare Diseases

\* Program partnered with Sanofi  
 † Program partnered with Teva and Mitsubishi Tanabe Pharma Corporation (Asia)



**REGENERON**

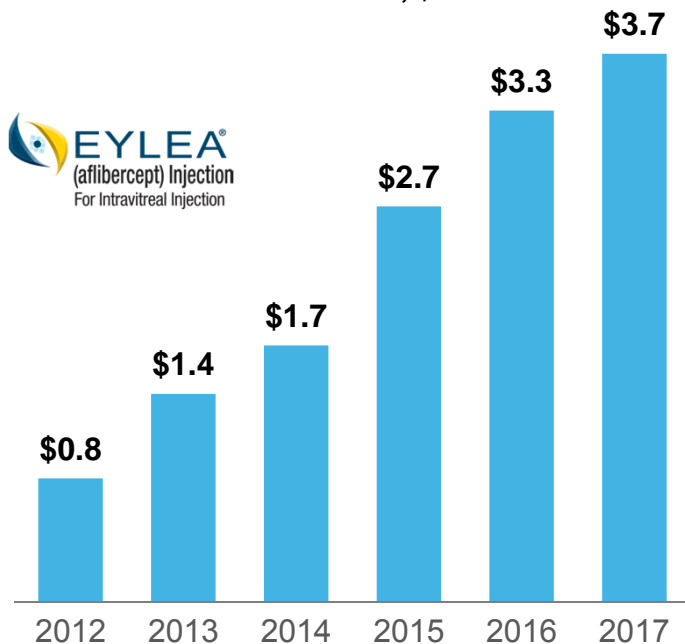
This slide includes pipeline drug candidates currently undergoing clinical testing in a variety of diseases. The safety and efficacy of these drug candidates have not been evaluated by any regulatory authorities for the disease categories described here.

## YTD 2018 HIGHLIGHTS

CLINICAL & REGULATORY PROGRESS	<ul style="list-style-type: none"> <li>✓ EYLEA® - Positive topline data reported from Phase 3 PANORAMA study in non-proliferative diabetic retinopathy, sBLA submitted</li> <li>✓ EYLEA® - Approved for use in a modified 12-week dosing schedule after one year of effective therapy</li> <li>✓ EYLEA® - sBLA submitted for EYLEA in a pre-filled syringe</li> <li>✓ Praluent® - Positive data presented from the 18,000-patient cardiovascular ODYSSEY OUTCOMES study; PDUFA date: 04/28/2019</li> <li>✓ Dupixent® - Approved and launched for moderate-to-severe atopic dermatitis (AD) in Japan</li> <li>✓ Dupilumab - Regulatory filings submitted in both the U.S. and EU for asthma; PDUFA date: 10/20/2018</li> <li>✓ Dupilumab - Positive data reported in adolescent (ages 12-17) Phase 3 AD study; U.S. regulatory submission planned for Q3 2018</li> <li>✓ Dupilumab - Phase 2 study in grass immunotherapy initiated</li> <li>✓ Cemiplimab (PD-1) - Submitted for regulatory approval in both the U.S. (PDUFA date: 10/28/2018) and EU in advanced cutaneous squamous cell carcinoma</li> <li>✓ Evinacumab (ANGPTL3) - Initiated a Phase 3 study in HoFH and a Phase 2 study in severe hypertriglyceridemia</li> <li>✓ Trevogrumab (GDF8) + Garetosmab (Activin-A) - Positive data reported from early stage muscle program</li> <li>✓ REGN3500 - Initiated Phase 2 studies in asthma and COPD</li> <li>✓ REGN-EB3 - Delivered to the Democratic Republic of the Congo for potential use in Ebola patients</li> <li>✓ 4 new candidates entered clinical development - 1) REGN4461 - Agonist antibody to leptin receptor (LEPR), 2) REGN4018 - MUC16xCD3 bispecific antibody, 3) REGN4659 - antibody to CTLA4, 4) REGN5069</li> </ul>
COMMERCIAL PROGRESS	<ul style="list-style-type: none"> <li>✓ EYLEA - 2Q18 U.S. net sales of \$992MM</li> <li>✓ Dupixent® - ~27% increase in total prescriptions and number of patients on treatment from Q1'18 to Q2'18</li> <li>✓ Launch preparations underway for Dupixent in asthma and cemiplimab in advanced CSCC</li> </ul>
ADVANCES IN GENETICS	<ul style="list-style-type: none"> <li>✓ Formed consortium to accelerate the sequencing of 500,000 exomes from the U.K. Biobank</li> <li>✓ Announced collaborations – 1) Alnylam Pharmaceuticals to discover new treatments for NASH and 2) bluebird bio to discover, develop, and commercialize new cell therapies for cancer</li> </ul>
CORPORATE PROGRESS	<ul style="list-style-type: none"> <li>✓ Announced acceleration and expanded investment for dupilumab and cemiplimab development programs</li> </ul>

# EYLEA® (AFLIBERCEPT) INJECTION

U.S. Net Sales, \$Bn



- 2Q'18 Sales:

- U.S. EYLEA® net sales of \$992MM
- Ex-U.S. EYLEA® net sales of \$666MM†

- Clinical Updates:

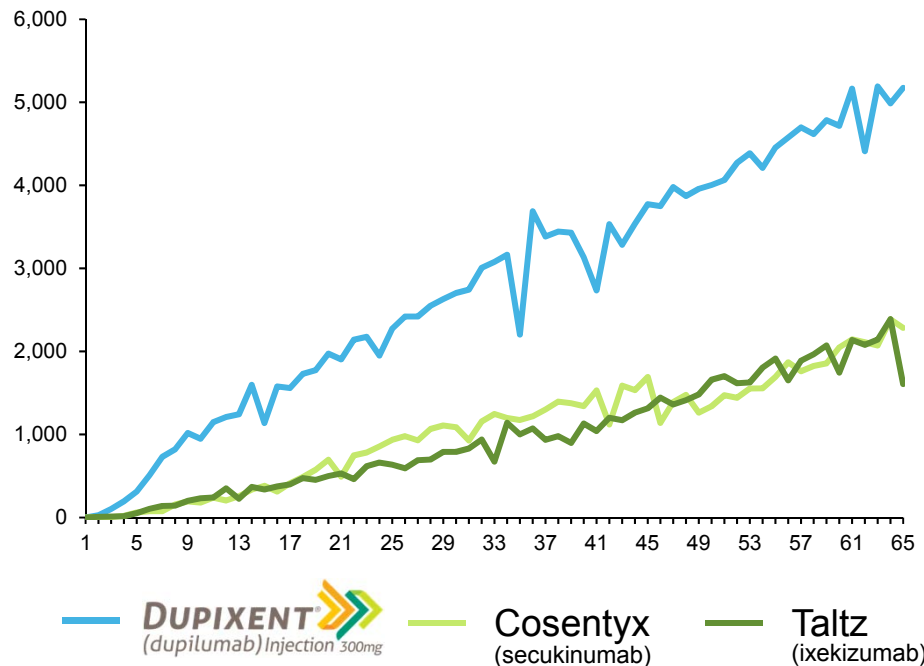
- Positive topline data from Phase 3 PANORAMA study in diabetic retinopathy reported in 1Q'18, sBLA submitted
- sBLA submitted for EYLEA® in a pre-filled syringe
- Approved for use in a modified 12-week dosing schedule after one year of effective therapy

