

# CORPORATE PRESENTATION



CELEBRATING

YFARS

1988-2018

### 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® (aflibercept) Injection, Dupixent® (dupilumab) Injection, Praluent® (alirocumab) Injection, Kevzara® (sarilumab) Injection, Libtayo® (cemiplimab) Injection, fasinumab, evinacumab, Regeneron's earlierstage 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, Dupixent, Praluent, Kevzara, Libtayo, fasinumab, and evinacumab; the likelihood and timing of achieving any of the anticipated milestones described in this presentation; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications: ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as EYLEA, Dupixent, Praluent, Keyzara, and Libtavo), 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 and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's products and product candidates; the availability and extent of reimbursement of the Company's products from third-party pavers, including private paver healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; 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, labeling, distribution, and other steps related to Regeneron's products and product candidates; 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; risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation proceedings relating to EYLEA. Dupixent, and 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; 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 September 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 also include the income tax effect of reconciling items. The Company makes such adjustments and other ron-GAAP measures for planning, 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 measures of financial measures of financial performance or with GAAP.

### COMBINING SCIENCE AND TECHNOLOGY TO IMPROVE PATIENTS' LIVES



## **ROBUST PIPELINE ACROSS MANY THERAPEUTIC AREAS**

	REGN5069 (GFRα3)		
	REGN4461 (LEPR agonist antibody)		
	REGN1908-1909 (Fel d 1 antibody)		
Skeletal Diseases	Trevogrumab ( <i>GDF</i> 8 antibody) + Garetosmab (Activin-A antibody)		
Oncology/IO Immunology & Inflammation	REGN4659* (CTLA-4 antibody)		
<ul> <li>Infectious Diseases</li> <li>Cardiovascular &amp; Metabolic</li> </ul>	Cemiplimab* (PD-1 antibody)		Evinacumab (ANGPTL3 antibody)
Pain Ophthalmology	REGN3767* (LAG-3 antibody)	Garetosmab (Activin-A antibody)	Alirocumab* (PCSK9 antibody)
Rare Diseases	REGN1979 (CD20xCD3 bispecific)	Cemiplimab* (PD-1 antibody)	Cemiplimab* (PD-1 antibody)
	REGN4018* (MUC16xCD3 bispecific)	REGN3500* (IL-33 antibody)	Dupilumab* (IL-4R antibody)
	REGN3048-3051 (MERS virus infection)	Dupilumab* ( <i>IL-4R antibody)</i>	Sarilumab* (IL-6R antibody)
* Program partnered with Sanofi <sup>†</sup> Program partnered with Teva and Mitsubishi	REGN-EB3 <i>(Ebola virus cocktail)</i>	Sarilumab* ( <i>IL-6R antibody)</i>	Fasinumab <sup>†</sup> <i>(NGF antibody)</i>
Tanabe Pharma Corporation (Asia)	Pozelimab <i>(C5 antibody)</i>	Evinacumab (ANGPTL3 antibody)	Aflibercept (VEGF Trap)
	PHASE 1	PHASE 2	PHASE 3

#### 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	* * * * * * * * * *	EYLEA <sup>®</sup> - Approved for use in a modified every 12-week dosing schedule in wet AMD after one year of effective therapy EYLEA <sup>®</sup> - Reported positive topline Phase 3 PANORAMA results in non-proliferative DR, sBLA accepted; PDUFA date: 05/13/201 Dupixent <sup>®</sup> - Approved and launched for moderate-to-severe asthma in adolescents and adults in the U.S. Dupilumab - FDA accepted the sBLA for an expanded AD indication in adolescents (12-17 years old); PDUFA date: 03/11/2019 Dupilumab - Announced positive top-line results from both Phase 3 studies in adults with CRSwNP Dupilumab - Initiated a Phase 2/3 study in eosinophilic esophagitis (EoE), and two Phase 2 studies in grass and peanut allergy Praluent <sup>®</sup> - Approved for heterozygous familial hypercholesterolemia (HeFH) undergoing apheresis Praluent <sup>®</sup> - FDA accepted the sBLA for reduction of cardiovascular events (DYSSEY OUTCOMES study); PDUFA date: 04/28/20' Libtayo <sup>®</sup> - Approved for patients with advanced CSCC in the U.S.; EU decision expected in 1H19 Fasinumab (NGF) - Announced positive top-line results from a Phase 3 study in chronic pain from osteoarthritis of the knee or hip REGN3500 - Initiated Phase 2 study in asthma and COPD 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 - antibody to GFRα3	19
COMMERCIAL PROGRESS	* * * *	EYLEA - 3Q18 U.S. net sales of \$1022MM Dupixent <sup>®</sup> - ~17% increase in total prescriptions from Q218 to Q318 Dupixent <sup>®</sup> - Approved and launched for moderate-to-severe asthma in adolescents and adults in the U.S. Libtayo <sup>®</sup> - Approved for patients with advanced CSCC in the U.S.; EU decision expected in 1H19	
ADVANCES IN GENETICS	✓ ✓	Formed consortium to accelerate the sequencing of 500,000 exomes from the U.K. Biobank; expected to be completed ahead of schedule 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	
CORPORATE PROGRESS	~	Announced acceleration and expanded investment for dupilumab and cemiplimab development programs	
REGENE	'RQ	<b>N</b> 5	

