

A blue-tinted photograph of a doctor sitting on the floor talking to a child in a hospital setting. The doctor is a woman with curly hair, wearing a white lab coat and a stethoscope. She is looking towards the child. The child is sitting on the floor, looking back at the doctor. In the background, there are other people, including a woman sitting on a chair and another person standing. The overall scene is a clinical or hospital environment.

# J.P.Morgan Healthcare Conference

JANUARY 8, 2024

**REGENERON®**

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

J.P.Morgan Healthcare Conference 2024

## 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® (afibercept) Injection, EYLEA HD (afibercept) Injection 8 mg, Dupixent® (dupilumab) Injection, Libtayo® (cemiplimab) Injection, Praluent® (alirocumab) Injection, Kevzara® (sarilumab) Injection, Evkeeza® (evinacumab) Injection, Veopoz™ (pozelimab) Injection, odronextamab, itepekimab, fianlimab, garetosmab, linvoseltamab, REGN5713-5714-5715, Regeneron's other oncology programs (including its costimulatory bispecific portfolio), 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 late-stage 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; 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, filling, 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 Medicaid; 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, including without limitation capital expenditures, 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 litigation initiated by 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 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 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.

**2023 achievements  
across key strategic  
priorities position  
Regeneron to  
deliver long-term  
shareholder value**

**REGENERON**  
**SCIENCE TO MEDICINE®**

FDA approval and successful launch of **Eylea HD** positions retinal franchise for prolonged leadership

Exceptional **Dupixent clinical and commercial execution**; unprecedented data in eosinophilic COPD to enable potential 2024 launch

Significant **immuno-oncology** pipeline progress across checkpoint inhibitor, CD3 bispecific, and CD28 costimulatory bispecific platforms, including **BLA submissions for odronextamab and linvoseltamab**

Emerging data from **hematology, genetic medicine, and obesity** pipelines support advancing multiple potential first- and best-in-class opportunities

# Delivered on key goals presented at J.P.Morgan 2023

## Ophthalmology

- FDA approval for EYLEA in ROP ✓
- BLA acceptance for aflibercept 8 mg in DME and wAMD ✓
- FDA approval and U.S. launch of EYLEA HD ✓
- Two-year data for PHOTON (DME) and PULSAR (wAMD) studies ✓

## Dupixent

- sBLA acceptance for CSU ✓
- EC decision on pediatric AD (6mo – 5yr) ✓
- Report data for Phase 3 study in Type 2 COPD ✓
- sBLA acceptance for pediatric EoE ✓
- FDA decision on CSU – received CRL

## Veopoz (anti-C5 antibody)

- FDA acceptance of CHAPLE BLA ✓
- FDA decision on CHAPLE (PDUFA August 20, 2023) ✓

## Solid Organ Oncology

- Fianlimab + Libtayo:
  - Initiate Phase 2/3 studies in 1L advanced NSCLC ✓
  - Initiate Phase 2 study in perioperative melanoma – 2024
  - Initiate Phase 2 study in perioperative NSCLC – 2024
- Report additional data for PSMaxCD28+Libtayo – 2024/2025
- Report initial data across solid organ oncology, including for CD3 bispecifics and CD28 costimulatory bispecifics ✓
- EC decision for Libtayo in combination with chemotherapy in 1L advanced NSCLC ✓

## Odronextamab (CD20xCD3)

- Initiate confirmatory studies in FL & DLBCL, including earlier lines ✓
- Initiate Phase 1 study in combination with REGN5837 (CD22xCD28) in aggressive DLBCL ✓
- BLA and MAA acceptance in B-NHL ✓

## Linvoseltamab (BCMAxCD3)

- Report updated pivotal Phase 2 data in R/R Multiple Myeloma ✓
- Initiate confirmatory study in MM, including in earlier lines ✓
- Initiate Phase 1 study in combination with TAAxCD28 in MM – 2024
- BLA submission in 3L+ MM ✓

# EYLEA HD approved by FDA for wAMD, DME, and DR



has the potential to become the **next-generation standard-of-care anti-VEGF treatment**

4Q 2023 U.S. Net Product Sales\*:

# \$123 million

achieved in first full quarter following launch



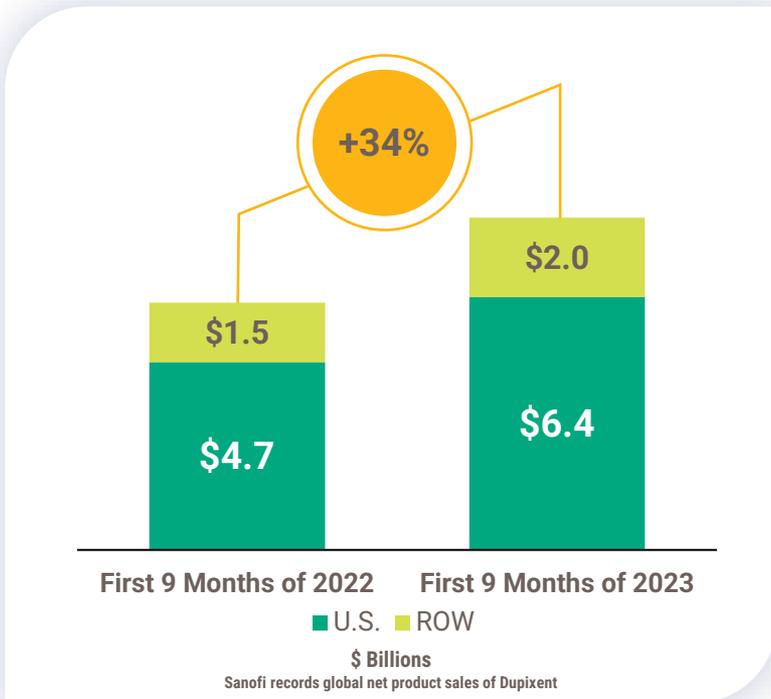
4Q 2023 combined EYLEA HD + EYLEA U.S. net product sales of **\$1.46 billion\***

- ✓ **FDA approval** for wAMD, DME and DR received in August 2023
- ✓ Early indicators suggest **broad initial uptake** across treatment landscape
- ✓ **Strong 2-year data** from pivotal PULSAR and PHOTON studies presented in 2H 2023, supporting **best-in-class** efficacy, safety, and durability profile
- ✓ **~2/3 of eligible lives have coverage**; vast majority of covered lives have **first-line or single-step-edit access** to Eylea HD
- ✓ **100% of Medicare jurisdictions** have confirmed paid claims
- ✓ Remain on track for **permanent J-Code** on April 1, 2024

# Dupixent global net product sales grew 34% and reached nearly \$8.4 billion through first nine months of 2023

In the third quarter of 2023, Dupixent global net sales grew 33% to ~\$3.1 billion

Incremental market penetration, new indications, and younger populations represent significant opportunity for continued growth



**>750,000** patients on therapy globally

Approved in **FIVE** indications, positive pivotal results in **SEVEN** Type 2 allergic diseases

- ✓ NBRx – #1 prescribed biologic in all 5 approved indications
- ✓ TRx – #1 prescribed biologic in 4 out of 5 approved indications

