# ESMO 2022 Regeneron Investor Event

September 12, 2022

REGENERON®

This non-promotional presentation is intended for the investor audience and contains investigational data as well as forward-looking statements; actual results may vary materially.

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These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators or licensees (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products, product candidates being developed by Regeneron and/or its collaborators or licensees (collectively, "Regeneron Product Candidates") and research and clinical programs now underway or planned, including without limitation Libtayo® (cemiplimab) (as monotherapy or in combination with certain Regeneron Product Candidates discussed or referenced in this presentation or other therapies), odronextamab (a CD20xCD3 bispecific antibody), ubamatamab (a MUC16xCD3 bispecific antibody), REGN5093 (a METxMET bispecific antibody), and other Regeneron Product Candidates discussed or referenced in this presentation; uncertainty of the utilization, market acceptance, and commercial success of Regeneron's Products and Regeneron Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed or referenced in this presentation, on any of the foregoing or any potential regulatory approval of Regeneron's Products and Regeneron Product Candidates; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron Product Candidates and new indications for Regeneron's Products; 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 and/or its collaborators or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; the ability of Regeneron's collaborators, licensees, 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 Product Candidates; the ability of Regeneron and/or its collaborators to manufacture and manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products and Regeneron Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron Product Candidates in clinical trials; 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 Product Candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer 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 payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron Product Candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply 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; 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® (aflibercept) Injection, Dupixent® (dupilumab), Praluent® (alirocumab), and REGEN-COV® (casirivimab and imdevimab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, 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, including its Form 10-K for the year ended December 31, 2021 and its Form 10-Q for the quarterly period ended June 30, 2022. 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.

**David Weinreich, MD**
EVP, Global Clinical Development

**Israel Lowy, MD, PhD**
SVP, Translational and Clinical Sciences, Oncology

**Justin Holko**
VP, Global Commercial Business Unit, Oncology

# Agenda

- Oncology Overview
- ESMO 2022 Data Updates
- Other Oncology Programs
- Q&A

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# Oncology Overview

**David Weinreich, MD**
EVP, Global Clinical Development



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# Committed to Becoming a Leader in Immuno-Oncology with Libtayo as Foundation

**Accomplishments: Initial approvals, novel platform validation and signals of activity**

**Potential upcoming regulatory submissions, approvals and data readouts**

**Leader in immuno-oncology by investigating the power of informed combinations**

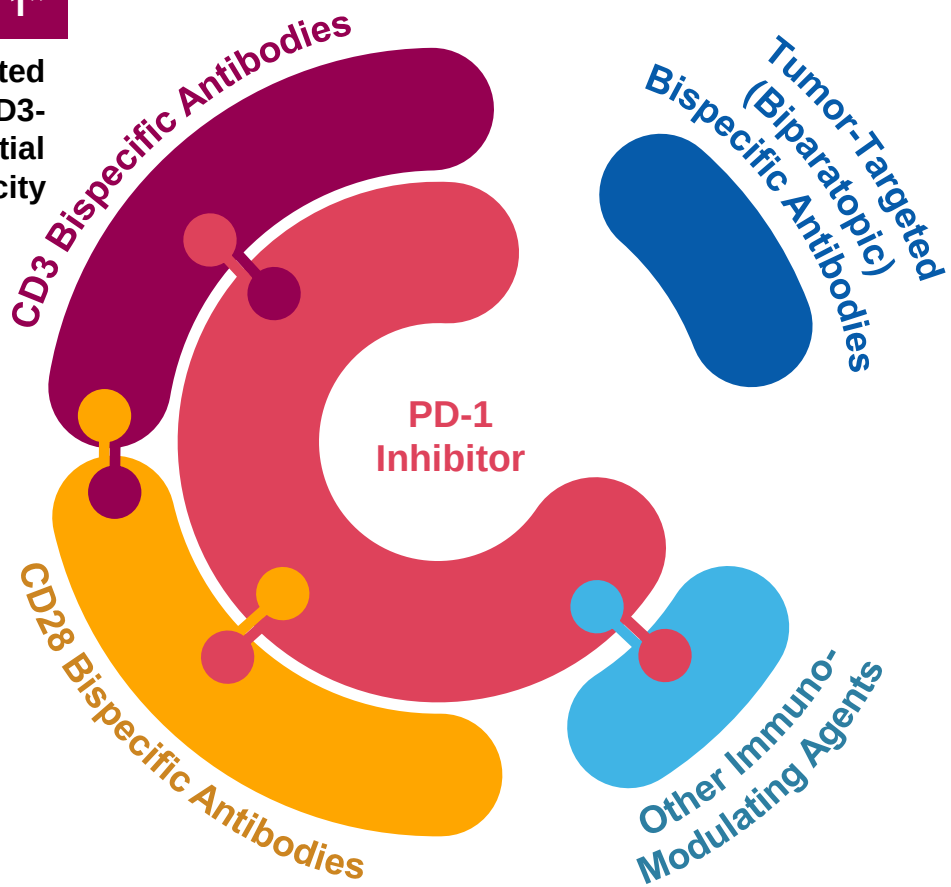
# Unique flexibility of internally-developed pipeline drives potential for novel and differentiated combinations

## CD3 Bispecifics: "Signal 1"

Designed to bridge tumor-associated antigens on cancer cells with CD3-expressing T cells, resulting in potential local T-cell activation and cytotoxicity

## CD28 Bispecifics: "Signal 2"

Designed to increase the activity of T cells that recognize tumor antigens by augmenting costimulatory signals




## Tumor-Targeted Biparatopics

Designed to disrupt cellular signaling and/or deliver a cytotoxic drug to tumor cells

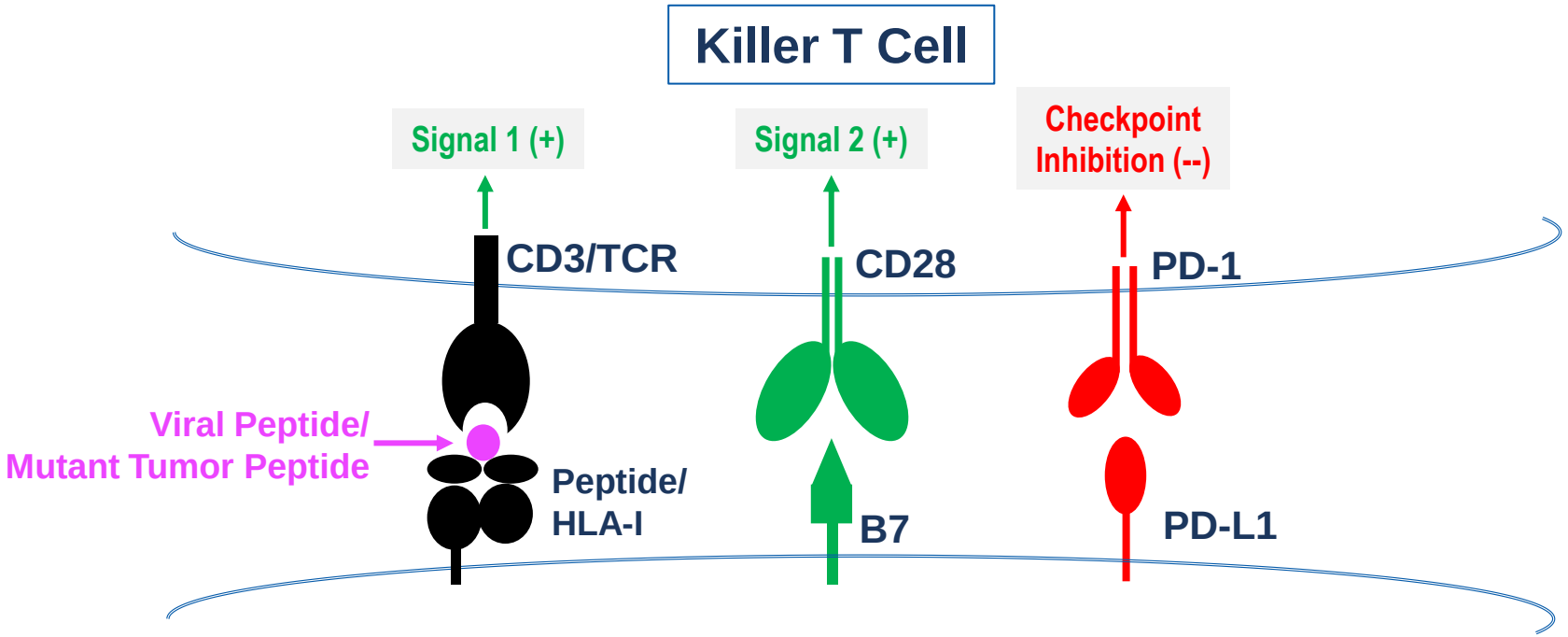
## Modulating immune response

Designed to overcome the tumor suppressive microenvironment

# How Killer T Cells Recognize and Attack Target Cells

**Killer T cell activation requirements**

Signal 1: Recognize target cell via T Cell Receptor (CD3/TCR)
Signal 2: Promote killing signal using costimulatory receptor (CD28)
(Signal 3: Cytokine amplification: e.g., IL-2, IFNγ, IL-12)
Then: Rapid suppression, via checkpoint inhibition (e.g. PD-1 and LAG-3), to prevent auto-immunity




**Target Cell:**
Virally-infected or Tumor Cell – "CD3/TCR" recognizes foreign viral peptide or mutated tumor peptide on HLA



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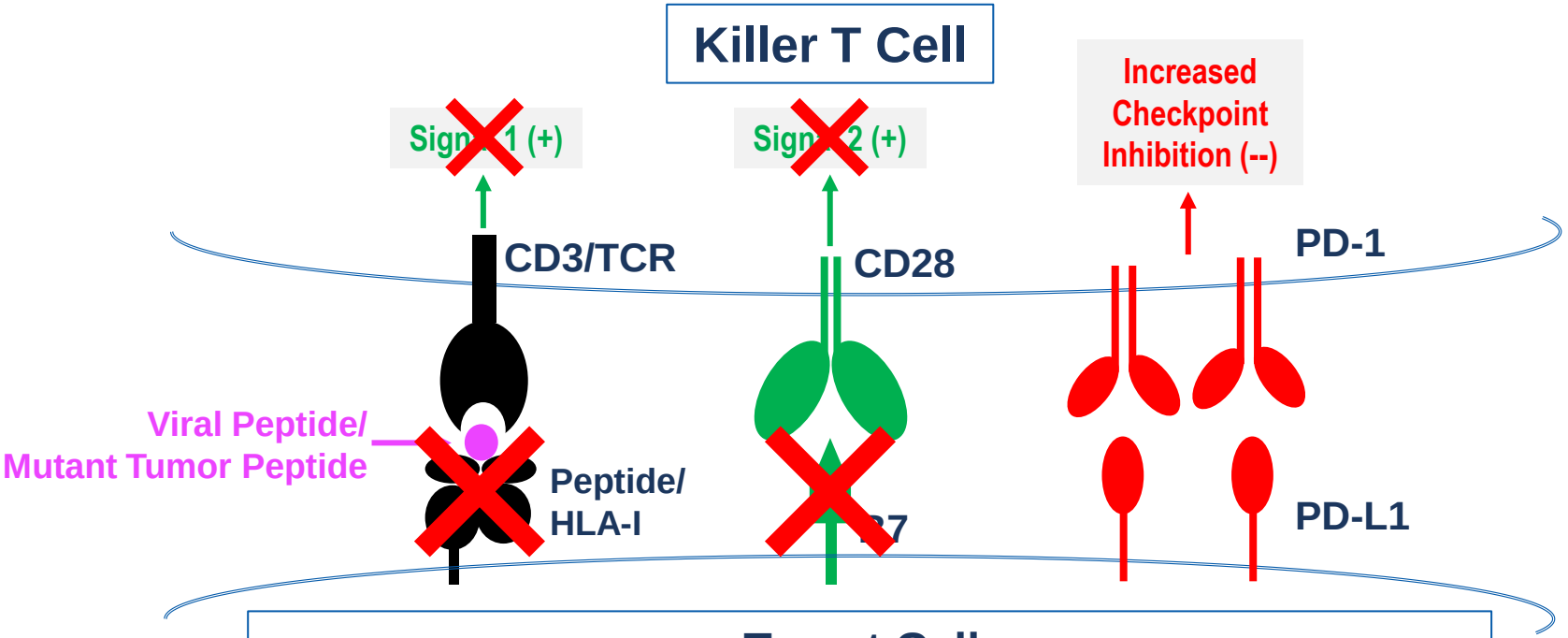
# “Cold Tumors” can evade Killer T Cells

**Tumors eliminate Signal 1 and/or 2, and increase checkpoint inhibition**

- **Signal 1: Tumors do not present any (or very few) mutant peptides**
- **Signal 2: Tumors do not present any (or little) costimulatory ligand (B7)**
- **Tumors over-express checkpoint (e.g. PD-1 and LAG-3) ligands**

