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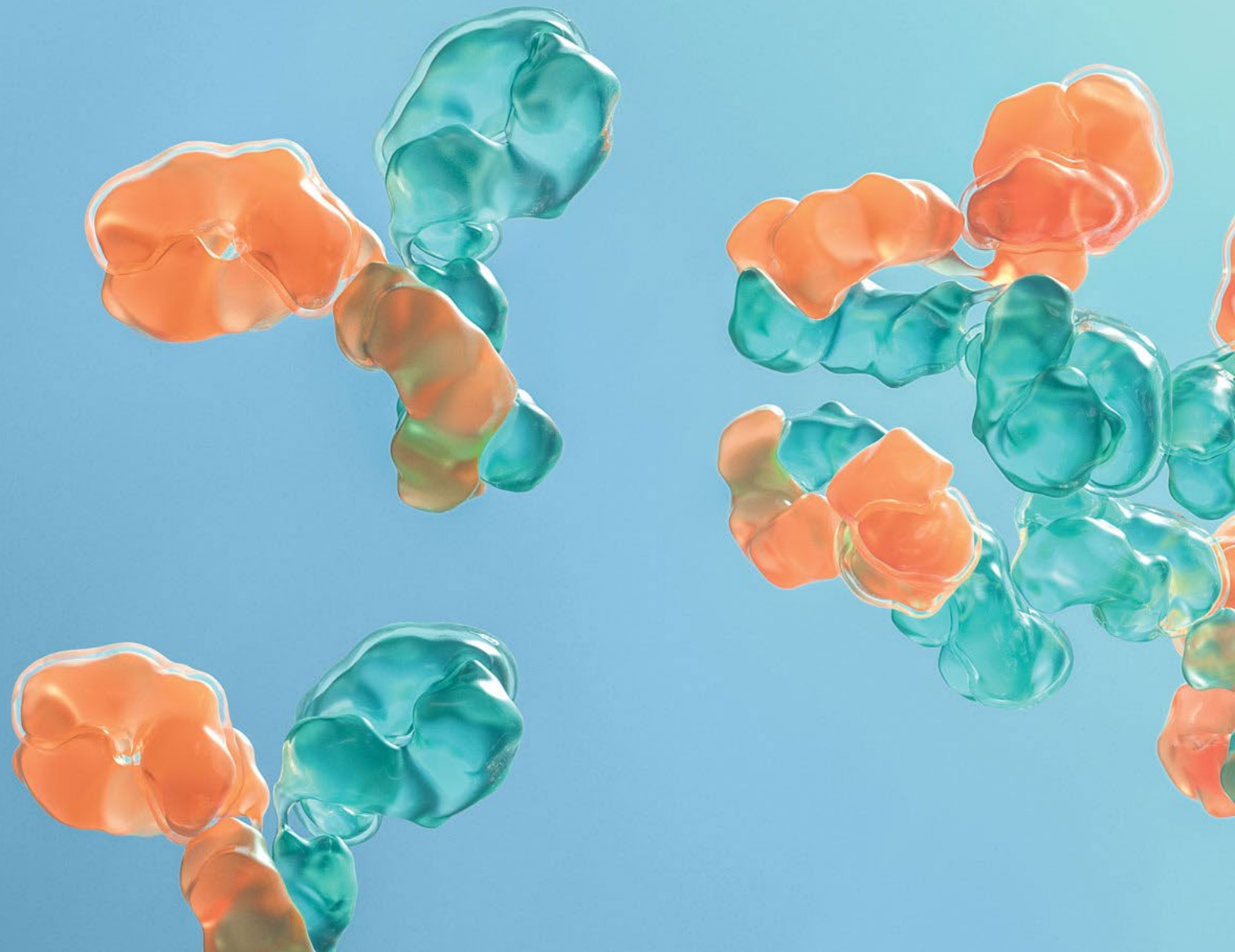
2021 Virtual R&D Update and ASH Data Review

December 14, 2021

Live via Webcast



Forward looking statement

This presentation contains forward looking statements. The words “believe”, “expect”, “anticipate”, “intend” and “plan” and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation. Genmab does not undertake any obligation to update or revise forward looking statements in this presentation nor to confirm such statements to reflect subsequent events or circumstances after the date made or in relation to actual results, unless required by law.

