ASH 2022 Investor Event

December 14, 2022

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

Note regarding forward-looking statements

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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 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 odronextamab (a CD20xCD3 bispecific antibody), linvoseltamab (a BCMAxCD3 bispecific antibody), and other of Regeneron's Product Candidates discussed or referenced in this presentation (such as REGN5837 (a CD22xCD28 bispecific antibody)); 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David Weinreich, MD
EVP, Global Clinical Development

Andres Sirulnik, MD, PhD
SVP Clinical Development – Hematology

Agenda

- **Oncology & Hematology Overview**
- **ASH 2022 Program Updates**
  - Odronextamab (FL / DLBCL)
  - REGN5837 (CD22xCD28) costimulatory bispecific
  - Linvoseltamab (MM)
- **Classical Hematology**
- **Closing Remarks and Q&A**

ASH 2022 IR EVENT

Oncology & Hematology Overview

David Weinreich, MD
EVP, Global Clinical Development

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Committed to becoming a leader in oncology and hematology

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.

Together, they provide us with unique combinatorial flexibility to develop customized and potentially synergistic cancer treatments.

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

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; FDA-approved, under EMA review ✓

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

Approved as monotherapy in high PD-L1 expressors and in combination with chemotherapy irrespective of PD-L1 expression levels

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

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

Advancing broad oncology and hematology pipeline in 2022

Tumor Type	Initial Indication	Data Disclosures 2H 2022
Hematology	Lymphoma	Odronextamab ✪ ✓
	Multiple myeloma	Linvoseltamab ✪ ✓
Dermato-oncology	Neoadjuvant CSCC	Cemiplimab ✓
	First-line advanced melanoma	Fianlimab + Cemiplimab ✓
Other Solid Tumors	MET-altered advanced NSCLC	METxMET ✓
	Advanced NSCLC	Fianlimab + Cemiplimab ✓
	Ovarian cancer (2L+)	MUC16xCD3 ✓
	Metastatic castration-resistant prostate cancer	PSMAxCD28 + Cemiplimab ✓

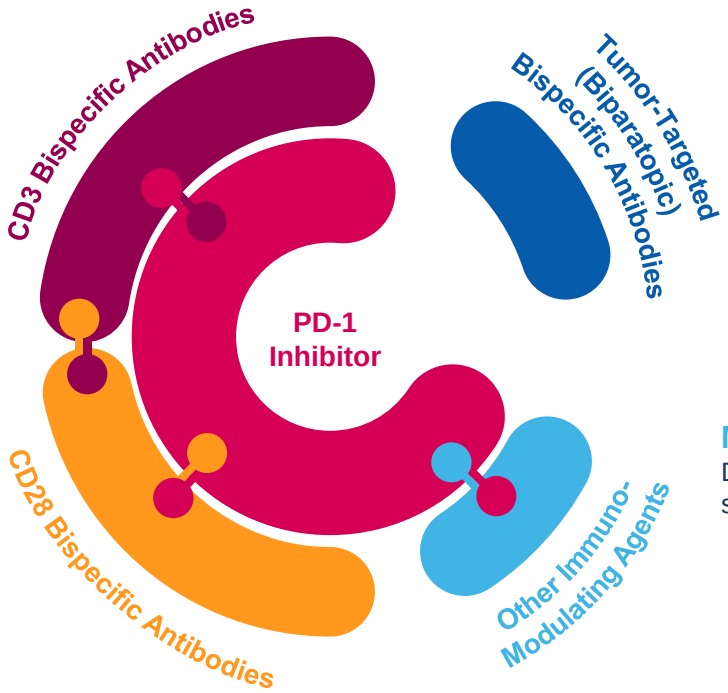
✪ indicates potentially pivotal study ✓ indicates data readout

2L+, Second line and beyond; BCMA, B-cell maturation antigen; CSCC, Cutaneous squamous cell carcinoma; MUC16, Mucin 16; NSCLC, Non-small cell lung cancer; PSMA, Prostate-specific membrane antigen.

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

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Foundational bispecific programs to be discussed

CD3 Bispecifics: "Signal 1"

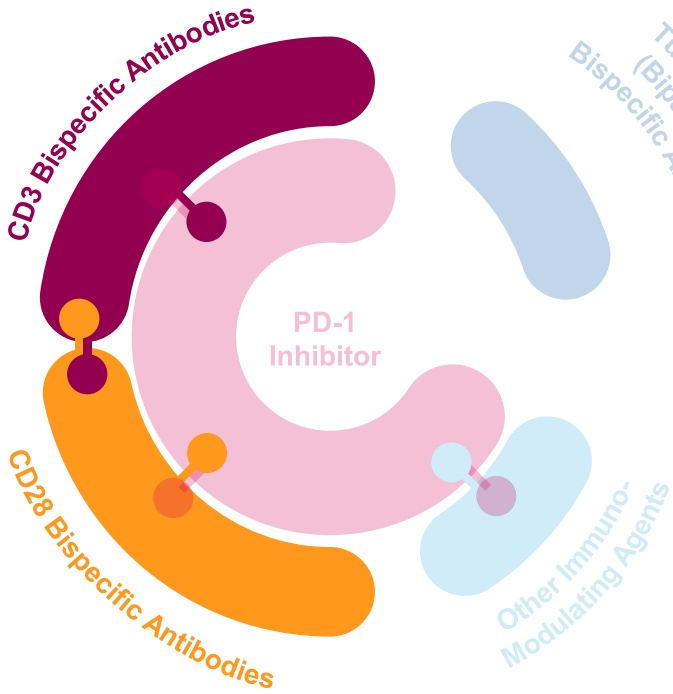
Designed to bridge tumor-associated antigens on cancer cells with CD3-expressing T cells, resulting in potential local T-cell activation and cytotoxicity

- Odronextamab (CD20xCD3) — R/R B-NHL
- Linvoseltamab (BCMAxCD3)D — R/R Multiple Myeloma

CD28 Bispecifics: "Signal 2"

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

- Odronextamab (CD20xCD3) + REGN5837 (CD22xCD28) — R/R B-NHL
- Linvoseltamab (BCMAxCD3) + TAAxCD28 — R/R Multiple Myeloma



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

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ASH 2022 Updates

Andres Sirulnik, MD, PhD
SVP Clinical Development – Hematology

ASH 2022: Advancing hematology pipeline across multiple blood cancers and disorders

Select Presentations/Posters	#/Type
Odronextamab (CD20xCD3)	
Odronextamab in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL): Results from a prespecified analysis of the pivotal Phase II study ELM-2	#444 Oral Presentation
Odronextamab in patients with relapsed/refractory (R/R) follicular lymphoma (FL) Grade 1–3a: Results from a prespecified analysis of the pivotal Phase II study ELM-2	#949 Oral Presentation
Linvoseltamab (BCMAxCD3)	
Updated safety and efficacy of REGN5458, a BCMAxCD3 bispecific antibody, treatment for relapsed/refractory multiple myeloma: A Phase 1/2 first-in-human study	#4555 Poster Presentation

*…plus **14 more** posters and presentations including first clinical data from two Phase 2 studies evaluating pozelimab (C5 antibody) in combination with cemdisiran (siRNA C5 inhibitor) in patients with paroxysmal nocturnal hemoglobinuria (PNH)*

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Odronextamab in Relapsed / Refractory FL & DLBCL

Follicular Lymphoma (FL) - Oral Presentation #949
Presented Monday, December 12, 2022

Diffuse Large B-Cell Lymphoma - Oral Presentation #444
Presented Sunday, December 11, 2022

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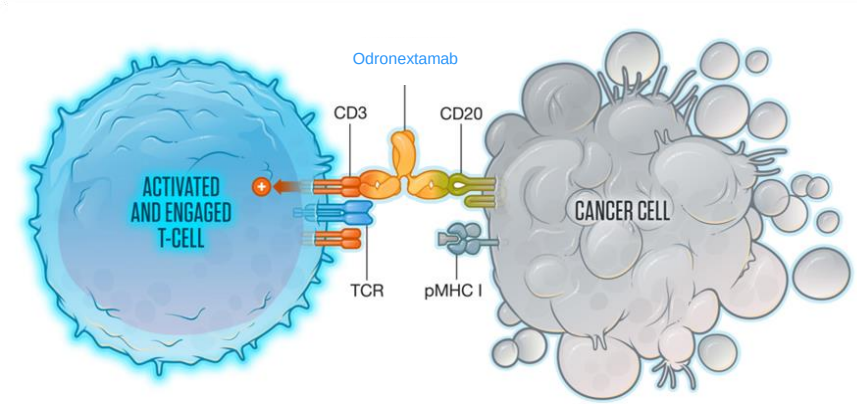
Odronextamab (CD20xCD3): Regeneron's most advanced bispecific