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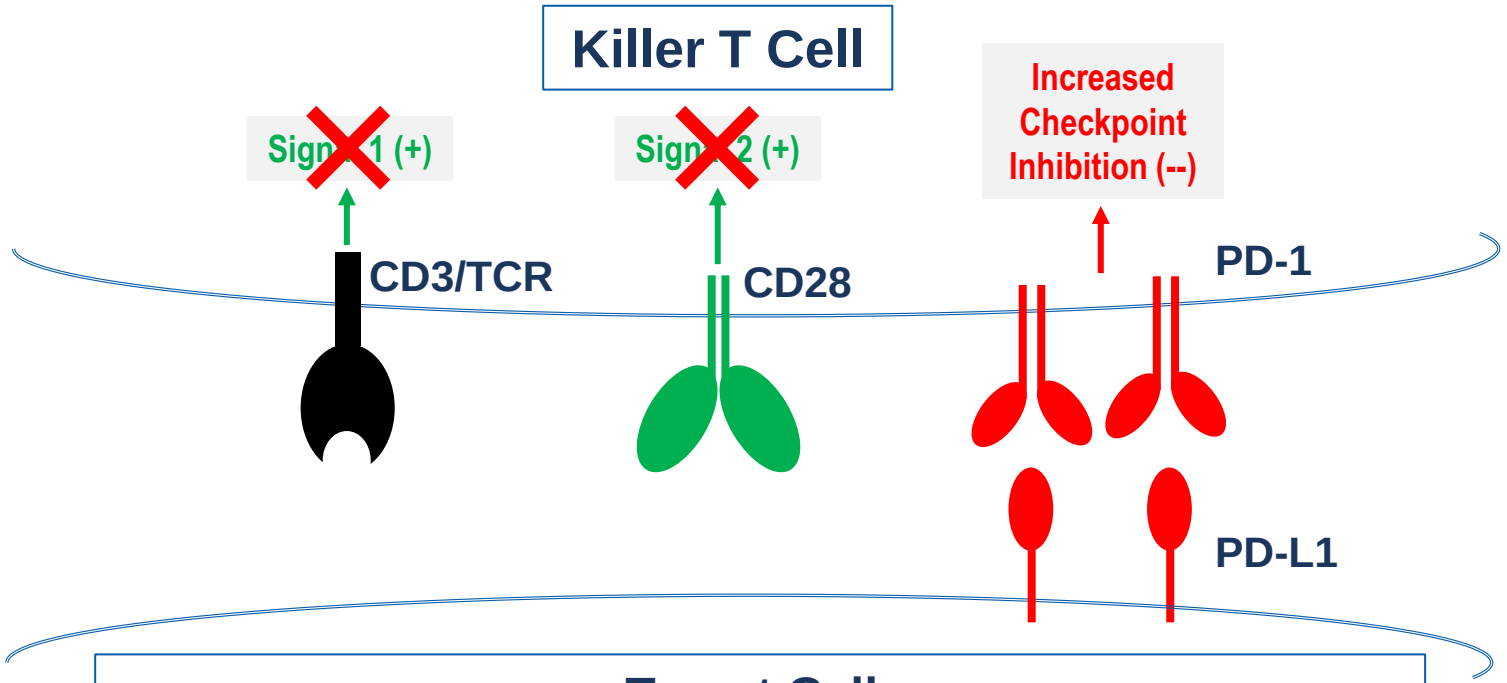


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# Turning “cold” tumors into “hot” tumors:
## Restore Signal 1 & 2 in killer T cells, block checkpoint inhibition

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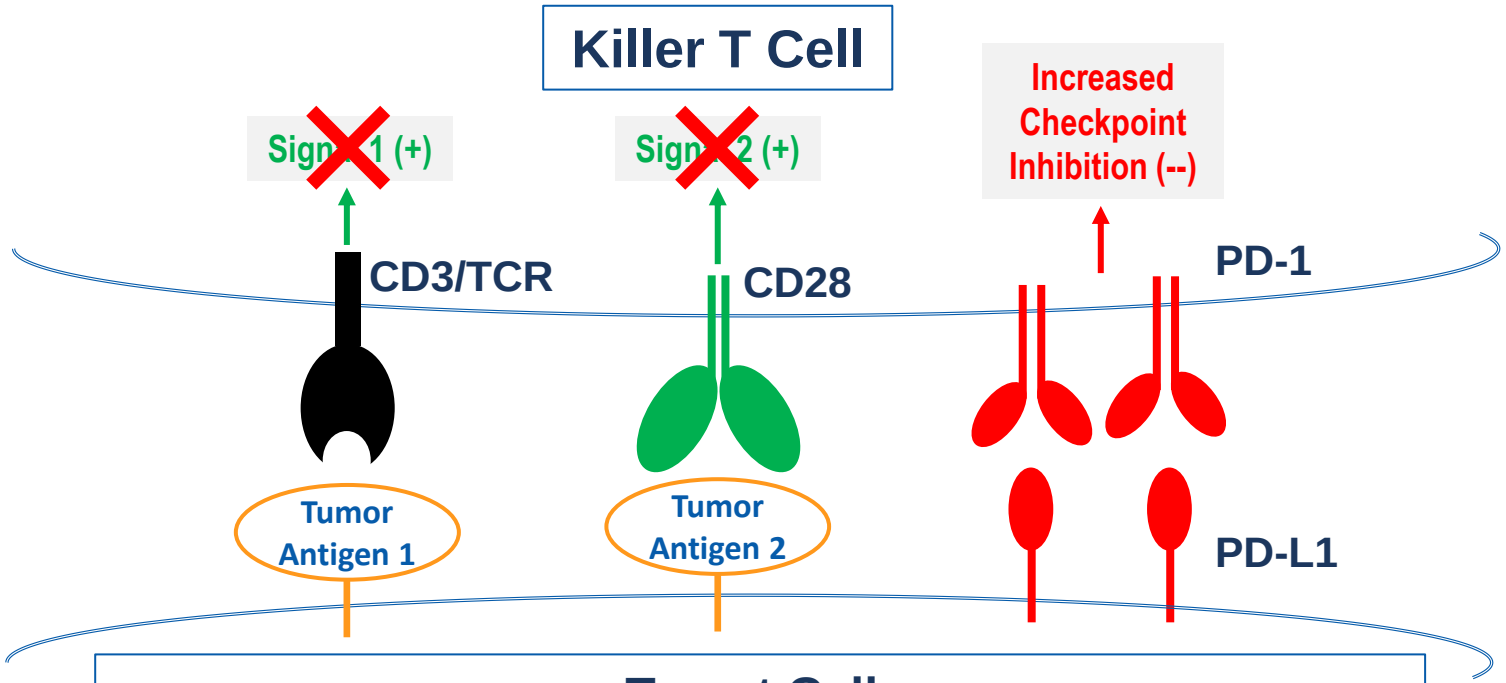


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Tumors do not present any (or very few) mutant peptides, and/or do not express any (or little) costimulatory ligand, and/or over-express checkpoint (e.g. PD-1 and LAG-3) ligands



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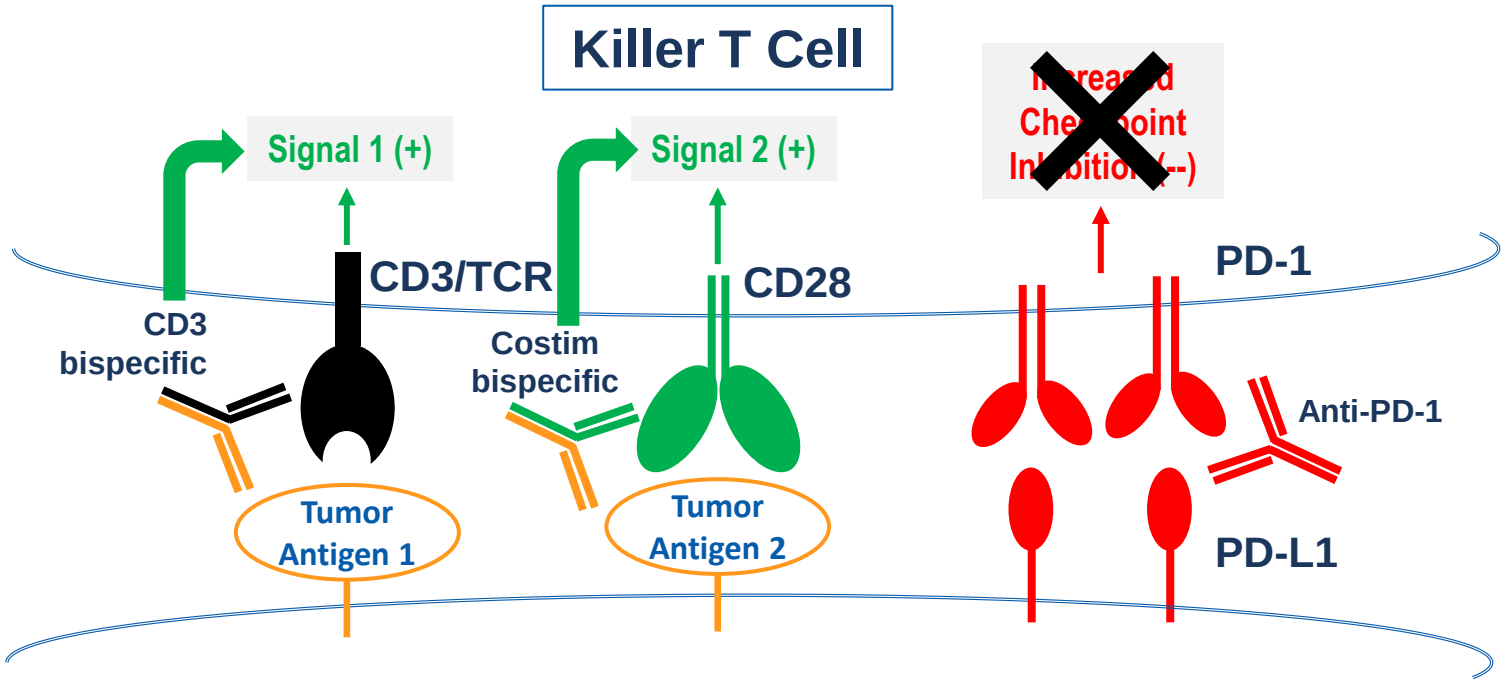
# Turning “cold” tumors into “hot” tumors:
## Restore Signal 1 & 2 in killer T cells, block checkpoint inhibition

Signal 1: Restore Signal 1 using “CD3 BiSpecific”
Signal 2: Restore Signal 2 using “CoStim BiSpecific”
Block “Checkpoint Inhibitors” using anti-PD1 (or anti-LAG-3)




- ✓ Regeneron has clinically validated its checkpoint blockers (anti-PD-1 and anti-LAG-3) and CD3-bispecifics as potentially best-in-class
- ✓ First-in-class costimulatory bispecifics have minimal clinical activity or toxicity as monotherapy
- ✓ Preclinical studies have shown profound synergy when any of these above agents are combined



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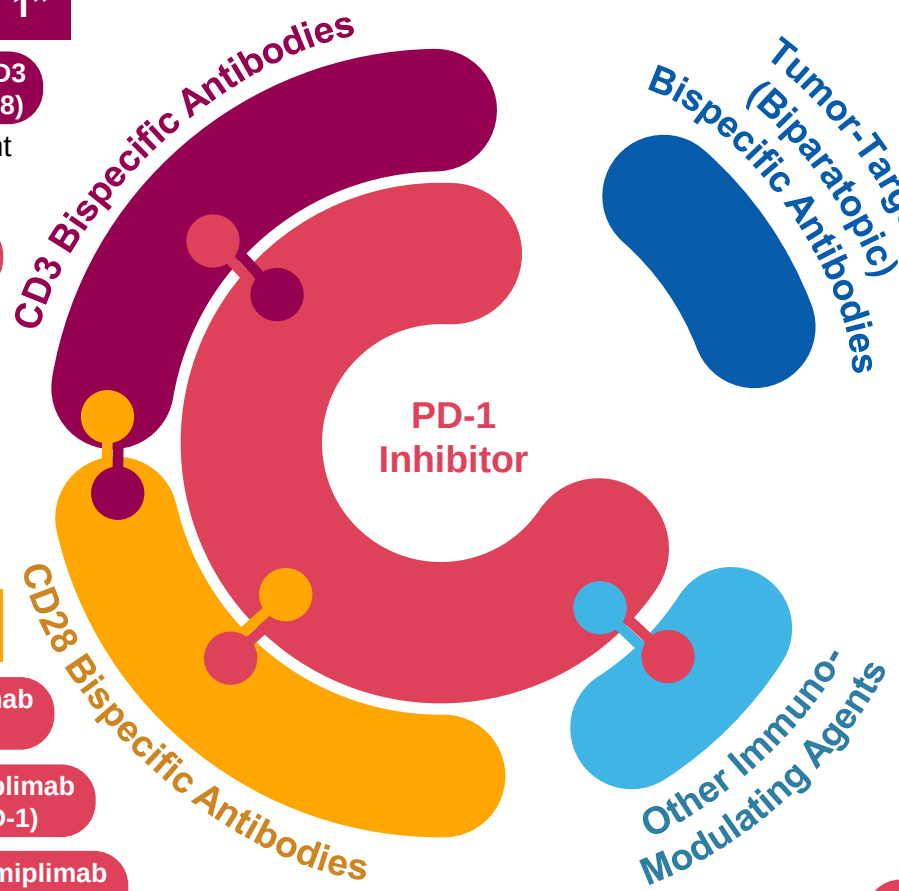
# Unique flexibility of internally-developed pipeline drives potential for novel and differentiated combinations

## CD3 Bispecifics: "Signal 1"

- Odronextamab (CD20xCD3) — R/R B-NHL, CLL
- BCMAxCD3 (REGN5458) — R/R Multiple Myeloma
- PSMAxCD3 (REGN4336) — Metastatic prostate cancer
- MUC16xCD3 (REGN4018) — Recurrent ovarian cancer
- PSMAxCD3 (REGN4336) + Cemiplimab (PD-1) — Metastatic prostate cancer
- MUC16xCD3 (REGN4018) + Cemiplimab (PD-1) — Recurrent ovarian cancer
- MUC16xCD3 (REGN4018) + MUC16xCD28 (REGN5668) — Recurrent ovarian cancer
- PSMAxCD3 (REGN4336) + PSMAxCD28 (REGN5678) — Metastatic prostate cancer

## CD28 Bispecifics: "Signal 2"

- PSMAxCD28 (REGN5678) + Cemiplimab (PD-1) — Metastatic prostate cancer
- EGFRxCD28 (REGN7075) + Cemiplimab (PD-1) — Solid tumors
- MUC16xCD28 (REGN5668) + Cemiplimab (PD-1) — Recurrent ovarian cancer




## Tumor-Targeted Biparatopics

- METxMET (REGN5093) — MET-altered advanced NSCLC
- METxMET ADC (REGN5093-M114) — MET over-expressing advanced NSCLC

## Modulating immune response

- Cemiplimab (PD-1) + Fianlimab (LAG3) — Melanoma & other advanced malignancies
- Cemiplimab (PD-1) + GITR (REGN6569) — HNSCC
- Cemiplimab (PD-1) + vidutolimod (TLR9) — CSCC, Merkel cell carcinoma

