## J.P. Morgan Healthcare Conference

JANUARY 13, 2025

### **REGENERON**<sup>®</sup>

This non-promotional presentation contains investigational data as well as forward-looking statements; actual results may vary materially.

J.P. Morgan Healthcare Conference 2025

## **Strategy & Business Update**



### Leonard S. Schleifer, MD, PhD

Co-Founder, Board Co-Chair, President & Chief Executive Officer



## Note regarding forward-looking statements

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 products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products") and product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation EYLEA HD® (aflibercept) Injection 8 mg, EYLEA® (aflibercept) Injection, Dupixent® (dupilumab) Injection, Libtayo® (cemiplimab) Injection. Praluent<sup>®</sup> (alirocumab) Injection, Kevzara<sup>®</sup> (sarilumab) Injection, Evkeeza<sup>®</sup> (evinacumab) Injection, Veopoz<sup>™</sup> (pozelimab) Injection, Ordspono<sup>™</sup> (odronextamab), itepekimab, fianlimab, garetosmab, linvoseltamab, Regeneron's other oncology programs (including its costimulatory bispecific portfolio), REGN5713-5715, nexiguran ziclumeran (Nex-z, NTLA-2001), REGN1908-1909, mibavademab. DB-OTO, Regeneron's and its collaborators' earlier-stage programs, and the use of human genetics in Regeneron's research programs; the likelihood and timing of achieving any of the anticipated milestones discussed or referenced in this presentation; safety issues resulting from the administration of Regeneron's Products and Regeneron's Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, such as those listed above; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; ongoing regulatory obligations and oversight impacting Regeneron's Products, 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 Regeneron's Product Candidates: competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates (including biosimilar versions of Regeneron's Products); uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) or recommendations and guidelines from governmental authorities and other third parties on the commercial success of Regeneron's Products and Regeneron's Product Candidates; Regeneron's ability to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; the availability and extent of reimbursement of Regeneron's Products from third-party payors, including private payor healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicarid; coverage and reimbursement determinations by such payors and new policies and procedures adopted by such payors; unanticipated expenses; the costs of developing, producing, and selling products; Regeneron's ability to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi and Bayer (or their respective affiliated companies, as applicable), to be cancelled or terminated; the impact of public health outbreaks, epidemics, or pandemics (such as the COVID-19 pandemic) on Regeneron's business; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA), other litigation and other proceedings and government investigations relating to the Company and/or its operations (including the pending civil proceedings initiated or joined by the U.S. Department of Justice and the U.S. Attorney's Office for the District of Massachusetts), the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. 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. Any forwardlooking 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 or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

## Driven by science and innovation

## **REGENERON** SCIENCE TO MEDICINE®

Differentiated technology platforms have delivered 4 'blockbuster' products discovered by Regeneron



For Intravitreal Injection



Unprecedented research and discovery capabilities drive best-in-class pipeline of ~40 product candidates

 Includes many near-term opportunities with potential to address therapeutic categories expected to exceed an aggregate of \$220 billion in 2030

Regeneron Genetics Center<sup>®</sup> has created the **world's largest DNA sequence-linked healthcare database**. Largescale proteomics-linked database underway

 For drug discovery and development as well as healthcare analytics and management

## Driving long-term shareholder value creation

## **1** Continued strong execution across our in-line brands

**DUPIXENT Dupixent** now treating over 1 million patients worldwide across 7 approved indications, with new indications expected in 2025

COPD launch underway; potential U.S. launches for CSU and BP in 2025

EYLEA HD + EYLEA U.S. net product sales grew 1%\* in 2024
 EYLEA HD pre-filled syringe submission completed; mid-2025 launch planned
 2<sup>nd</sup> year of PHOTON and PULSAR data under FDA review (April 20 PDUFA)
 EYLEA HD FDA submissions for RVO and Q4W dosing planned for Q1 2025

**VIBTAYO** LIBTAYO to be Regeneron's fourth 'blockbuster' product

• First immunotherapy to demonstrate statistically significant disease free survival benefit in high-risk adjuvant CSCC

2 Advancing our differentiated pipeline

> Potential best-in-class opportunities across large and growing therapeutic categories

3 Positioning for the future with genetics, proteomics, & targeted medicine

> Expanding the world's largest DNA sequence-linked healthcare database and empowering it with large-scale proteomics to prepare for the future of healthcare analytics & management



## Continued growth and expansion in multiple Type 2 indications

Q3 2024 Dupixent global net sales of \$3.8B (+23% YoY), annualizing at over \$15 billion

>1 million patients on therapy globally

Approved in <u>SEVEN</u> indications globally

Chronic spontaneous urticaria sBLA resubmitted (PDUFA April 18)

Bullous pemphigoid sBLA submitted in Q4 2024 (pending FDA acceptance)

Driving growth through increased penetration of biologic-eligible patients across all indications





## **COPD** launch underway in U.S.

Dupixent approved by FDA in late September 2024 as an add-on maintenance treatment of adult patients with inadequately controlled COPD and an eosinophilic phenotype

- Potential to address ~300,000 patients in the U.S.
- **Top commercial and Medicare payers** authorized Dupixent coverage "to label" within first 90 days of approval
- 2025 <u>Global initiative for Chronic Obstructive Lung Disease</u> (GOLD) guidelines include Dupixent as the only biologic recommended as treatment for COPD patients who continue to experience exacerbations after optimized inhaled therapy
- Launch efforts focused on increasing awareness of Type 2 inflammation in COPD among physicians and patients to drive momentum in 2025