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Strategic Partnerships, Collaborations and Licensing Agreements

As part of the Genmab 2021 Virtual R&D Update and ASH Data Review presentation, we will discuss products developed in collaboration with strategic partners or that are the result of product or technology licenses with other companies. This slide is an acknowledgement of those relationships.

- **Partners for Genmab owned products ≥50%:**
- Seagen Inc. (Seagen): TIVDAK™
- AbbVie Inc: epcoritamab, DuoHexaBody®-CD37 (GEN3009)
- BioNTech SE: DuoBody®-CD40x4-1BB (GEN1042) & DuoBody-PD-L1x4-1BB (GEN1046)
- Janssen Biotech, Inc. (Janssen)*: HexaBody®-CD38 (GEN3014)
- **Companies developing products created by Genmab or that incorporate Genmab's innovation:**
- Janssen: DARZALEX®, RYBREVANT®, teclistamab, talquetamab
- Novartis Pharma AG (Novartis): Kesimpta®
- H. Lundbeck A/S: Lu AF82422
- Novo Nordisk A/S: Mim8
- Global Blood Therapeutics, Inc.: inclacumab

*Genmab is developing HexaBody-CD38 in an exclusive worldwide license and option agreement with Janssen Biotech, Inc.

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Agenda

14.00	Welcome & Introduction	Dr. Jan van de Winkel, President & CEO
14.10	Proprietary Next-Generation Technology Platforms	Dr. Janine Schuurman, Senior Vice President, Head of Antibody Research & Technology
14.30	Epcoritamab at ASH	Dr. Martin Hutchings, Department of Hematology, Rigshospitalet, Copenhagen University Hospital
14.53	Live Q&A	Dr. Jan van de Winkel, Dr. Janine Schuurman and Dr. Kim Linton, Clinical Senior Lecturer in Medical Oncology, University of Manchester, Dr. Judith Klimovsky, EVP & CDO, DR. Tahamtan Ahmadi, EVP & CMO
14.11	2022 & Beyond: Positioned for Continued Success	Dr. Jan van de Winkel
15.21	Live Q&A	

Well Positioned for Future Growth

- Consistent and solid track record
- Experienced world-class team
- Innovative proprietary technologies and first-in-class / best-in-class pipeline including Genmab's first approved medicine
- Partnerships with innovators and industry leaders
- Strong financials to invest in growth opportunities

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Evolution into Fully-integrated Biotech Innovation Powerhouse

Summary of Key 2021 Events: Pipeline and Capabilities

First Genmab-owned product on the market

- TIVDAK
- Collaboration with Seagen
- First and only approved ADC for treatment of patients with metastatic cervical cancer with disease progression on or after chemotherapy
- Genmab & Seagen focused on strong commercial execution

tivdak™
tisotumab vedotin-tftv
for injection 40 mg

- Continued growth of internal capabilities
- First Phase 3 studies for tisotumab vedotin and epcoritamab
- First GEN1046 Phase 2
- GEN1042 expansion cohorts
- New investigational medicines enter the clinic
- Multiple data presentations and publications across portfolio
- Bolt Biotherapeutics collaboration

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Progress with Early-stage Product Candidates

- HexaBody-CD38 (GEN3014)
  - Dose-escalation ongoing in Ph 1/2 study in relapsed or refractory MM and other hematologic malignancies
  - Early signs of activity
  - No safety signals

- DuoHexaBody-CD37 (GEN3009)
  - Dose-escalation ongoing in Ph 1/2 study in relapsed or refractory B-cell NHL
  - Early signs of activity
  - No safety signals

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Summary of Key 2021 Events: Genmab's Innovation in Action

Updates for previously approved therapies

- DARZALEX (Janssen)
  - Additional approvals: U.S., EU, Japan, China
- Kesimpta (Novartis)
  - Approvals in EU & Japan

Data presentations / publications, new studies announced for multiple programs incorporating Genmab's innovation