EGFR, Epidermal growth factor receptor; MUC16, Mucin 16; PSMA, Prostate-specific membrane antigen; R/R, Relapse/refractory; B-NHL, B-cell Non-Hodgkin lymphoma; BCMA, B-cell maturation antigen; NSCLC, Non-small cell lung cancer; SCCHN, Squamous cell carcinoma of the head and neck; CSCC, Cutaneous squamous cell carcinoma; ADC, Antibody drug conjugate; LAG-3, Lymphocyte-activation gene 3; GITR, Glucocorticoid-induced TNFR-related protein



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

# Programs to be discussed today

## CD3 Bispecifics: "Signal 1"

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## CD28 Bispecifics: "Signal 2"

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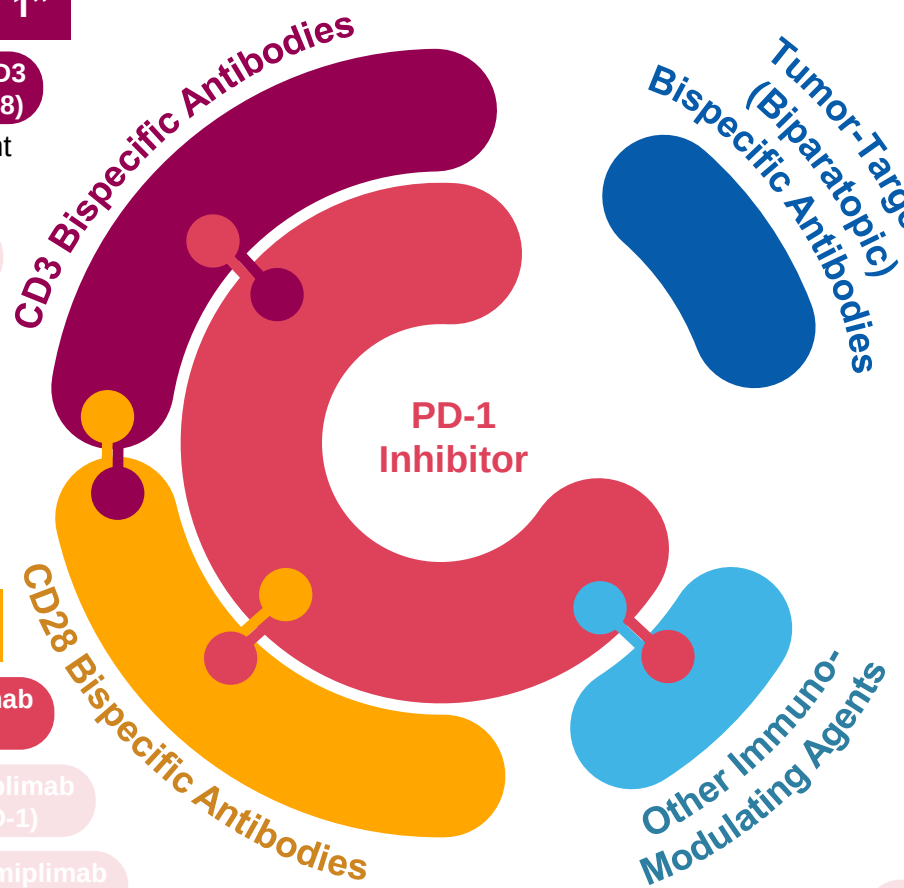


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# ESMO 2022 Updates

**Israel Lowy, MD, PhD**
SVP, Translational and Clinical Sciences, Oncology

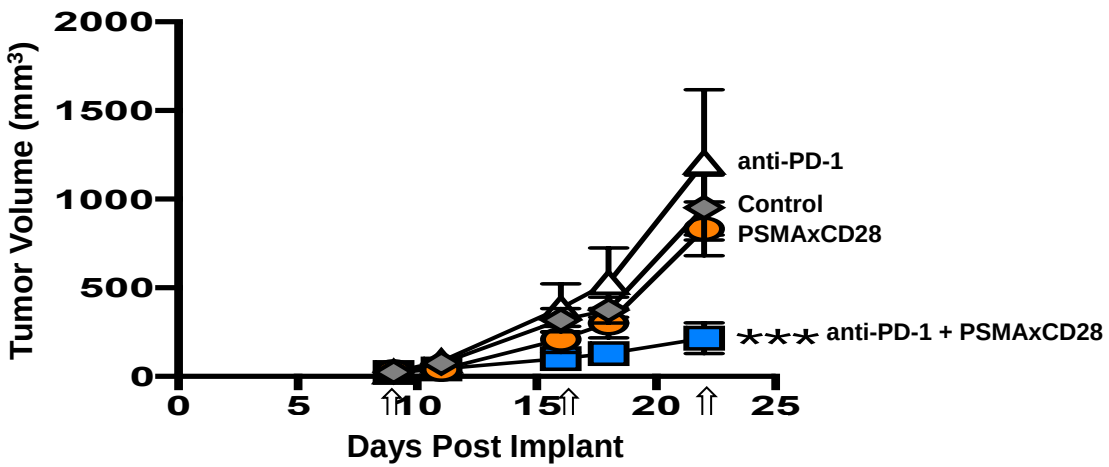
Data update

# First-in-class costim bispecific PSMAxCD28 + Libtayo in development for late-stage prostate cancer

In August 2022, we shared encouraging early clinical data from the dose escalation study

- Prostate cancer is the 2nd leading cause of cancer death in men in the U.S.[1]
- REGN5678 (PSMAxCD28) is one of our three clinical-stage costimulatory bispecifics, which are designed to augment CD28 signaling in T cells to increase anti-tumor activity in combination with Libtayo or a CD3 bispecific
- In preclinical models, PSMAxCD28 in combination with an anti-PD-1 inhibited growth of established tumors[2]

**Humanized prostate cancer mouse model**




- August 2022: Encouraging topline clinical data released for the eight cohorts of the FIH study
- Broad combination development approach for prostate cancer:
  - PSMAxCD28 in combination with Libtayo and/or REGN4336 (PSMAxCD3)
  - PSMAxCD3 monotherapy and with Libtayo

2022 readout:

PSMAxCD28 (REGN5678) + Cemiplimab (PD-1)

2024+ readouts:

PSMAxCD3 (REGN4336) + PSMAxCD28 (REGN5678)

PSMAxCD3 (REGN4336)

PSMAxCD3 (REGN4336) + Cemiplimab (PD-1)



1. Siegel RL et al. CA Cancer J Clin. 2020. 2. Waite JC et al. Sci. Transl. Med 2020. FIH, first-in-human.

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# PSMAxCD28 + Libtayo: Initial Clinical Data Supporting Profound Synergy with CoStim BiSpecs & anti-PD-1

## Proof-of-principle for the broader costimulatory bispecific platform

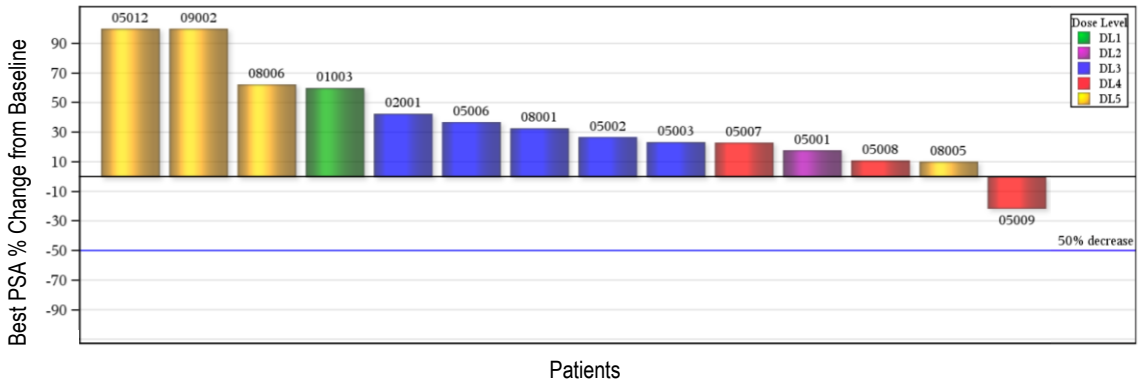
**Note: Prostate cancer shows <10% response rates to PD1 Monotherapy (unless tumors have mismatch repair defects); note recent Keytruda Phase 3 failure**

First clinical data from ongoing Phase 1/2 trial showed dose-dependent anti-tumor activity for REGN5678 (PSMAxCD28) when combined with standard dose Libtayo, suggesting potential to overcome mCRPC resistance to PD-1 inhibition

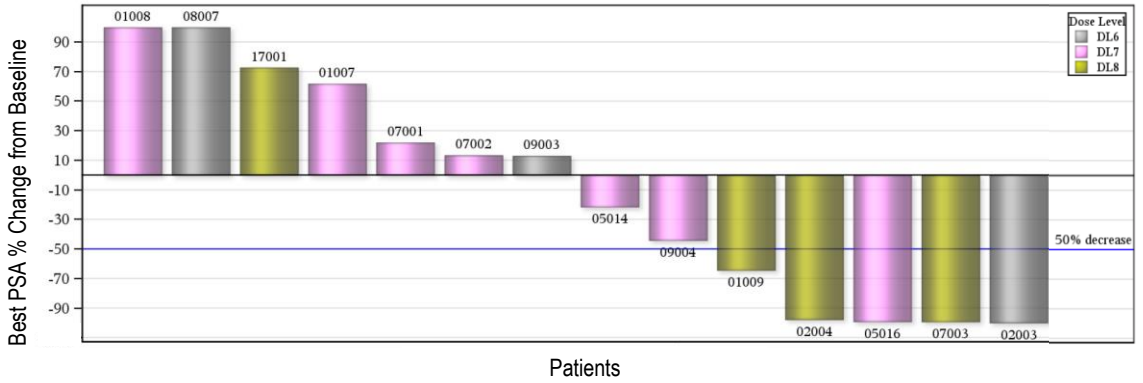
**Efficacy and safety**:

- **Dose Levels 1-5 (n=17): Minimal anti-tumor activity and no ≥Gr3 irAEs**
  - 0/17 response by PSA across these 5 dose levels
- **Dose Levels 6-8 (n=16): Dose-dependent responses observed with correlated irAEs**
  - DL6: 1/4 patients had response -- a 100% decrease in PSA and a complete response in target lesions, maintained for ~12 months
    - Responder discontinued therapy due to a Gr3 irAE of skin; CR maintained
  - DL7: 3/8 patients had responses -- 99%, 44% and 22% respective decrease in PSA
    - Two of the responders had a Gr3 AE, which resolved
  - DL8: 3/4 patients had responses -- 99%, >99% and 82% respective decreases in PSA
    - One of the responders had a Gr3 AE that resolved
    - One of the responders had an irAE resulting in death
- **No additional Gr4 irAEs or ≥Gr2 CRS have been observed in the trial to date**
- **All ≥Gr3 irAEs only occurred in patients with anti-tumor activity**

### Patients from Dose Levels 1 to 5




### Patients from Dose Levels 6 to 8




NOTE: Patient 01009 had further PSA reduction to 82% at a subsequent analysis.

PSA, prostate-specific antigen; CR, complete response; Gr, grade; irAE, immune-related adverse event; CRS, cytokine release syndrome.
Preliminary, unmonitored data.



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# PSMAxCD28 + Libtayo demonstrated 75% response rate at dose level 8

Advanced metastatic castration-resistant prostate cancer shows <10% response rates to anti-PD-1 monotherapy

**Dose Level 8: 3/4 patients had profound responses**

- **Patient 1009: 82% reduction in PSA at week 9**
  - PSA at baseline >30 ng/mL; PSA continued to rise to >50 ng/mL until cemiplimab initiated at week 3
  - No ≥Gr3 AEs reported
  - Treatment paused at week 9; observation continues
- **Patient 7003: 99% reduction in PSA at week 9**
  - PSA at baseline >200 ng/mL; PSA continued to rise until cemiplimab initiated at week 3
  - Developed Gr3 mucocitis at week 8 that has since resolved
  - Remains on treatment through week 15
- **Patient 2004: >99% reduction in PSA at week 6**
  - PSA at baseline >500 ng/mL; PSA continued to rise to >600 ng/mL until cemiplimab initiated at week 3
  - Developed Gr3 case of acute inflammatory demyelinating polyradiculopathy (AIDP) shortly after initial cemiplimab administration
  - AIDP developed into hemophagocytic lymphohistiocytosis (HLH) at week 9 and patient passed away at week 13

## Graphs of three responders at dose level 8

### Prostate-Specific Antigen (PSA) vs. time (weeks)




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# Regeneron ESMO 2022 titles

| Libtayo (cemiplimab) | Indication | Presentation title |
|---|---|---|
| monotherapy | Skin cancer | Neoadjuvant cemiplimab in patients with stage II–IV CSCC: Primary analysis of a Phase 2 study |
| monotherapy | Skin cancer | Phase 2 study of cemiplimab in patients with advanced CSCC: Final analysis from EMPOWER-CSCC-1 Groups 1, 2 and 3 |
| monotherapy | Skin cancer | Phase 2 confirmatory study of cemiplimab in patients with locally advanced or metastatic CSCC: Study 1540 Group 6 |
| monotherapy | Skin cancer | Prospective study of the safety and efficacy of cemiplimab in patients with advanced CSCC in a real-world setting |
| monotherapy | Cervical cancer | Phase 3 EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 trial of cemiplimab in recurrent or metastatic cervical cancer: Long-term survival analysis |
| monotherapy + chemo | Lung cancer | Continued cemiplimab with addition of chemotherapy in patients with progressive disease after first line cemiplimab monotherapy for advanced NSCLC: analysis from EMPOWER-Lung 1 |
| monotherapy + chemo | Lung cancer | Cemiplimab with platinum-based chemotherapy for first-line locally advanced NSCLC: EMPOWER-Lung 3 subgroup analysis |
| monotherapy | Lung cancer | Clinical interchangeability of PD-L1 immunohistochemistry assays for the treatment of first-line NSCLC with cemiplimab |
| monotherapy | Lung cancer | Patient-reported outcomes of cemiplimab vs chemotherapy in advanced NSCLC: EMPOWER-Lung 1 histology subgroups |
| monotherapy | Lung cancer | Factors associated with not receiving first-line immune checkpoint inhibitor treatment among patients with advanced NSCLC and high PD-L1 expression: an evaluation by age |
| monotherapy | Lung cancer | Outcomes of real-world patients with advanced NSCLC and high PD-L1 expression receiving first line immune checkpoint inhibitor therapy |

| Other Pipeline | Indication | Presentation Title |
|---|---|---|
| Fianlimab, Libtayo | Skin cancer | Phase 1 study of fianlimab, a human lymphocyte activation gene-3 (LAG-3) monoclonal antibody, in combination with cemiplimab in advanced melanoma |
| Ubamatamab | Ovarian cancer | Ubamatamab (REGN4018, MUC16xCD3 bispecific antibody) monotherapy in patients with recurrent ovarian cancer: Phase 1 dose-escalation analysis |
| REGN5093 (METxMET) | Lung cancer | Early safety, tolerability, and efficacy of REGN5093 in patients with MET-altered advanced NSCLC from a first in human study |
| Vidutolimod | Skin cancer | Vidutolimod + pembrolizumab as 2L+ treatment in patients with anti-PD-1 refractory melanoma and adrenal insufficiency: subgroup analyses of a Phase 1b study |
| N/A | Blood cancer | Real-world health-related quality of life in patients with Follicular Lymphoma: Comparisons by line of therapy and region (Europe vs US) |