**Demonstrated clinical and real-world safety profile**

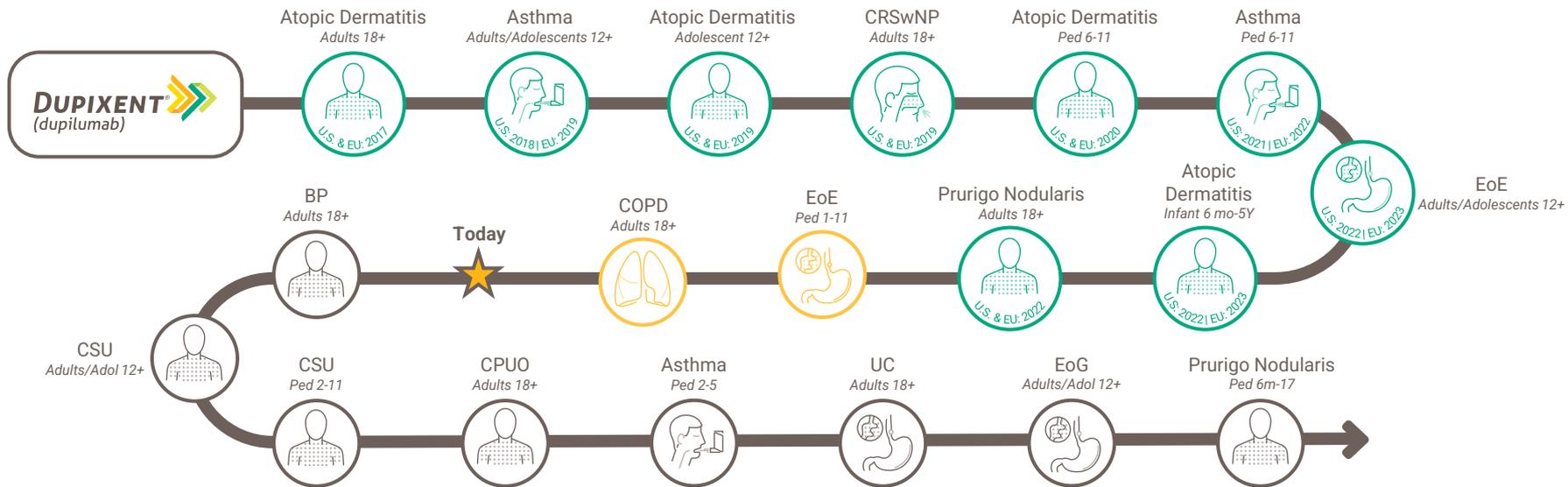
- ✓ >60 clinical trials with >10,000 patients

**Chronic Obstructive Pulmonary Disease**

- ✓ Reported positive results for pivotal BOREAS and NOTUS studies
- ✓ sBLA submission completed in December 2023; under review in EU

# Delivering on “pipeline in a product” potential

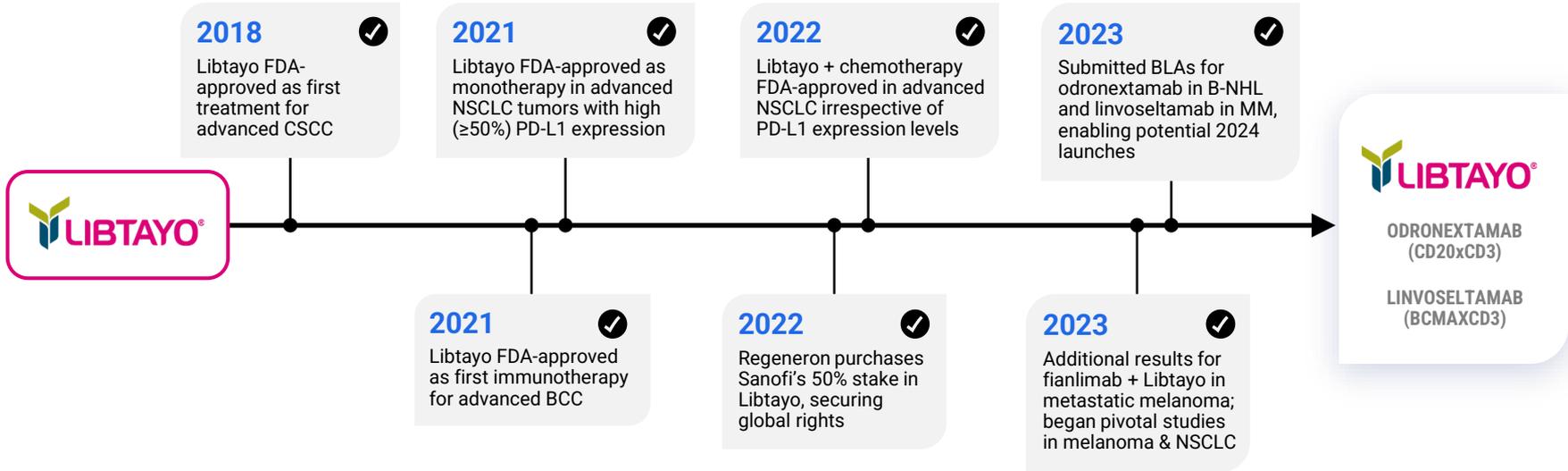
Dupilixent clinical trials have demonstrated that IL-4 and IL-13 are key drivers of multiple Type 2 allergic diseases



**Potential new indications for Dupixent provide opportunity to add up to ~1 million additional eligible patients in the U.S.**

# Striving for global leadership in oncology

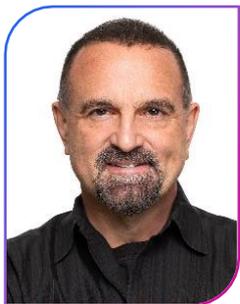
Potential for up to three FDA-approved products by end of 2024, spanning solid and hematological malignancies



**Libtayo poised to exceed \$1 billion in global net product sales in 2024;  
Robust oncology pipeline driven primarily by Libtayo combinations**

J.P.Morgan Healthcare Conference 2024

## Research & Pipeline Update



**George D. Yancopoulos, MD, PhD**

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

# Relentless Innovation

After 35 years, Regeneron is still pushing the boundaries of science and technology

2023 was another year of scientific “firsts”

## Dupixent in COPD\*

First biologic to achieve clinically meaningful reduction in COPD exacerbations and improvement in lung function

## CRISPR gene editing†

First to initiate a pivotal study using *in vivo* CRISPR gene editing cleared by U.S. FDA

## CD28 costimulatory bispecifics

First to dose patients with costimulatory bispecific in combination with a CD3 bispecific for both solid and heme tumors

## siRNA in CNS†

First clinical results demonstrating silencing of a pathological gene in human brain

## Antibody + siRNA targeting C5

Generated first data combining antibody and siRNA therapeutic classes (for targeting C5 in PNH)

## Gene therapy for hearing loss

Restored hearing in profoundly deaf child with otoferlin gene therapy

## Reversing severe allergy

Published preclinical results on potential groundbreaking approach for reversing severe allergy

Collaboration with:

\* Sanofi; † Alnylam; ‡ Intellia

# Harnessing the immune system to fight cancer

Regeneron has validated 3 independent classes of internally-developed immuno-oncology agents

- One approved medicine, two under regulatory review
- Robust pipeline of immuno-oncology combinations

## Checkpoint Inhibitors (anti-PD-1 & anti-LAG-3)

 **LIBTAYO**<sup>®</sup>  
(cemiplimab-rwlc)  
Injection 350 mg  
(anti-PD-1)  
CSCC, BCC, NSCLC

**Fianlimab**  
(anti-LAG-3)  
Melanoma, NSCLC

## CD3 Bispecifics ("Signal 1")

**Odronextamab**  
(CD20xCD3)  
B-NHL

**Ubatamamab**  
(MUC16xCD3)  
Ovarian Cancer

**Linvoseltamab**  
(BCMAxCD3)  
MM

**REGN4336**  
(PSMAxCD3)  
Prostate Cancer

## CD28 Costimulatory Bispecifics ("Signal 2")

**REGN5678**  
(PSMAxCD28)  
Prostate Cancer

**REGN5668**  
(MUC16xCD28)  
Ovarian Cancer

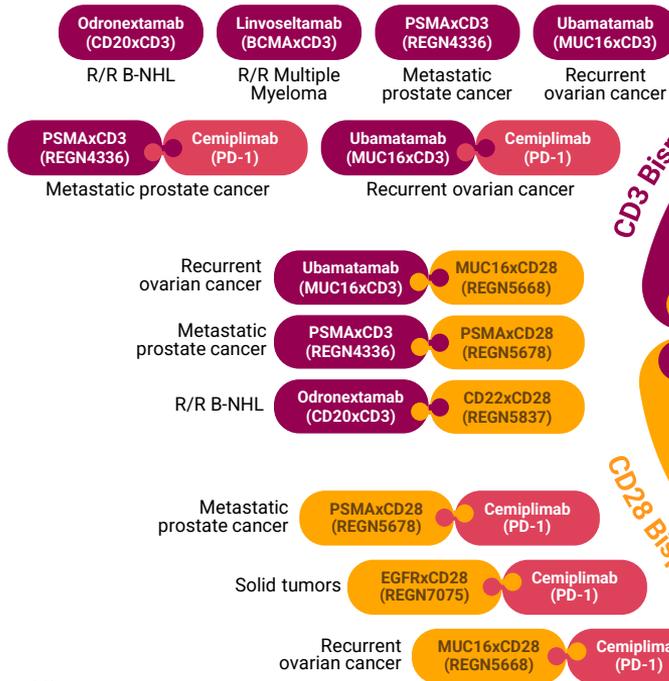
**REGN7075**  
(EGFRxCD28)  
Solid Tumors