EYLEA® continues to be the market-leading product among FDA-approved anti-VEGF agents for its approved indications

† Outside the United States, EYLEA net product sales comprise sales by Bayer in countries other than Japan and sales by Santen Pharmaceutical Co., Ltd. in Japan under a co-promotion agreement with an affiliate of Bayer; Regeneron shares profits and losses from such sales.

## DUPIXENT® (DUPILUMAB): LAUNCH IN ATOPIC DERMATITIS PROGRESSING WELL

Weekly TRx since launch

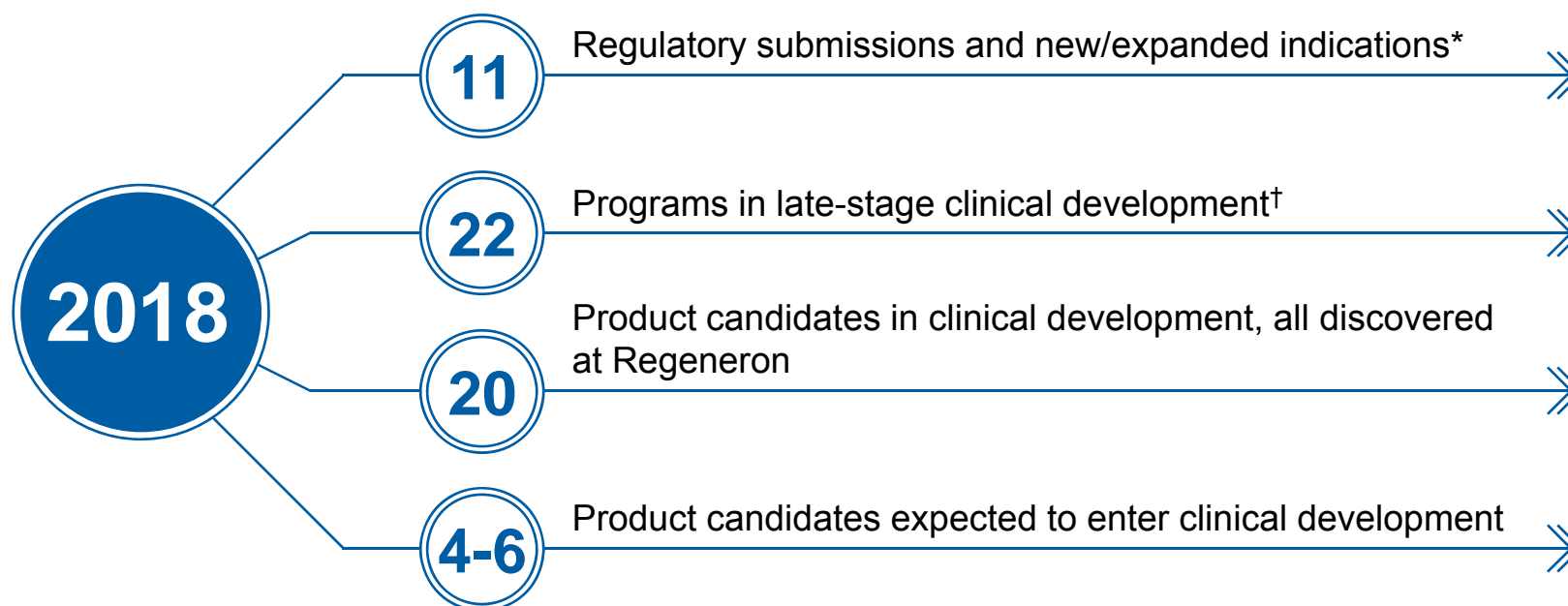


- Underlying demand for Dupixent remains strong
  - Total prescriptions up ~27% sequentially from Q1'18 to Q2'18\*
  - On average, ~550 new patients/week are dispensed drug\*
- Patient refill rate and persistence rates remain high

Source: IQVIA

\*Prescription data as of Aug 2, 2018 (2Q financial and operating results release)

## IMPORTANT PIPELINE ADVANCES



\* Regulatory application submitted

† Programs in Phase 2 or Phase 3 development



## 2018 SELECT MILESTONES

EYLEA	<input type="checkbox"/> Report one-year data from Phase 3 PANORAMA study for the treatment of non-proliferative diabetic retinopathy in patients without diabetic macular edema (DME)
Dupixent (dupilumab)	<input type="checkbox"/> FDA decision on sBLA for asthma in adult/adolescent patients (target action date of October 20, 2018) <input type="checkbox"/> Additional regulatory agency decisions on applications for atopic dermatitis in adults outside the United States <input type="checkbox"/> Submit sBLA and MAA for treatment of atopic dermatitis in adolescent patients (12–17 years of age) <input type="checkbox"/> Report data from Phase 3 studies in nasal polyps <input type="checkbox"/> Initiate Phase 3 study in EoE and Phase 2 studies in peanut allergy
Praluent (alirocumab)	<input type="checkbox"/> Initiate Phase 3 pediatric studies in HoFH
Kevzara (sarilumab)	<input type="checkbox"/> Initiate Phase 3 study in giant cell arteritis and polymyalgia rheumatica
Cemiplimab (PD-1 Antibody)	<input type="checkbox"/> FDA decision on BLA for advanced CSCC (target action date of October 28, 2018) <input type="checkbox"/> Continue patient enrollment in Phase 3 study for first-line treatment of non-small cell lung cancer, as well as various other studies
Fasimumab (NGF Antibody)	<input type="checkbox"/> Continue patient enrollment in Phase 3 long-term safety and efficacy studies in osteoarthritis
REGN3500 (IL-33 Antibody)	<input type="checkbox"/> Initiate Phase 2 studies in atopic dermatitis
Bispecific Antibodies	<input type="checkbox"/> Initiate Phase 2 study for REGN1979 (CD20xCD3 Antibody) in Follicular Lymphoma <input type="checkbox"/> Submit Investigational New Drug Application (IND) for BCMAXCD3 antibody