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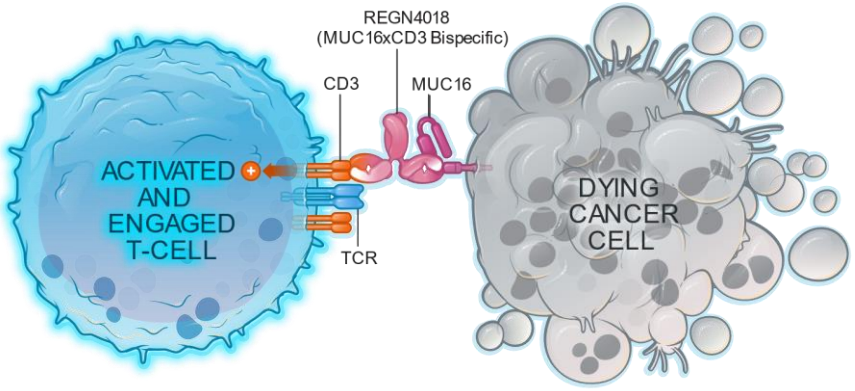
# Ubamatamab: first-in-class MUC16xCD3 for solid tumors

Vision for ubamatamab: develop a highly effective and well tolerated treatment for ovarian cancer and potentially other MUC16 expressing tumors (e.g. pancreatic, endometrial) as monotherapy or in combination

- There is a high unmet need for improved therapies for women with rOVCA, with about 14,000 deaths/year in the U.S.[1,2]
  - The median survival is only ~12 months in the platinum resistant rOVCA[3]
- Ubamatamab (REGN4018) is a human bispecific antibody, designed to bridge MUC16 on cancer cells with CD3-expressing T cells to facilitate T-cell activation and killing of cancer cells[4]

**Ubamatamab**
**(MUC16xCD3 bispecific)**




- ESMO 2022: Initial ubamatamab monotherapy clinical data
  - Activity across a wide range of doses (ORR and DCR)
  - Responses appear enriched in MUC16-high tumors
  - mDOR was 12.2 months by Kaplan-Meier analysis
  - Tolerability across a wide range of doses, with AEs most commonly occurring during step-up dosing
- Developed as monotherapy and in combination with Libtayo and/or REGN5668 (MUC16xCD28), next steps:
  - Phase 2 dose-ranging portion of this study (monotherapy and with Libtayo)

2022 readout:

- MUC16xCD3 (REGN4018)

2023 readouts:

- MUC16xCD3 (REGN4018) + Cemiplimab (PD-1)
- MUC16xCD3 (REGN4018) + MUC16xCD28 (REGN5668)
- MUC16xCD28 (REGN5668) + Cemiplimab (PD-1)



1. National Cancer Institute. Available at: https://seer.cancer.gov/statfacts/html/ovary.html 2. Siddiqui MK et al. Gynecol Oncol. 2017;146:44–51. 3. Pujade-Lauraine et al. J Clin Oncol. 2014; 13:1302-8 4. Crawford A et al. Sci Transl Med. 2019;11:1–13
rOVCA, recurrent ovarian cancer; ORR, objective response rate, DCR, disease control rate; mDOR, median duration of response.

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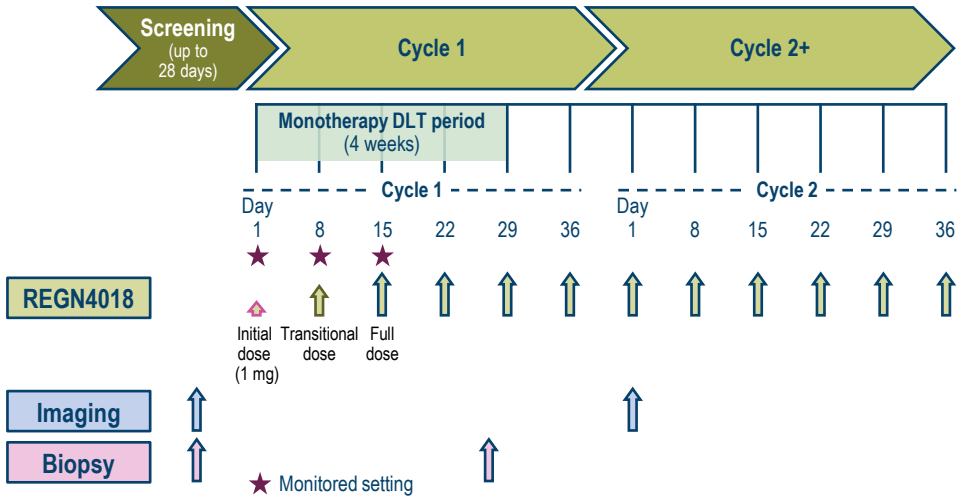
# Ubamatamab first-in-human trial for advanced ovarian cancer

## Heavily pretreated ovarian cancer patients enrolled in a step-up monotherapy dose escalation study

FIH ubamatamab (MUC16xCD3) monotherapy dose escalation (NCT03564340)




- Dosed IV weekly, doses ranging from 0.1–800 mg
- Modified 3+3 design (4+3)
- Step-up dosing for initial two doses utilized to mitigate risk of CRS
- **Primary objectives:** Safety and PK
- **Secondary objectives:** Preliminary ORR per RECIST 1.1
- **Key inclusion criteria:**
  - Women ≥18 years of age
  - Relapsed advanced epithelial ovarian, primary peritoneal, or fallopian tube cancer
  - ≥1 prior cycle of platinum-based therapy
  - CA125 ≥2X the upper limit of normal

| Demographics | Total (n=78) |
|---|---|
| Age in years, median (range) | 61 (31.0–80.0) |
| Number of lines of prior therapy, median (range) | 4.5 (1–17) |
| Histology, n (%) | |
| High-grade serous | 71 (91.0) |
| Clear cell | 2 (2.6) |
| High-grade endometroid | 1 (1.3) |
| Low-grade serous | 1 (1.3) |
| Other | 3 (3.8) |
| Other Features | |
| CA-125 baseline serum U/mL, median (range) | 709 (107–10,000) |
| Visceral Metastases, n (%) | 26 (33) |
| >75% PS2+ IHC staining,* n (%) | 30 (58) |

* Out of 52 patients with available MUC16 score

| | |
|---|---|
| Duration of exposure, median (range), weeks | 12 (0.4–145) |



CA-125, cancer antigen 125; FIH, first-in-human; CRS, cytokine release syndrome; IV, intravenous; ORR, objective response rate; PK, pharmacokinetics; RECIST, Response Evaluation Criteria in Solid Tumors. Data cut-off date: March 16, 2022.

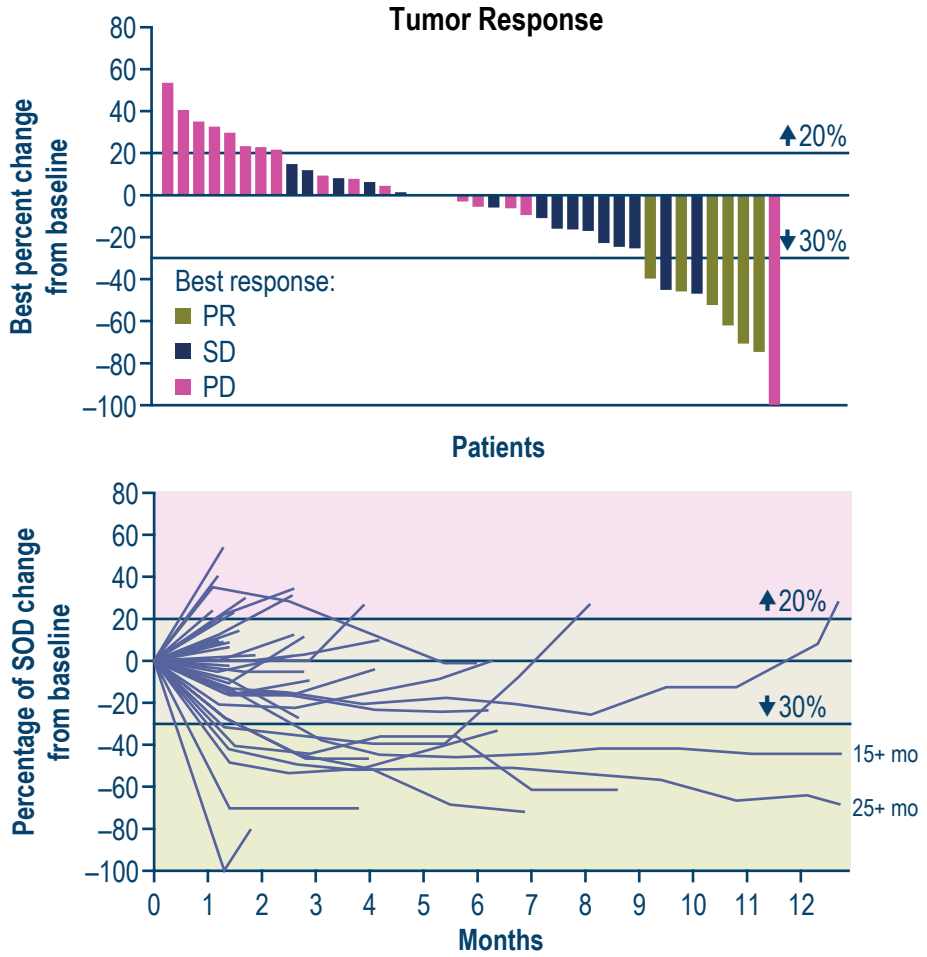
# Ubamatamab: durable responses at doses 20 mg – 800 mg

mDOR of 12.2 months, 57% disease control rate with the first-in-class single-agent MUC16xCD3 – promising activity in a solid tumor

Responses seem enriched in MUC16-high tumors (31% ORR)

| | Results |
|---|---|
| Response in patients who received at least one dose of ≥ 20 mg, % (n) | (n=42) |
| ORR (complete response + partial response) | 14.3% (6) |
| DCR (complete response + partial response + stable disease) | 57.1% (24) |
| CA-125 response | 23.8% (10) |
| Patients with no visceral metastases (exploratory subset), n (%) | (n=29) |
| ORR (complete response + partial response) | 20.7% (6) |
| DCR (complete response + partial response + stable disease) | 72.4% (21) |
| CA-125 response | 31.0% (9) |
| Patients with >75% of tumour cells with 2+ baseline MUC16 IHC staining (preliminary exploratory subset), n (%) | (n=13*) |
| ORR (complete response + partial response) | 30.8% (4) |
| DCR (complete response + partial response + stable disease) | 61.5% (8) |
| CA-125 response | 46.2% (6) |

- mDOR = 12.2 months
  (Kaplan-Meier estimate in patients with confirmed response)




* Across all dose levels, IHC was evaluated in 52 patients; 58% had >75% of tumor cells with 2+ baseline MUC16. Data for 26 patients were available at the time of analysis, 13 of which had >75% of tumor cells with 2+ baseline MUC 16 staining. Data cut-off date: March 16, 2022.

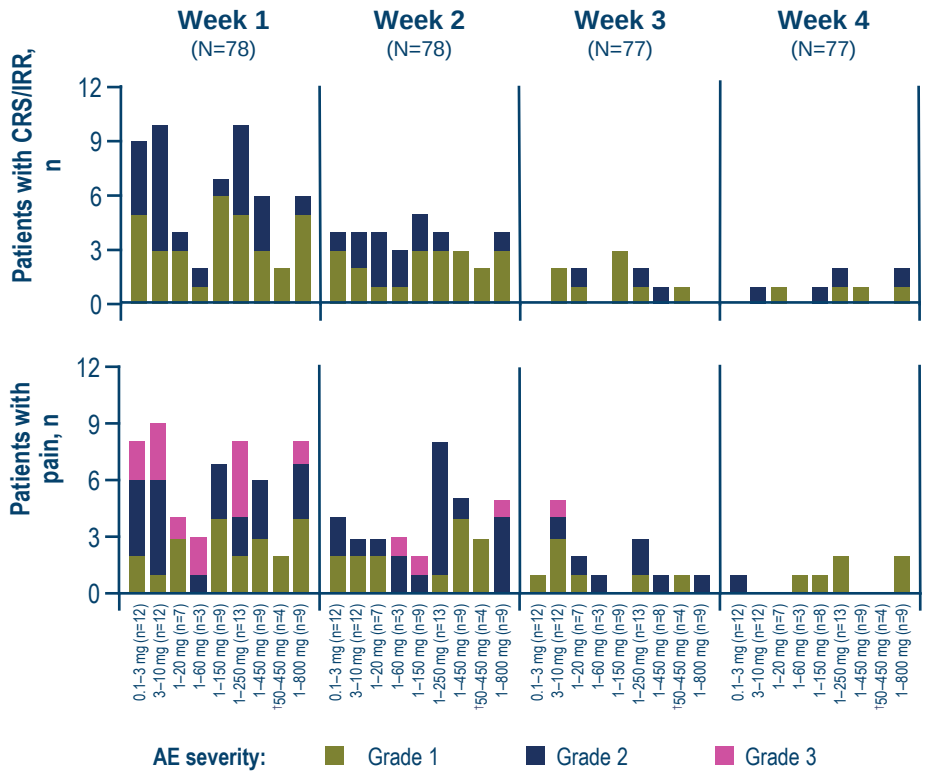
mDOR, median duration of response, CA-125, cancer antigen 125; ORR, objective response rate; DCR, disease control rate; IHC, immunohistochemical; CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SOD, Sum of the Diameters.