**REGN5837**  
(CD22xCD28)  
DLBCL

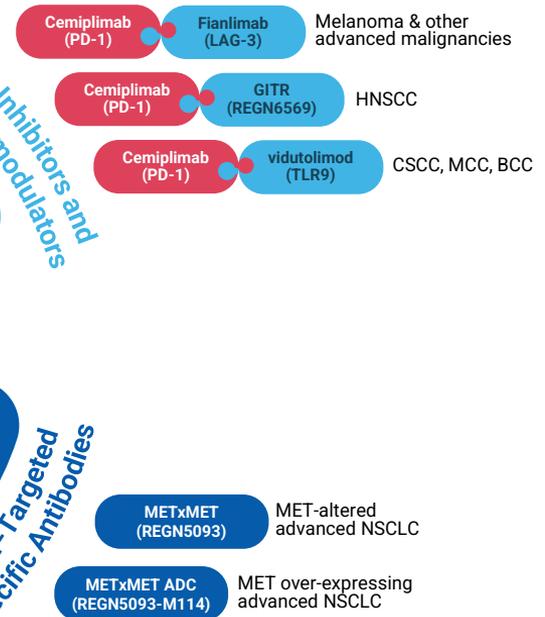
Broad pipeline of clinical-stage assets and numerous  
preclinical assets planned to advance to clinical studies

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

## Bispecifics and Checkpoint Inhibitor Combos



## Checkpoint Inhibitor Combos



# Fianlimab (anti-LAG-3) + cemiplimab (anti-PD-1): Combining two checkpoint inhibitors

Results from three independent 1L metastatic melanoma cohorts from the FIH study demonstrated strong efficacy signal, including in patients treated with adjuvant anti-PD-1 therapy

		Phase 1	Phase 2	Phase 3	Results in 1L Metastatic Melanoma							
<b>Melanoma</b>	1L Metastatic Melanoma	Potentially pivotal data expected 2H24			<b>fianlimab + cemiplimab</b> FIH POC study <sup>1</sup>	<b>ORR</b>	<b>DCR</b>	<b>mPFS</b> (KM-estimate)				
	Adjuvant Melanoma	Enrolling							<b>Cohort MM1</b> (n=40) <i>Initial</i>	63%	80%	24 mo
	Perioperative Melanoma	Initiating 1H24							<b>Cohort MM2</b> (n=40) <i>Confirmatory</i>	63%	80%	15 mo
<b>Lung (NSCLC)</b>	Advanced NSCLC	Enrolling Initial data expected 2H24			<b>Cohort MM3</b> (n=18) <i>PD-1 in adjuvant setting</i>	56%	67%	12 mo				
	Perioperative NSCLC	Initiating 1H24			<b>Combined</b> (n=98)	<b>61%</b>	<b>78%</b>	<b>15 mo</b>				
<b>Other solid tumors</b>	Perioperative HCC	Enrolling			<b>RELATIVITY-047 Phase 3<sup>2</sup></b>							
	Perioperative CSCC	Initiating 2024			nivolumab (n=359)	33%	51%	4.6 mo				
	Perioperative HNSCC	Initiating 2024			nivolumab + relatlimab (n=355)	43%	63%	10.2 mo				

**Safety profile of fianlimab + cemiplimab combination similar to anti-PD-1 monotherapy**

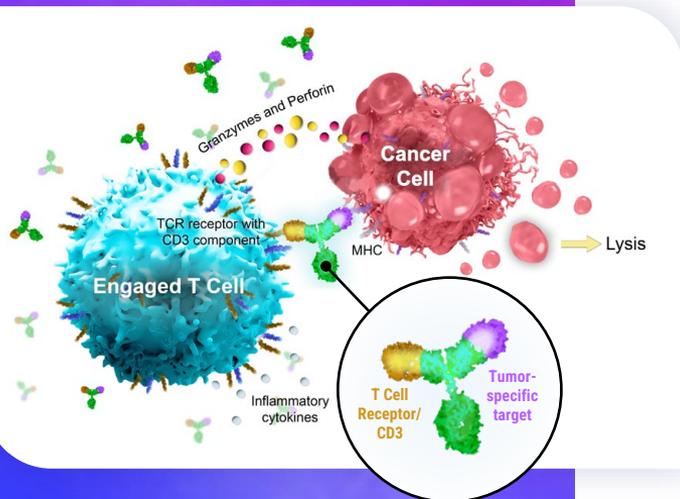
<sup>1</sup>Hamid, O. Significant durable response with fianlimab (anti-LAG-3) and cemiplimab (anti-PD-1) in advanced melanoma: post adjuvant PD-1 analysis, ASCO 2023.

<sup>2</sup>Long, G. Relatlimab and nivolumab versus nivolumab in previously untreated metastatic or unresectable melanoma: Overall survival and response rates from RELATIVITY-047, ASCO Plenary Series, March 2022.

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

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.

# Regeneron's leading CD3 bispecifics



Our blood cancer research is focused on bispecific antibodies that are being investigated both as monotherapies and in combination with each other and emerging therapeutic modalities

## Linvoseltamab (BCMAxCD3) – MM

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

Confirmatory Phase 3 study underway; expanding into early stages of disease

BLA submitted in December 2023 for R/R multiple myeloma, pending FDA acceptance

EU submission planned for 1Q 2024

## Odronextamab (CD20xCD3) – NHL

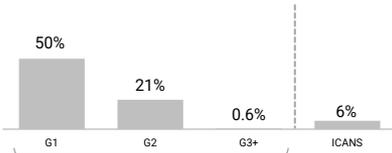
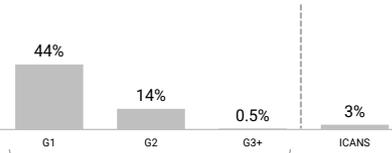
Odronextamab can treat both indolent and aggressive lymphomas with potential best-in-class efficacy in FL and a competitive profile in DLBCL, including patients previously treated with CAR-T therapy

Confirmatory Phase 3 OLYMPIA program underway and enrolling patients in earlier lines of therapy

BLA accepted by FDA for R/R FL & DLBCL (PDUFA March 31, 2024)

EU submission completed; decision expected 2H 2024

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

	<b>Teclistamab</b> - FDA Approved (per U.S. FDA Prescribing Information*)	<b>Elranatamab</b> - FDA approved (per U.S. FDA Prescribing Information*)	<b>Linvoseltamab*</b> (per LINKER-MM1 primary analysis*)
 <b>Efficacy</b>	<p>ORR  62%</p> <p>sCR + CR  28%</p> <p>Follow-up 7.4-months among responders</p>	<p>ORR  58%</p> <p>sCR + CR  26%</p> <p>Follow-up 11.1-months among responders</p>	<p>200mg dose</p> <p>ORR  71%</p> <p>sCR + CR  46%</p> <p>Follow-up 11.0-months all patients</p>
 <b>Safety</b>	<p></p> <p><b>CRS</b></p> <p>CRS median time to onset: 2 days median duration: 2 days</p>	<p></p> <p><b>CRS</b></p> <p>CRS median time to onset: 2 days median duration: 2 days</p>	<p></p> <p><b>CRS</b></p> <p>CRS median time to onset: 1 day median duration: within 1 day</p>
 <b>Hospitalization, Administration &amp; Dosing schedule</b>	<p> <b>x 6 days</b></p> <p>3 X 48-hr hospitalization requirements during step-up dosing (over initial ~9 days)</p> <p><b>Subcutaneous</b> (by HCP only)</p> <p>QW </p>	<p> <b>x 3 days</b></p> <p>1 X 48-hr + 1 X 24-hr hospitalization requirements during step-up dosing (over initial ~5 days)</p> <p><b>Subcutaneous</b> (by HCP only)</p> <p>QW  Q2W</p> <p>Weeks 1-24                      Week 25+ for responders</p>	<p> <b>x 2 days</b></p> <p>1 X 24-hrs in W1 + 1 x 24-hrs in W2; Hospitalized for 1 day during step-up dosing on <b>Day 1 &amp; Day 8*</b></p> <p><b>Intravenous</b> (Week 3+ = 30-min+)</p> <p>QW  Q2W  Q4W</p> <p>Weeks 1-14      Weeks 15-23                      Week 24+ if VGPR+</p>

\* Data source: Regeneron press release from Dec 7, 2023. † Per Protocol. ‡ 30-min as long as patient tolerability allows; discretion at Day 8.