## DIABETIC EYE DISEASES PRESENT IMPORTANT OPPORTUNITIES FOR EYLEA

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### Diabetic Macular Edema (DME)

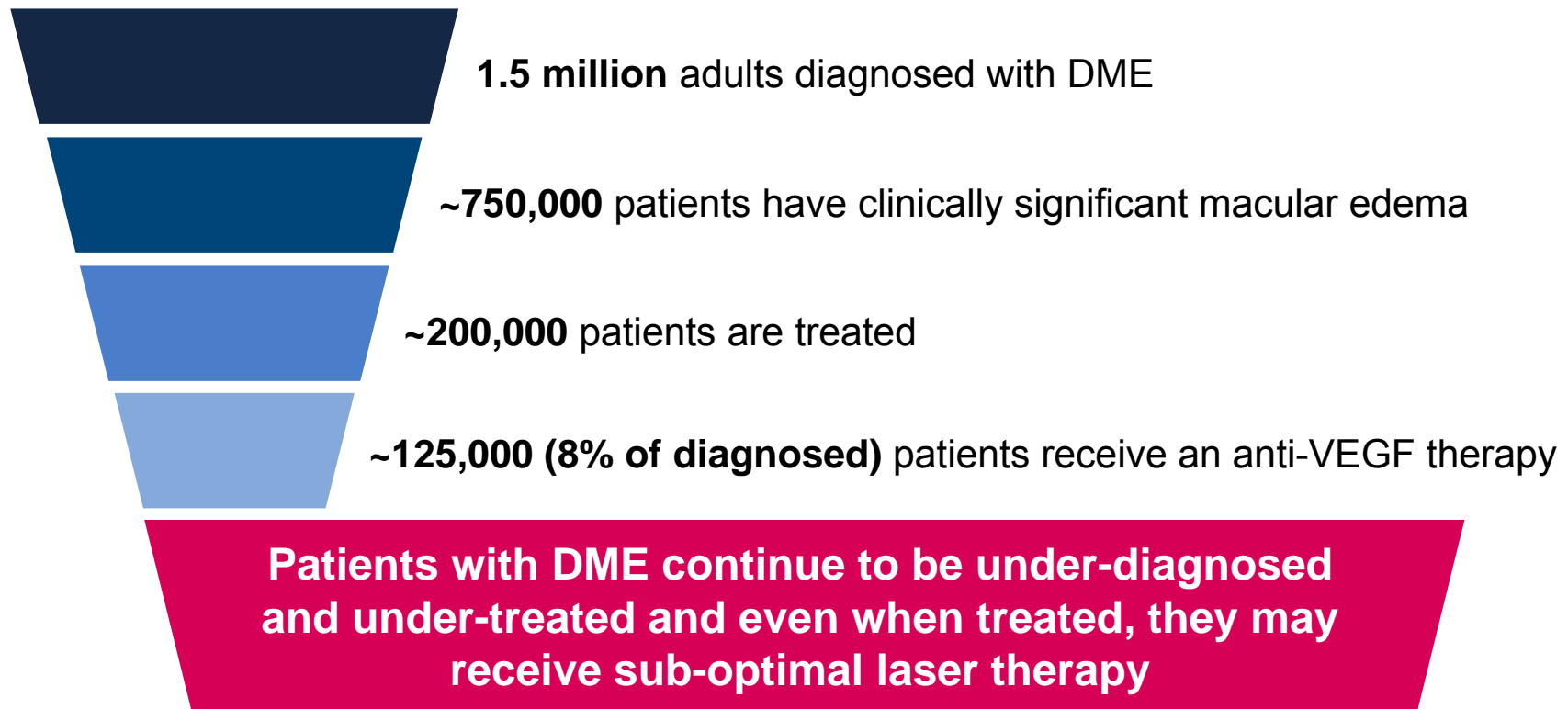
Characterized by visual loss due to edema or swelling in the most important part of the retina

### Diabetic Retinopathy (DR)

Characterized by vascular abnormalities that can lead to profound vision loss, by causing edema, hemorrhage, or vascular proliferation

## DIABETIC MACULAR EDEMA (DME) IS AN IMPORTANT OPPORTUNITY FOR EYLEA

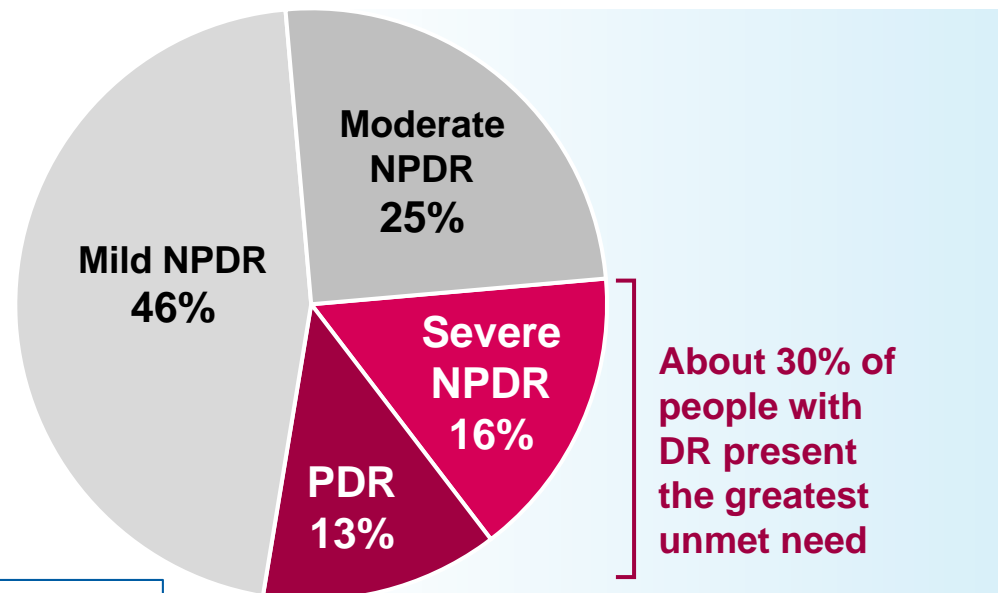
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## DIABETIC RETINOPATHY WITHOUT DME IS AN IMPORTANT RELATED POTENTIAL OPPORTUNITY FOR EYLEA

**3.5 million people in the U.S. are diagnosed with diabetic retinopathy without DME<sup>1,2</sup>**

- Severe, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) may result in profound vision loss and represent a potential opportunity for EYLEA
- The majority of people with PDR are now treated with pan-retinal photocoagulation (laser) therapy, which was inferior to EYLEA in the CLARITY study
- Positive topline results in Phase 3 NPDR trial (PANORAMA)
  - 58% of EYLEA-treated patients experienced a two-step or greater improvement from baseline on the Diabetic Retinopathy Severity Scale (DRSS) at week 24, compared to 6% of patients receiving sham injection ( $p < 0.0001$ )
  - There were no new safety signals in the trial



sBLA submitted for the treatment of diabetic retinopathy

<sup>1</sup> NHANES 2005-2008, projected to 2012 US population; American Diabetes Association. <sup>2</sup> BioTrends Research Group, Treatment Trends®: Diabetic Retinopathy / Diabetic Macular Edema (US) 2013.