# **EYLEA® (AFLIBERCEPT) INJECTION**



#### 3Q18 Sales:

- U.S. EYLEA® net sales of \$1022MM
- Ex-U.S. EYLEA® net sales of \$655MM<sup>†</sup>

#### Clinical and Regulatory Updates:

- Positive topline data from Phase 3 PANORAMA study in diabetic retinopathy reported, sBLA submitted (PDUFA date May 13, 2019)
- Approved for use in a modified 12-week dosing schedule after one year of effective therapy
- sBLA resubmission for EYLEA ® pre-filled syringe expected in the first half of 2019, on track for an expected 2019 launch

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

<sup>†</sup> 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): ATOPIC DERMATITIS LAUNCH CONTINUES TO PROGRESS WELL



#### Atopic Dermatitis

- Underlying demand for Dupixent remains strong
  - Total prescriptions up ~17% sequentially from 2Q18 to 3Q18\*
  - On average, ~550 new patients/week are dispensed drug\*
- Patient refill rate and persistence rates remain high

\*Prescription data as of 3Q financial and operating results release



Source: IQVIA

### DUPIXENT<sup>®</sup>: NOW APPROVED FOR ADULTS AND ADOLESCENTS WITH MODERATE-TO-SEVERE ASTHMA

- A highly differentiated biologic for the treatment of asthma
- Approved for two types of patients:
  - Moderate-to-severe disease within eosinophilic phenotype
  - Oral corticosteroid (OCS) required to manage disease
- Only asthma biologic that offers self-administration
- ~775,000 to 900,000 adult and adolescent patients in the U.S. with moderate-to-severe asthma have uncontrolled symptoms despite SOC and may be suitable for treatment with a biologic
  - Currently, only ~11% of these patients are treated with a biologic
  - ~25%-30% of these patients are OCS-dependent

FDA approved for asthma on October 20, 2018; launch underway



### LIBTAYO<sup>®</sup>(CEMIPLIMAB-RWLC): NOW APPROVED FOR PATIENTS WITH ADVANCED CSCC

- Libtayo (PD-1 antibody) is the first FDA-approved treatment for patients with advanced Cutaneous Squamous Cell Carcinoma (CSCC) advanced CSCC who are not candidates for curative surgery or curative radiation
- CSCC results in ~4,000 to 8,000 deaths/year in US<sup>1</sup> (compared to 9,700 deaths from melanoma)





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 approved on September 28, 2018; EU decision expected in 1H19