#### \*Based on preliminary, unaudited results.

8

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# EYLEA HD + EYLEA remained the U.S. anti-VEGF category leader in 2024

## Goal to establish EYLEA HD as new standard of care for retinal diseases

- Q4 2024 U.S. net product sales of \$305M\*
- FY 2024 U.S. net product sales of \$1.20B\* comprised 20% of FY 2024 EYLEA + EYLEA HD net sales

# EYLEA remains #1 anti-VEGF treatment for retinal diseases

- Q4 2024 U.S. net product sales of \$1.19B\*
- FY 2024 U.S. net product sales of \$4.77B\*



**EYLEAHD**°

(aflibercept) Injection 8 mg





## **Strengthening EYLEA HD product profile in 2025**

Delivering key enhancements to EYLEA HD product offering to further unlock ongoing launch



- Best-in-class efficacy and durability profile provide potential to become the new standard-of-care for retinal diseases
- · Safety profile consistent with the established safety profile of EYLEA
- Long-term data from PHOTON and PULSAR extension studies and real-world experience continue to support differentiated profile

#### Planned for 2025

#### **Convenient Administration**

- Pre-Filled Syringe (PFS) submission completed; <u>U.S.</u> launch anticipated by mid-2025
- Same PFS device approved in Europe in 2024
- Strong physician preference; 95% of EYLEA administered via PFS

#### Addressing More Retinal Diseases

- Positive Phase 3 data in retinal vein occlusion (RVO) announced in December 2024
- RVO was ~17% of EYLEA sales in 2024
- sBLA submission in Q1 2025

### Extended Dosing Intervals

- 2<sup>nd</sup> year of PHOTON and PULSAR data under FDA review (April 20 PDUFA)
- Potential to offer wAMD and DME patients the longest dosing interval (up to every-24-week dosing) of any approved anti-VEGF therapy

#### Maximizing Dosing Flexibility

 <u>sBLA submission in Q1</u> <u>2025</u> for every-4-week dosing (Q4W) for wAMD, DME, and DR indications

Opportunity for EYLEA HD to have broadest indication set with greatest dosing flexibility in anti-VEGF category



## Key growth driver and foundational to oncology portfolio

LIBTAYO to become Regeneron's next internally-discovered drug to reach >\$1B in annual net sales

### Strong and consistent growth

- WW net sales \$850M through 9 months of 2024 (+36% YoY)
- Expanding global commercial footprint



- One of two PD-1 antibodies FDA-approved for use in combination with chemotherapy irrespective of histology or PD-L1 expression levels
- Continuing to grow market share in monotherapy
   and in combination with chemotherapy



Leading anti-PD-1/L1 therapy in advanced CSCC and BCC

Advanced CSCC

First and only immunotherapy to show a statistically significant disease-free survival benefit in high-risk CSCC in the adjuvant setting (KEYTRUDA<sup>®</sup> failed in this setting)



Prior to July 1, 2022, Sanofi recorded net product sales of Libtayo outside the United States. Included in these amounts for the years ended December 31, 2023 and 2022 is approximately \$6 million and \$34 million, respectively, of net product sales recorded by Sanofi in connection with sales in certain markets outside the United States (Sanofi recorded net product sales in such markets during a transition period).

# Differentiated pipeline opportunities to potentially address categories expected to exceed \$220 billion annually in 2030

Category	Product	Anticipated Launch Year	Indication(s)	Value Proposition
Eosinophilic COPD	Dupixent	2024	COPD with Type 2 inflammation	First and only biologic approved for eosinophilic COPD
COPD in former smokers	itepekimab	2026	COPD in former smokers	Potential first-in class opportunity to address up to 1 million former smokers with COPD globally
Non-melanoma skin cancers	Libtayo	2025-2026	Adjuvant CSCC	First and only immunotherapy to show a statistically significant DFS benefit in high-risk adjuvant CSCC
Solid tumors	fianlimab + Libtayo	2026 (Melanoma)	Melanoma, NSCLC, HNSCC	Emerging as a potentially differentiated treatment option in multiple solid tumors
Myeloma	linvoseltamab	2025 (3L+ MM only)	Multiple myeloma & pre-cursor conditions	Potentially best-in-class BCMA bispecific to disrupt current treatment paradigm in earlier lines
Lymphoma	odronextamab	2025 (3L+ FL only)	FL, DLBCL	Potentially best-in-class CD20 bispecific (in FL) to disrupt current treatment paradigm in earlier lines
Complement- mediated diseases	pozelimab + cemdisiran	2027 (gMG)	gMG, PNH, GA	Complete inhibition of C5 has potential to improve efficacy and convenience
Anticoagulants	REGN7508 & REGN9933	2028	Coagulation disorders	Potential to improve efficacy and safety relative to current standards of care
Obesity	trevogrumab ± garetosmab	2028	Obesity, T2DM	Potential to improve quality of weight loss when combined with GLP-1 therapy
Food allergy treatment	Dupixent + linvoseltamab	TBD	IgE-mediated food allergies	Groundbreaking approach to potentially reverse severe food allergy