# Ubamatamab safety: most common TEAEs occurred with initial doses

No Grade ≥3 cytokine release syndrome (CRS) observed

| | All grades (n=78) | Grade ≥3 (n=78) |
|---|---|---|
| Total TEAEs, n | 1403 | 103 |
| Patients with any TEAE, n (%) | 78 (100.0) | 51 (65.4) |
| Patients with any TEAE resulting in death,* n (%) | 3 (3.8) | 3 (3.8) |
| Primary toxicities experienced during step up dosing, n (%) | | |
| CRS | 58 (74.4) | 0 (0) |
| Grade 1 | 31 (39.7) | n/a |
| Grade 2 | 27 (34.6) | n/a |
| Patients with any TEAE with pain | 68 (87.2) | 18 (23.1) |
| Abdominal pain | 58 (74.4) | 16 (20.5) |
| Back pain | 29 (37.2) | 6 (7.7) |
| Non-cardiac chest pain | 14 (17.9) | 1 (1.3) |
| ICANS | 1 (1.3) | 1 (1.3) |
| Other G3 AEs observed in >5% of patients, n (%) | | |
| Anaemia | 40 (51.3) | 19 (24.4) |
| Neutropaenia | 10 (12.8) | 6 (7.7) |

**CRS/IRR and pain AEs over the first four doses of ubamatamab**






*Sepsis (1), cardiac arrest (2), none attributed to ubamatamab based on sponsor assessment; †Translational dose of 2–25mg. Data cut-off date: March 16, 2022.
AEs, adverse events; CRS, cytokine release syndrome; G3, Grade 3; ICANS, immune effector cell-associated neurotoxicity syndrome; IRR, infusion-related reactions; n/a, not applicable; TEAE, treatment-emergent adverse event.

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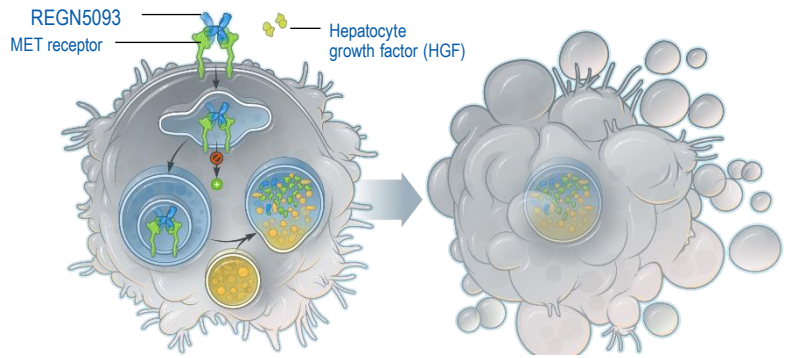
Initial data

# METxMET first-in-class bispecific demonstrates preliminary efficacy in MET-altered advanced NSCLC

## Initial data set encouraging for the differentiated METxMET ADC, data anticipated in 2023

- Long-term survival remains an unmet need in advanced NSCLC with mesenchymal epithelial transition (MET) alterations
  - Resistance to MET-targeting TKIs frequently occurs
- REGN5093 (METxMET bispecific) targets two distinct epitopes on the MET receptor, enabling rapid internalization, rather than activation of the MET receptor
- Preclinical data:
  - In MET-driven tumor models, our biparatopic antibody exhibits significantly better activity than the parental monoclonal antibodies
  - METxMET-ADC promotes substantial and durable tumor regression in xenografts with moderate to high MET expression, including models that exhibit innate or acquired resistance to MET blockers

*METxMET bispecific induces death of the tumor cell by disrupting its cell-survival signaling*




- ESMO 2022: among the population of heavily treated patients with MET-altered advanced NSCLC, REGN5093 monotherapy demonstrated:
  - Preliminary efficacy signals among patients with all three types of MET alterations: MET exon 14 mutations, MET gene amplification and/or MET protein overexpression
  - Tumor response was enhanced with centrally confirmed biomarker selection
  - Acceptable safety profile – no DLTs, Gr≥3 AEs in 26% patients

**Expansion cohorts: REGN5093 2000 mg Q3W IV**

| Cohort 1A | Cohort 1B | Cohort 2A | Cohort 2B | Cohort 2C |
|---|---|---|---|---|
| **MET exon 14 mutation (MET TKI experienced)** | **MET exon 14 mutation (MET TKI naïve)** | **MET gene amplification (MET TKI naïve)** [MET/CEP7 ratio ≥4 or MET gene fold change of ≥2* or MET fold change ≥2 in ctDNA; or MET GCN ≥6] | **MET protein overexpression (MET TKI naïve)** [IHC 3+ or H score of ≥200] | **MET gene amplification & protein overexpression (MET TKI naïve)** [MET/CEP7 ratio ≥4 or MET gene fold change of ≥2* or MET fold change ≥2 in ctDNA; or MET GCN ≥6] and [IHC 3+ or H score of ≥200] |

Patients in expansion cohorts were enrolled based on local results of MET alteration.



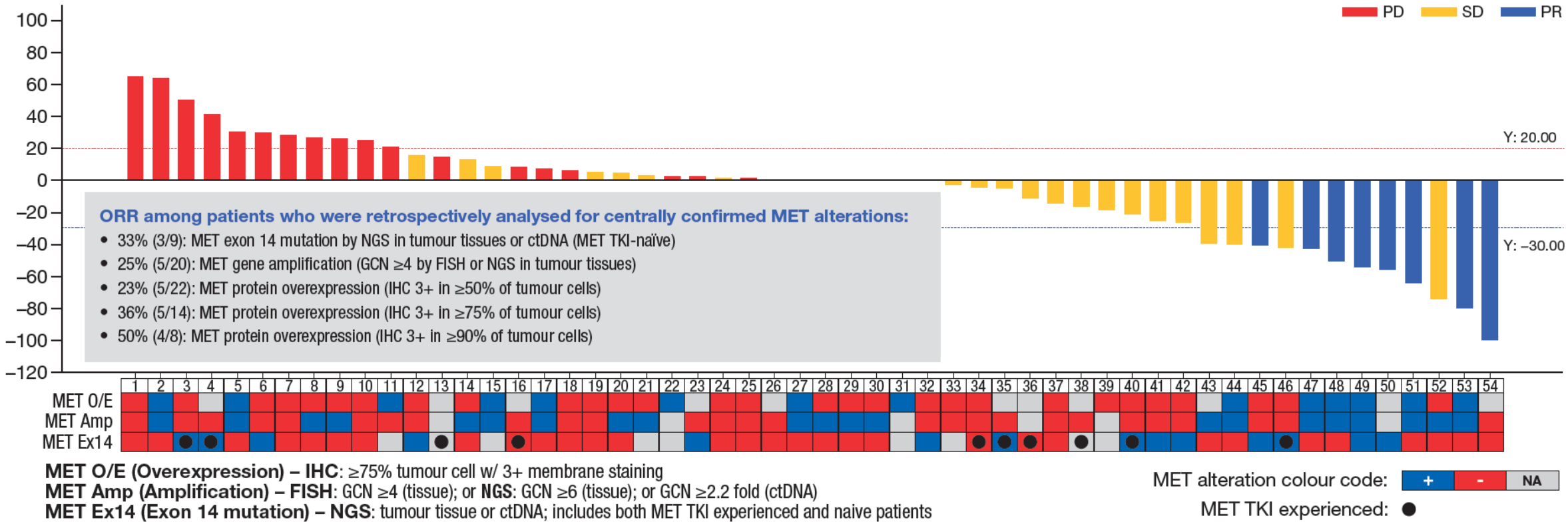
NSCLC, non-small cell lung cancer; ADC, antibody-drug conjugate; TKIs, tyrosine kinase inhibitors; DLT, dose limiting toxicity; AE, adverse event.

REGENERON

# Tumor response to METxMET is enriched by MET alteration

Promising early efficacy signals supporting a biomarker-driven strategy

## Tumor Response by Centrally Confirmed MET Alterations



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# METxMET safety: no DLTs observed

- No DLTs were observed
- Similar safety profile observed in dose-escalation and dose-expansion, notably with Grade 1/2 peripheral oedema in 9% patients
- Grade≥3 TEAEs reported in 26% patients

| Summary of safety data | Total (N=69) | |
|---|---|---|
| **Duration of exposure, median (range), weeks** | 9.3 (1-82) | |
| **TEAEs, n (%)** | **Any grade** | **Grade 3–5** |
| Overall | 59 (86) | 18 (26) |
| Serious | 16 (23) | 12 (17) |
| Led to discontinuation | 3 (4) | 2 (3) |
| Led to death | 1 (1) | 1 (1) |
| Occurred in ≥5% of patients | | |
| Nausea | 9 (13) | 0 |
| Fatigue | 7 (10) | 1 (1) |
| Oedema peripheral | 6 (9) | 0 |
| Pruritis | 6 (9) | 0 |
| ALT increased | 5 (7) | 2 (3) |
| AST increased | 5 (7) | 1 (1) |
| COVID-19 | 5 (7) | 1 (1) |
| Constipation | 5 (7) | 0 |
| Dizziness | 5 (7) | 0 |

| Summary of safety data, continued | Total (N=69) | |
|---|---|---|
| **Duration of exposure, median (range), weeks** | 9.3 (1-82) | |
| **TEAEs, n (%)** | **Any grade** | **Grade 3–5** |
| Headache | 5 (7) | 0 |
| Insomnia | 5 (7) | 0 |
| Pneumonia | 4 (6) | 3 (4) |
| Back pain | 4 (6) | 3 (4) |
| Decreased appetite | 4 (6) | 0 |
| Dyspnea | 4 (6) | 2 (3) |
| Hypoalbuminaemia | 4 (6) | 0 |
| Musculoskeletal chest pain | 4 (6) | 0 |
| Pleural effusion | 4 (6) | 2 (3) |
| Pulmonary embolism | 4 (6) | 1 (1) |
| Vomiting | 4 (6) | 0 |
| **Treatment-related AEs, n (%)** | | |
| Overall | 27 (39) | 3 (4) |
| Serious | 2 (3) | 2 (3) |



DLT, dose-limiting toxicity; TEAE, treatment-emergent adverse event.

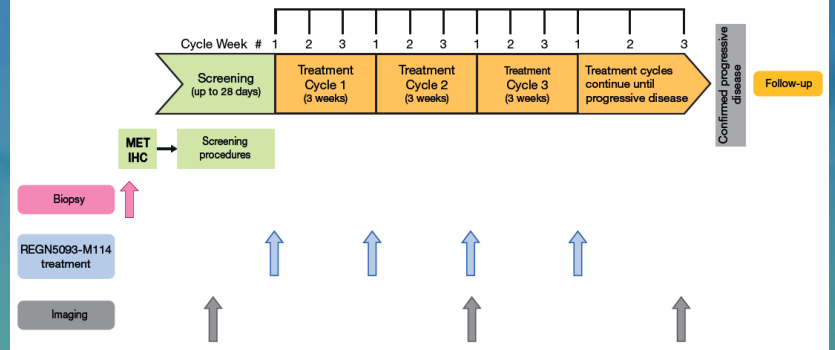
# Next steps for REGN5093 (METxMET)

**METxMET (REGN5093)** **METxMET ADC (REGN5093-M114)**

- MET-overexpression may render lung cancer susceptible to METxMET-directed rapid receptor internalization and antitumor activity
- These data show promise for upcoming METxMET ADC in MET-overexpressing NSCLC (expected 2023)
- METxMET ("naked" or ADC) could be combined with Libtayo for lung cancer
- Combinations with tyrosine kinase inhibitors (TKIs) also possible

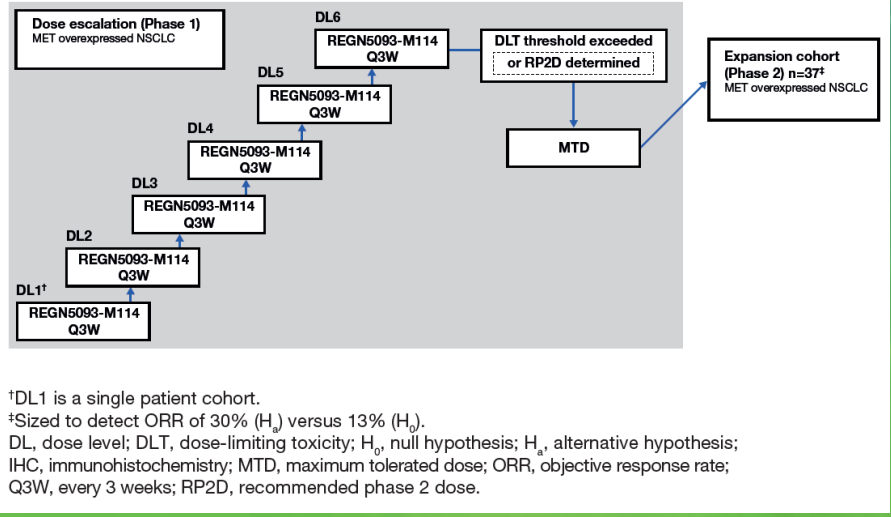
# METxMET-ADC (REGN5093-M114) Trial in Progress

## Study flow diagram




IHC, immunohistochemistry.