Binds CD20 on malignant B-cells and CD3 on T cells, to elicit T-cell-mediated cytotoxicity

Odronextamab is an investigational **single, off-the-shelf bispecific**, effective in both indolent and aggressive lymphomas, including patients who failed CAR-Ts

- **Odronextamab was investigated in the ELM-1 Phase 1 trial***

  Encouraging efficacy and manageable safety was observed in heavily pre-treated patients in relapsed/refractory (R/R) follicular lymphoma (FL) and R/R diffuse large B-cell lymphoma (DLBCL)

- **At ASH 2022, first interim data from the ELM-2 Phase 2 trial† in R/R FL and R/R DLBCL were presented in two separate oral presentations**

- **To date, over 550 patients dosed across the program**

Confirmatory Phase 3 OLYMPIA program will initiate in early 2023

Intend to submit BLA for R/R DLBCL and R/R FL in 2H23

*NCT02290951; †NCT03888105

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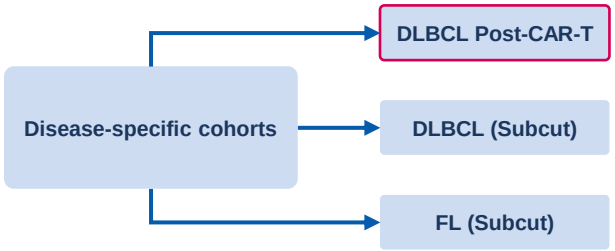
Odronextamab: ELM-1 / ELM-2 program design

ELM-1*

Phase 1, open-label, multi-cohort, multicenter study of odronextamab monotherapy for patients with R/R B-NHL

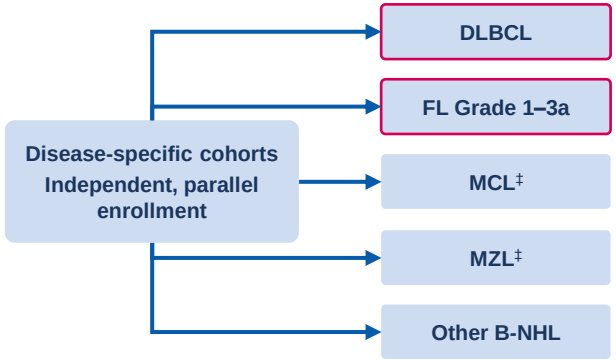


Previously presented encouraging efficacy and manageable safety profile in heavily pre-treated patients in relapsed/refractory (R/R) follicular lymphoma and R/R diffuse large B-cell lymphoma

Subcutaneous administration initiated, DLBCL post CAR-T cohort on track to complete enrollment in 4Q22

ELM-2†

Phase 2, open-label, multi-cohort, multicenter study of odronextamab monotherapy for patients with R/R B-NHL



Primary endpoint

- ORR§ by ICR

Key secondary endpoints

- ORR§ by local investigator
- CR, DOR, PFS, and OS
- Safety and tolerability

*NCT02290951; †NCT03888105. ‡New enrolment is currently paused. §According to Lugano criteria[1]
B-NHL, B-cell non-Hodgkin's lymphoma; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance score; FL, follicular lymphoma; ICR, independent central review; IV, intravenous; MCL, mantle cell lymphoma; MZL, marginal zone lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory; Q2W, every 2 weeks.

[1]Cheson BD, et al. *J Clin Oncol*. 2014;32(27):3059–3068.

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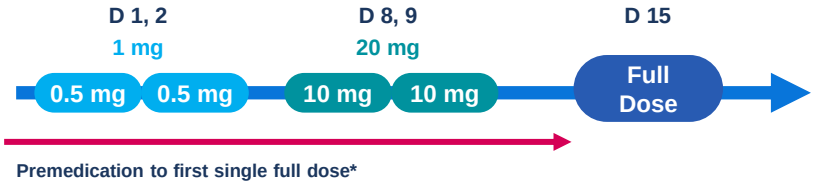
Odronextamab: Modified step-up dosing regimen has improved safety profile with similar efficacy

Prior Regimen: 1/20 mg



FL: 80 – 160mg‡
DLBCL: 160 – 320mg§

New Regimen: 0.7/4/20 mg

Modified step-up dosing regimen have improved safety profile with similar efficacy, resulting in lower rates of treatment discontinuations, interruptions, dose reductions and dose delays

Approximately 50% of patients on each regimen in FL and DLBCL

*20 mg IV dexamethasone 1 to 3 hours prior to each split or initial single infusion; †10 mg dexamethasone orally 12 to 24 hours prior to the first split infusion. On each day of split or single infusion: dexamethasone 20 mg IV 1 to 3 hours before infusion; diphenhydramine 25 mg IV or orally and acetaminophen 650 mg orally 30 to 60 minutes before infusion. ‡Cycles 2–4 80mg Days 1, 8,15; Cycle 5 onwards 160mg Q2W; Treatment until disease progression. §Cycles 2-4 160mg Days 1, 8,15; Cycle 5 onwards 320mg Q2W; Treatment until disease progression
CRS, cytokine release syndrome

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Follicular Lymphoma: Potential best-in-class efficacy profile

Consistent efficacy observed regardless of step-up regimen in heavily pre-treated, highly refractory patient population

Best Overall Response

	All Patients N=121*
Objective response rate (ORR)†	**81.8%** [95% CI: 73.8–88.2%]
Complete response	75.2%
Partial response	6.6%
Stable disease	5.8%
Progressive disease	4.1%

~92% of responders had a Complete Response

Week 12 Assessment

1/20 step-up regimen N=68	0.7/4/20 step-up regimen N=53
72.1% [95% CI: 59.9–82.3%]	**75.5%** [95% CI: 61.7–86.2%]
61.8%	71.7%

Consistent efficacy observed at Week 12 regardless of step-up regimen

Data cut-off date: Sep 15, 2022.
*Efficacy evaluable (with an opportunity for assessment at 12 weeks); †ORR = complete responses + partial responses.
CI, confidence interval; ORR, objective response rate.

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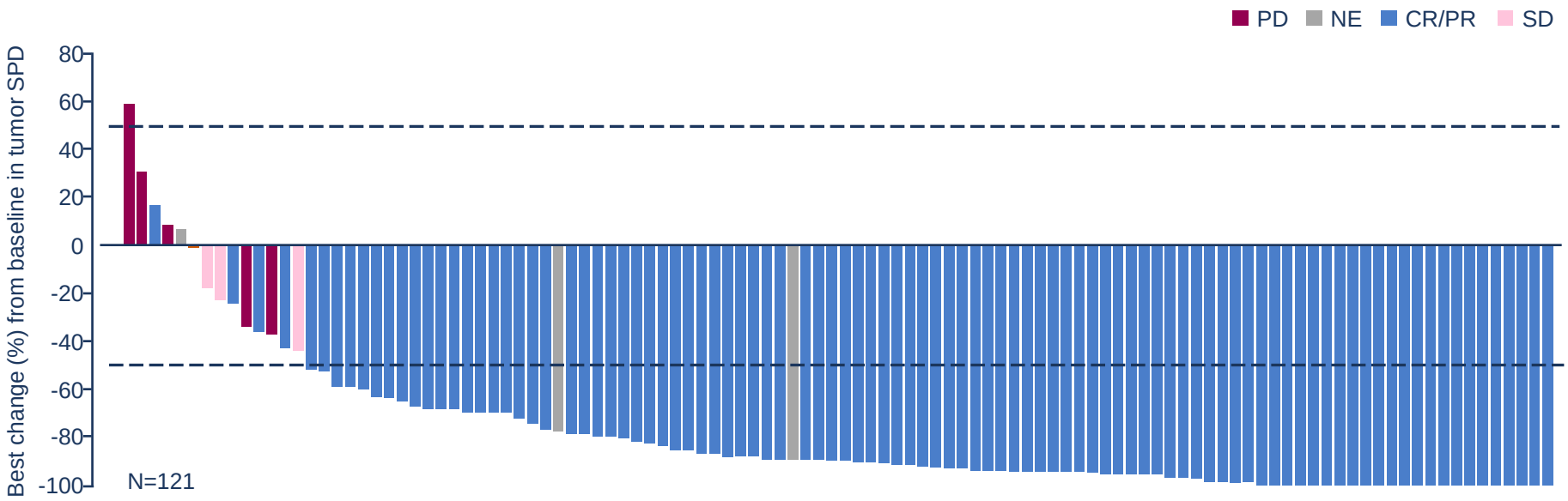
Follicular Lymphoma: Majority of patients had substantial tumor shrinkage