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# Progressing CD28 costimulatory bispecifics

	Dose Escalation	Proof-of-Mechanism	Dose Expansion	Status / Next Steps	Combined with:
 <p><b>PSMAxCD28</b> Prostate Cancer</p>				Enrolling monotherapy cohort; combo with PSMAxCD3 to start 1H24	 
 <p><b>EGFRxCD28</b> Solid Tumors</p>				Expansion cohorts with cemiplimab to initiate in 1H24 in multiple tumors	
 <p><b>MUC16xCD28</b> Ovarian Cancer</p>				Presented initial dose escalation results with cemiplimab; expansion cohorts expected to initiate in 2024; enrolling dose escalation with ubamatamab	 
 <p><b>CD22xCD28</b> DLBCL</p>				Enrolling dose escalation cohorts	
 <p><b>CD38xCD28</b> MM</p>				Initiating Phase 1 study in 2024	

Additional costimulatory bispecifics expected to enter the clinic in 2024 and beyond

# Potential to change the COPD treatment paradigm with Dupixent and itepekimab

**DUPIXENT**<sup>®</sup>  (anti-IL4/13)  
(dupilumab)

Positive results in Phase 3 BOREAS and NOTUS studies in eosinophilic COPD reported during 2023

sBLA submission completed in December 2023

	BOREAS	NOTUS
<b>Primary endpoint:</b> Significant reduction in moderate or severe COPD exacerbations over 52 weeks compared to placebo	<b>30%</b> (p=0.0005)	<b>34%</b> (p=0.0002)
<b>Key secondary endpoint:</b> Significant improvement in lung function at week 12 compared to placebo*	<b>+83 mL</b> (p<0.0001)	<b>+82 mL</b> (p=0.0001)

Lung function benefit vs. placebo observed at Week 12 sustained at Week 52

Safety findings generally consistent with known safety profile of Dupixent

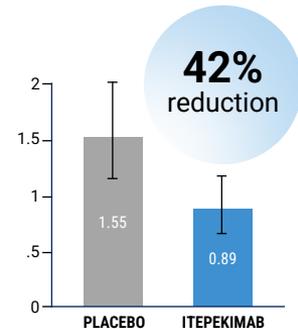
**Itepekimab**  
(anti-IL-33)

Positive data in former smokers in Phase 2 COPD study informed Phase 3 trial design

Phase 3 AERIFY studies passed interim futility analysis in 2023

- Demonstrated 42% reduction in exacerbations in former smokers vs. placebo in Phase 2 study
- RGC-generated human genetics data support rationale for IL-33 blockade to treat COPD
- Pivotal results from both AERIFY studies expected in 2025

**Phase 2 COPD Trial**  
Itepekimab led to 42% reduction in exacerbations in former smokers



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

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

## ALLERGY

A therapeutic strategy to target distinct sources of IgE and durably reverse allergy

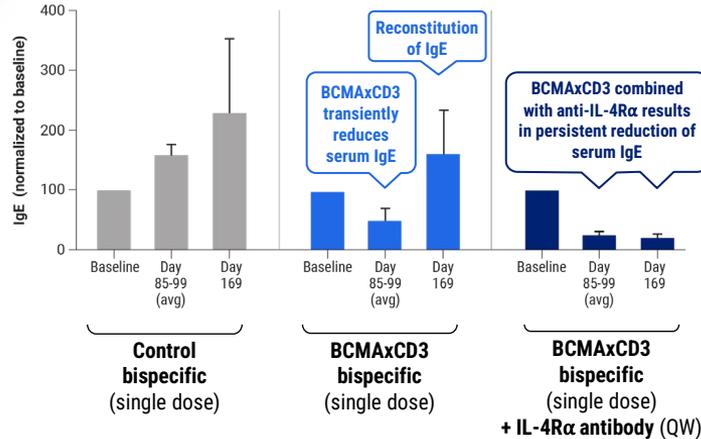
Andre Limnander, Navneet Kaur, Seblewongel Asrat, Carley Tasker, Anita Boyapati, Li-Hong Ben, John Janczy, Paulina Pedraza, Pablo Abreu, Wen-Chi Chen, Stephen Godin, Benjamin J. Daniel, Harvey Chin, Michelle DeVeaux, Karen Rodriguez Lorenc, Andres Sirulnik, Olivier Harari, Neil Stahl, Matthew A. Sleeman, Andrew J. Murphy, George D. Yancopoulos, Jamie M. Orengo\*

**Linvoseltamab and Dupixent regimen could eliminate IgE: potential groundbreaking approach for controlling severe allergy**

- **Immunoglobulin E (IgE)** is the key driver of allergic reactions, such as food allergies; long-lived plasma cells consistently produce IgE<sup>2</sup>
- In atopic patients, **transient linvoseltamab treatment with Dupixent maintenance** has the potential of permanently eliminating IgE and durably reversing severe allergies, while allowing the restoration of other immunoglobulins

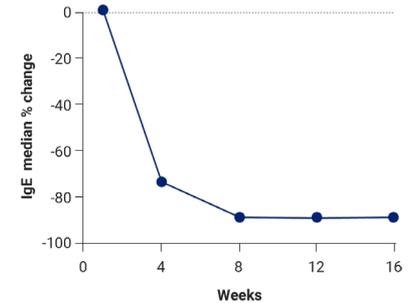


**Transient plasma cell depletion with BCMAxCD3 plus sustained IL-4Rα blockade durably eliminates IgE production in cynomolgus monkeys<sup>1</sup>**



**Myeloma patients treated with linvoseltamab rapidly reduce IgE levels<sup>1</sup>**

Median concentrations of serum IgE over time in MM patients (n=12) receiving QW linvoseltamab\*



- Linvoseltamab effectively eliminates BCMA-expressing cells, including long-lived plasma cells
- IgE reduction seen in myeloma patients supports the two-drug regimen for severe food allergies

**Clinical trial with the two-drug regimen in patients with severe food allergies to begin in 2024**

<sup>1</sup>Adapted from Limnander et al, Sci. Transl. Med. 2023.<sup>2</sup>Asrat et al, Sci. Immunol. 2020.