# PRALUENT® (ALIROCUMAB): ODYSSEY OUTCOMES PROVIDES STRONG CLINICAL EVIDENCE OF PATIENT BENEFIT FROM LONG-TERM THERAPY<sup>1</sup>



## Transformational Study

- High risk patients with ACS event between 1 and 12 months
- Patient follow-up for up to 5 years with >40% of patients followed-up for more than 3 years
- >90% of patients enrolled in the study were on maximally tolerated statin therapy



## Positive Results

- Primary endpoint met: Significant reduction in MACE
- Reduction in all-cause mortality<sup>2</sup>
- No new safety signals in the trial: Well tolerated in the longest PCSK9 inhibitor trial



## Potential Patient Impact

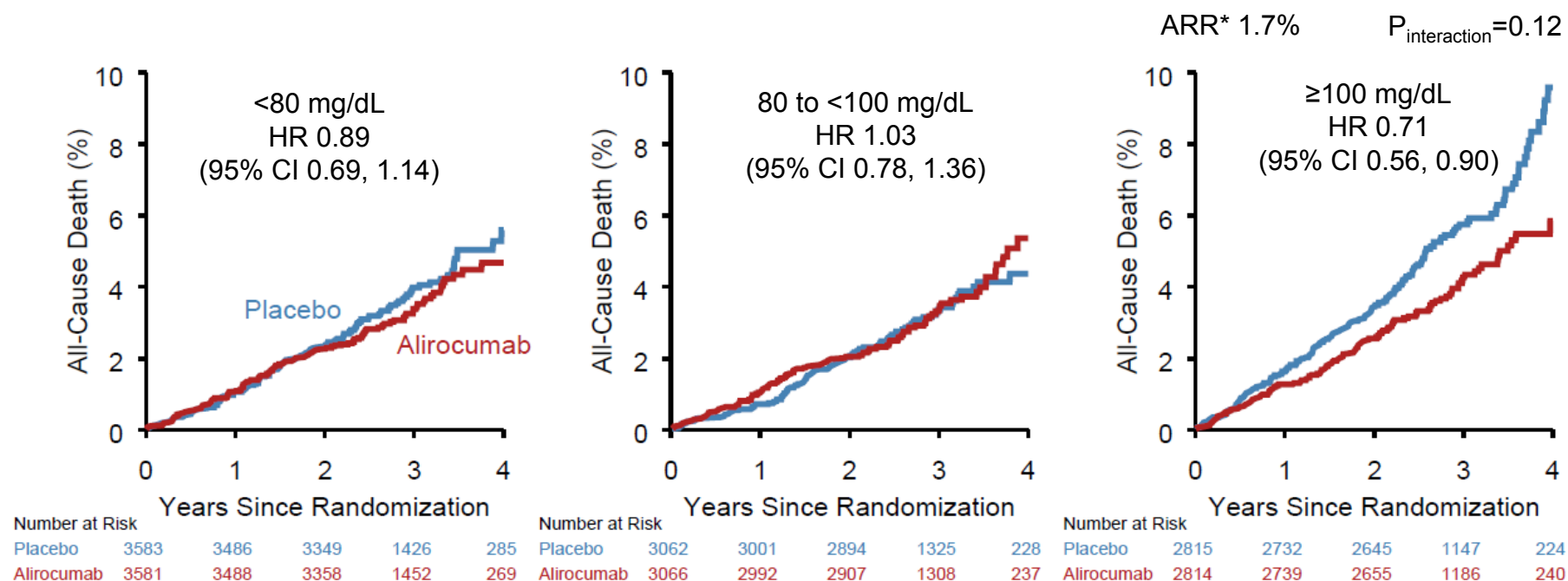
- Greatest clinical benefit was seen in high risk post-ACS patients
- In highest risk patients with LDL-C  $\geq 100$ mg/dL, Praluent was associated with a 28% reduction in the risk of CHD death, 31% reduction in CV death, and 29% reduction in all-cause death<sup>3</sup>

FDA target action date for sBLA for cardiovascular risk reduction is April 28, 2019

ACS=Acute Coronary Syndrome; MACE=Major Adverse Cardiac Event;  
CV=Cardiovascular; CHD=Cardiac Heart Disease

(1) In addition to maximally tolerated statin therapy  
(2) HR= 0.85; CI 0.73-0.98; nominal p value = 0.0261  
(3) Post-hoc analyses; HR=0.71, CI: 0.56-0.90

# PRALUENT® ODYSSEY OUTCOMES POST HOC ANALYSIS: ALL-CAUSE DEATH BY BASELINE LDL-C SUBGROUPS



\*Based on cumulative incidence

**PRALUENT® ODYSSEY OUTCOMES EFFICACY: SUBGROUP WITH BASELINE LDL-C  $\geq$ 100 MG/DL (MEDIAN BASELINE LDL-C 118 MG/DL)**

Endpoint, n (%)	Alirocumab (N=2814)	Placebo (N=2815)	Absolute risk reduction (%)	HR (95% CI)
MACE	324 (11.5)	420 (14.9)	3.4	<b>0.76</b> (0.65, 0.87)
CHD death	69 (2.5)	96 (3.4)	1.0	<b>0.72</b> (0.53, 0.98)
CV death	81 (2.9)	117 (4.2)	1.3	<b>0.69</b> (0.52, 0.92)
All-cause death	114 (4.1)	161 (5.7)	1.7	<b>0.71</b> (0.56, 0.90)

## PRALUENT® ODYSSEY OUTCOMES SAFETY (1)

Treatment-emergent adverse events, n (%)	Alirocumab (N=9451)	Placebo (N=9443)
Any	7165 (75.8)	7282 (77.1)
Serious	2202 (23.3)	2350 (24.9)

Laboratory value	Alirocumab	Placebo
ALT >3 × ULN, n/N (%)	212/9369 (2.3)	228/9341 (2.4)
Creatine kinase >10 × ULN, n/N (%)	46/9369 (0.5)	48/9338 (0.5)