J.P. Morgan Healthcare Conference 2025

## **Research & Pipeline Update**



### George D. Yancopoulos, MD, PhD

Co-Founder, Board Co-Chair, President & Chief Scientific Officer



## **Regeneron: A History of Relentless Innovation**

Technological breakthroughs yield turnkey platforms that repeatedly deliver practice-changing medicines



### **Technological Breakthroughs Have Delivered Commercial Blockbusters**

- 12 FDA-approved or authorized medicines\*, including 4 internally-discovered 'blockbusters'
- Pipeline of ~40 product candidates with significant commercial potential spanning many therapeutic areas
- World's largest and most diverse DNA sequence-linked healthcare database, for drug discovery and development, as well as healthcare analytics and management

### Next Generation of Technological Breakthroughs Delivering Future Opportunities

- Silencing pathological genes in brain with siRNAs
- Combining antibodies with siRNAs
- Validating and combining two classes of bispecifics (xCD3s and xCD28s)
- · Combining bispecifics with immune-regulating antibodies
- Using CRISPR to silence genes in the liver and correct genetic deficiencies
- Restoring hearing in profoundly deaf children

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## Key 2025 clinical milestones to drive long-term shareholder value

**Opportunity to address areas of high unmet need in large commercial categories** 



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# Itepekimab (IL-33): Regeneron's next innovation in COPD with pivotal results anticipated in 2H 2025

Building upon Dupixent's clinical success, potential for benefit in broader COPD population

RGC. Regeneron Genetics Center Our RGC found that IL-33 is genetically linked to COPD and asthma via risk-increasing variants and protective loss-of-function variants

IL-33 Loss-of-Function Protects From COPD (~20% Decreased Risk) and Gain of Function Increases Risk (Up to ~10% Increased Risk)

GOF genotypes that increase IL-33 signaling are associated with higher risk of COPD

LOF genotype that decreases IL-33 signaling is associated with lower risk of COPD



Phase 2 study showed overall reduction in exacerbations; post-hoc analysis informed Phase 3 trial design

Phase 3 AERIFY studies passed interim futility analysis in 2023; results expected in 2H 2025





# Regeneron's oncology strategy: Using the immune system to defeat cancer with 5 classes of immunomodulatory agents

Regeneron has clinically validated these first 3 classes, several with potentially best-in-class clinical efficacy



### **Earlier-stage Programs**



- REGN has clinically validated the first 3 classes
- Can be used across multiple tumor types and in combination

### Indication areas of focus

Hematological Lymphomas, Myelomas, Myeloid malignancy

Lung Cancer NSCLC; potential for SCLC

Dermato-Oncology CSCC; BCC; Melanoma

**Genitourinary** Prostate; RCC; potential for bladder

**Gyn-Onc** Ovarian; endometrial; cervical

GI CRC; esophageal / gastric; HCC HNSCC

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## Unique flexibility of internally-developed oncology pipeline drives potential for novel and differentiated combinations



This slide contains investigational drug candidates that have not been approved by any regulatory authority.

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# First immunotherapy to show statistically significant benefit in DFS in high-risk adjuvant Cutaneous Squamous Cell Carcinoma (CSCC)

## LIBTAYO (anti-PD1) in CSCC

LIBTAYO's leading position in metastatic CSCC, together with the recent failure of KEYTRUDA® in adjuvant CSCC, position Regeneron for continued leadership in non-melanoma skin cancer



#### **Primary Endpoint:**

#### **Disease Free Survival (DFS)** Time from randomization to disease recurrence or death

#### **Secondary Endpoints:**

- Freedom from
   locoregional recurrence
- Freedom from distant metastases
- Cumulative occurrence of Second Primary Tumors (SPTs)
- Overall Survival (OS)
- Safety and tolerability
- PK and Immunogenicity



## **Topline Results**

At the first pre-specified interim analysis for DFS, adjuvant LIBTAYO demonstrated a 68% reduction in the risk of disease recurrence or death, compared to placebo

HR: 0.32 (0.20, 0.51) p < 0.0001

Safety profile generally consistent with what has been established in other cemiplimab monotherapy studies

Anticipate presenting full results at a medical meeting this year

Global regulatory submissions planned for this year

## Combining two potentially best-in-class checkpoint inhibitors: Fianlimab (anti-Lag3) & LIBTAYO (anti-PD1) in 1L metastatic melanoma\*

### Emerging as potentially differentiated treatment option for 1L metastatic melanoma

Table depicts randomized Phase 3 data for four FDA-approved treatments as well as pooled, post-hoc data from three independent cohorts from initial trial of fianlimab + cemiplimab; there are no randomized, head-to-head clinical trials between these products. Study data being provided for descriptive purposes only. Caution is advised when drawing conclusions based on cross-trial comparisons.



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\*This slide contains data for the unapproved combination fianlimab + cemiplimab. All other products listed are FDA-approved therapies. There are no randomized, head-to-head clinical trials between these products. Study data being provided for descriptive purposes only. Caution is advised when drawing conclusions based on cross-trial comparisons.