\* Pooled data from n=12 multiple myeloma patients from the LINKER-MM1 Phase 1 study, treated with six different dose levels of linvoseltamab

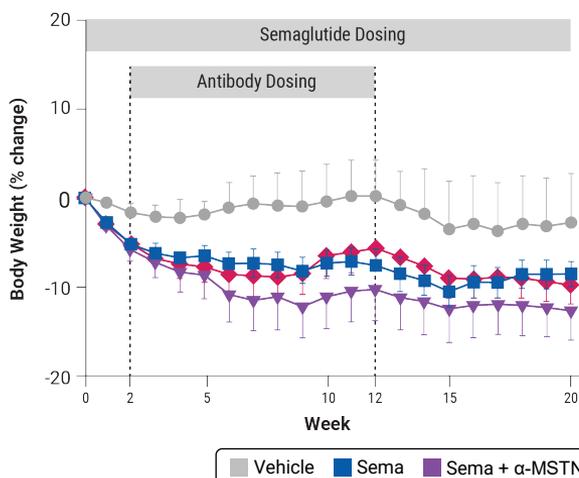
# Regeneron's approach to obesity: combinations with leading medicines aim to improve quality of weight loss

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

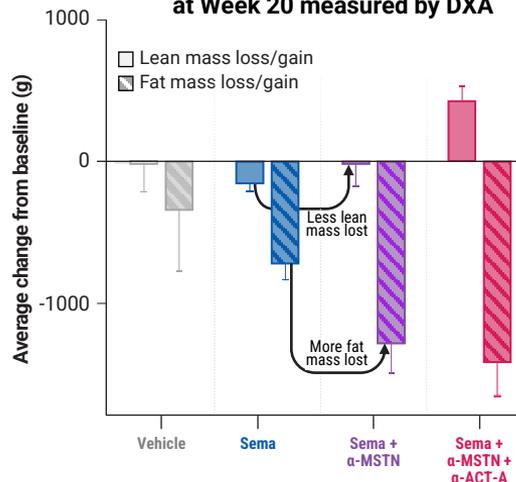
Novel approaches for obesity		
	Rationale	Program status
Incretin-based therapy	Improving upon once weekly standard of care in obesity/T2DM	NHP studies underway for our <b>antibody-tethered GLP-1 ligand</b>
+ $\alpha$ -MSTN + $\alpha$ -ACT-A	Improving <b>quality of weight loss</b> by preserving lean muscle during weight loss	Mid-2024: Start Phase 2 study of semaglutide with <b>trevogrumab</b> (anti-myostatin) $\pm$ <b>garetosmab</b> (anti-activin A)
<b>GPR75</b>	GPR75 gene mutations are associated with <b>protection against obesity</b>	siRNA, small molecule, and antibody candidate identification and screening underway

## Adding myostatin blockade to semaglutide leads to greater fat loss and less lean mass loss compared to semaglutide monotherapy in obese non-human primates<sup>2</sup>

Change in Body Weight through 20 Weeks



Change in Body Composition at Week 20 measured by DXA



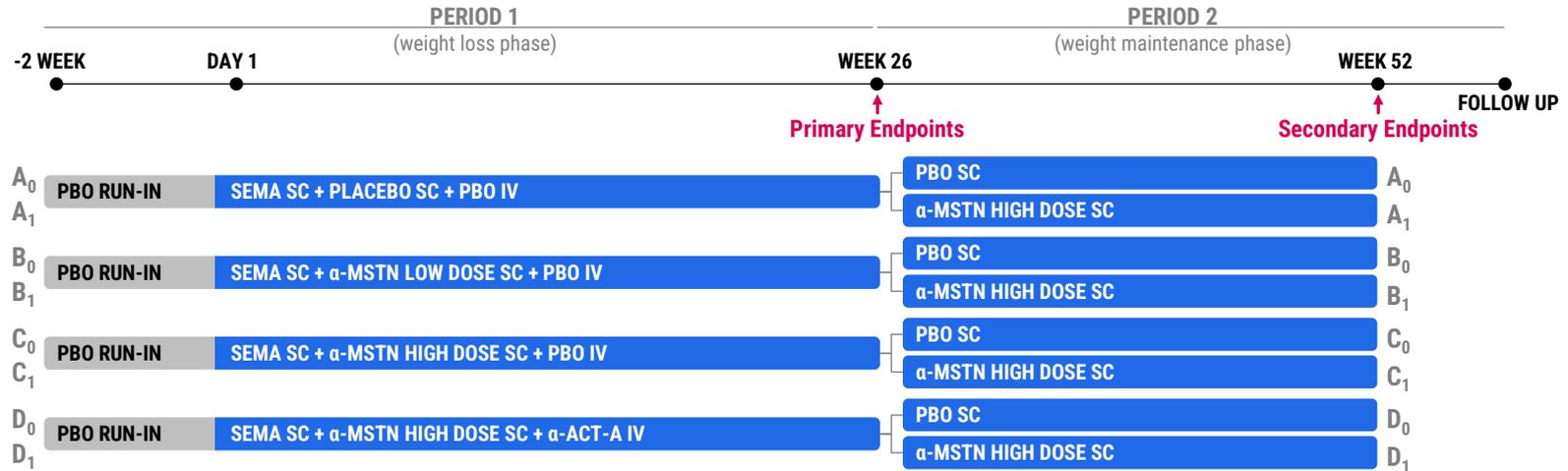
# Obesity clinical program to start in mid-2024

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

- Obese patient enrollment starting mid-2024, pending safety and tolerability trial of high dose trevogrumab in healthy volunteers

## Phase 2 General Obesity Trial Design

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



# Leveraging Regeneron's novel genetics discovery – GPR75 as a target for obesity

Exome sequencing of ~640,000 individuals revealed that gene variants in *GPR75* are associated with reduced risk of obesity; Individuals with at least one inactive copy of the *GPR75* gene had lower BMI and, on average, tended to weigh about 12 pounds less<sup>1</sup>

Regeneron is pursuing three modalities to target *GPR75*:

- siRNA collaboration with Alnylam
- Small molecule collaboration with AstraZeneca
- Antibody approach

## GPR75: a novel target for obesity

*Gpr75* knockout mice

People with an inactive copy of *GPR75* gene

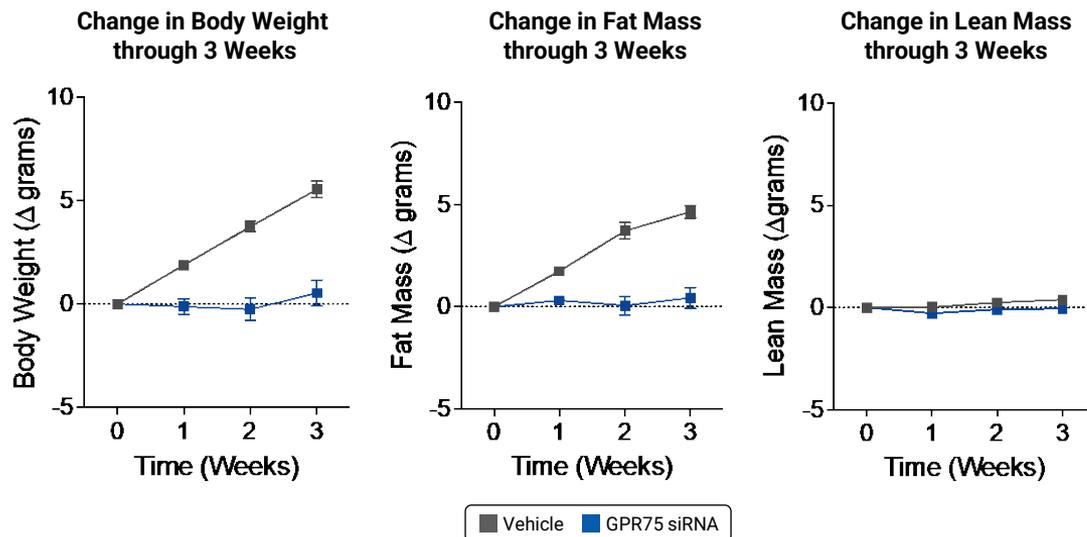
Body Weight



Physical Activity

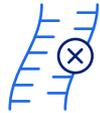


GPR75 siRNA treatment halts weight gain and fat mass gain without lean mass loss in high fat diet fed obese mice<sup>2</sup>



# Regeneron Genetic Medicines: multiple investigational approaches for treatment of genetic diseases

Established clinical proof-of-principle across several diseases with novel genetic medicine technologies



## siRNA Gene Silencing

(alone and antibody combos)

- First clinical results demonstrating silencing of a pathological gene in human brain (**APP**)\*
- Pioneers in siRNA + antibody combo (**C5**)