## PRALUENT® ODYSSEY OUTCOMES SAFETY (2)

Event	Alirocumab (N=9451)	Placebo (N=9443)
Diabetes worsening or diabetic complications: <i>pts w/DM at baseline</i> , n/N (%)	506/2688 (18.8)	583/2747 (21.2)
New onset diabetes; <i>pts w/o DM at baseline</i> , n/N (%)	648/6763 (9.6)	676/6696 (10.1)
General allergic reaction, n (%)	748 (7.9)	736 (7.8)
Hepatic disorder, n (%)	500 (5.3)	534 (5.7)
Local injection site reaction, n (%)*	360 (3.8)	203 (2.1)
Neurocognitive disorder, n (%)	143 (1.5)	167 (1.8)
Cataracts, n (%)	120 (1.3)	134 (1.4)
Hemorrhagic stroke, n (%)	9 (<0.1)	16 (0.2)

## PRALUENT®: COMMITTED TO MAKE PRALUENT ACCESSIBLE FOR PATIENTS WITH GREATEST HEALTH RISK AND UNMET NEED

- Regeneron and Sanofi lowered the net price of Praluent in exchange for, straightforward, more affordable access for Express Scripts patients
- Exclusive agreement



- For payers willing to reduce access barriers for high-risk patients, companies will offer net price within a cost-effective range, leveraging a new Institute for Clinical and Economic Review (ICER) analysis

## KEVZARA® (SARILUMAB): LAUNCHED IN RHEUMATOID ARTHRITIS; PLANNING PIVOTAL STUDIES IN ADDITIONAL INDICATIONS

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- Launch ongoing in rheumatoid arthritis in U.S., EU and Japan
- Increased formulary coverage started in January 2018
- FDA approved single-dose pre-filled pen, the only IL-6 inhibitor with an auto-injector device
- Studies planned in additional indications
  - Giant Cell Arteritis (U.S. prevalence >228,000)<sup>1</sup>
  - Polymyalgia Rheumatica (U.S. prevalence ~711,000)<sup>1</sup>

<sup>1</sup>Lawrence RC, Felson DT, Helmick CG, et al; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part II. Arthritis Rheum. 2008;58(1):26-35

## REGENERON AND SANOFI ACCELERATE AND EXPAND INVESTMENT FOR CEMIPIMAB AND DUPILUMAB DEVELOPMENT PROGRAMS

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- **Investment in cemiplimab to be increased by ~\$1 billion**
  - Companies will continue to equally fund cemiplimab development
  - The companies will also continue their additional investment in other immuno-oncology programs under their existing Immuno-oncology Discovery Agreement
- **Additional investment in dupilumab and anti-IL-33 (REGN3500) development program**
  - To accelerate planned new studies of dupilumab in chronic obstructive pulmonary disease, peanut and grass allergy, and in patients with multiple allergic disorders
  - The additional investment will also accelerate and expand development of REGN3500 with studies expected to be conducted in atopic dermatitis, asthma and chronic obstructive pulmonary disease (COPD)
  - Funding pursuant to existing antibody collaboration with Sanofi

## 2018 FINANCIAL GUIDANCE<sup>1</sup>

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<b>Non-GAAP Unreimbursed R&amp;D</b>	<b>\$1,210MM - \$1,260MM</b>
<b>Non-GAAP SG&amp;A</b>	<b>\$1,340MM - \$1,390MM</b>
<b>Sanofi Collaboration Revenue: Reimbursement of Regeneron Commercialization-Related Expenses</b>	<b>\$455MM - \$485MM</b>
<b>Effective Tax Rate</b>	<b>13%-16%</b>
<b>Capital Expenditures</b>	<b>\$410MM - \$450MM</b>

1) As of August 2<sup>nd</sup>, 2018. The guidance does not assume the completion of any significant business development transaction that had not been completed as of the date of the guidance. Regeneron does not undertake any obligation to update publicly any financial projection or guidance, whether as a result of new information, future events, or otherwise.

# DUPIUMAB: AN IL-4/IL-13 BLOCKER WITH POSITIVE DATA IN MANY ALLERGIC DISEASES

## Atopic Dermatitis

- Approved in U.S., EU and Japan
- Positive data reported in adolescent (ages 12-17) Phase 3 study; U.S. regulatory submission planned in Q3 2018
- Studies ongoing in pediatric populations



Dupilumab

## Asthma

- Efficacy demonstrated in 3 pivotal studies; Oct 20, 2018 FDA target action date
- Largest Phase 3 biologic program in asthma
- Pediatric studies ongoing



## Nasal Polyps

- Positive Phase 2 proof-of-concept data reported
- Both Phase 3 studies fully enrolled



## Eosinophilic Esophagitis

- Positive Phase 2 proof-of-concept data reported
- Phase 3 studies to be initiated in 2018



Phase 2 studies in grass immunotherapy initiated in 2Q'18

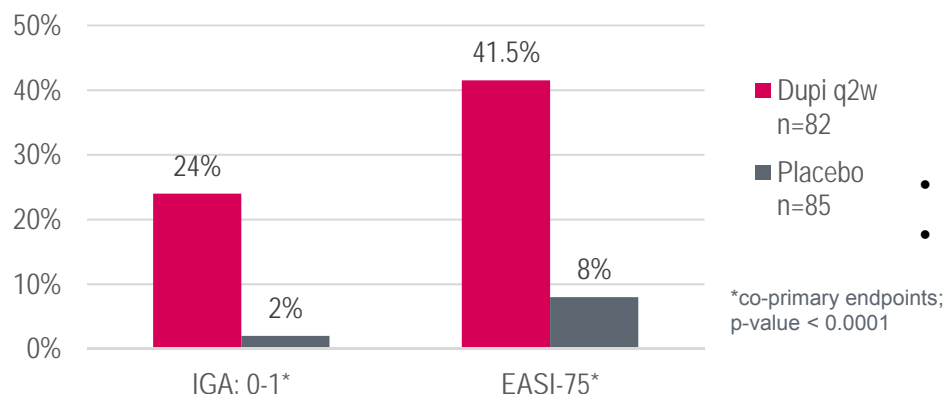
Phase 2 studies in peanut allergy, co-morbid allergic disorders, and COPD planned



# PEDIATRIC ATOPIC DERMATITIS REPRESENTS A HIGH DISEASE BURDEN WITH LIMITED TREATMENT OPTIONS

## ADOLESCENTS (AGES 12-17 YEARS)

- Positive data reported in Phase 3 AD study; U.S. regulatory submission planned for Q3 2018



- The overall rate of treatment-emergent adverse events was comparable between the dupilumab group (72%) and placebo (69%). The rate of overall infections and infestations was numerically lower in the dupilumab group (11%) vs. placebo (20%).
- There were no serious adverse events or events leading to treatment discontinuation in the dupilumab treatment group.