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# Advancing Fianlimab (anti-Lag3) & LIBTAYO (anti-PD1) combination in Melanoma and across several solid tumor cancers

Combining two potentially "best-in-class" checkpoint inhibitors: Fianlimab (anti-LAG-3) & LIBTAYO (cemiplimab, anti-PD-1) – potential for differentiated efficacy and safety vs. current standard-of-care

		Phase 1 Phase 2	Phase 3	
	1L Metastatic Melanoma (vs. pembrolizumab)	Enrolling – Pivotal data in 2H	2025	Dual LAG-3 and PD-1 blockade may
Melanoma	1L Metastatic Melanoma (vs. nivolumab+relatlimab)	Enrolling		provide enhanced immune activation vs. anti-PD-1 alone
	Adjuvant Melanoma	Enrolling		ALL WILL
	Perioperative Melanoma	Enrolling		RECN7767 (Anti-LAG-3) LAG-3 pMIC I
NSCLC	Advanced NSCLC	Enrolling – Initial data 1H25		APC PAHC II RE-ACTIVATED T-CELL DUING CANCER CELL
	Perioperative NSCLC	Enrolling		
	Perioperative HCC	Enrolling		(Anti-PD-1) (Anti-PD-1)
Other solid tumors	1L HNSCC (PD-L1+; HPV+ and HPV-)	Initiating 2025		
	Perioperative HNSCC	Initiating 2025		

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## Pipeline of CD28 costimulatory bispecifics progressing

**Combined with:** 

		Dose Escalation	Proof-of- Mechanism	Dose Expansion	Status / Next Steps	Checkpoint Inhibitors	xCD3 bispecifics
	Nezastomig (PSMAxCD28) Prostate Cancer; RCC	Data	expected in 20	025	Enrolling monotherapy and combination cohorts	Cemiplimab	PSMAxCD3
(a) (a)	EGFRxCD28 Solid Tumors	Data	expected in 20	)25	Expansion cohorts (NSCLC, HNSCC, CSCC, CRC) in combination with cemiplimab and with chemotherapy now enrolling	Cemiplimab	
<b>M</b>	MUC16xCD28 Ovarian Cancer				Expansion cohorts in combination with cemiplimab expected to initiate in 2025; enrolling dose escalation with ubamatamab	Cemiplimab	Ubamatamab (MUC16xCD3)
<u>:</u> 0	CD22xCD28 DLBCL				Enrolling dose escalation cohorts		Odronextamab (CD20xCD3)
00	CD38xCD28 MM				Enrolling dose escalation cohorts		Linvoseltamab (BCMAxCD3)

## Regeneron's differentiated CD3 bispecifics



### ORDSPONO (odronextamab, CD20xCD3) Non-Hodgkin lymphoma (NHL)

Regeneron's first approved bispecific antibody (in EU) in relapsed/refractory (R/R) follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL)

#### 80% ORR / 73% CR in r/r FL

Highest response rate observed in the class in this late-line setting

#### Approved in Europe in 2024

Enrollment underway for confirmatory study to support BLA resubmission for FL

**BLA resubmission planned for Q1 2025** 

### LINVOSELTAMAB (BCMAxCD3) Multiple myeloma (MM)

Linvoseltamab has the potential to be the best-in-class BCMAxCD3 bispecific with its differentiated clinical profile, dosing, and administration

### 71% ORR / 50% CR in r/r MM<sup>+</sup>

Nearly double the CR rate of other bispecifics at similar follow-up

Third-party fill/finish manufacturer currently in compliance

#### BLA recently resubmitted: FDA approval anticipated by mid-2025

Differentiated Phase 3 programs in earlier lines of therapy using monotherapy and novel combinations underway for both ORDSPONO and linvoseltamab

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## **Broad ORDSPONO phase 3 program currently enrolling** patients, including in earlier lines of FL and DLBCL



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Monotherapy efficacy in late lines supports differentiated approach using monotherapy and novel combinations in earlier lines

	Line of therapy U.S. treated population	Study	Phase 1	Phase 2	Phase 3		
	Third line+ ~1,900	<b>ELM-2</b> * (odro mono, pivotal)	Phase 2				
Follicular Lymphoma Incidence: U.S. ~13,100 WW ~120,000	Second line ~4,100	<b>OLYMPIA-5</b> * (odro-lenalidomide vs. rituximab-lenalidomide)	Phase 3			Now approved in Europe	
	<b>First line</b> ~11,300	OLYMPIA-1 ( <u>odro mono v</u> s. R-CHOP)	Phase 3			RI A resubmission for D/D EI	
	First line ~11,300 OLYMPIA-2 (odro-chemo vs. R-chemo)		Phase 3			planned for Q1 2025	
	Third line+ ~3,600	<b>ELM-2</b> * (odro mono, pivotal)	Phase 2				
DLBCL		ATHENA-1 (odro-CD22xCD28)	FIH, Phase 1			Exploring differentiated combinations (with CD22xCD28)	
Incidence: U.S. ~31,000 WW ~163,000		CLIO-1 (odro-cemiplimab)	Phase 1				
	Second line ~8,600	OLYMPIA-4 (odro vs. SOC)	Phase 3			Advancing to carlier	
	<b>First line</b> ~27,000	OLYMPIA-3 (odro-CHOP vs. R-CHOP)	Phase 3			lines of therapy	

Incidence - new cases diagnosed annually.