Data cut-off date: Sep 15, 2022.
Responses as per investigator assessment.
CR complete response; FL, follicular lymphoma; NE, not evaluable; R/R relapsed/refractory; PD, progressive disease; PR, partial response; SD, stable disease; SPD, sum of the products of diameters

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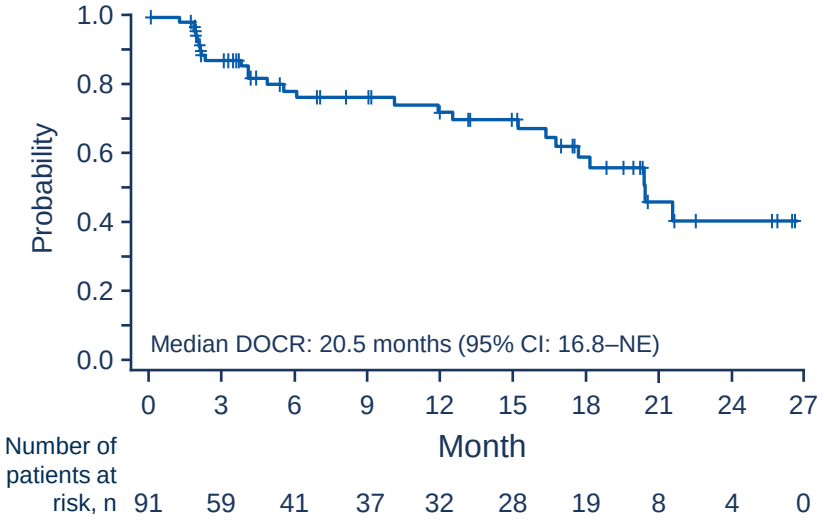
Follicular lymphoma: Encouraging durability of responses

Duration of complete response

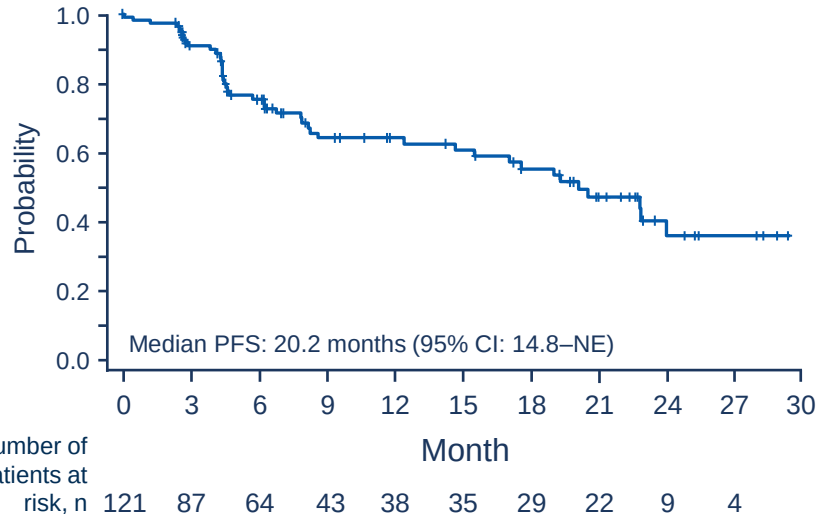
Independent central review



- Durable responses observed with median DOR of 20.5 months
- Complete responses also durable, with median DOCR of 20.5 months

Progression-free survival

Independent central review



- Median PFS was 20.2 months
- Median OS not yet reached

Data cut-off date: Sep 15, 2022.

CI, confidence interval; DOCR, duration of complete response; DOR, duration of response; NE, not estimable, OS, overall survival; PFS, progression-free survival.

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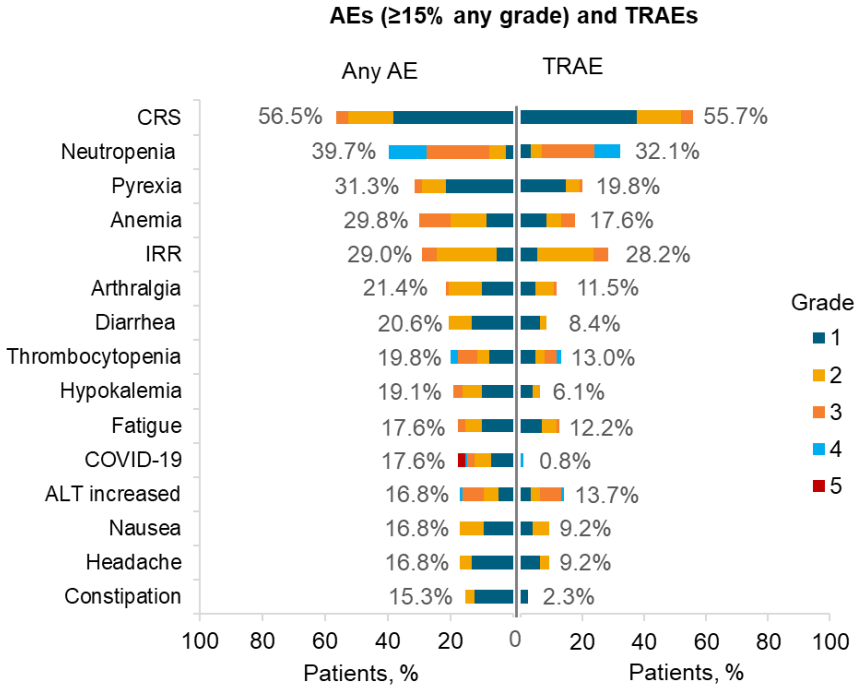
Follicular lymphoma: Safety profile

Treatment-emergent adverse events, n (%)	Patients N=131 All events	TRAEs
Any TEAE	**131 (100%)**	**118 (90.1%)**
Grade ≥3 TEAE	102 (77.9%)	73 (55.7%)
Serious AE	81 (61.8%)	53 (40.5%)
Grade 5 TEAE	17 (13.0%)	3 (2.3%)
Related to COVID-19	7 (5.3%)	0
Other grade 5 events	10 (7.6%)	3 (2.3%)
TEAE leading to treatment discontinuation	15 (11.5%)	10 (7.6%)



Data cut-off date: Sep 15, 2022.
AEs per NCI-CTCAE v5.0. CRS per Lee 2019.
AE, adverse event; ALT, alanine aminotransferase; CRS, cytokine release syndrome; IRR, infusion related reaction; PML, Progressive multifocal leukoencephalopathy; TEAE, treatment-emergent adverse event; TRAE, treatment-related AE.
Grade 5 TRAEs: pneumonia, PML, systemic mycosis (n=1 each)

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Follicular lymphoma: Safety improvements from modified step-up dosing regimen

n, (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)
CRS any Grade	**38 (55.9%)**	**36 (57.1%)**
Grade 1	22 (32.4%)	28 (44.4%)
Grade 2	**12 (17.6%)**	**7 (11.1%)**
Grade 3	**4 (5.9%)**	**1 (1.6%)**
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	11 (16.2%)	17 (27.0%)
Received tocilizumab	9 (13.2%)	12 (19.0%)
Received vasopressors	4 (5.9%)	1 (1.6%)

n (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)	All patients (N=131)
ICANS, any grade	**1 (1.5%)**	**0**	**1 (0.8%)**
Grade ≥3	0	0	0
Infusion related reaction, any grade	**21 (30.9%)**	**16 (25.4%)**	**37 (28.2%)**
Grade ≥3	4 (5.9%)	2 (3.2%)	6 (4.6%)
Infection, any grade	**51 (75.0%)**	**35 (55.6%)**	**86 (65.6%)**
Grades 1–2	23 (33.8%)	21 (33.3%)	44 (33.6%)
Grades 3–4	**19 (27.9%)**	**11 (17.5%)**	**30 (22.9%)**
Grade 5	**9 (13.2%)**	**3 (4.8%)**	**12 (9.2%)**
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	1 (1.5%)	0	1 (0.8%)