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



## **IMPORTANT PIPELINE ADVANCES**



\* Regulatory application submitted

† Programs in Phase 2 or Phase 3 development



# **SELECT MILESTONES: NEXT 12 MONTHS**

EYLEA (aflibercept)	FDA decision on sBLA for the treatment of diabetic retinopathy (PDUFA date of May 13, 2019) Re-submission of Prior-Approval Supplement (PAS) for pre-filled syringe Initiate a study of higher dose formulations of aflibercept
Dupixent (dupilumab)	FDA decision on sBLA for expanded atopic dermatitis indication in adolescent patients (12–17 years of age) (PDUFA date of March 11, 2019) EMA decision on regulatory application for asthma Submit sBLA for CRSwNP Initiate Phase 2/3 program in COPD
Praluent (alirocumab)	FDA (PDUFA date of April 28, 2019) and EMA decisions on applications for cardiovascular risk reduction FDA decision on sBLA for first-line treatment of hyperlipidemia (target action date of April 29, 2019)
Kevzara (sarilumab)	Initiate Phase 3 study in giant cell arteritis
Libtayo (cemiplimab)	Regulatory agency decision for advanced CSCC in the EU Continue patient enrollment in NSCLC and various other studies Initiate additional studies in various indications
Fasinumab (anti-NGF)	Continue patient enrollment in Phase 3 long-term safety study and Phase 3 efficacy studies in osteoarthritis
REGN3500 (anti-IL-33)	Initiate Phase 2 study in atopic dermatitis
Bispecific Antibodies	Initiate Phase 2 study for REGN1979 (CD20xCD3) in follicular lymphoma Initiate Phase 2 study for REGN1979 (CD20xCD3) in diffuse large B-cell lymphoma (DLBCL) Submit Investigational New Drug Application (IND) for BCMAxCD3

### DIABETIC EYE DISEASES PRESENT IMPORTANT OPPORTUNITIES FOR EYLEA

### **Diabetic Macular Edema (DME)**

### **Diabetic Retinopathy (DR)**

Characterized by <u>visual loss</u> due to edema or swelling in the most important part of the retina Characterized by vascular abnormalities that <u>can lead to profound vision loss</u>, by causing edema, hemorrhage, or vascular proliferation



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





### 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 panretinal photocoagulation (laser) therapy, which was inferior to EYLEA in the CLARITY study
- Positive topline results in Phase 3 NPDR trial (PANORAMA)
  - The trial met its 52-week primary endpoint: 80% and 65% of EYLEA-treated patients (Q8W and Q16W after initial monthly dosing, respectively) experienced a twostep or greater improvement from baseline on the Diabetic Retinopathy Severity Scale (DRSS), compared to 15% of patients receiving sham injection (p<0.0001)</li>
  - o There were no new safety signals in the trial



sBLA accepted for the treatment of diabetic retinopathy -- PDUFA date: May 13, 2019

<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>



#### 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

# ODYSSEY OUTCOMES DETAILED RESULTS PUBLISHED IN NEJM: PRALUENT<sup>®</sup> SIGNIFICANTLY REDUCES MACE BY 15%



The NEW ENGLAND JOURNAL of MEDICINE



- ODYSSEY met its primary endpoint, showing that Praluent® reduced the risk of major adverse cardiovascular events (MACE) in patients with an acute coronary syndrome (ACS)
  - MACE occurred in 903 patients (9.5%) in the Praluent group vs 1,052 patients (11.1%) in the placebo group (HR 0.85; p<0.001)</li>
- Praluent was associated with a 15% lower risk of death from any cause
  - 3.5% patients in the Praluent group vs 4.1% patients in the placebo group (HR 0.85; p<0.001)</li>
- AHA 2018: Mortality risk reduction greater in patients treated for at least 3 years or those with baseline LDL-C levels of at least 100 mg/dL

Composite Primary Endpoint Met -- Praluent Reduced Risk of MACE compared to placebo<sup>1</sup>



FDA action date on April 28, 2019

<sup>1</sup>Schwartz GG, et al; Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 7



# 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



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



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



- Within the IL-6 subcutaneous class Kevzara now has 42% dispensed NBRx share and 20% share of TRx<sup>1</sup>
- FDA approved single-dose pre-filled pen, the only IL-6 inhibitor with an auto-injector device
  - Button-free auto-injector with ergonomic features (comfortable grip and circular cap) to enhance patient convenience in RA
  - Phase 3 studies in additional indications:
    - Initiated Polymyalgia Rheumatica (U.S. prevalence ~711,000)<sup>2</sup>
  - Planned Giant Cell Arteritis (U.S. prevalence >228,000)<sup>2</sup>

<sup>1</sup>Source: IQVIA; \*Prescription data as of Nov 6, 2018 (3Q financial and operating results release)

<sup>2</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 CEMIPLIMAB AND DUPILUMAB DEVELOPMENT PROGRAMS

- 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 immunooncology 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 conducted in asthma and chronic obstructive pulmonary disease (COPD); expected in atopic dermatitis
  - Funding pursuant to existing antibody collaboration with Sanofi

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

Non-GAAP Unreimbursed R&D	\$1,190MM - \$1,225MM
Non-GAAP SG&A	\$1,330MM - \$1,370MM
Sanofi Collaboration Revenue: Reimbursement of Regeneron Commercialization-Related Expenses	\$430MM - \$455MM
Effective Tax Rate	11%-13%
Capital Expenditures	\$360MM - \$390MM

<sup>1</sup> As of November 6, 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.