## Dose escalation and dose expansion




†DL1 is a single patient cohort.
‡Sized to detect ORR of 30% ($H_a$) versus 13% ($H_0$).
DL, dose level; DLT, dose-limiting toxicity; $H_0$, null hypothesis; $H_a$, alternative hypothesis; IHC, immunohistochemistry; MTD, maximum tolerated dose; ORR, objective response rate; Q3W, every 3 weeks; RP2D, recommended phase 2 dose.

Drilon A et al. TPS ASCO 2022



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

# Libtayo monotherapy provides strong foundation for oncology combinations

## Dermato-oncology

**Advanced Cutaneous Squamous Cell Carcinoma**
- First FDA-approved anti-PD-1

**Advanced Basal Cell Carcinoma**
- First FDA-approved anti-PD-1

**Adjuvant Cutaneous Squamous Cell Carcinoma**
- Phase 3 enrolling

**First-line Advanced Melanoma**
- Phase 3 enrolling in combination with fianlimab (anti-LAG3)

**Second-line Advanced Melanoma**
- Combinations with multiple candidates

**Libtayo is first-in-class and considered standard of care in FDA-approved non-melanoma skin cancer indications**

## NSCLC

**First-line Advanced Non-Small Cell Lung Cancer**
- FDA-approved as monotherapy in tumors with high (≥50%) PD-L1 expression

**First-line Advanced Non-Small Cell Lung Cancer**
- Combination with chemotherapy; under FDA and EMA review

**Building presence in NSCLC monotherapy in advance of potential chemo-combo approval**



Indicates U.S. Food and Drug Administration (FDA) and European Commission (EC) approval

Indicates FDA and EMA (European Medicines Agency) regulatory review is ongoing.

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

Initial data

Cemiplimab

# Libtayo Phase 2 data in neoadjuvant CSCC support our continued investment into our leadership in skin cancer

## Potentially significant near-term opportunity

- Libtayo is the leader in advanced CSCC with no curative treatment options
- No currently approved systemic therapy for CSCC in the curative setting
  - Neoadjuvant therapy (prior to surgery) may improve outcomes in patients by lowering the risk of surgical burden, reducing failure rates, complications and deformity in advanced CSCC patients who are candidates for surgery
  - ~20,000 CSCC U.S. patients may be candidates for neoadjuvant treatment[1]
- At ESMO 2019, reported results from the MD Anderson pilot study of single-arm Libtayo in neoadjuvant CSCC[2]
  - N=20; **55%** pathologic Complete Response (pCR) and **15%** Major Pathologic Response (MPR)
  - Initiated Regeneron-sponsored confirmatory Phase 2 study (NCT04154943)

PARIS 2022 ESMO congress

- Today at ESMO 2022, reported encouraging results from the single-arm Phase 2 study; concurrent publication in *New England Journal of Medicine*
  - In N=79 patients**, 63.3%** achieved combined pathologic response (**50.6%** pCR + **12.7%** MPR); 68.4% ORR by RECIST 1.1
  - No new Libtayo safety signals; Gr≥3 AEs occurred in 17.7% of patients
  - Reductions in tumor allowed for less extensive and less disfiguring surgery
- These data are shared with regulators, and we are determining next steps for the program



1. Regeneron internal market research 2. Ferrarotto R. Clin Cancer Res 2021;27:4557–4565 and ESMO 2019 Gross et al.
CSCC, cutaneous squamous cell carcinoma; AEs, adverse events. pCR: 0% viable tumor cells; MPR: >0 and ≤10% viable tumor cells

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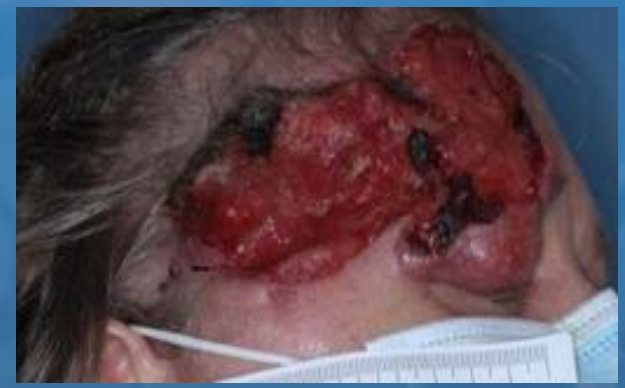
# Majority of patients in this study of Libtayo in neoadjuvant CSCC achieved clinically meaningful pathologic responses

63.3% achieved combined pathologic response (50.6% pCR + 12.7% MPR) at surgery;
68.4% ORR by RECIST 1.1

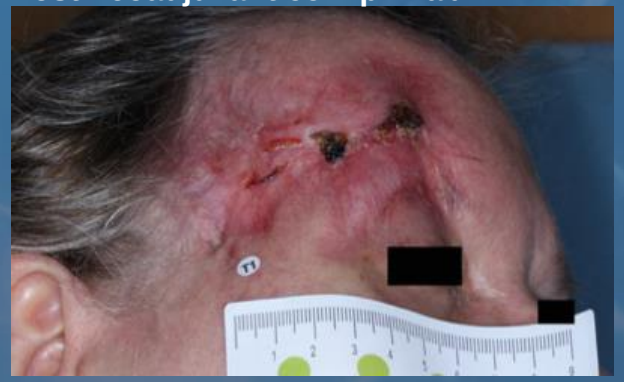
| | Neoadjuvant cemiplimab (N=79) | |
|---|---|---|
| **Pathologic response** | **ICPR N (%) [95% CI]** | **Local pathology review N (%) [95% CI]** |
| **pCR (0% viable tumor cells)** | **40 (50.6) [39.1–62.1]** | 42 (53.2) [41.6–64.5] |
| MPR (>0% and ≤10% viable tumor cells) | 10 (12.7) [6.2–22.0] | 10 (12.7) [6.2–22.0] |
| Combined pathologic response (pCR + MPR) | 50 (63.3) [51.7–73.9] | 52 (65.8) [54.3–76.1] |
| Non-pCR/MPR | 20 (25.3) | NA* |
| Not evaluable (no surgery) | 9 (11.4) | 9 (11.4) |
| **Radiological response** | | **Local imaging review N (%) [95% CI]** |
| Objective response rate (ORR), RECIST 1.1 | | 54 (68.4) [56.9–78.4] |
| Best overall response | | |
| Complete response | | 5 (6.3) |
| Partial response | | 49 (62.0) |
| Stable disease | | 16 (20.3) |
| Progressive disease | | 8 (10.1) |
| Not evaluable | | 1 (1.3) |

**Example**

**Baseline**



**Post neoadjuvant cemiplimab**



**Patient's eye was saved due to response to neoadjuvant Libtayo prior to her surgery**

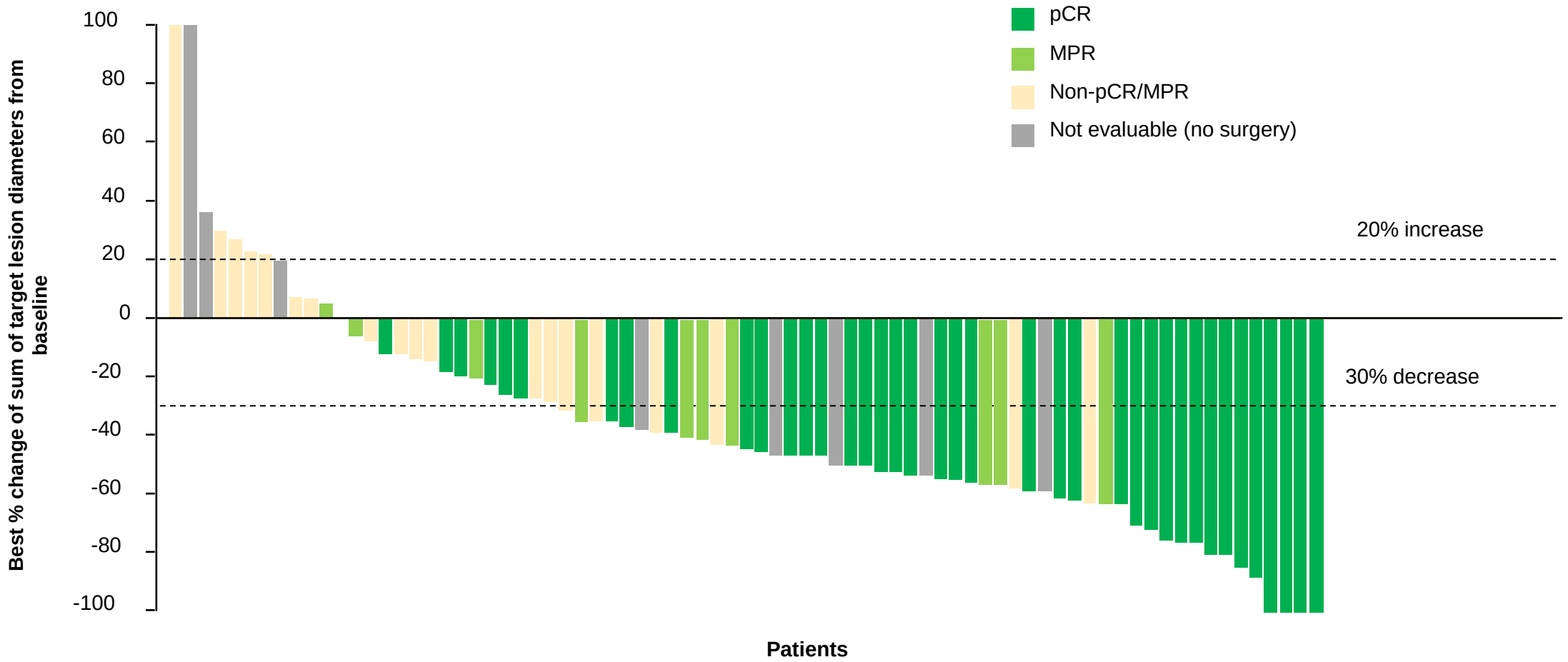
*Local pathology review only reported the categories of pCR, MPR, and other.
CSCC, cutaneous squamous cell carcinoma; CI, confidence interval; ICPR, independent central pathology review; MPR, major pathologic response; NA, not available; pCR, complete pathologic response. Data cut-off date: 1 December 2021

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

# Meaningful responses to Libtayo in neoadjuvant CSCC

63.3% patients achieved combined pathologic response at surgery

## Imaging (RECIST 1.1) and pathologic response assessment (per ICPR)




Horizontal lines indicate criteria for partial radiological response (≥30% decrease in the sum of target lesion diameters) and progressive disease (≥20% increase in the target lesion diameters).
CSCC, cutaneous squamous cell carcinoma; ICPR, independent central pathology review; MPR, major pathologic response; pCR, pathologic complete response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1. Data cut-off date: 1 December 2021

# No new Libtayo safety signals in neoadjuvant CSCC setting

Treatment-emergent adverse events (TEAEs)

- 1 treatment discontinuation
- 4 deaths (3 unrelated to treatment by investigator)

| TEAEs regardless of attribution | Cemiplimab 350 mg Q3W (N=79) | |
|---|---|---|
| n, (%) | Any Grade | Grade ≥3 |
| Any | 69 (87.3) | 14 (17.7) |
| Serious | 13 (16.5) | 10 (12.7) |
| Led to discontinuation | 1 (1.3) | 1 (1.3) |
| Led to death | 4 (5.1) | 4 (5.1) |
| Occurred in >10% of patients (any grade) or ≥1 patient (Grade ≥3) | | |
| Fatigue | 24 (30.4) | 1 (1.3) |
| Diarrhea | 11 (13.9) | 1 (1.3) |
| Nausea | 11 (13.9) | 0 |
| Rash maculo-papular | 11 (13.9) | 0 |
| Constipation | 9 (11.4) | 0 |
| Pruritus | 8 (10.1) | 0 |
| Anemia | 5 (6.3) | 1 (1.3) |
| Hyponatremia | 3 (3.8) | 2 (2.5) |
| Insomnia | 3 (3.8) | 1 (1.3) |
| Confusional state | 2 (2.5) | 2 (2.5) |
| **Myocardial infarction** | 2 (2.5) | 1 (1.3)* |

| TEAEs regardless of attribution | Cemiplimab 350 mg Q3W (N=79) | |
|---|---|---|
| n, (%) | Any Grade | Grade ≥3 |
| **Acute myocardial infarction** | 1 (1.3) | 1 (1.3)* |
| Agitation | 1 (1.3) | 1 (1.3) |
| Cellulitis | 1 (1.3) | 1 (1.3) |
| **Cardiac failure congestive** | 1 (1.3) | 1 (1.3)* |
| Cholelithiasis | 1 (1.3) | 1 (1.3) |
| **COVID-19 pneumonia** | 1 (1.3) | 1 (1.3)* |
| Delusion | 1 (1.3) | 1 (1.3) |
| Dermatitis bullous | 1 (1.3) | 1 (1.3) |
| Glucose tolerance impaired | 1 (1.3) | 1 (1.3) |
| Hepatic enzyme increased | 1 (1.3) | 1 (1.3) |
| Immune-mediated hepatitis | 1 (1.3) | 1 (1.3) |
| Hypertension | 1 (1.3) | 1 (1.3) |
| Procedural hemorrhage | 1 (1.3) | 1 (1.3) |
| Pulmonary embolism | 1 (1.3) | 1 (1.3) |



Safety was assessed in all patients who received at least one dose of neoadjuvant cemiplimab. *Grade 5 TEAEs are in bold text. Data cut-off date: 1 December 2021.