## CRISPR

### Knockout and Insertion Genome Editing

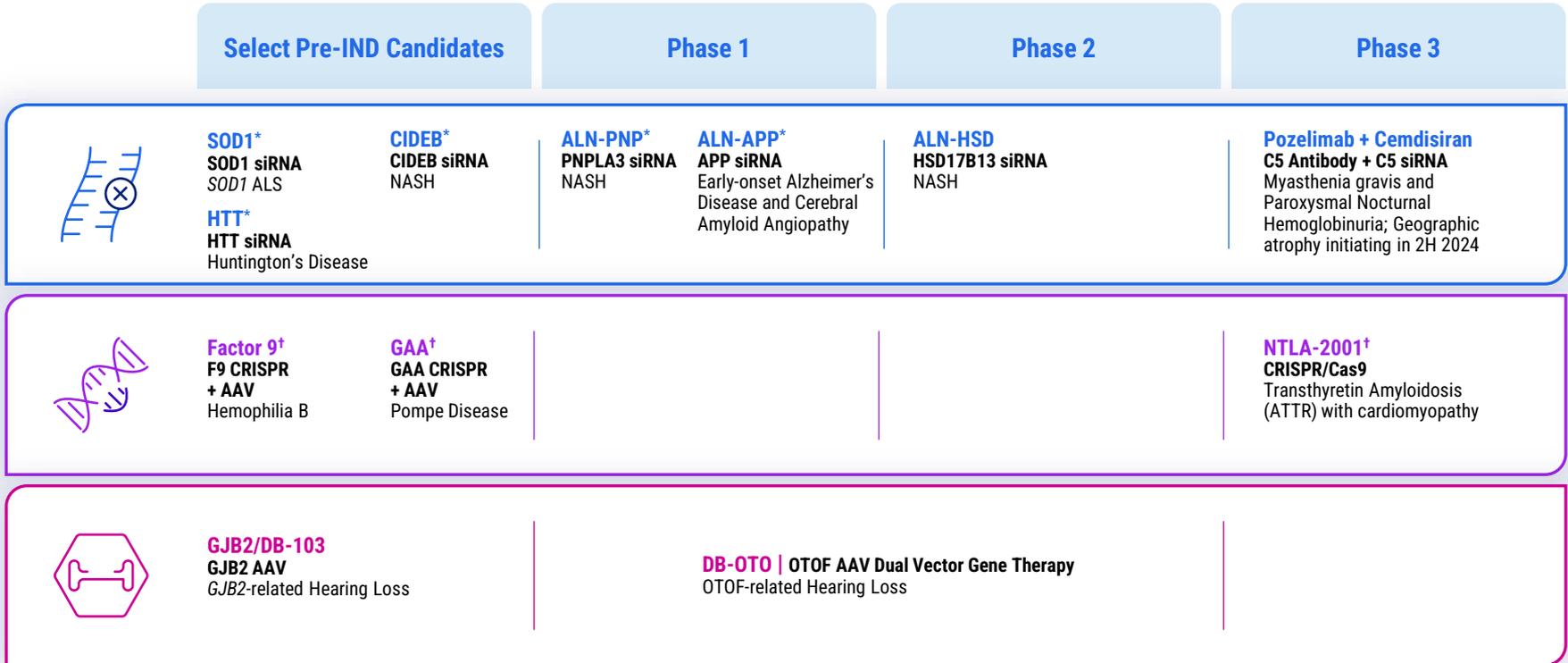
- Gene knockout: first clinical results demonstrating genome editing in humans; Phase 3 started (**TTR**)<sup>†</sup>
- Gene insertion: clinical program to start in 2024, pending regulatory approval (**Factor 9**)<sup>†</sup>



## AAV Gene Therapy

- Local delivery: restored hearing in first treated patient (**OTOF**)
- Antibody-targeted delivery: proof-of-concept in non-human primates; clinical approach in development (**muscle disorders**)

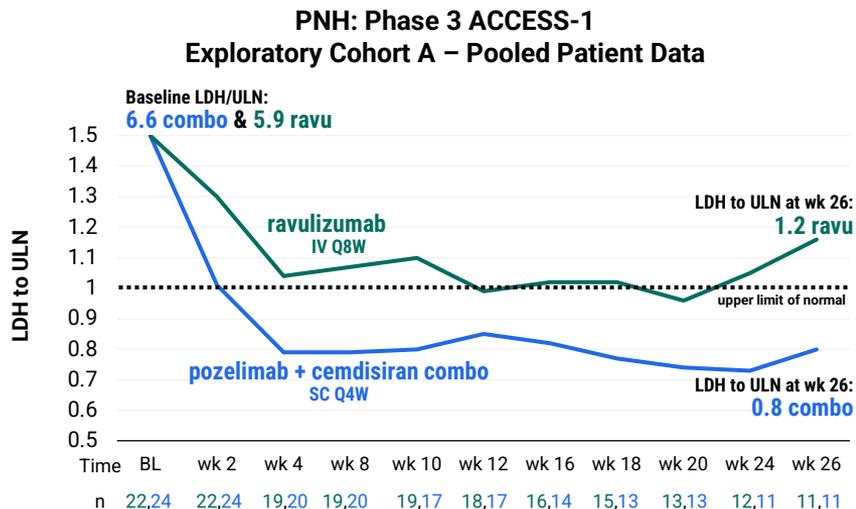
# Regeneron Genetic Medicines pipeline



# Regeneron pioneers first combination of siRNA + antibody therapeutic classes

siRNA reduces target load so that antibody can completely block target for extended period

Prior to this combination, no treatment has reduced and sustained average LDH to normal levels in PNH patients



**Pozelimab + cemdisiran – reduces LDH levels in almost all patients**

**Prior to this combination, no treatment has reduced and sustained average LDH to normal levels in PNH patients**

**Primary Endpoint:** the percent change in lactate dehydrogenase (LDH) from baseline to week 26. LDH is a well-accepted biomarker of hemolysis – with adequate control and normalization defined as  $\leq 1.5$  and  $\leq 1.0$  times the upper limit of normal (ULN), respectively. Only patients that completed 26 weeks of the study were evaluated for efficacy at the time of the data cut.

	Overview	Status
<b>PNH</b>	<b>Phase 3 ACCESS-1</b> Complement inhibitor-naïve patients	<ul style="list-style-type: none"> <li>Cohort A: Interim results recently reported</li> <li>Cohort B: Enrolling, data expected in 2024/2025</li> </ul>
<b>gMG</b>	<b>Phase 3 NIMBLE</b> Patients with symptomatic generalized myasthenia gravis	<ul style="list-style-type: none"> <li>Study enrolling</li> <li>Data expected in 2025</li> </ul>
<b>GA</b>	Patients with geographic atrophy secondary to age-related macular degeneration  Systemic administration - <i>Single subcutaneous injection to treat bilateral disease</i>	<ul style="list-style-type: none"> <li>Phase 3 pivotal program initiating in 2H 2024</li> </ul>

**Our antibody + siRNA combination has the potential to improve on current standards of care across many diseases including complement mediated disorders:**

- Complete and sustained C5 inhibition at a lower dose
- Reduced dosing frequency
- Convenient subcutaneous formulation

# Geographic atrophy (in dry AMD): Extending our C5 siRNA + antibody approach to ophthalmology

Pivotal Phase 3 program to initiate in 2H 2024

## Program Overview

*(Trials to initiate in 2H 2024)*

Two Phase 3 pivotal trials (multi-center, randomized, double-masked) in geographic atrophy secondary to age-related macular degeneration

	Current Geographic Atrophy Landscape	Regeneron Opportunity (Pozelimab + Cemdisiran Combo)
 <b>Market Opportunity</b>	<ul style="list-style-type: none"> <li>~1M diagnosed in U.S.</li> <li>Increasing diagnosis and drug-treatment rates</li> <li>2 approved agents, many more in development</li> </ul>	<ul style="list-style-type: none"> <li>Leadership in ophthalmology</li> <li>Differentiated MOA</li> </ul>
 <b>Route of Administration</b>	<ul style="list-style-type: none"> <li>Q4W/Q8W intravitreal injections</li> <li>Bilateral disease requires injections in each eye</li> </ul>	<ul style="list-style-type: none"> <li>Less invasive treatment option</li> <li>Systemic administration enables treatment of bilateral disease</li> <li>Q4W systemic treatment</li> </ul>
 <b>Ocular Safety</b>	<ul style="list-style-type: none"> <li>Reported cases of occlusive retinal vasculitis along with other ocular safety events</li> </ul>	<ul style="list-style-type: none"> <li>Systemic administration potentially reduces risk of ocular safety events</li> </ul>
 <b>Efficacy</b>	<ul style="list-style-type: none"> <li>Approved agents lack evidence of maintenance of visual function</li> </ul>	<ul style="list-style-type: none"> <li>Opportunity to demonstrate greater reduction in lesion growth rate along with preservation of visual function</li> </ul>
 <b>Office Visits</b>	<ul style="list-style-type: none"> <li>Administered in office by retinal specialist</li> </ul>	<ul style="list-style-type: none"> <li>Potential for self-administration (subcutaneous coformulation)</li> </ul>