With optimized step-up dosing regimen:

- **CRS was mostly grade 1 and generally occurred with Cycle 1 step-up**
- **No cases of ICANS or TLS**

Data cut-off date: Sep 15, 2022.
CRS per Lee 2019.
CRS, cytokine release syndrome; ICU, intensive care unit, ICANS, immune effector cell-associated neurotoxicity syndrome; TLS, tumor lysis syndrome

DLBCL: Competitive efficacy profile

Consistent efficacy observed regardless of step-up regimen in heavily pre-treated, highly refractory patient population in ELM-2 study

Best Overall Response

	All Patients N=130*
Objective response rate (ORR)†	**49.2%** [95% CI 40.4%–58.1%]
Complete response	**30.8%**
Partial response	18.5%
Stable disease	3.8%
Progressive disease	22.3%

~63% of responders had a Complete Response

Week 12 Assessment

1/20 step-up regimen N=67	0.7/4/20 step-up regimen N=63
46.3% [95% CI: 34.0–58.9%]	**42.9%** [95% CI: 30.5–56.0%]
26.9%	20.6%

Consistent efficacy observed at Week 12 regardless of step-up regimen

Data cut-off date from ELM-2: Sep 15, 2022
*Efficacy evaluable (with an opportunity for assessment at 12 weeks); †ORR = complete responses + partial responses.
CI, confidence interval; ORR, objective response rate.

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DLBCL: Similar efficacy observed regardless of prior CAR-T experience

Best Overall Response

	CAR-T Naïve *(ELM-2)* N=130*	Post-CAR-T *(ELM-1)* N=31†
Objective response rate (ORR) ‡	**49.2%** [95% CI 40.4%–58.1%]	**48.4%** [95% CI 30.2%–66.9%]
Complete response	**30.8%**	**32.3%**
Partial response	18.5%	16.1%
Stable disease	3.8%	6.5%
Progressive disease	22.3%	9.7%

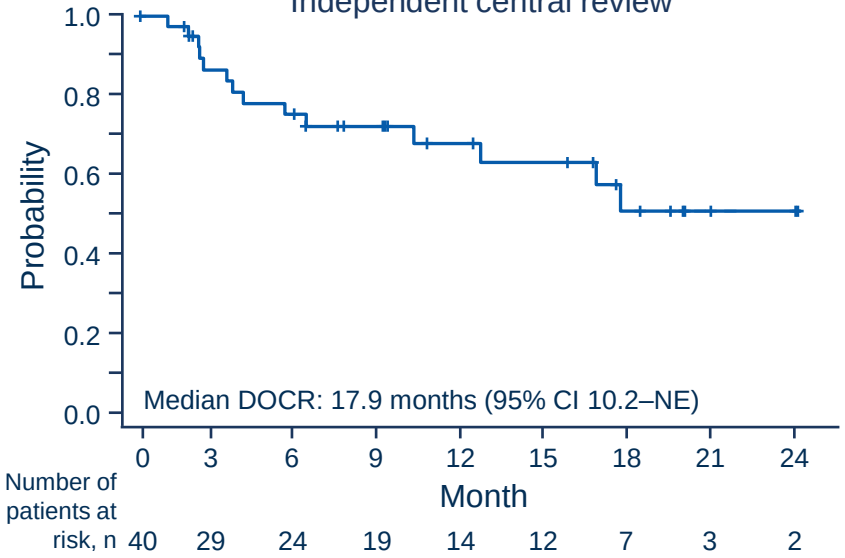
Comparable ORR observed regardless of CAR-T experience

*Data cut-off date from ELM-2: Sep 15, 2022, Efficacy evaluable (with an opportunity for assessment at 12 weeks). †Data cut-off date from ELM-1: Aug 11, 2022. ‡ORR = complete responses + partial responses.
CAR T, chimeric antigen receptor T cell; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; NE, not evaluable; ORR, objective response rate.

DLBCL: Encouraging durability of responses

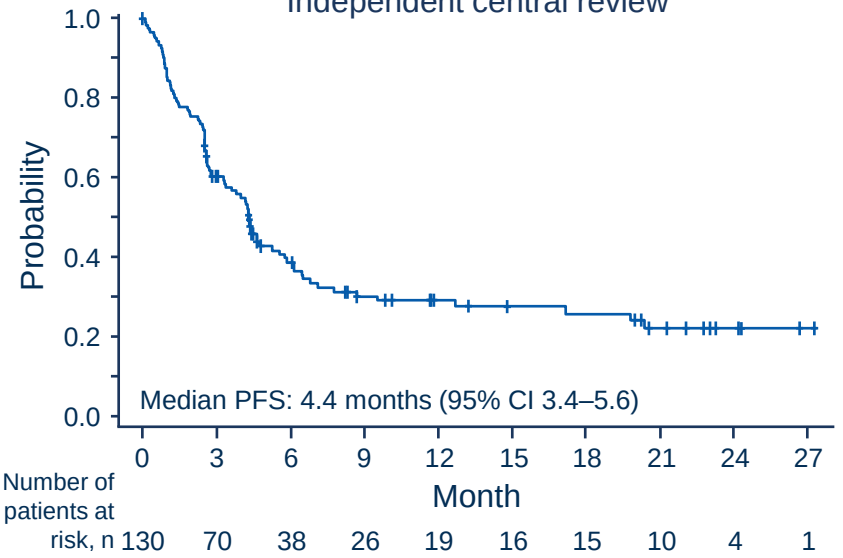
Duration of complete response

Independent central review



Progression-free survival

Independent central review



- Durable responses observed with median DOR of 10.2 months
- Complete responses appear particularly durable, with median DOCR of 17.9 months

- Median PFS was 4.4 months

Data cut-off date from ELM-2: Sep 15, 2022

CI, confidence interval; DOCR, duration of complete response; DOR, duration of response; NE, not evaluable; PFS, progression-free survival.

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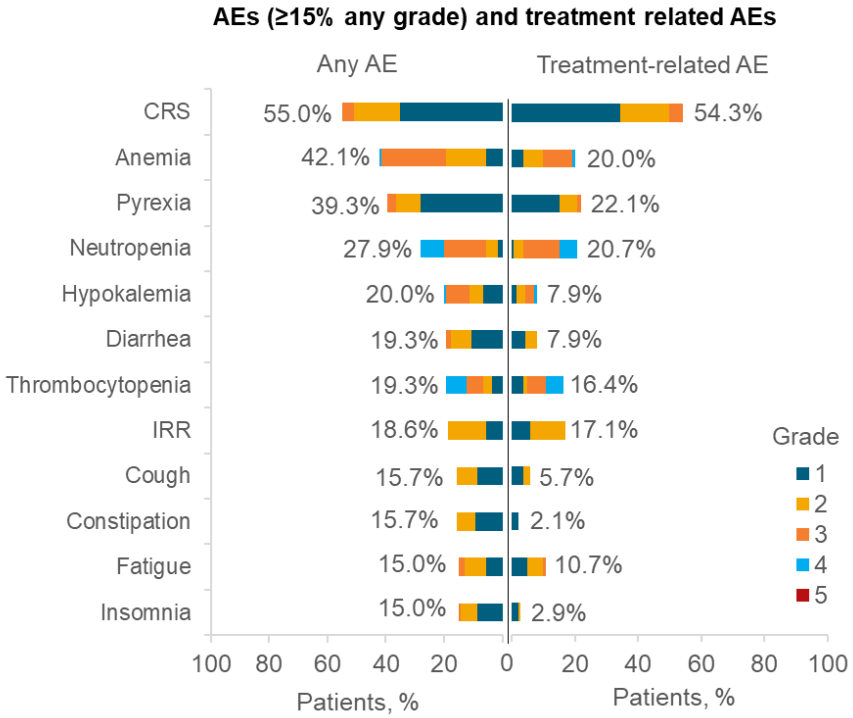
DLBCL: Safety profile