IGA: Investigator's Global Assessment, EASI: Eczema Area and Severity Index

## PEDIATRICS (AGES 6 MONTHS -11 YEARS)

- Prevalence of AD is ~10% of U.S. pediatric population<sup>1</sup>
  - 1%–2% of these pediatric AD patients have severe disease<sup>2,3,4</sup>, which includes patients with more than 50% of their skin surface covered with lesions
- Limited treatment options currently available
- Pediatric studies ongoing:
  - In children between 6 and 11 years ongoing
  - In children between 6 mos. and 5 years ongoing

<sup>1</sup>Shaw et al., J In Derm, Eczema Prevalence in the United States; Data from the 2003 National Survey of Children's Health, 2011, 131, 67-73

<sup>2</sup>Charman CR, Williams HC. Epidemiology. In: Bieber T, Leung DYM, editors. Atopic Dermatitis. New York: Dekker; 2002. pp. 21–42

<sup>3</sup>Emerson RM, Williams HC, Allen BR. Severity distribution of atopic dermatitis in the community and its relationship to secondary referral. British Journal of Dermatology. 1998;139(1):73–6

<sup>4</sup> Atopic Eczema in Children: Management of Atopic Eczema in Children from Birth up to the Age of 12 Years. NICE Clinical Guidelines, No. 57. National Collaborating Centre for Women's and Children's Health (UK). London: RCOG Press; 2007 Dec

# DUPIUMAB IN ASTHMA: COMPREHENSIVE CLINICAL PROGRAM DEMONSTRATES EFFICACY IN BROAD PATIENT POPULATION



The NEW ENGLAND  
JOURNAL of MEDICINE

Dupilumab  
in asthma

- **In three pivotal studies (DRI, QUEST, VENTURE) dupilumab reduced exacerbations in both the overall patient population and in patients with eosinophilic phenotype**
  - 46%-70% reductions in overall patient population
  - 66%-81% reductions in eosinophilic population (>300 eos/mL)
- **Clinically significant and sustained improvement observed in lung function (FEV1)**
  - 0.13L-0.22L increase in FEV1 vs. placebo in overall patient population
  - 0.21L-0.32L increase in FEV1 vs. placebo in eosinophilic population (>300 eos/mL)
- **In the VENTURE study (severe, oral steroid-dependent asthma), dupilumab substantially reduced use of oral steroids, while reducing exacerbations and improving lung function**
  - Half the patients were able to completely eliminate use of oral steroids
  - 59% reduction in exacerbations in overall patient population, and 71% reduction in eosinophilic population (>300 eos/mL)
  - 0.22L increase in FEV1 vs. placebo in overall patient population, and 0.32L increase in eosinophilic patient population (>300 eos/mL)

FDA target action date for sBLA is October 20, 2018

DRI ClinicalTrials.gov Identifier: NCT01854047  
QUEST ClinicalTrials.gov Identifier: NCT02414854  
VENTURE ClinicalTrials.gov Identifier: NCT02528214

**REGENERON**



## REGN3500 (IL-33) CLINICAL DEVELOPMENT UNDERWAY

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- **Role of IL-33 in respiratory disease has been validated by genetic associations (Regeneron Genetics Center®)**
  - Genetic link established to asthma:
    - Common “gain-of-function” (GOF) variants in IL-33 and its receptor increase the risk of asthma
    - Rare “loss-of-function” (LOF) variants in IL-33 decrease risk of eosinophilic asthma by more than 50%
- **Preclinical models have shown REGN3500 can have additive and complementary effects with dupilumab**
- **Initial clinical study showed favorable pharmacokinetics and safety profile in healthy volunteers**
- **Phase 2 study in asthma initiated in Q1’18 and Phase 2 study in COPD initiated in Q2’18. Further studies planned in atopic dermatitis\***

\* These studies are planned to include combination arms with dupilumab

# FASINUMAB: OPPORTUNITY EXISTS FOR A NOVEL CLASS OF NON-OPIOID PAIN THERAPIES

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- **Fasinumab (NGF) presents a novel, non-opioid approach to addressing chronic pain**
  - Partnered with Teva and Mitsubishi Tanabe Pharma (MTPC) outside of the U.S.
- **Approximately 50 million U.S. adults suffer from significant chronic or severe pain; treatments with novel mechanisms of action are desperately needed<sup>1</sup>**
  - NSAIDs are associated with serious CV and GI side effects, which can be troublesome, particularly in elderly patients
  - Opioids have limited efficacy in osteoarthritis (OA) pain and are associated with serious issues with chronic tolerability and abuse potential
- **In August 2018, announced positive topline Phase 3 results in patients with chronic pain from osteoarthritis of the knee or hip**
  - At the week 16 primary efficacy analysis, the study met both co-primary endpoints<sup>2</sup>
  - Fasinumab was generally well tolerated, with similar adverse events (AEs) as those observed in previous fasinumab trials
  - Among the approximately 65% of patients who had completed their first radiographic assessment, the placebo-adjusted rate of adjudicated arthropathies was approximately 2%

1) American Pain Society, "Estimates of Pain Prevalence and Severity in Adults: United States, 2012." Available at [http://www.jpain.org/article/S1526-5900\(15\)00679-3/pdf](http://www.jpain.org/article/S1526-5900(15)00679-3/pdf). Last accessed: March 2016.

2) Co-primary Efficacy Endpoints: change from baseline to week 16 in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) pain subscale score and change from baseline to week 16 in the WOMAC physical function subscale score

## TREVOGRUMAB (ANTI-GDF8) + GARETOSMAB (ANTI ACTIVIN-A) DEMONSTRATED SIGNIFICANT INCREASE IN MUSCLE MASS AT 8 WEEKS

		Pbo	Trevogrumab	Garetosmab	Trevogrumab + Garetosmab	Trevogrumab+ Garetosmab	Trevogrumab+ Garetosmab
	Dose	-	High	High	Low	Mid	High
	N	12	6	6	6	6	12
Week 8 change from baseline	LS Mean (SE)	<b>0.88%</b> (1.05)	<b>4.61%</b> (1.49)	<b>2.85%</b> (1.49)	<b>3.51%</b> (1.49)	<b>6.19%</b> (1.48)	<b>7.73%</b> (1.05)
	p-Value vs. placebo		0.047	0.287	0.16	0.006	<0.0001