REGENERON

Data update

# Fianlimab (anti-LAG3) + Libtayo: melanoma and beyond

## Additional data in PD-(L)1 naïve melanoma confirm previous promising results, unlock potential for a broader IO opportunity

- BMS trial for anti-LAG-3 + anti-PD-1 treatment demonstrated higher mPFS and ORR vs. anti–PD-1 monotherapy in a Phase 2/3 trial for untreated advanced melanoma[1]
  - RELATIVITY-047 study showed an **ORR of 43.1%** (95% CI, 37.9-48.4) and **median PFS of 10.2 months** (95% CI, 6.5-14.8) (N=355)[2]

- **ASCO 2021:** Regeneron's fianlimab + cemiplimab in patients (cohort 6) with PD-(L)1 naïve advanced melanoma showed **ORR of 66.7%** (N=33)[3]

- ESMO 2022: Updated results from Cohort 6 and second independent cohort (Cohort 15) **confirms early efficacy signal** in PD-(L)1 naïve melanoma patients

| Cohort | N | ORR, % (n) | mPFS (months) | mDOR (months) |
|---|---|---|---|---|
| 6 | 40 | **62.5%** (25) | 24.0 (95% CI: 4.2-NE) | NR (95% CI: 11.9-NE) |
| 15 | 40 | **65.0%** (26) | NR (95% CI: 7.5-NE) | NR (95% CI: 6.3-NE) |

  - 7 complete responses, 44 partial responses across both cohorts
  - Responses observed across PD-L1 expression levels, and in patients associated with poor prognosis (high LDH and liver metastasis)
  - Safety profile similar to anti-PD-1 monotx; Gr≥3 AEs occurred in 20% patients

### FIH Phase 1 fianlimab + Libtayo (NCT03005782)

**Expansion cohorts 6 and 15**
**Anti–PD-1/PD-L1 naive**

**Fianlimab 1600 mg + cemiplimab 350 mg IV every 3 weeks, for up to 51 weeks**

**Expansion cohort 7**
**Anti–PD-1/PD-L1 experienced**

- **Tumour response assessed by investigators**
- **Response assessments every 6 or 9 weeks (RECIST 1.1) to determine ORR**

**Primary endpoint**
- ORR per RECIST 1.1 criteria

**Secondary endpoints**
- Safety, PK and ADA

**Key inclusion criteria**
- ≥18 years of age
- ECOG PS of 0 or 1
- At least one lesion measurable by RECIST 1.1
- Metastatic or inoperable locally advanced nonuveal melanoma

**Key exclusion criteria**
- Prior treatment with LAG-3–targeting biologic or small molecule
- Radiation therapy within 2 weeks prior to enrolment

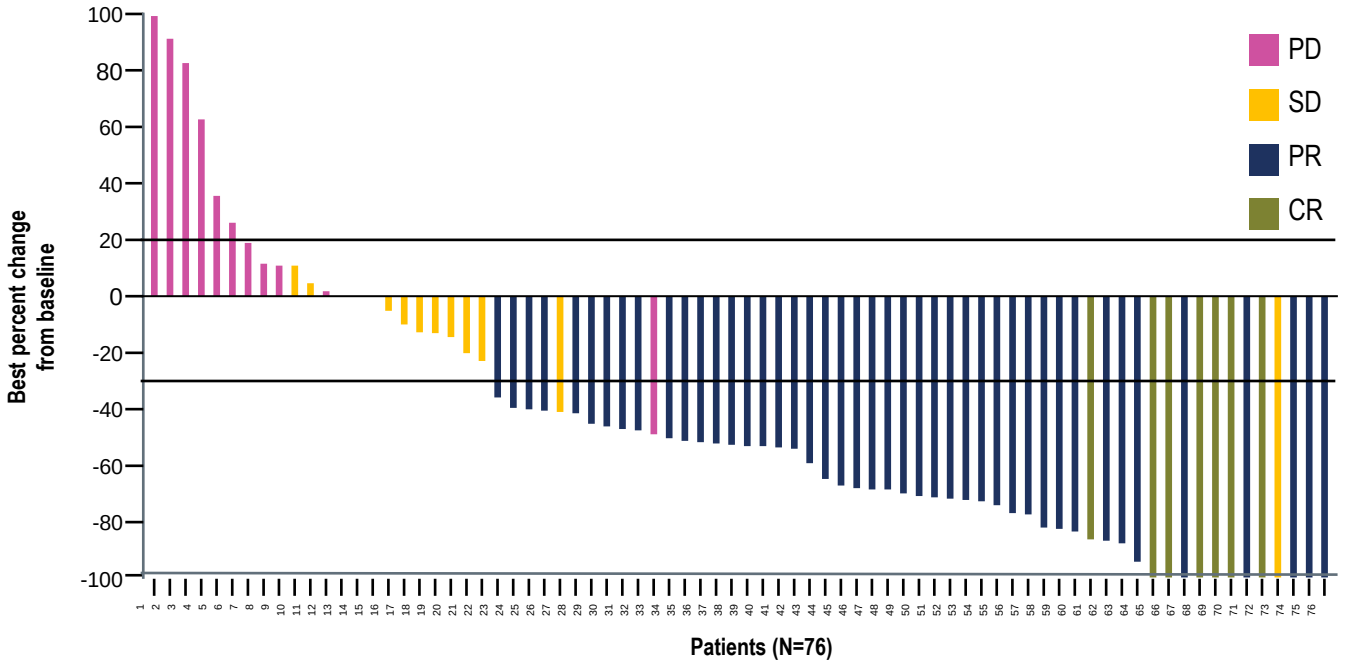


1. Tawbi HA et al. N Engl J Med. 2022;386:24–34. 2. Long GV et al. J Clin Oncol. 2022;40(suppl 36): 360385. 3. Hamid O et al. J Clin Oncol. 2021;39(suppl 15):9515 and ASCO 2021 Hamid at al. LAG-3, lymphocyte activation gene-3; FIH, first-in-human; mPFS, median progression-free survival; ORR, objective response rate; mDOR, median duration of response; AE, adverse events; ADA, antidrug antibody; ECOG PS, Eastern Cooperative Oncology Group performance score; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

# Fianlimab + Libtayo: competitive efficacy in 1L melanoma

Pooled data from PD-(L)1 naïve melanoma cohorts show 63.8% ORR

**Tumor Response waterfall plot by investigator assessment**
(melanoma anti–PD-(L)1-naïve patients, cohorts 6 and 15)




| % (n), unless otherwise stated | Anti–PD-(L)1 naive* | | Cohorts 6 + 15 (N=80) |
|---|---|---|---|
| | Cohort 6 (N=40) | Cohort 15 (N=40) | |
| **ORR, % (95% CI)** | **62.5 (45.8, 77.3)** | **65.0 (48.3, 79.4)** | **63.8 (52.2, 74.2)** |
| Complete response | 15.0 (6) | 2.5 (1) | 8.8 (7) |
| Partial response | 47.5 (19) | 62.5 (25) | 55.0 (44) |
| Stable disease | 17.5 (7) | 15.0 (6) | 16.3 (13) |
| Progressive disease | 15.0 (6) | 15.0 (6) | 15.0 (12) |
| NE | 5.0 (2) | 5.0 (2) | 5.0 (4) |
| DCR | 80.0 (32) | 80.0 (32) | 80.0 (64) |
| **KM-estimated PFS, median (95% CI), months** | **24 (4.2, NE)** | **NR (7.5, NE)** | **24 (9.9, NE)** |
| DOR, median (95% CI), months | NR (11.9, NE) | NR (6.3, NE) | NR (22.6, NE) |
| ORR: baseline LDH, n/N1 (%) | | | |
| LDH > ULN | 10/17 (58.8) | 6/11 (54.5) | 16/28 (57.1) |
| LDH normal | 15/23 (65.2) | 18/24 (75.0) | 33/47 (70.2) |
| ORR: liver metastasis, n/N2 (%) | | | |
| Yes | 6/14 (42.9) | 3/5 (60.0) | 9/19 (47.4) |
| No | 19/26 (73.1) | 23/35 (65.7) | 42/61 (68.9) |

*Prior systemic therapies, including prior adjuvant therapies, excluded for cohort 15.
CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease. Data cut-off date: 1 Jul 2022



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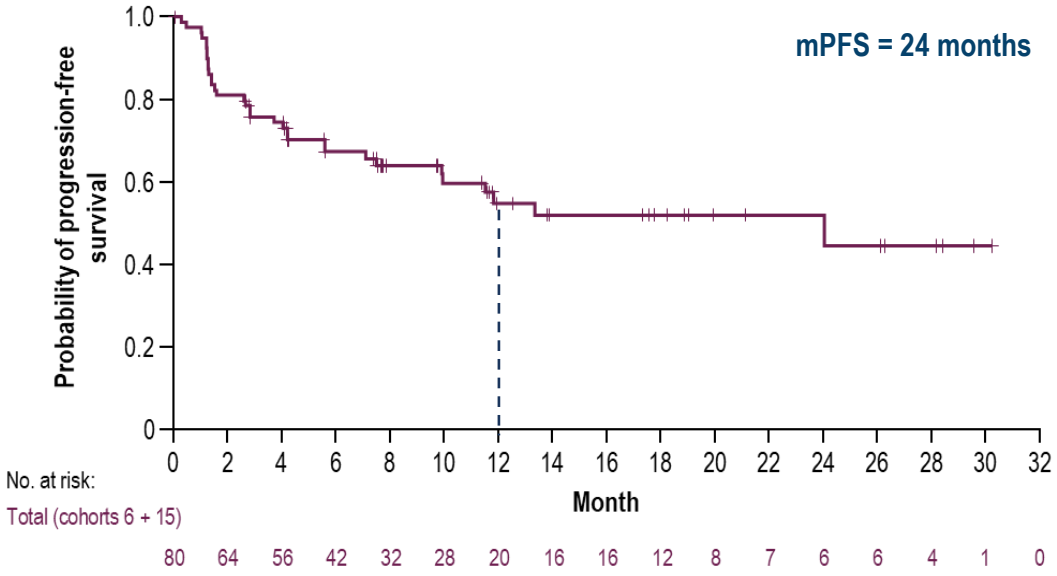
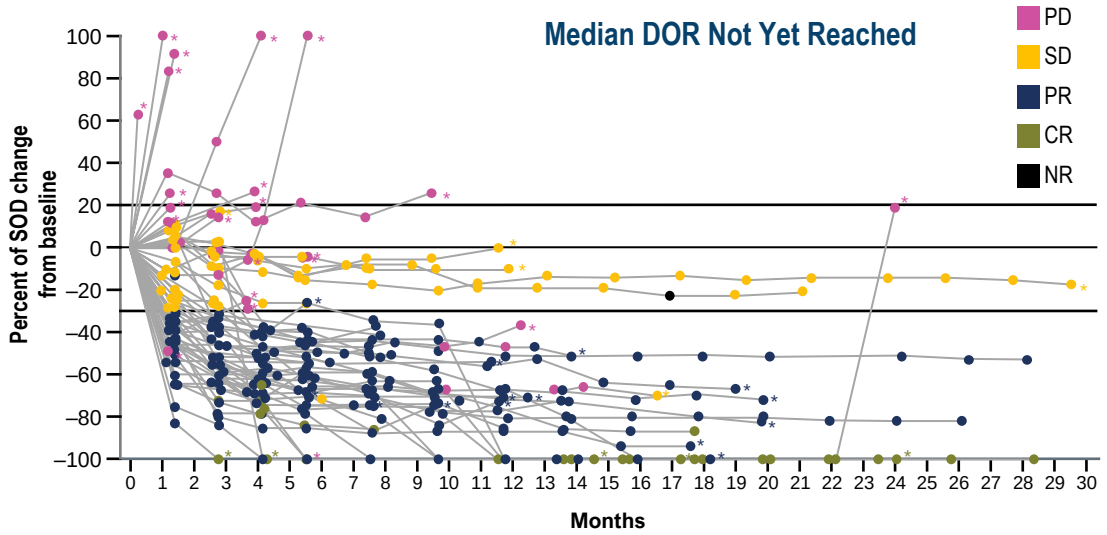
# Fianlimab + Libtayo: competitive efficacy in 1L melanoma

Pooled data from PD-(L)1 naïve melanoma cohorts show 63.8% ORR and 24mo mPFS; median DOR not yet reached

**Progression-free survival**
(melanoma anti–PD-(L)1-naïve patients, cohorts 6 and 15)




| Kaplan-Meier Estimation of PFS by Investigator Assessment | Anti–PD-(L)1 naïve (n=80) |
|---|---|
| Median PFS, (95% CI) months | 24.0 (9.9, NE) |
| Estimated Event-Free Probability (%) (95% CI) at 12 Months | 55.0 (41.6, 66.5) |
| Duration of exposure, median (range), weeks | 30.9 (2.0–110.0) |

CI, confidence interval; CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease. Data cut-off date: 1 Jul 2022



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# Fianlimab + Libtayo in 1L melanoma: safety profile similar to anti-PD-1 monotherapy

- In the PD-(L)1 naïve population:
  - Grade ≥3 treatment-related AE rate was 20%
  - Rate of discontinuation due to treatment-related AEs was 15%, with two deaths considered related to treatment (colitis and cardiac shock)
  - Rate of treatment-emergent adrenal insufficiency was 10%

| % (n), unless otherwise stated | Anti–PD-(L)1 naive‡ (N=80) | | Anti–PD-(L)1 experienced (N=15) | |
|---|---|---|---|---|
| **Duration of exposure, median (range), weeks** | **30.9 (2.0–110.0)** | | **9.0 (6.0–57.0)** | |
| **Patients with treatment-emergent AEs regardless of attribution** | **Any grade** | **Grade 3–5** | **Any grade** | **Grade 3–5** |
| Overall | 96.3 (77) | 40.0 (32) | 80.0 (12) | 46.7 (7) |
| Serious | 28.8 (23) | 25.0 (20) | 33.3 (5) | 26.7 (4) |
| **Patients with treatment-related AEs** | | | | |
| Overall | 80.0 (64) | 20.0 (16) | 53.3 (8) | 20.0 (3) |
| Serious | 13.8 (11) | 13.8 (11) | 13.3 (2) | 13.3 (2) |

| Treatment-emergent immune-mediated AEs, % (n) | Anti–PD-(L)1 naive‡ (N=80) | | Anti–PD-(L)1 experienced (N=15) | |
|---|---|---|---|---|
| | **Any grade** | **Grade 3–5** | **Any grade** | **Grade 3–5** |
| **Overall** | **65.0 (52)** | **11.3 (9)** | **33.3 (5)** | **13.3 (2)** |
| **Occurred in >5% of patients (any grade)** | | | | |
| Rash | 23.8 (19) | 0 | 26.7 (4) | 0 |
| Pruritis | 15.0 (12) | 0 | 0 | 0 |
| Hypothyroidism | 13.8 (11) | 0 | 0 | 0 |
| Arthralgia | 12.5 (10) | 0 | 6.7 (1) | 0 |
| Diarrhoea | 12.5 (10) | 0 | 13.3 (2) | 0 |
| Myalgia | 10.0 (8) | 0 | 6.7 (1) | 0 |
| Adrenal Insufficiency | 8.8 (7) | 2.5 (2) | 6.7 (1) | 0 |
| Colitis | 7.5 (6) | 3.8 (3) | 0 | 0 |
| Pneumonitis | 6.3 (5) | 0 | 6.7 (1) | 6.7 (1) |