Treatment-emergent adverse events, n (%)	Patients N=140 All events	TRAEs
Any TEAE	**139 (99.3%)**	**123 (87.9%)**
Grade ≥3 TEAE	110 (78.6%)	74 (52.9%)
Serious AE	85 (60.7%)	64 (45.7%)
Grade 5 TEAE	20 (14.3%)	5 (3.6%)
Related to COVID-19	5 (3.6%)	1 (0.7%)
Other grade 5 events	15 (10.7%)	4 (2.9%)
TEAE leading to treatment discontinuation	14 (10.0%)	11 (7.9%)



Data cut-off date from ELM-2: Sep 15, 2022
AEs per NCI-CTCAE v5.0. CRS per Lee 2019 criteria.
AE, Adverse Event; CRS, cytokine release syndrome; IRR, infusion related reaction; TEAE, treatment-emergent AE; TRAE, treatment-related AE.
Grade 5 TRAEs: pneumonia (n=3), COVID-19 (n=1) and pseudomonal sepsis (n=1)

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DLBCL: Safety improvements from modified step-up dosing regimen

n, (%)	1/20 regimen (N=67)	0.7/4/20 regimen (N=73)
CRS any Grade	**38 (56.7%)**	39 (53.4%)
Grade 1	21 (31.3%)	28 (38.4%)
Grade 2	**12 (17.9%)**	**10 (13.7%)**
Grade 3	**5 (7.5%)**	**1 (1.4%)**
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	13 (19.4%)	15 (20.5%)
Received tocilizumab	10 (14.9%)	19 (26.0%)
Received vasopressors	5 (7.5%)	1 (1.4%)

n (%)	1/20 regimen (N=67)	0.7/4/20 regimen (N=73)	All patients (N=140)
ICANS, any grade	**3 (4.5%)**	**1 (1.4%)**	**4 (2.9%)**
Grade ≥3	1 (1.5%)*	0	1 (0.7%)
Infusion related reaction, any grade	**16 (23.9%)**	**8 (11.0%)**	**24 (17.1%)**
Grade ≥3	0	0	0
Infection, any grade	**40 (59.7%)**	**43 (58.9%)**	**83 (59.3%)**
Grades 1–2	13 (19.4%)	24 (32.9%)	37 (26.4%)
Grades 3–4	**21 (31.3%)**	**12 (16.4%)**	**33 (23.6%)**
Grade 5	6 (9.0%)	7 (9.6%)	13 (9.3%)
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.7%)
Grade ≥3	1 (1.5%)	0	1 (0.7%)

With optimized step-up dosing regimen:

- **CRS was mostly grade 1 and generally occurred with Cycle 1 step-up**
- **Only 1 instance of ICANS, no Gr3+ ICANS**

Data cut-off date from ELM-2: Sep 15, 2022
CRS per Lee 2019.
*Grade 3 ICANS event = encephalopathy.
CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

REGENERON

Advancing REGN5837 (CD22xCD28) costimulatory bispecific in combination with odronextamab

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER IMMUNOTHERAPY

CD22-targeted CD28 bispecific antibody enhances antitumor efficacy of odronextamab in refractory diffuse large B cell lymphoma models

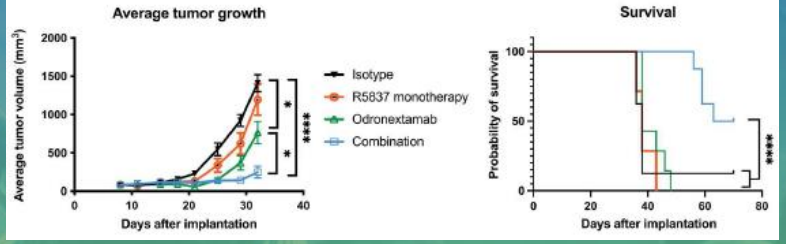
Recent Science Translation Medicine publication:

- REGN5837, a bispecific antibody that clusters CD22-expressing tumor cells with CD28-expressing T cells, enhances odronextamab by potentiating T cell activation and cytolytic function
- REGN5837 monotherapy shows limited activity and no toxicity in primate studies, it augments T cell activation when dosed in combination with odronextamab
- In DLBCL models using mice with reconstituted human immune system, REGN5837 promotes antitumor activity of odronextamab and induces intratumoral expansion of functional T cells
- The combination of these two bispecific antibodies may provide a chemotherapy-free approach for the treatment of DLBCL

Skokos, D., Wei, J., et al. (2022). CD22-targeted CD28 bispecific antibody enhances antitumor efficacy of odronextamab in refractory diffuse large B cell lymphoma models. *Science Translational Medicine*. https://doi.org/10.1126/scitranslmed.abn1082

REGN5837 markedly enhanced the antitumor activity of odronextamab in preclinical NHL models

REGN5837-mediated costimulation enhances odronextamab antitumor efficacy against a B cell malignancy tumor model in a therapeutic treatment setting
(WSU-DLCL2 tumors implanted into NSG mice)



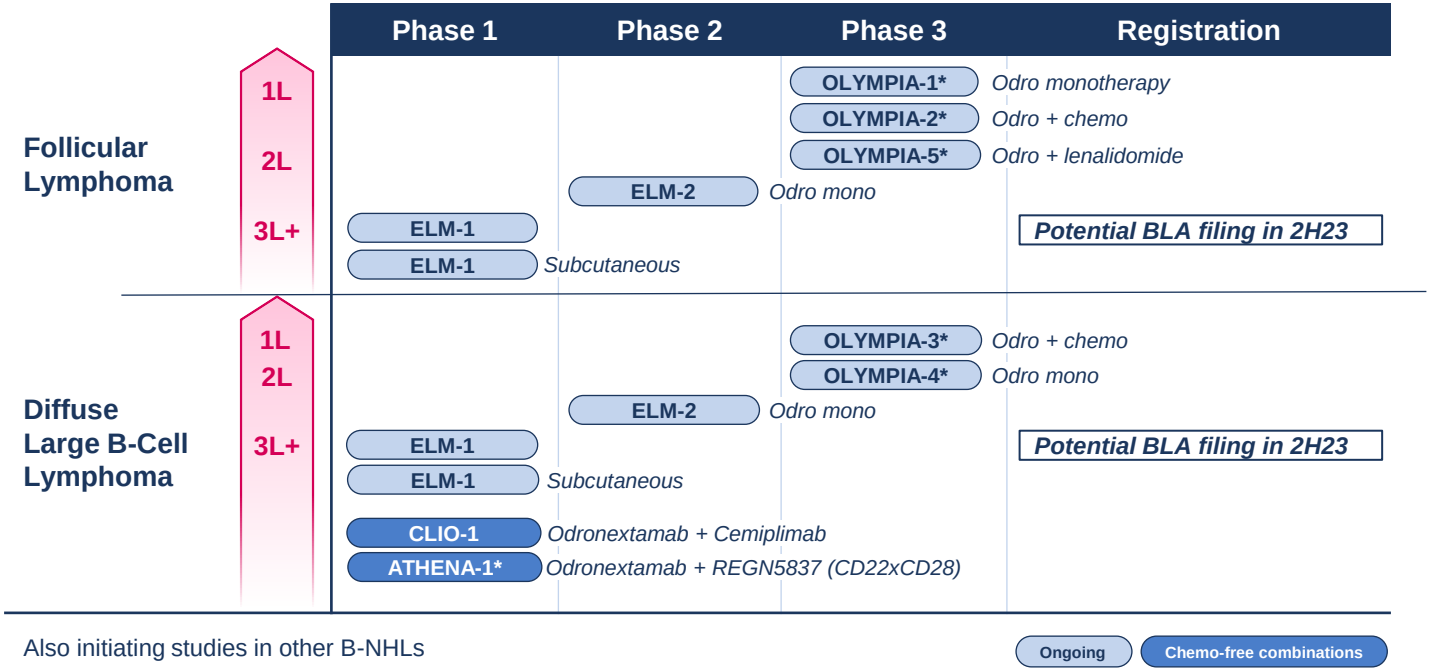
Combining odronextamab, a CD3xCD20 bispecific ('Signal 1" activator) with REGN5837, a CD22xCD28 costimulatory bispecific ("Signal 2" activator) has the potential to increase the breadth and durability of responses to odronextamab alone

Our FIH Phase 1 program combining REGN5837 (CD22xCD28) with odronextamab (CD20xCD3) in aggressive B-NHL patients is expected to initiate in early 2023