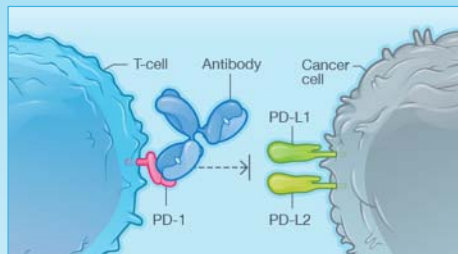
- Regeneron scientists identified Activin-A as a second “myostatin” that appears to be a more important regulator of muscle mass in primates
- The addition of garetosmab (anti-Activin A/REGN2477) to trevogrumab (anti-GDF8/REGN1033) in healthy volunteers, resulted in:
  - Dose-dependent increase in thigh muscle volume of up to ~8%
  - Decreased fat mass
  - Acceptable safety profile
- Additional combination studies in muscle indications planned
- Regeneron scientists identified aberrant Activin-A activity as the cause of the ultra-orphan disease known as Fibrodysplasia Ossificans Progressiva (FOP)
  - Garetosmab is being studied as monotherapy in FOP

# A MULTI-PRONGED APPROACH TO IMMUNO-ONCOLOGY

## CHECKPOINT INHIBITORS

that block targets such as PD-1 and LAG-3, helping T-cells to recognize and attack cancer cells

**Cemiplimab** (Anti-PD-1)    **REGN3767** (Anti-LAG-3)    **REGN4659** (Anti-CTLA4)

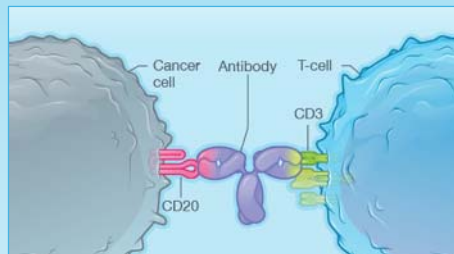


- Cemiplimab, REGN3767, and REGN4659 antibodies in clinical development
- Cemiplimab in development as backbone for mono and combination therapy
- Expanding size of our ongoing monotherapy Phase 3 study in non small cell lung cancer. Read out expected in 2020.

## BISPECIFIC ANTIBODIES

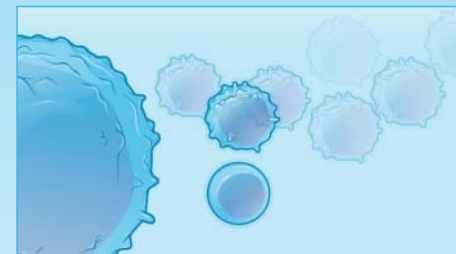
that can bind two different molecular targets, allowing for diverse approaches to targeting and killing cancer cells

**REGN1979** (CD20xCD3 Bispecific Antibody)



- REGN1979 (CD20xCD3) and REGN4018 (MUC16xCD3) in clinical development
- Additional BCMAxCD3 bispecific to enter the clinic in 2018

## OTHER MODALITIES



- Several targets in preclinical development, including GITR agonistic antibody
- Novel approach for generating peptide in HLA antibodies
- CAR-T approaches

## PIVOTAL STUDY IN ADVANCED CSCC DEMONSTRATED HIGH RESPONSE RATE AND DURABLE RESPONSES

- ~1M cases of Cutaneous Squamous Cell Carcinoma (CSCC) annually in the U.S.
- While most are well-treated with surgery, CSCC results in 3,900 to 8,800 deaths/year in US<sup>1</sup> (compared to 9,700 deaths from melanoma)
- There are no FDA-approved CSCC therapies



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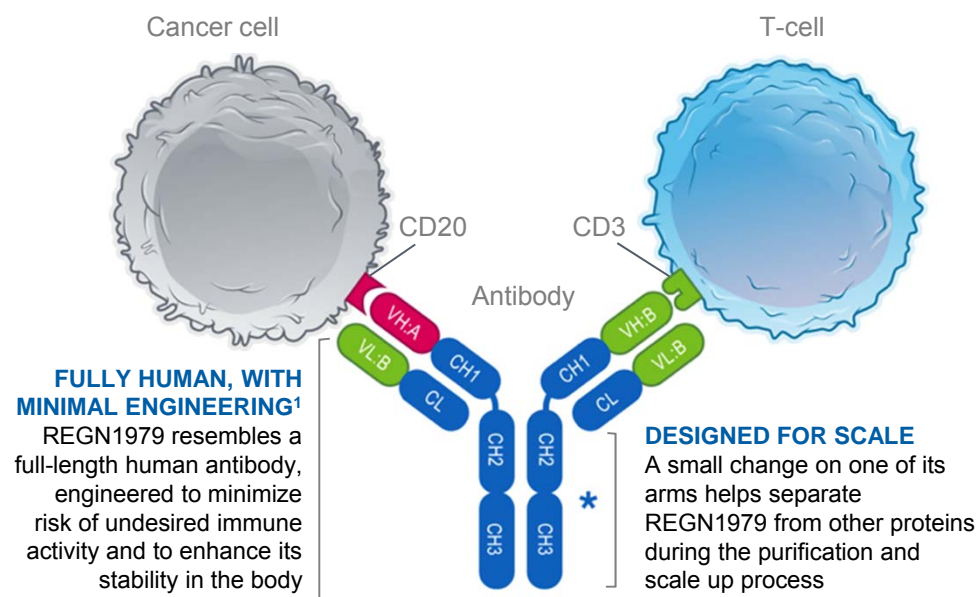
June 2018 NEJM publication details Phase 2 study results in 59 metastatic CSCC patients:

- **Primary endpoint: 47.5% Overall Response Rate (ORR)** by independent review
- **Durable Disease Control Rate (DDCR) of 61%**
- **Median duration of response and progression-free survival have not been reached**
- Cemiplimab was associated with adverse events that are similar to those seen with other PD-1 inhibitors

FDA target action date is October 28, 2018 and EU decision expected in 1Q19

<sup>1</sup>Karia PS et al. J Am Acad Dermatol. 2013;68:957–66

## CD20XCD3 BISPECIFIC ANTIBODY (REGN1979): POSITIVE DATA OBSERVED IN B-CELL MALIGNANCIES



- REGN1979 monotherapy demonstrated response rates of 50% at highest tested doses in heavily pre-treated/Rituxan-refractory NHL<sup>1,2</sup>
  - Dose escalation ongoing
  - Manageable safety profile thus far without any dose limiting toxicities
  - REGN1979 is being tested in combination with cemiplimab (anti-PD-1), which may result in enhanced anti-tumor activity<sup>2</sup>

<sup>1</sup>Bannerji R, et al. Presented at the 59th ASH Annual Meeting & Exposition. 2017. Atlanta, GA. <sup>2</sup>Topp MS, et al. Presented at the 59th ASH Annual Meeting & Exposition. 2017. Atlanta, GA.