# Regeneron restores hearing in a profoundly deaf child

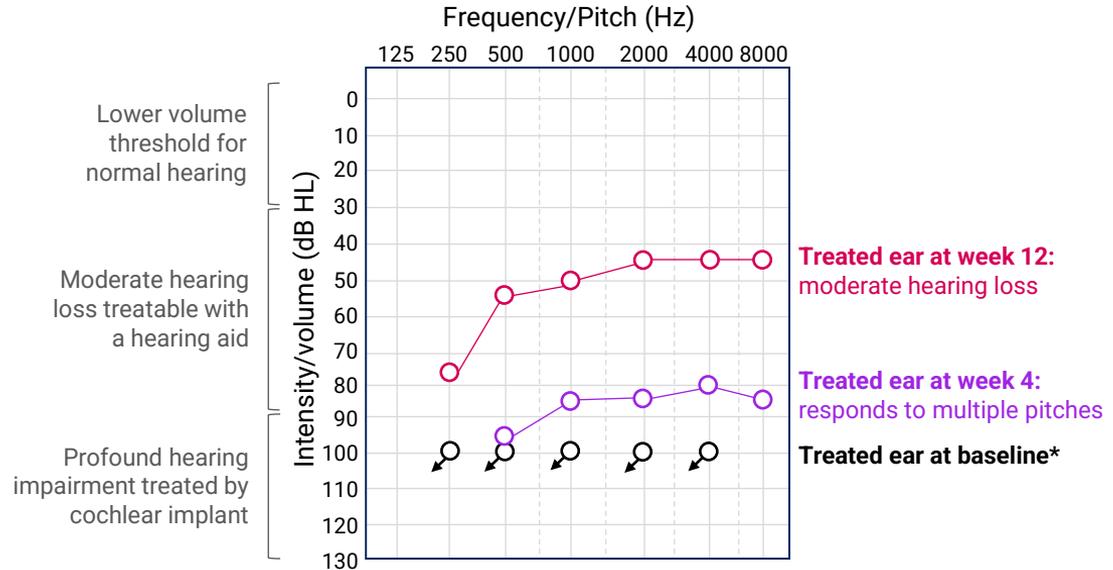
DB-OTO AAV-based dual-vector gene therapy delivered to the inner ear to rescue hearing in infants

## Gene therapy for genetic hearing loss

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

- DB-OTO is a surgically delivered AAV-based dual-vector gene therapy that selectively expresses functional OTOF in the inner ear hair cells of patients, enabling the ear to transmit sound to the brain
- Preliminary, positive safety and efficacy results from the first patient (<2 years old) continue to show improvements in auditory responses, now through week 12, compared to baseline
- Paves the way for next gene therapy for genetic hearing loss – GJB2
  - Currently in IND-enabling studies

**Preliminary results for first patient dosed:**  
Profoundly deaf child at baseline, demonstrates markedly improved hearing at 12 weeks post-treatment

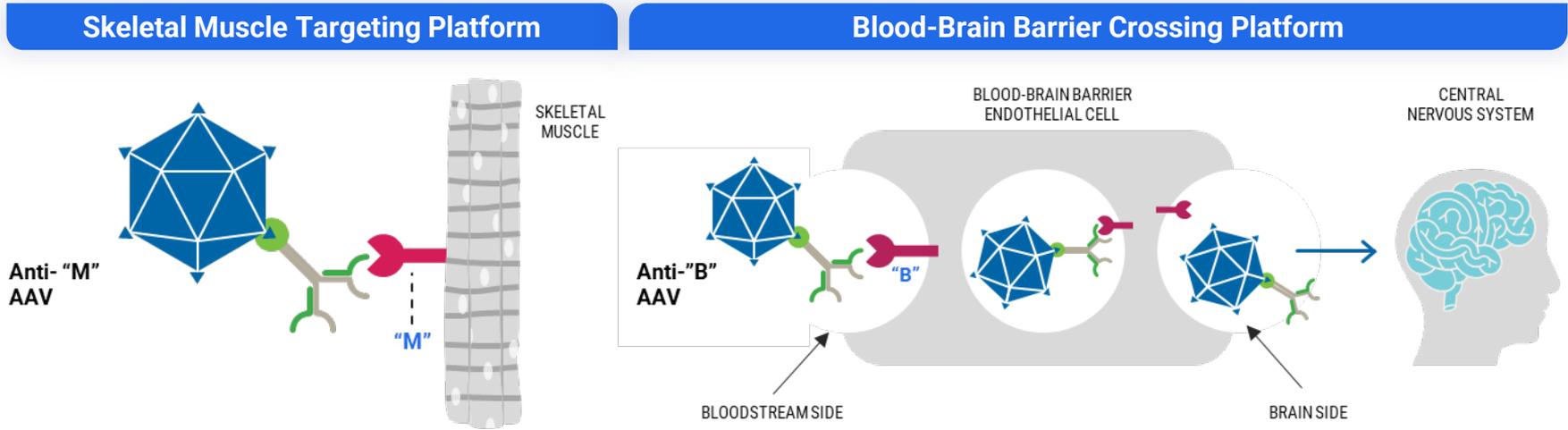


Behavioral pure tone audiogram – a plot of softest sounds a patient can hear in an individual ear

\*Arrows indicate no response at maximum level tested

# Optimizing genetic medicines with antibody-targeted delivery

Targeting of vector delivery with the skeletal muscle cell-specific protein ("M") and blood-brain barrier endothelial cell-specific protein ("B")



"M"- and "B"-mediated AAV9 delivery results in enhanced targeting to skeletal muscles and the central nervous system, respectively, as well as de-targeting other organs like the liver and heart

# 2024 key upcoming milestones

## Ophthalmology

- EU decision for aflibercept 8 mg in wAMD and DME – **Now Approved** ✓
- Japan decision for aflibercept 8 mg in wAMD and DME (1H)
- Initiate pivotal RVO study of Eylea HD to enable FDA filing (mid)
- Obtain permanent J-code for EYLEA HD (2Q)
- Initiate pivotal studies of pozelimab + cemdisiran combination in geographic atrophy (2H)

## Dupixent / I&I

- Regulatory decisions for pediatric (1-11 yrs) eosinophilic esophagitis (U.S. Q1, EU 2H)
- sBLA acceptance for COPD with a Type 2 inflammatory phenotype (Q1); potential FDA approval (mid/2H)
- Report results from ongoing Phase 3 study in CSU (4Q)
- Initiate Phase 1 study in severe food allergy following transient linvoseltamab treatment
- Complete enrollment of Phase 3 studies of itepekimab in COPD (2H)

## Obesity

- Initiate Phase 2 proof-of-concept study of combination of semaglutide and trevogrumab (anti-myostatin) with and without garetosmab (anti-Activin A) (mid)

## Solid Organ Oncology

- Report potentially pivotal interim analysis of Libtayo in Adjuvant CSCC (mid)
- Report potentially pivotal results from Phase 2/3 study of fianlimab + cemiplimab in 1L metastatic melanoma (2H); initial data in 1L advanced NSCLC (2H)
- Initiate potentially pivotal Phase 2 studies for fianlimab + cemiplimab in perioperative melanoma (1H) and perioperative NSCLC (1H)
- Initiate dose-expansion cohorts of EGFRxCD28 + cemiplimab in EGFR-high tumors (1H)
- Initiate cohorts combining PSMAxCD28 + PSMAxCD3 in mCRPC as well as PSMAxCD28 monotherapy in RCC (1H)