AE, adverse event. Data cut-off date: 1 Jul 2022

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# Robust fianlimab + Libtayo clinical program underway

**Melanoma**

- Phase 3 in 1L advanced melanoma ongoing (NCT05352672)
- Phase 3 adjuvant melanoma initiating soon
- ➢ Potential for best in class

**Non-small cell lung cancer**

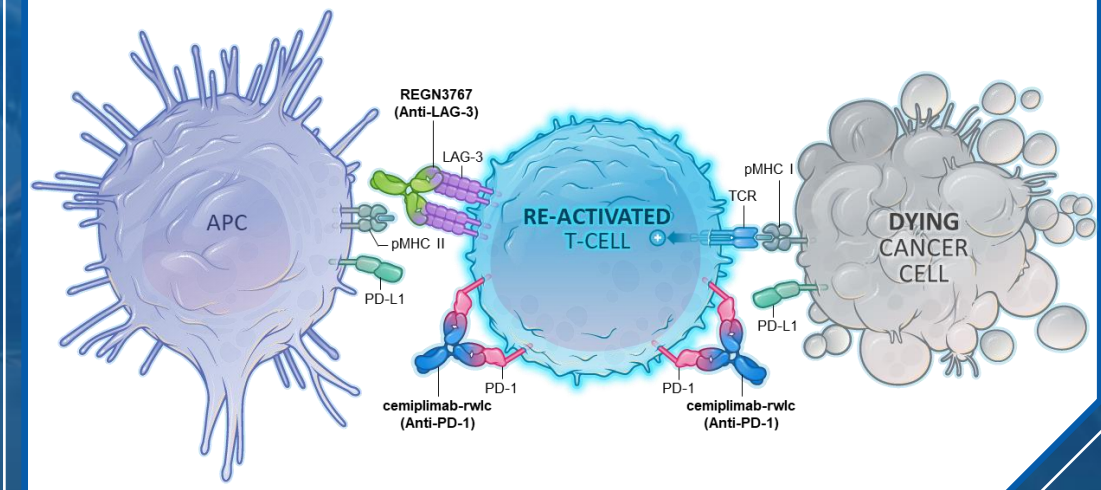
- Expansion cohort of the FIH study in PD-(L)1 naïve NSCLC, data in in 2H22
- Initiating further studies in 1L NSCLC
- ➢ Potential for first in class

**Exploring Additional Indications**

- Neoadjuvant breast cancer: I-SPY study of fianlimab+Libtayo+paclitaxel, data in 2H22
- ➢ Science-led development for additional indications

# Potential for differentiated efficacy and safety vs. current SOC

## Dual LAG-3 and PD-1 blockade may provide enhanced immune activation vs. anti-PD-1 alone




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



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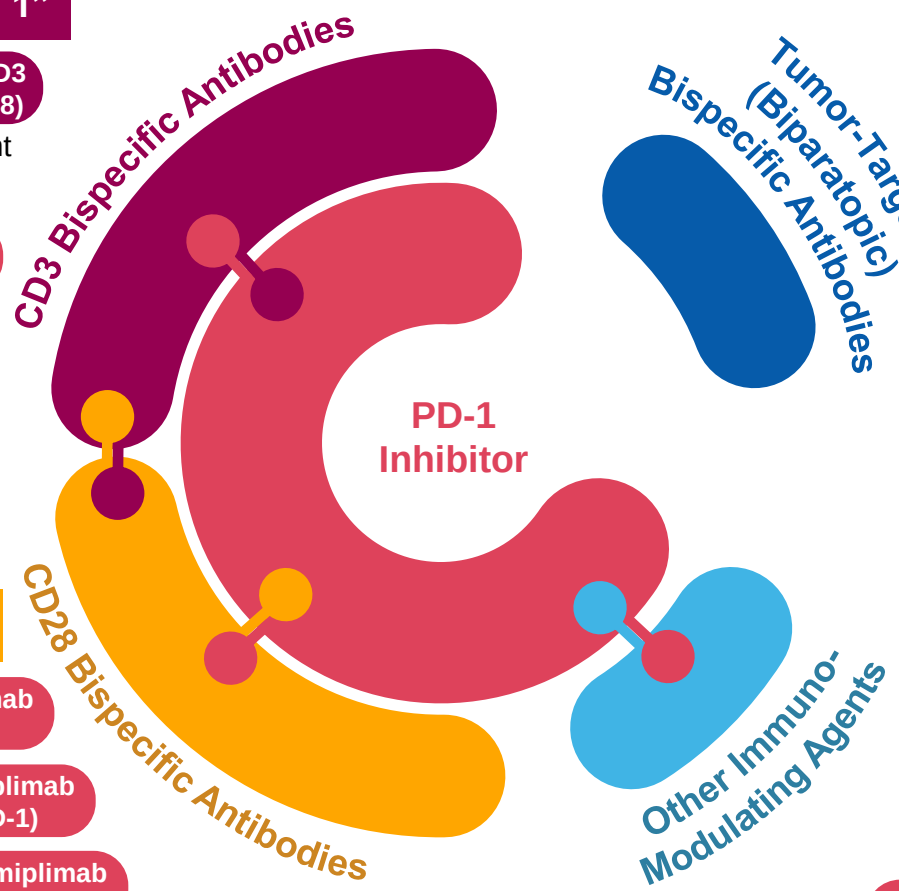
# Unique flexibility of internally-developed pipeline drives potential for novel and differentiated combinations

## CD3 Bispecifics: "Signal 1"

- Odronextamab (CD20xCD3) — R/R B-NHL, CLL
- BCMAxCD3 (REGN5458) — R/R Multiple Myeloma
- PSMAxCD3 (REGN4336) — Metastatic prostate cancer
- MUC16xCD3 (REGN4018) — Recurrent ovarian cancer
- PSMAxCD3 (REGN4336) + Cemiplimab (PD-1) — Metastatic prostate cancer
- MUC16xCD3 (REGN4018) + Cemiplimab (PD-1) — Recurrent ovarian cancer
- MUC16xCD3 (REGN4018) + MUC16xCD28 (REGN5668) — Recurrent ovarian cancer
- PSMAxCD3 (REGN4336) + PSMAxCD28 (REGN5678) — Metastatic prostate cancer

## CD28 Bispecifics: "Signal 2"

- PSMAxCD28 (REGN5678) + Cemiplimab (PD-1) — Metastatic prostate cancer
- EGFRxCD28 (REGN7075) + Cemiplimab (PD-1) — Solid tumors
- MUC16xCD28 (REGN5668) + Cemiplimab (PD-1) — Recurrent ovarian cancer




## Tumor-Targeted Biparatopics

- METxMET (REGN5093) — MET-altered advanced NSCLC
- METxMET ADC (REGN5093-M114) — MET over-expressing advanced NSCLC

## Modulating immune response

- Cemiplimab (PD-1) + Fianlimab (LAG3) — Melanoma & other advanced malignancies
- Cemiplimab (PD-1) + GITR (REGN6569) — HNSCC
- Cemiplimab (PD-1) + vidutolimod (TLR9) — CSCC, Merkel cell carcinoma

EGFR, Epidermal growth factor receptor; MUC16, Mucin 16; PSMA, Prostate-specific membrane antigen; R/R, Relapse/refractory; B-NHL, B-cell Non-Hodgkin lymphoma; BCMA, B-cell maturation antigen; NSCLC, Non-small cell lung cancer; SCCHN, Squamous cell carcinoma of the head and neck; CSCC, Cutaneous squamous cell carcinoma; ADC, Antibody drug conjugate; LAG-3, Lymphocyte-activation gene 3; GITR, Glucocorticoid-induced TNFR-related protein



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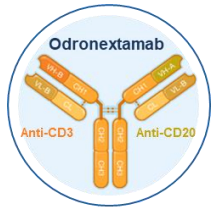
# Other Oncology Updates & Closing Remarks

**David Weinreich, MD**
EVP, Global Clinical Development

# Bispecifics for heme malignancies: promising results from maturing CD3 programs

Odronextamab: potential to be the first CD20xCD3 to be approved for both major types of advanced B cell lymphomas




## Odronextamab (CD20xCD3)*

**Summary** – A **single, off-the-shelf bispecific**, effective in both indolent and aggressive lymphomas, including patients who failed CAR-Ts

- R/R FL: **ORR=90% CR=70%** (N=30)
- R/R DLBCL: CAR-T naïve **ORR=55% CR=55%** (N=11)
  post-CAR-T ORR=33% CR=21% (N=24)

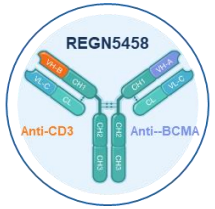
- **Durable responses** (up to 3.5 years so far in FL)
- Manageable safety profile observed with revised step-up dosing

**Progress to Date:**

- Received Fast Track designation in FL and DLBCL
- Over 500 patients dosed to date across program

**Upcoming Milestones:**

- Report additional results from potentially pivotal Phase 2 study (2H22)
- Potential U.S. regulatory submission in FL and DLBCL (2H22)
- Initiate OLYMPIA Phase 3 program and additional combinations, including TAAxCD28 costim




## REGN5458 (BCMAxCD3)**

**Efficacy** – Early, deep, and durable responses:

- **75% ORR**, with **58% VGPR or better** at higher doses (200-800 mg)
- 51% ORR among all enrolled patients
- 86% of responders with VGPR or better; 43% with CR or better
- Median DOR was not reached

**Safety** – Acceptable safety and tolerability profile:

- No Grade 3+ CRS; no grade 3+ ICANS
- CRS reported in 38% patients, vast majority of events were Gr1
- All patients experienced some grade of TEAEs, with 42% Grade 3 and 33% Grade 4
- Maximum tolerated dose was not reached

**Upcoming Milestones**:

- Report data from potentially pivotal Phase 2 study (2H22)
- Potential U.S. regulatory submission R/R MM (2023)
- Initiate additional combinations with TAAxCD28 costim

**Additional data updates submitted to ASH 2022**



DLBCL, Diffuse Large B Cell Lymphoma; FL, Follicular Lymphoma; ORR, objective response rate; VGPR, very good partial response; CR, complete response; DOR, duration of response; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; SOC, standard of care

*Data from ASH 2020
**Data from ASH 2021

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# Several data read-outs at ESMO with more to come in 2023+

| Tumor Type | Initial Indication | Upcoming Data Disclosure: 2H 2022 | 2023 | 2024+ |
|---|---|---|---|---|
| Hematology | Lymphoma | Odronextamab ✪ | | |
| | Multiple myeloma | ✓ PARIS 2022 ESMO | BCMAxCD3 ✪ | |
| Dermato-oncology | Neoadjuvant CSCC | Cemiplimab | | |
| | Adjuvant CSCC | | | Cemiplimab ✪ |
| | Advanced CSCC (2L) | | | Vidutolimod – Cemiplimab |
| | Adjuvant melanoma | | | Fianlimab – Cemiplimab ✪ |
| | First-line advanced melanoma | | | Fianlimab – Cemiplimab ✪ |
| Other Solid Tumors | MET-altered advanced NSCLC | ✓ PARIS 2022 ESMO METxMET | METxMET ADC | |
| | Ovarian cancer (2L+) | ✓ PARIS 2022 ESMO MUC16xCD3 | MUC16xCD3 – Cemiplimab<br>MUC16xCD28 – Cemiplimab<br>MUC16xCD3 – MUC16xCD28 | |
| | Metastatic castration-resistant prostate cancer | ✓ PSMAxCD28 – Cemiplimab | | PSMAxCD28 – Cemiplimab<br>PSMAxCD3 – Cemiplimab<br>PSMAxCD3 – PSMAxCD28 |
| | SCCHN | | | GITR – Cemiplimab |
| | EGFR+ solid tumors | | EGFRxCD28 – Cemiplimab | |



CSCC, Cutaneous squamous cell carcinoma; NSCLC, Non-small cell lung cancer; 2L+, Second line and beyond; SCCHN, Squamous cell carcinoma of the head and neck; EGFR, Epidermal growth factor receptor; MUC16, Mucin 16; PSMA, Prostate-specific membrane antigen; BCMA, B-cell maturation antigen

✪ indicates pivotal study

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# Regeneron is well positioned for future growth and leadership in oncology

Breaking ground with new technologies in IO-unresponsive tumors that saw limited success so far

- **REGN5678 (PSMAxCD28) + Libtayo in advanced prostate cancer**: first costimulatory bispecific to show encouraging early efficacy and safety data
- **Ubamatamab (MUC16xCD3) monotherapy in advanced ovarian cancer**: first and only MUC16 targeting bispecific to demonstrate durable responses in late-stage ovarian cancer; continuing development as monotherapy, and look forward to combinations with Libtayo and costims in 2023
- **REGN5093 (METxMET) in MET-NSCLC**: initial data confirms monotherapy activity with acceptable safety profile; shows potential for increased activity with METxMET ADC and combination approach
- **Libtayo in neoadjuvant CSCC**: results further Libtayo's leadership in CSCC and have potential to influence standard of care in the neoadjuvant setting – additional ~20k eligible U.S. patients, if approved
- **Fianlimab + Libtayo in PD-1 naïve melanoma**: potentially best-in-class efficacy and safety; exploring combination in NSCLC and other cancers



CSCC, Cutaneous squamous cell carcinoma; NSCLC, Non-small cell lung cancer; ADC, Antibody drug conjugate.

# Questions & Answers

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EVP, Global Clinical Development

**Israel Lowy, MD, PhD**
SVP, Translational and Clinical Sciences, Oncology

**Justin Holko**
VP, Global Commercial Business Unit, Oncology