## BROAD DEVELOPMENT PROGRAM WITH A FOCUS ON NON-SMALL CELL LUNG CANCER (NSCLC)

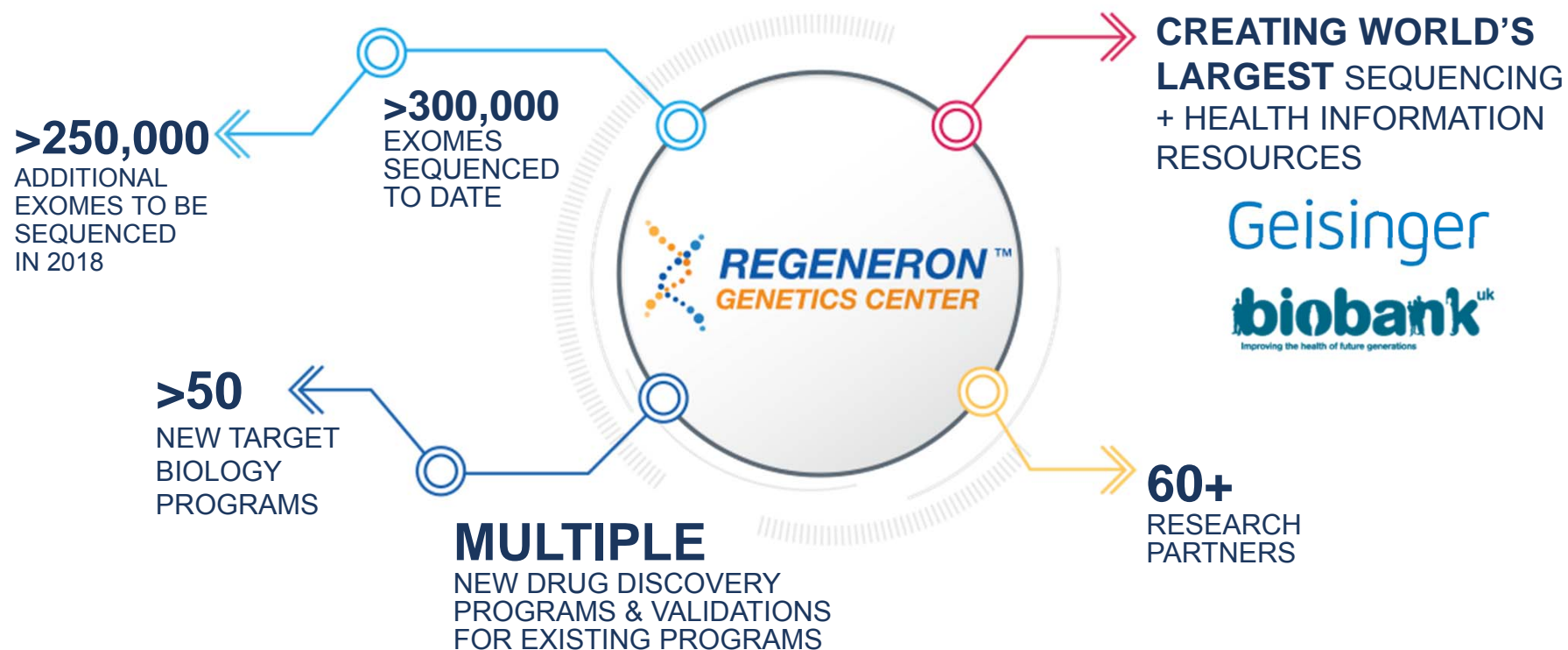
TARGET CONDITION/DISEASE	STUDY	STATUS
Advanced CSCC	Chemo naïve or experienced, monotherapy cemiplimab	Target FDA action date of Oct 28, 2018
1 <sup>st</sup> Line NSCLC $\geq$ 50% PD-L1	Monotherapy: cemiplimab vs platinum doublet	Ongoing
1 <sup>st</sup> Line NSCLC < 50% PD-L1	Chemo vs chemo+cemiplimab vs abbreviated chemo+cemiplimab+ipilumumab	Ongoing
1 <sup>st</sup> Line NSCLC $\geq$ 50% PD-L1	Pembrolizumab vs cemiplimab+ipilumumab vs cemiplimab+abbreviated chemo+ipilumumab	Ongoing
2 <sup>nd</sup> Line NSCLC	Phase 2 study with cemiplimab alone or with ipilumumab	Ongoing
Platinum-refractory cervical cancer	Phase 3 study in 2 <sup>nd</sup> line setting with cemiplimab	Ongoing

## ADDITIONAL INDICATIONS AND COMBINATIONS BEING STUDIED

TARGET CONDITION/DISEASE	STUDY	STATUS
<b>Cemiplimab combinations with candidates from collaborators</b>		
Glioblastoma	Phase 1/2 (DNA vaccines + cemiplimab; Inovio)	Ongoing
Renal Cell Carcinoma	Phase 1/2 (Oncolytic virus + cemiplimab; SillaJen)	Ongoing
Squamous Cell Carcinoma of the Head and Neck	Phase 2 (HPV-SLP vaccine + cemiplimab; ISA)	Planned
Multiple Myeloma; Solid Tumors	Phase 1/2 (anti-CD38 + cemiplimab; Sanofi)	Ongoing
Solid Tumors	Phase 1 (anti-TGFbeta + cemiplimab; Sanofi)	Ongoing
<b>Cemiplimab combinations with new REGN candidates</b>		
Anti LAG-3: Solid and Hematologic Tumors	Phase 1/2 monotherapy and with cemiplimab	Ongoing
CD20xCD3: B Cell Malignancies, NHL/CLL	Studies in monotherapy and with cemiplimab	Ongoing
MUC16xCD3: Ovarian Cancer	Phase 1/2 monotherapy and with cemiplimab	Ongoing
Anti-GITR: Solid Tumors	Phase 1/2 monotherapy and with cemiplimab	Planned
BCMAxCD3: Multiple Myeloma	Phase 1/2 monotherapy and with cemiplimab	Planned



## REGENERON GENETICS CENTER (RGC): LARGE SCALE INTEGRATION OF HUMAN GENETICS INTO DRUG DISCOVERY AND DEVELOPMENT



## LEADING A NEW LIFE SCIENCES CONSORTIUM TO BUILD AN UNPRECEDENTED, ACCESSIBLE 'BIG DATA' RESOURCE

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- RGC to sequence exomes from 500,000 people by end of 2019; data will be paired with detailed, de-identified health information
- All data will be openly available to the global research community
- Largest database of its kind may have profound impact on human health



**INVENTING  
TECHNOLOGIES  
THAT ADDRESS  
BOTTLENECKS &  
COMPLEMENT  
BIOLOGY**