REGENERON

Odronextamab: Broad development pipeline in lymphoma

Confirmatory Phase 3 trials initiating in earlier lines of therapy



*Initiating 1H23

REGENERON

Odronextamab: ASH 2022 summary

Rapidly advancing development of novel bispecific platform

R/R Follicular Lymphoma
- **ORR=82%, CR=75%**
- N=121
- Median PFS: 20 months
- Median OS: NR

R/R DLBCL (CAR-T naïve)
- **ORR=49%, CR=31%**
- N=130
- Median PFS: 4.4 months
- mDOCR: 18 months

R/R DLBCL (post-CAR-T)
- **ORR=48%, CR=32%**
- N=31
- mDOCR: NR

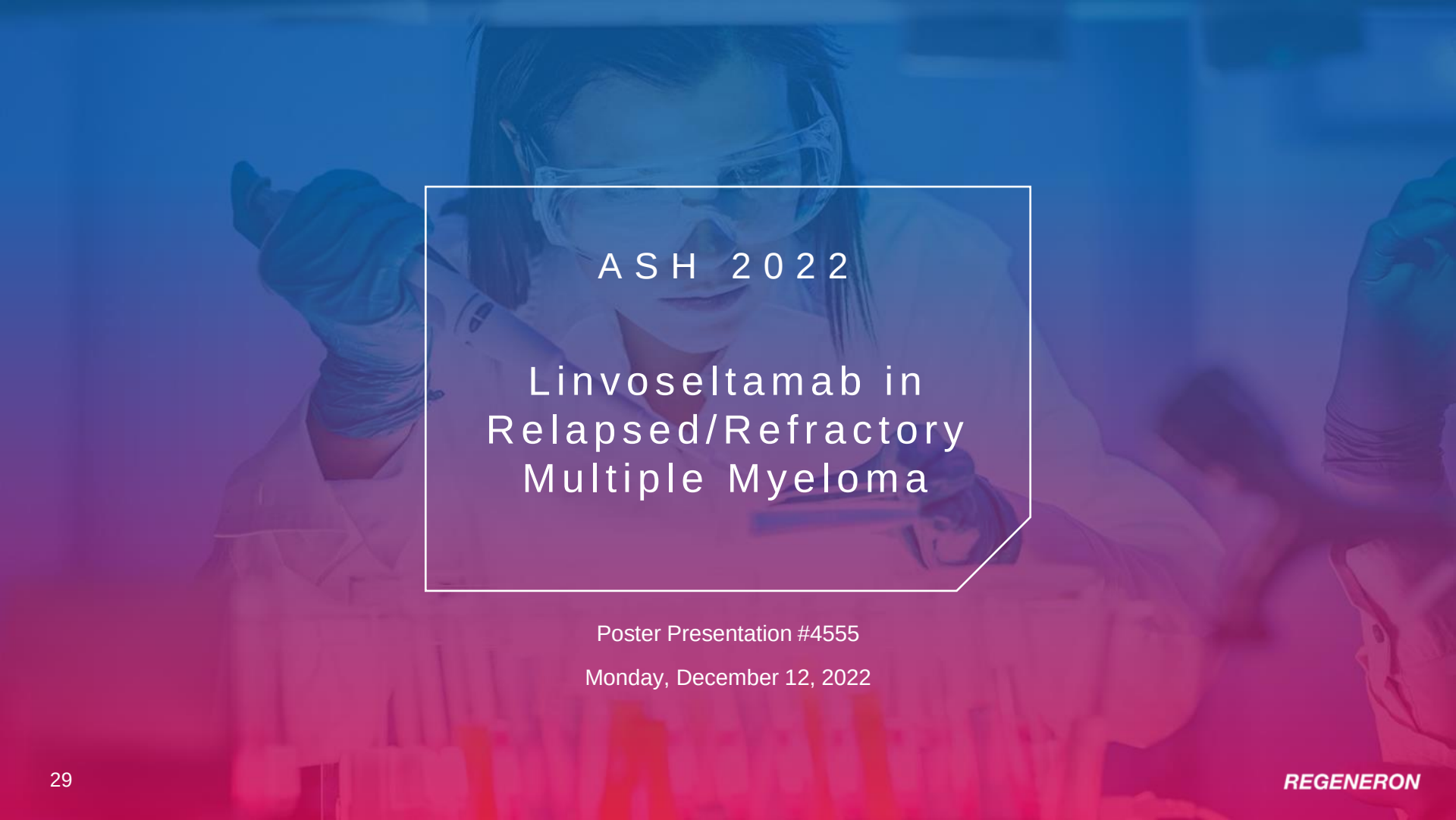
- **FL:** highest CR rates observed in this late-stage setting to date
- **DLBCL:** encouraging ORR seen in patients regardless of CAR-T experience
- Encouraging durability of response and PFS for both indications
- Consistent responses and improved safety observed with revised step-up dosing regimen
- Initiating confirmatory Phase 3 studies in early 2023 to support BLA filing in DLBCL and FL in 2H23

Safety (FL & DLBCL)

Generally manageable safety profile with the optimized step-up regimen

- No Grade 4-5 CRS in FL or DLBCL
- Incidence of Grade 2-3 CRS was reduced with modified step-up dosing regimen
- CRS was mostly grade 1 and occurred mainly with Cycle 1 step-up
- Median time to resolution of 2 days

mDOCR, median duration of complete response; NR, not reached; OS, overall survival; PFS, progression-free survival; CRS, cytokine release syndrome; CAR-T, chimeric antigen receptor T-Cell



ASH 2022

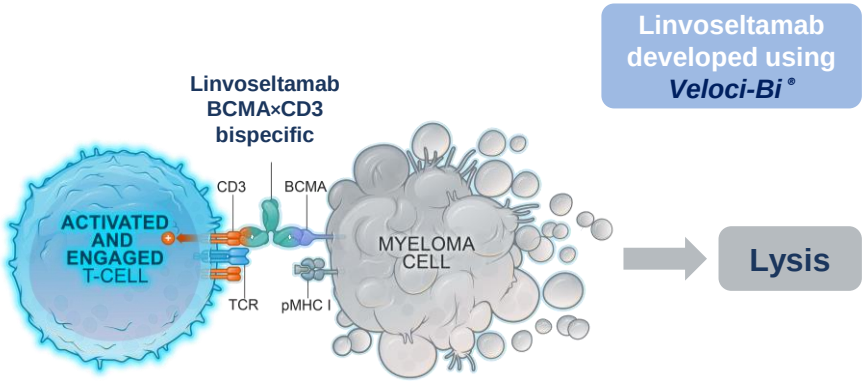
Linvoseltamab in Relapsed/Refractory Multiple Myeloma

Poster Presentation #4555

Monday, December 12, 2022

REGENERON

Linvoseltamab (BCMAxCD3): Rapidly advancing bispecific



Linvoseltamab (REGN5458) is an investigational B-cell maturation antigen (BCMA) × CD3 bispecific antibody that targets T-cell effector function to induce cytotoxicity of BCMA-expressing multiple myeloma cells

- **At ASH 2021** – we presented updated data from Phase 1 dose escalation portion of the study:
  - Linvoseltamab induced early, deep, and durable responses with a manageable safety profile in patients with relapsed/refractory multiple myeloma
- **At ASH 2022** – we presented updated Phase 1/2 safety and efficacy data from the dose escalation and dose expansion portion of the study

The Phase 2 dose escalation portion of the study is fully enrolled and pending FDA discussion we intend to file in 2H23

REGENERON

Linvoseltamab: Updated efficacy and safety data presented from potentially pivotal clinical program

First-in-human Phase 1/2*, dose-escalation and dose-expansion study of linvoseltamab in patients with relapsed/refractory MM

Objectives (Phase 2)

Primary Objective:

- To assess the antitumor activity as measured by objective response rate (ORR) as determined by a blinded independent review committee (IMWG criteria)

Secondary Objectives:

- ORR (by investigator assessment), DOR, PFS, MRD status, and OS

Patient eligibility (Phase 2)

- Active MM by International Myeloma Working Group (IMWG)
- Progression on or after ≥3 lines of therapy including an immunomodulatory drug (IMiD), a proteasome inhibitor (PI), and an anti-CD38 antibody, or triple-refractory (≥1 IMiD, 1 PI, and one anti-CD38 antibody)