23 \* Also investigating patients with marginal zone lymphoma (MZL)

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# Recent data from safety lead-in portion of Ph3 Olympia-1 Trial >>>Odronextamab monotherapy: 12 of 12 complete responses in 1L FL



Unprecedented ORR in late-line setting provides confidence for monotherapy approach in earlier lines; Phase 3 OLYMPIA-1 trial designed to explore novel, chemotherapy-free, fixed-duration treatment in an outpatient setting in 1L FL



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# Within the BCMA bispecific class, linvoseltamab emerging with differentiated and compelling clinical profile in r/r multiple myeloma

There are no randomized, head-to-head clinical trials between these products. Study data being provided for descriptive purposes only. Caution is advised when drawing conclusions based on cross-trial comparisons.



25 \* Data source: Jagannath, S. Linvoseltamab, a B-cell maturation antigen-targeted T-cell-engaging bispecific antibody in patients with relapsed or refractory multiple myeloma, including difficult-to-treat subgroups, AACR 2024 \$US PI as of April 2024 † Per Protocol. ‡ 30-min as long as patient tolerability allows; discretion at Day 8.

#### This slide contains investigational drug candidates that have not been approved by any regulatory authority.

## Broad linvoseltamab development program to evaluate monotherapy and simplified combinations in earlier stages of disease

Unprecedented late-line responses rates provide confidence to explore monotherapy and novel combinations in earlier disease settings to simplify treatment approaches

		U.S. treated population	Study	Phase 1	Phase 2	Phase 3		
			LINKER-MM3 <sup>§</sup> (Linvo vs. EPd)	Phase 3				
Multiple Myeloma	<b>A4</b> 1.1 1	Third line+ ~4,000 in 4L+/ ~8,000 in 3L	LINKER-MM1 (Linvo mono)	FIH/Phase 1	/2		BLA resubmitted, app anticipated by mid-2	proval 025
	Multiple Myeloma		(Linvo + CD38xCD28)	FIH/Phase 1	/2		Exploring differentia	ted
	U.S. ~35,000 WW >176,000	Second line ~16,000	LINKER-MM2 (cohorts of Linvo + SOC / novel therapies)	Phase 1			combinations (with C	CD38xCD28)
		<b>First line</b> ~30,000	LINKER-MM4 (Linvo mono)	Phase 1/2			Advancing to earlier	
			Studies in maintenance, transplant ineligible, transplant eligible	Phase 3s pla	anned		lines of therapy	
	Multiple Myeloma	High Risk (HR) Smoldering MM	Study 2256 (Linvo mono)	Phase 2			U.S. Epidemiology MM Prec (clinically detected cases only, actu higher; estimates not as well-charac	cursor Conditions al population may be sterized as MM)
 (	Conditions	HR MGUS / non-HR Smoldering MM	LINKER-MGUS1 (Linvo mono)	Phase 2			HR SMM, incidence:	1,200 - 1,600
	AL Amyloidosis	Second line+	LINKER-AL2 (Linvo mono)	Phase 1/2		Non-HR SMM, incidence:	3,000 - 3,500	
	Incidence: U.S. ~4,500					HR MGUS, prevalence*:	11,000 - 19,000	

§Linvoseltamab mono vs. EPd (Elotuzumab + Pomalidomide + dexamethasone); 3L+ in the U.S.; earlier line of therapy eligible in some geographies based on regional SOC Incidence – new cases diagnosed annually. \*Prevalence provided instead of incidence as MGUS is a slow progressing disease.

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26

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# Two-pronged approach to anticoagulation offers potential for improved blood clot prevention and lower bleeding risk

Two Factor XI antibodies advancing to pivotal trials in 2025: REGN7508 (catalytic domain) and REGN9933 (A2 domain)

## Current market for thrombosis disorders:

- Existing SoC includes LMWH, DOAC's and aspirin, including \$20 billion SPAF market
- Challenges with existing SoC include:
  - Factor Xa effectively reduce thrombotic events, but carry elevated risk of bleeding
  - Utilization rate for DOAC's in SPAF is only ~50%, mainly due to bleeding risk

#### Future vision: Factor XI Ab's

- More specific inhibition of the intrinsic coagulation pathway
- Two FXI antibodies may address unmet need in thrombosis prevention, with unique profiles<sup>1</sup>:
  - REGN7508 mimics FXI deficiency: improved anticoagulation vs. SoC
- REGN9933 mimics FXII deficiency: low bleeding risk may enable broader usage

#### **Genetic data:**

- FXI deficiency<sup>2</sup>: trend toward reduced risk of MI, stroke with minimal increased bleeding risk
- FXII deficiency: no increased bleeding risk



<sup>1</sup>Based on maximal aPTT prolongation in human plasma; aPTT - activated Partial Thromboplastin Time – an assay measuring activity of the coagulation pathway; Chalothorn D, et al., THSNA 2024 poster <sup>2</sup>Sharman Moser S, et al., The Association between Factor XI Deficiency and the Risk of Bleeding, Cardiovascular, and Venous Thromboembolic Events. Thromb Haemost. 2022. doi: 10.1055/s-0041-1735971



# Regeneron's Factor XI antibodies: Potential for maximal anti-coagulation with minimal bleeding

Positive proof-of-concept data for REGN7508 (catalytic) and REGN9933 (A2) announced in December 2024



Therapy	Target	VTE Rate*	Initiation of dosing (hrs)
REGN7508	FXI (catalytic)	7%	12-24 postop
REGN9933	FXI (A2)	17%	12-24 postop
Enoxaparin	Multiple	21%	12-24 postop
Apixaban	FXa	12%	12-24 postop
Historical Control (pbo)	N/A	48% <sup>1</sup>	N/A