## Hematology

- FDA decision on odronextamab in R/R FL and R/R DLBCL (1Q); EU decision (2H)
- BLA acceptance for linvoseltamab in R/R multiple myeloma (1Q); potential FDA approval (2H); EU submission (1Q)
- Initiate Phase 1 study of linvoseltamab in combination with CD38xCD28 costimulatory bispecific in multiple myeloma
- Report Phase 2 proof-of-concept results for Factor XI antibody (2H)

## Genetic Medicines

- Initiate Phase 1 study of *Factor 9* gene insertion in hemophilia (mid)
- Report additional proof-of-concept data for DB-OTO
- Initiate proof-of-concept study of SOD1 siRNA in ALS

# Our mission:

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

## Three responsibility focus areas all 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



### Build sustainable communities

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

Member of  
**Dow Jones  
Sustainability Indices**  
Powered by the S&P Global CSA



### Foster a culture of integrity and excellence

- Product quality and safety
- Diverse, healthy and engaged workforce
- Ethics and integrity



# Q&A



**Leonard  
S. Schleifer,  
MD, PhD**

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



**George D.  
Yancopoulos,  
MD, PhD**

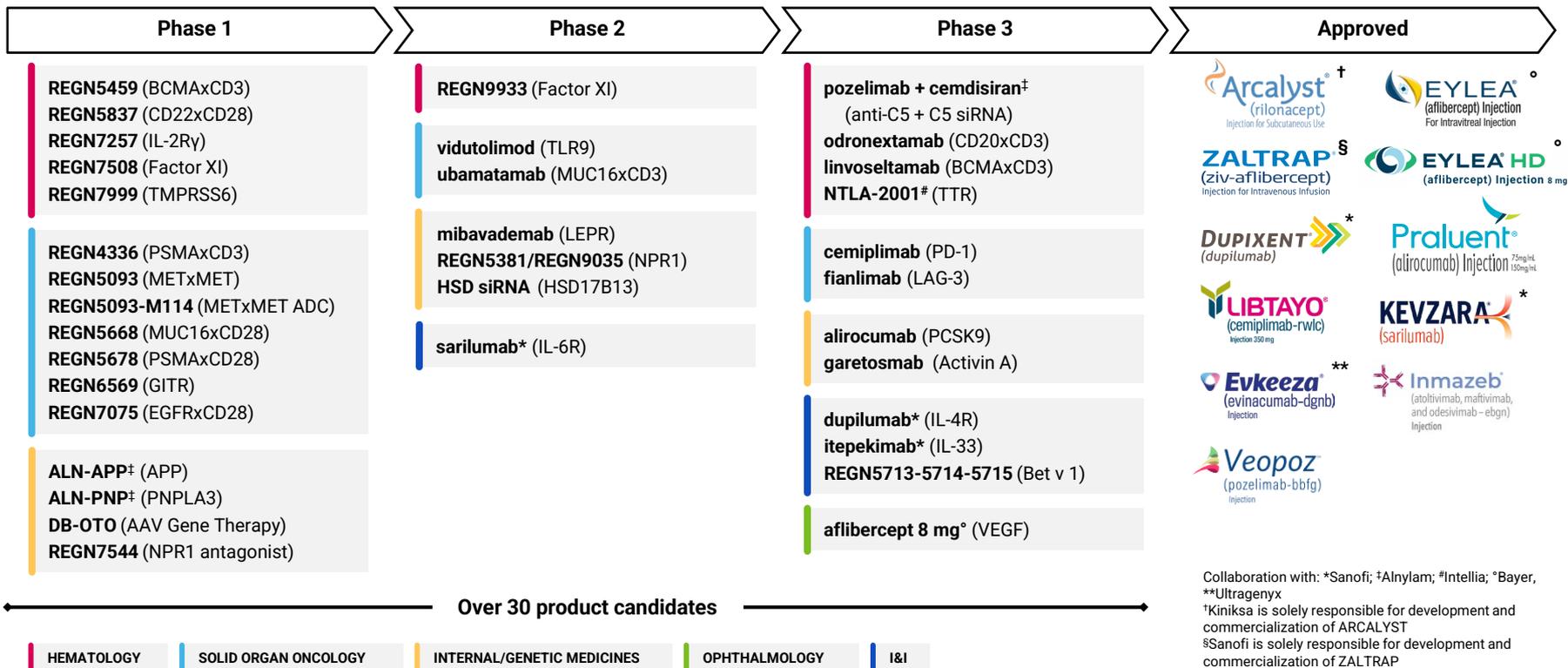
Co-Founder, Board  
Co-Chair, President &  
Chief Scientific Officer



**Marion  
McCourt**

EVP, Head of Commercial

# Regeneron-discovered, approved and investigational medicines across a diverse set of diseases



Collaboration with: \*Sanofi; †Alnylam; ‡Intellia; °Bayer, \*\*Ultragenyx  
 †Kiniksa is solely responsible for development and commercialization of ARCALYST  
 §Sanofi is solely responsible for development and commercialization of ZALTRAP

# Abbreviations and Definitions

Abbreviation	Definition
1L	First line
AAV	Adeno-associated virus
ALS	Amyotrophic lateral sclerosis
APP	Amyloid precursor protein
BCC	Basal cell carcinoma
BCMA	B-cell maturation antigen
BLA	Biologics license application
B-NHL	B-cell non-Hodgkin's lymphoma
BP	Bullous pemphigoid
CAR-T	Chimeric antigen receptor T-cell
CIndU-COLD	Chronic inducible urticaria – cold
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CPUO	Chronic pruritis of unknown origin
CR	Complete response
CRS	Cytokine release syndrome
CRSwNP	Chronic sinusitis with nasal polyposis
CSCC	Cutaneous squamous cell carcinoma
CSU	Chronic spontaneous urticaria
dB HL	Decibel hearing loss
DCR	Duration of complete response
DLBCL	Diffuse large B-cell lymphoma
DME	Diabetic macular edema
DR	Diabetic retinopathy
DXA	Dual-energy X-ray absorptiometry
EC	European Commission
EGFR	Epidermal growth factor receptor
EoE	Eosinophilic esophagitis
EoG	Eosinophilic gastroenteritis

Abbreviation	Definition
FIH	First in human
FL	Follicular lymphoma
GA	Geographic atrophy
GAA	Alpha glucosidase
GITR	Glucocorticoid-induced TNFR-related protein
GLP-1	Glucagon-like peptide 1
GLP-1R	Glucagon-like peptide 1 receptor
gMG	Generalized myasthenia gravis
HCC	Hepatocellular carcinoma
HCP	Healthcare Provider
HNSCC	Head and neck squamous cell carcinoma
Hz	Hertz
ICANS	Immune effector cell-associated neurotoxicity syndrome
IND	Initial new drug application
IV	Intravenous
KM	Kaplan-Meier curve
LAG-3	Lymphocyte-activation gene 3
LDH	Lactate dehydrogenase
LEPR	Leptin receptor
MAA	Marketing authorization application
MCC	Merkel cell carcinoma
mCRPC	Metastatic castration-resistant prostate cancer
MM	Multiple myeloma
MOA	Mechanism of action
mPFS	Median progression-free survival
MUC16	Mucin 16
NASH	Non-alcoholic steatohepatitis
NBRx	New to Brand Prescriptions
NHP	Non-human primate

Abbreviation	Definition
NSCLC	Non-small cell lung cancer
ORR	Overall Response Rate
OTOF	Otoferrin
PBO	Placebo
PD-1/PD-(L)1	Programmed cell death protein/(ligand) 1
PDUFA	Prescription Drug User Fee Act
PNH	Paroxysmal nocturnal hemoglobinuria
POC	Proof-of-concept
PSMA	Prostate-specific membrane antigen
R/R	Relapsed/Refractory
RCC	Renal cell carcinoma
RGC	Regeneron Genetics Center
ROW	Rest of world
RVO	Retinal vein occlusion
sBLA	Supplemental biologics license application
SC	Subcutaneous
sCR	Stringent complete response
siRNA	Small interfering RNA
T2DM	Type 2 diabetes mellitus
TAA	Tumor-associated antigen
TRx	Total prescriptions
TTR	Transthyretin protein
UC	Ulcerative colitis
ULN	Upper limit of normal
VEGF	Vascular endothelial growth factor
wAMD	Wet age-related macular degeneration