Phase 1 Dose Escalation:	**9 dose levels (3 to 800 mg)**
Phase 2 Dose Expansion:	**Two cohorts (50 mg and 200 mg) – each fully enrolled cohort has >100 patients**

Linvoseltamab IV dosing schedule for Phase 2 expansion cohorts

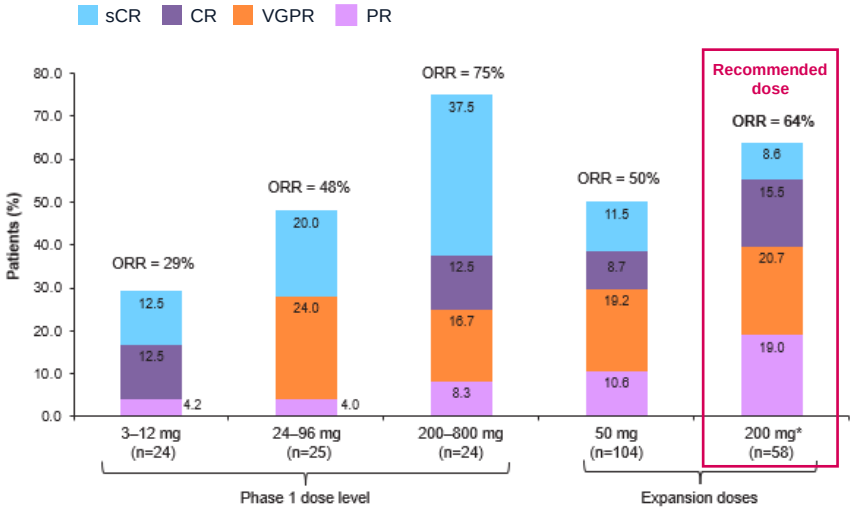
	W1–2 Step-up doses	W3–6 Cycle 1 Full dose	W7–14 Cycles 2–3	W16–23 Cycles 4–5	W24+ Cycle 6 onwards
50 mg cohort	5 / 25 mg	50 mg QW*	50 mg QW*	50 mg Q2W	50 mg Q2W
200 mg cohort	5 / 25 mg	200 mg QW	200 mg QW	200 mg Q2W	≥VGPR 200 mg Q4W <VGPR 200 mg Q2W

*Patients in the 50 mg cohort who progress after ≥4 weeks or ≤12 full doses of tx may dose escalate to 200 mg. For patients who undergo intra-patient dose escalation to 200 mg and who subsequently achieve VGPR or better and have received ≥24 weeks of tx at 200 mg, the frequency of administration will be decreased to Q4W.

*NCT03761108, LINKER-MM1

DOR, duration of response; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease; OS, overall survival; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; tx, treatment; VGPR, very good partial response; W, week; IMiD, Immunomodulatory imide drug; PI, proteasome inhibitor

Linvoseltamab: Higher response rates observed at higher dose levels, with 64% ORR at 200mg dose



- Responses observed across all dose levels, with a trend for higher response rates at higher doses
- At the recommended 200 mg dose: 64% ORR and 45% VGPR or better, with **consistent** responses in high-risk subgroups
  - ORR rate as well as depth of response may increase with further follow-up
- Among CR/sCR with available MRD data†:
  - **Phase 1**: 47% of patients MRD negative at 10^{-5}, with an additional 29%‡ MRD negative at 10^{-4};
  - **Phase 2**: 60% of patients MRD negative at 10^{-5} with an additional 40%‡ MRD negative at 10^{-4}

Early, deep, and durable responses were observed with linvoseltamab, responses may further improve with longer follow-up

Heavily pre-treated patients with high disease burden

- **84%** penta-exposed
- **37%** with BMPC ≥50%
- median soluble BCMA **0.43 mg/L**

Data cut-off date: 01 Sep 2022. Full analysis set - includes all patients who had opportunity for response assessment at 12 weeks. Median follow-up was 3.2 (range 0–30.4)
*Includes 12 patients from the dose escalation part of the study. †17 of 24 patients with CR/sCR in Phase 1, and 20 of 28 patients in Phase 2.
‡Patients had no detectable malignant plasma cells and failed to achieve a 10^{-5} threshold due to insufficient cell number for Euroflow.
CR, complete response; ORR, objective response rate; PR, partial response; sCR, stringent CR; VGPR, very good partial response; BMPC, bone marrow plasma cells; MRD, minimal residual disease

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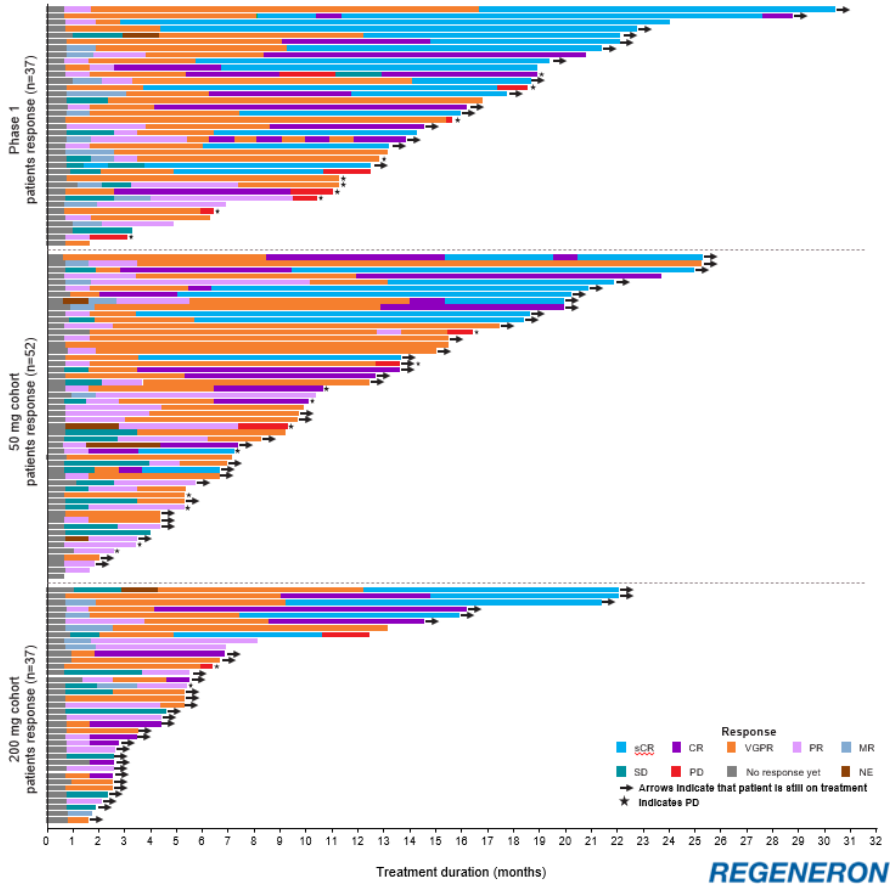
Linvoseltamab: Responses occurred early, were durable and deepen with time

- **Median time to response**
  - **50 mg cohort:** 0.77 months
  - **200 mg cohort**: 0.95 months
- **Probability of maintaining response (Kaplan–Meier method):**
  - **50 mg cohort**: 85% at 6 months, 64% at 12 months, and 60% at 16 months
  - **200 mg cohort**: 79% at 6 months; not estimable at 12 months
- **Longest responses (at latest data cut)**
  - **28+ months** (ongoing)
- **Six out of eight patients who dose escalated from 50 to 200 mg (protocol amendment) responded to treatment, including four VGPR**



Data cut-off date: 01 Sept. 2022.
CR, complete response; MR, minimal response; NE, not evaluable; PD, progressive disease; PR, partial response; sCR, stringent CR; SD, stable disease; VGPR, very good partial response.