PoC data support advancing both antibodies into a broad Phase 3 development program in multiple coagulation disorders and in patients with different risk factors for bleeding

Phase 3 trials expected to initiate in 2025

\*Results from ROXI-VTE I (REGN9933, apixaban) and ROXI-VTE II (REGN7508); enoxaparin VTE rate pooled across both studies

<sup>8</sup> <sup>1</sup>Fuji T, Fujita S, Tachibana S, Kawai Y. A dose-ranging study evaluating the oral factor Xa inhibitor edoxaban for the prevention of venous thromboembolism in patients undergoing total knee arthroplasty. J Thromb Haemost. 2010 Nov;8(11):2458-68. doi: 10.1111/j.1538-7836.2010.04021.x. PMID: 20723033.



# Regeneron's approach to obesity: novel combinations with leading medicines aim to improve quality of weight loss

GLP-1 based therapies, such as semaglutide (sema) and tirzepatide, are emerging as standards of care for weight loss; however, up to 40% of weight loss from these agents is due to decreases in muscle mass<sup>1</sup>



proof-of-concept studies in obesity are expected in 2H 2025





#### 29 <sup>1</sup>Wilding, Diabetes Obes Metab, 2022; PMID: 35441470, <sup>2</sup> Mastaitis J, et al. Manuscript in preparation and ADA 2023 presentation, n=10 per arm; DXA: dual-energy X-ray absorptiometry measurement



This slide contains investigational drug candidates that have not been approved by any regulatory authority.

# Obesity Phase 2 study fully enrolled; primary analysis expected to read-out in 2H 2025

Phase 2 study to investigate if addition of trevogrumab (anti-myostatin) to semaglutide with and without garetosmab (antiactivin A) improves the quality of weight loss and/or improves maintenance of weight loss post semaglutide discontinuation

#### Phase 2 General Obesity Trial Design (Part B)

Randomized (1:1:1:1:1:1) double-blind, active controlled trial



### **Primary Endpoints:**

- % change in body weight from baseline at week 26
- % change in total fat mass from baseline at week 26

#### Key Secondary Endpoint:

• % change in muscle mass from baseline at week 26

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# Leveraging decades of expertise to develop a robust pre-clinical obesity and cardiometabolic pipeline

Our **first wave** of therapeutics focuses on improving GLP1-based weight loss by preserving muscle

**Goal:** To provide the best suite of antibody + GLP1 combination therapies – either as coformulations or 'unimolecular' solutions – to improve quality of weight loss and long-term health outcomes Our **next wave** of therapeutics focuses on GLP1-independent mechanisms and targeting muscle growth and improved metabolism

**Goal:** To bring next-generation muscle and/or neuro-targeted therapies (androgens, siRNAs, gene therapies) to patients as the next cornerstone of healthy weight management therapy

Opportunity to combine novel, first-in-class muscle and/or neuro-targeting agents with appropriate weight loss interventions to provide benefit to distinct patient populations

REGENERON

## Novel treatment approach for potentially reversing severe allergy: Linvoseltamab (BCMAxCD3) plus Dupixent (anti-IL4Rα)

Linvoseltamab and Dupixent regimen has the potential to eliminate IgE: potential groundbreaking approach for controlling severe allergy

- Initial Data: A 20-year-old male with mild asthma, allergic rhinitis, atopic dermatitis and multiple severe IgE-mediated food allergies with documented recurrent anaphylaxis, ER visits and hospitalizations, which have significantly impacted his quality of life
- Safety: no unexpected adverse events to-date



Induction with short course (4 doses) of lowdose linvoseltamab led to rapid and profound (~90%) reduction in IgE with combined approach

**Immunoglobulin E (IgE)** is the key driver of allergic reactions, such as food allergies; long-lived plasma cells consistently produce IgE

Clinical trial with the two-drug regimen in patients with severe food allergies is ongoing; Additional patients enrolled with data updates anticipated in 2025

## World-class Regeneron Genetic Medicines (RGM) Program

RGM builds and utilizes 'turnkey' therapeutic platforms – customizing the choice of genetics technology (siRNA, CRISPR/Cas9, etc.) based on therapeutic application

Continuing to build in-house expertise and leverage groundbreaking industry collaborations



**Alnylam:** Exclusive siRNA collaboration in eye and CNS, with liver programs in MASH and additional RGC targets

**In-House:** Developing next-generation gene therapies combining novel payloads, viral vectors and antibodies to address difficult-to-treat diseases



Intellia: Exclusive CRISPR/Cas9 gene knockdown and gene insertion in the liver and ex vivo targets

Mammoth Biosciences: Ultracompact CRISPR gene editing systems to advance *in vivo* programs in multiple tissue and cell types

REGENERON

# DB-OTO demonstrates the potential to provide hearing to deaf children (from infancy to adolescence)

DB-OTO is an AAV-based dual-vector gene therapy delivered to the inner ear to enable hearing in children

#### Gene therapy for genetic hearing loss

Potentially first-in-class, one-time treatment to enable hearing in patients born with profound deafness due to biallelic OTOF mutations

- Twelve patients between the ages of 10 months and 16 years have now been dosed with DB-OTO (3 bilaterally)
- 10 of 11 treated patients with at least one post treatment assessment have shown a notable response, with improved hearing at various dBHL thresholds
- No DB-OTO related adverse events have been recorded to date