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



Phase 2 study in grass allergy initiated in 2Q18 Phase 2 study in peanut allergy initiated in 3Q18 Phase 2 studies in co-morbid allergic disorders and COPD planned

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

#### **ADOLESCENTS (AGES 12-17 YEARS)**





 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 SAEs or events leading to discontinuation in the treatment group

#### FDA action date on March 11, 2019

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

REGENERON

#### **PEDIATRICS (AGES 6 MONTHS TO 11 YEARS)**

- AD prevalence is ~10% in 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
  - In children between 6 months and 5 years

<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

# **REGN3500 (IL-33) CLINICAL DEVELOPMENT UNDERWAY**

- Role of IL-33 in respiratory disease has been validated by genetic associations (Regeneron Genetics Center<sup>®</sup>)
  - 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 1Q18 and Phase 2 study in COPD initiated in 2Q18; further studies planned in atopic dermatitis<sup>\*</sup>

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



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

- 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, we 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. 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 (GDF8) + GARETOSMAB (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
	Ν	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>
	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/REGN2477 (anti-Activin A) to trevogrumab/REGN1033 (anti-GDF8) 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 REGN3767 REGN4659 (Anti-PD-1) (Anti-LAG-3) (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

#### **BISPECIFIC ANTIBODIES**

that can bind two different molecular targets,

allowing for diverse approaches to targeting and

killing cancer cells

**REGN1979** 

**OTHER MODALITIES** 



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



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

#### 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/Rituxanrefractory NHL<sup>1,2,3</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>
  - Updated data to be presented at ASH on Dec 1, 2018<sup>3</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. <sup>3</sup>Bannerji R, et al. 60th ASH Annual Meeting & Exposition Abstract. 2018. San Diego, CA

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

TARGET CONDITION/DISEASE	STUDY	STATUS
Advanced CSCC	Chemo naïve or experienced, cemiplimab monotherapy	Approved in the U.S. EU approval exp. 1H19
1 <sup>st</sup> Line NSCLC ≥ 50% PD-L1	Cemiplimab monotherapy vs platinum doublet	Ongoing
1 <sup>st</sup> Line NSCLC < 50% PD-L1	Chemo vs cemiplimab+chemo / cemiplimab+abbreviated chemo+ipilimumab	Ongoing
1 <sup>st</sup> Line NSCLC ≥ 50% PD-L1	Pembrolizumab vs cemiplimab+ipilimumab / cemiplimab+abbreviated chemo+ ipilimumab	Ongoing
2 <sup>nd</sup> Line NSCLC	Cemiplimab monotherapy / +ipilimumab	Ongoing
2 <sup>nd</sup> Line cervical cancer	Cemiplimab monotherapy vs chemo (Phase 3)	Ongoing
Advanced BCC	Cemiplimab monotherapy (potentially pivotal)	Ongoing



### **ADDITIONAL INDICATIONS AND COMBINATIONS BEING STUDIED**

TARGET CONDITION/DISEASE	STUDY	STATUS				
Cemiplimab combinations with candidates from collaborators						
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-TGF $\beta$ + cemiplimab; Sanofi)	Ongoing				
Cemiplimab combinations with new REGN candidates						
Anti-LAG-3: Solid and Hematologic Tumors	Phase 1 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				
BCMAxCD3: Multiple Myeloma	Phase 1/2 monotherapy and with cemiplimab	Planned				
Anti-GITR: Solid Tumors	Phase 1/2 monotherapy and with cemiplimab	Planned				

#### 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.

### **REGENERON GENETICS CENTER:** UNPRECEDENTED SPEED, SCALE & INTEGRATION



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

- RGC to sequence exomes from 500,000 people well ahead of schedule; 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





# **COLLABORATING TO ADVANCE SCIENCE AND MEDICINE**



INVENTING TECHNOLOGIES THAT ADDRESS BOTTLENECKS & COMPLEMENT BIOLOGY