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Linvoseltamab: Safety and tolerability profile

Treatment-emergent adverse events (TEAEs)

- Almost all patients experienced a TEAE with 77% experiencing Grade ≥3
- Anemia was most common hematologic TEAE, CRS was most common non-hematologic TEAE

Potential ICANS events (neurotoxicity)

- Any Grade: 5.6% of patients; Grade ≥3: 1.2% of patients

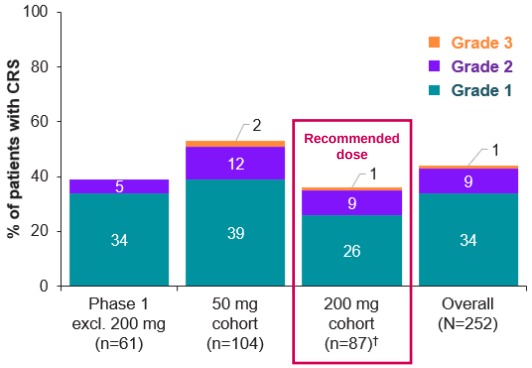
Infections

- Any Grade: 54% of patients; Grade ≥3: 29% of patients

Grade 5 AEs

- 14 patients, including sepsis/bacterial infection (n=6) and COVID-19 infection (n=4)
- None of the deaths were considered related to treatment per the treating physician

Severity of CRS* (% of patients)



Timing and Management of CRS

	Total (N=252)
Patients with CRS, n (%)	**111 (44)**
Median time to first CRS* onset‡ (range)	11.0 hours (0–47)
Median duration of CRS (range)	15.4 hours (0–377)
Patients with supportive measures to treat CRS, n (%)	
Tocilizumab	44 (18)
Steroids	24 (10)
Oxygen	10 (4)

Majority of patients did not develop CRS

- At the recommended 200mg dose: 37% of patients developed CRS; over 2/3 of CRS cases were Grade 1 with 1 transient Grade 3 CRS case
- Most CRS occurred during the step-up dosing (first 2 weeks of treatment), with onset on the day of dosing and resolved within 1 day

*Highest severity of CRS per ASTCT (Lee. *Biol Blood Marrow Transplant*. 2019) from each patient was included;
†Includes 12 patients from the dose escalation part of the study. ‡From the start of infusion of the most recent prior dose.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; excl., excluding.

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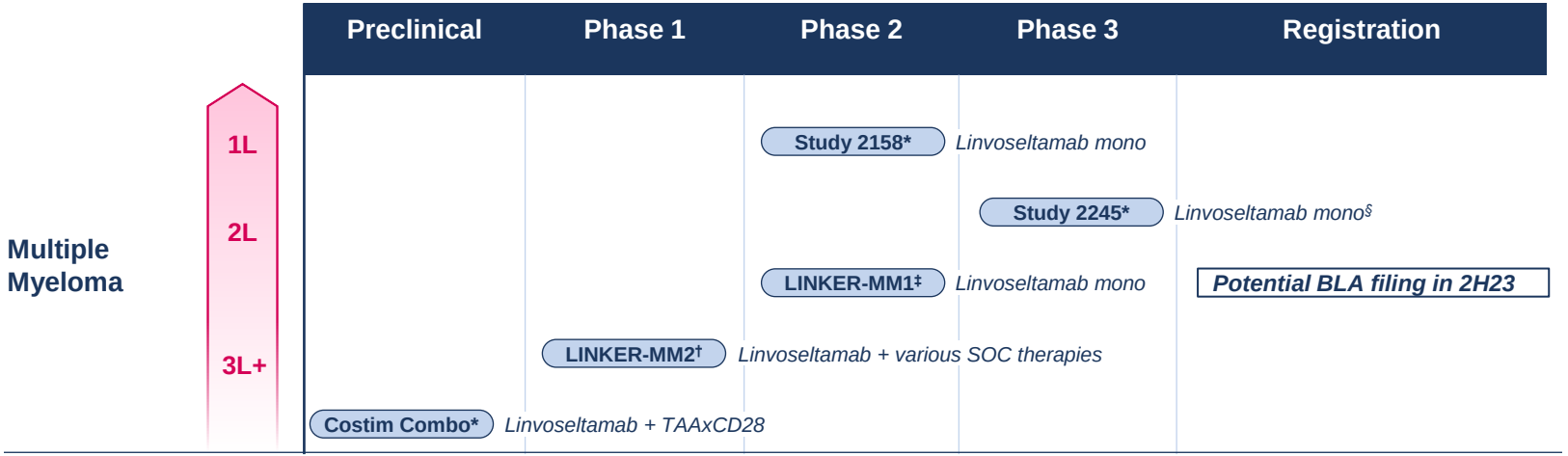
Linvoseltamab: Advancing clinical development program

Rapidly initiating confirmatory studies and advancing studies in earlier lines of therapy



Planning additional studies

*Initiating 1H23, †NCT05137054. ‡NCT03761108. §Linvoseltamab mono vs. Epd (Elotuzumab + Pomalidomide + Dexamethasone)
TAA: Tumor Associated Antigen

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Linvoseltamab: ASH 2022 summary

Compelling Phase 2 efficacy and generally manageable safety profile in heavily pre-treated multiple myeloma patients with high disease burden

Efficacy

- Recommended 200 mg dose: **ORR 64% and ≥VGPR 45%,** with an 79% probability of responders to maintain response at 6 months
- Responses may further improve with longer follow-up
- 60% of Phase 2 patients with CR/sCR were MRD negative at 10^{-5}
- Six out of eight patients who dose escalated from 50 to 200 mg responded to treatment, including four VGPR

Upcoming Milestones

- Phase 2 study fully enrolled, regulatory filings expected in 2H23
- Rapidly initiating confirmatory studies and advancing studies in earlier lines of therapy

Safety

- Recommended 200mg dose: 37% of patients developed CRS; over 2/3 of all CRS cases were Grade 1 with 1 transient Grade 3 CRS case
- Most CRS occurred during the step-up dosing (first 2 weeks of treatment), with onset on the day of dosing and resolved within 1 day

- **Encouraging efficacy** observed in a heavily pre-treated patient population with high disease burden
- Responses occur **early**, are **durable**, and **deepen** over time
- Generally manageable safety profile with majority of patients having no CRS
- Clinical program advancing with regulatory **filing expected in 2H23**

CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ORR, objective response rate; VGPR, very good partial response.

Classical Hematology

Hematology development pipeline

Our research and collaborations to develop potential treatments for rare blood disorders include explorations in antibody medicine, gene editing and gene-knockout technologies, and investigational RNA-approaches focused on depleting abnormal proteins or blocking disease-causing cellular signaling

Pre-Clinical	Phase 1	Phase 2	Phase 3
CD22xCD28 (REGN5837) Lymphoma	**IL2Rγ (REGN7257)** Aplastic Anemia	**odronextamab (CD20xCD3)** Lymphoma	**pozelimab (C5) + cemdisiran (ALN-CC5)** MG, PNH
TAAxCD28 Multiple myeloma	**TTR (NTLA-2001)*** Amyloidosis [Intellia]	**linvoseltamab (BCMAxCD3)** Multiple Myeloma	
Factor IX Gene Insertion CRISPR LNP + Viral [Intellia]	**BCMAxCD3 (REGN5459)** CKD patients awaiting transplant†	**pozelimab (C5)** CHAPLE	
	Factor XI (REGN9933) Thrombosis		
	TMPRSS6 (REGN7999) Transfusion dependent iron overload		

Heme Malignancies | Coagulation | Transplantation & Immunomodulation | Complement | Other | Collaborations

*collaborator leads development. †Desensitization of CKD patients awaiting kidney transplant.
CKD, Chronic Kidney Disease; gMG, generalized Myasthenia gravis; PNH, Paroxysmal Nocturnal hemoglobinuria..

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Closing Remarks

Anticipated proof of concept or pivotal data readouts across oncology pipeline

★ indicates potentially pivotal study ✓ indicates data readout

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

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

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ASH 2022 Key Takeaways

- Two advanced bispecific programs in hematologic malignancies with encouraging and durable efficacy and generally manageable safety profiles
- Rapidly advancing robust Phase 3 programs to the clinic to support potential 2H23 filings for odronextamab in FL and DLBCL and linvoseltamab in multiple myeloma
- Phase 3 programs to evaluate odronextamab and linvoseltamab vs. standard of care in earlier lines of therapy
- Plan to initiate studies in combination with novel CD28 costimulatory bispecifics
- Emerging hematology pipeline with diverse programs across hematological diseases, with Phase 3 studies for C5 antibody/ siRNA combination in PNH and MG

Rapidly progressing heme-onc programs with deep, durable responses and generally manageable safety toward 2023 filings

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

Q&A

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EVP, Global Clinical Development

Andres Sirulnik, MD, PhD
SVP Clinical Development – Hematology