Maturing data continues to demonstrate the potential of DB-OTO as a revolutionary treatment for children with genetic hearing loss



Behavioral pure tone audiogram - a plot of softest sounds a patient can hear in an individual ear

\*Arrows indicate no response at maximum level tested

# Our differentiated siRNA + antibody approach has the potential to address multiple complement-mediated diseases

Despite competitive markets, there is opportunity to improve upon the current standard of care with prolonged and complete inhibition of complement protein C5 (for multiple diseases)

siRNA (cemdisiran) lowers C5 target burden, allowing antibody (pozelimab) to more effectively block C5 function

		r rogram otatao
	<b>Geographic Atrophy</b> 2025 U.S. Prevalence (patients): ~1.1M Worldwide market sales* (2025e): ~\$1.0B Estimated market sales CAGR* (2025-2030): ~34%	<ul> <li>Phase 3 pivotal program initiated in 2H 2024</li> </ul>
<u> </u>	<b>Myasthenia Gravis</b> 2025 U.S. Prevalence (patients): ~90k Worldwide market sales* (2025e): ~\$5.0B Estimated market sales CAGR* (2025-2030): ~17%	<ul> <li>Study fully enrolled</li> <li>Phase 3 results expected in 2H 2025</li> </ul>
<b>^ ^ ^ </b>	Paroxysmal Nocturnal Hemoglobinuria 2025 U.S. Prevalence (patients): ~6k Worldwide market sales* (2025e): ~\$2.0B Estimated market sales CAGR* (2025-2030): ~12%	<ul> <li>Cohort A (exploratory): Updated Phase 3 data recently reported</li> <li>Cohort B (registrational): Study enrolling, data expected in 2026+</li> </ul>

**Drogram Statue** 

## Pozelimab + Cemdisiran (Poze-Cemdi) enables complete, rapid, uninterrupted and durable inhibition of terminal complement



Results from an exploratory cohort in the pivotal PNH trial; safety profile of poze-cemdi was generally consistent with approved C5 inhibitors

#### **Primary Endpoint:** % change in lactate dehydrogenase (LDH) from baseline to week 26 in PNH patients

#### More patients on Poze-Cemdi had improved control of LDH

 96% achieved adequate LDH control across study visits (weeks 8-26) on average with poze-cemdi, compared to 80% with ravulizumab

## Ravulizumab to pozelimab + cemdisiran switches

- At the start of the extension study (n=19), 68% (13 of 19) of patients taking ravulizumab had LDH ≤1.5×ULN
- After switching to poze-cemdi, all but one patient (95%; n=18) achieved LDH control during the extension study
- 4 of 5 patients previously uncontrolled on ravulizumab achieved adequate LDH control after switching to poze-cemdi



36 LDH is a well-accepted biomarker of hemolysis – with adequate control and normalization defined as ≤1.5 and ≤1.0 times ULN, respectively

#### This slide contains investigational drug candidates that have not been approved by any regulatory authority.

## **Regeneron genetic medicines pipeline**



Agreement with: \*Alnylam; †Intellia. 37 ALN-SOD is on U.S. FDA clinical hold, enrolling ex-U.S

REGENERON

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## 2025 key upcoming milestones

#### **EYLEA HD**

- RVO sBLA acceptance (1H) and FDA decision (2H)
- · Pre-filled syringe FDA decision and launch (mid)
- Addition of 2-year data in wAMD and DME to FDA label (PDUFA April 20)
- · Addition of Q4W dosing to FDA label for all indications (2H)

#### Dupixent / I&I

- Report pivotal data for itepekimab in COPD (2H); submit BLA (2H)
- Dupixent CSU FDA decision (PDUFA April 18)
- Dupixent BP sBLA acceptance (1H) and FDA decision (2H); EU submission (1H)
- Initiate additional Phase 3 studies for itepekimab (1H)
- · Report additional data for Dupixent + BCMA in severe food allergies

#### **Internal Medicine**

- Report proof-of-concept data of combination of semaglutide and trevogrumab with and without garetosmab in obesity (2H)
- Report proof-of-concept data for mibavademab with tirzepatide in obesity (2H)
- Report Phase 3 data for garetosmab in FOP (2H)

#### Solid Organ Oncology

- Submit sBLA for Libtayo in adjuvant CSCC (1H)
- Report results from Phase 3 study of fianlimab + cemiplimab vs. pembrolizumab monotherapy in 1L metastatic melanoma (2H); submit BLA pending results (2H)
- Report initial Phase 2 data for fianlimab + cemiplimab in 1L advanced NSCLC (1H)
- · Report additional data for ubamatamab (MUC16xCD3) in ovarian cancer
- Report additional data across solid tumor costimulatory bispecific programs:
  - Nezastomig (PSMAxCD28) + cemiplimab in mCRPC
  - EGFRxCD28 + cemiplimab -- dose expansion cohorts
  - MUC16xCD28 + ubamatamab in ovarian cancer

#### Hematology

- Resubmit BLA for odronextamab in R/R follicular lymphoma (Q1); FDA decision (2H)
- Resubmit BLA for linvoseltamab in R/R multiple myeloma  $\checkmark$ ; FDA decision (mid)
- Initiate Phase 3 program for Factor XI antibodies across multiple indications

#### **Genetic Medicines**

- Report additional data for DB-OTO (mid)
- Report pivotal Phase 3 data for pozelimab+cemdisiran in gMG (2H)

## Q&A



## Leonard S. Schleifer, MD, PhD Co-Founder, Board

Co-Founder, Board Co-Chair, President & Chief Executive Officer



## George D. Yancopoulos, MD, PhD

Co-Founder, Board Co-Chair, President & Chief Scientific Officer



## **REGENERON** SCIENCE TO MEDICINE®

### **OUR MISSION**

Use the power of science to repeatedly bring new medicines to people with serious diseases

Three responsibility focus areas reflect our "doing well by doing good" ethos Improve the lives of people with serious diseases

- Pipeline innovation
- Access to medicine and fair pricing
- Patient advocacy

Pharmaceutical Innovation and Invention Index 2024



### Foster a culture of integrity and excellence

- Product quality and safety
- · Diverse, healthy and engaged workforce
- · Ethics and integrity
- Responsible supply chain





#### **Build sustainable communities**

- STEM education sponsorship of top science competitions:
  - Regeneron Science Talent Search
  - Regeneron International Science and Engineering Fair
- Environmental sustainability







## **Abbreviations and Definitions**

Abbreviation	Definition
1L	First line
AAV	Adeno-associated virus
ALS	Amyotrophic lateral sclerosis
	Activated Partial
aPTT	Thromboplastin Time
BCC	Basal cell carcinoma
BCMA	B-cell maturation antigen
BLA	Biologics license application
BP	Bullous pemphigoid
CAR-T	Chimeric antigen receptor T-cell
CI	Confidence Interval
CNS	Central nervous system
	Chronic obstructive
COPD	pulmonary disease
CR	Complete response
CRC	Colorectal Cancer
CRS	Cytokine release syndrome
	Chronic sinusitis with nasal
CRSwNP	polyposis
0000	Cutaneous squamous
	Chronic spontaneous urticaria
dB HL	Decibel hearing loss
DFS	Disease-Free Survival
DLBCL	Diffuse large B-cell lymphoma
DLT	Dose-limiting toxicity
DME	Diabetic macular edema
DOAC	Direct oral anticoagulants

Abbreviation	Definition
DR	Diabetic retinopathy
DXA	Dual-energy X-ray absorptiometry
ECOG	Eastern Cooperative Oncology Grou
EGFR	Epidermal growth factor receptor
FIH	First in human
FL	Follicular lymphoma
	Follicular Lymphoma
FLIPI	International Prognostic Index
GA	Geographic atrophy
GAA	Alpha glucosidase
	Groupe d'Etude des
GELF	Lymphomes Folliculaires
GI	Gastrointestinal
GIP	Gastric inhibitory polypeptide
GLP-1	Glucagon-like peptide 1
gMG	Generalized myasthenia gravis
GOF	Gain of function
нсс	Hepatocellular carcinoma
НСР	Healthcare Provider
	Head and neck squamous
HNSCC	cell carcinoma
HPV	Human Papillomavirus
HR	Hazard Ratio
HTT	Huntingtin
	Immune effector cell-
ICANS	associated neurotoxicity syndrome
lgE	Immunoglobulin-E
IND	Initial new drug application

Abbreviation	Definition	Z
KM	Kaplan-Meier curve	1
LAG-3	Lymphocyte-activation gene 3	_
LDH	Lactate dehydrogenase	I
LEPR	Leptin receptor	
LMWH	Low molecular weight heparin	1
LOF	Loss of function	_
	Microtubule-associated	_
MAPT	protein tau	I
	Metabolic Dysfunction-Associated	
MASH	Steatohepatitis	1
	Metastatic castration-resistant	
mCRPC	prostate cancer	i
	Monoclonal gammopathy of	-
MGUS	unknown significance	
MM	Multiple myeloma	-
mOS	Median overall survival	-
mPFS	Median progression-free survival	-
MUC16	Mucin 16	_
NAFLD	Non-alcoholic fatty liver disease	_
NE	Not Estimable	_
NHP	Non-human primate	_
NR	Not Reached	_
(N)SCLC	(Non-)small cell lung cancer	_
ORR	Overall Response Rate	_
PBO	Placebo	_
PD	Progressive disease	1
	Programmed cell death	1
PD-1/PD-(L)1	protein/(ligand) 1	
PDUFA	Prescription Drug User Fee Act	١

Abbreviation	Definition
РК	Pharmacokinetic
	Paroxysmal nocturnal
PNH	hemoglobinuria
POC	Proof-of-concept
PR	Partial response
	Prostate-specific
PSMA	membrane antigen
R/R	Relapsed/Refractory
RCC	Renal cell carcinoma
RGC	Regeneron Genetics Center
RT	Radiotherapy
RVO	Retinal vein occlusion
	Supplemental biologics license
sBLA	application
SC	Subcutaneous
sCR	Stringent complete response
SD	Stable disease
siRNA	Small interfering RNA
SOC	Standard of care
SPAF	Stroke Prevention in Atrial Fibrillation
T2DM	Type 2 diabetes mellitus
TEAE	Treatment-emergent adverse events
TRAE	Treatment-related adverse events
ULN	Upper limit of normal
VEGF	Vascular endothelial growth factor
VTE	Venous thromboembolism
wAMD	Wet age-related macular degeneration