Strong validation for proprietary DuoBody technology platform

- Janssen programs:
  - RYBREVANT approved in U.S. & EU
  - Teclistamab BTD
  - Data at ASH

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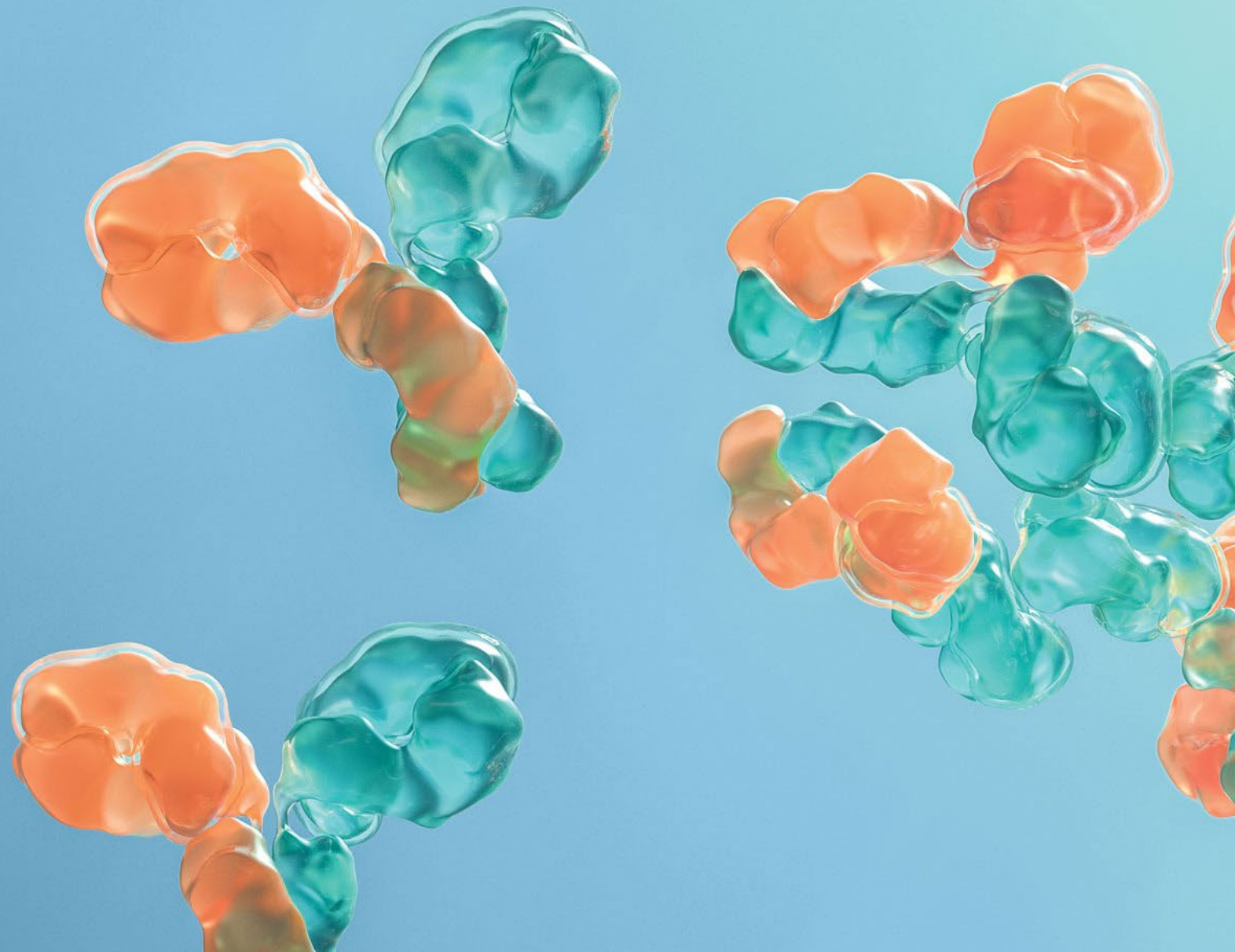
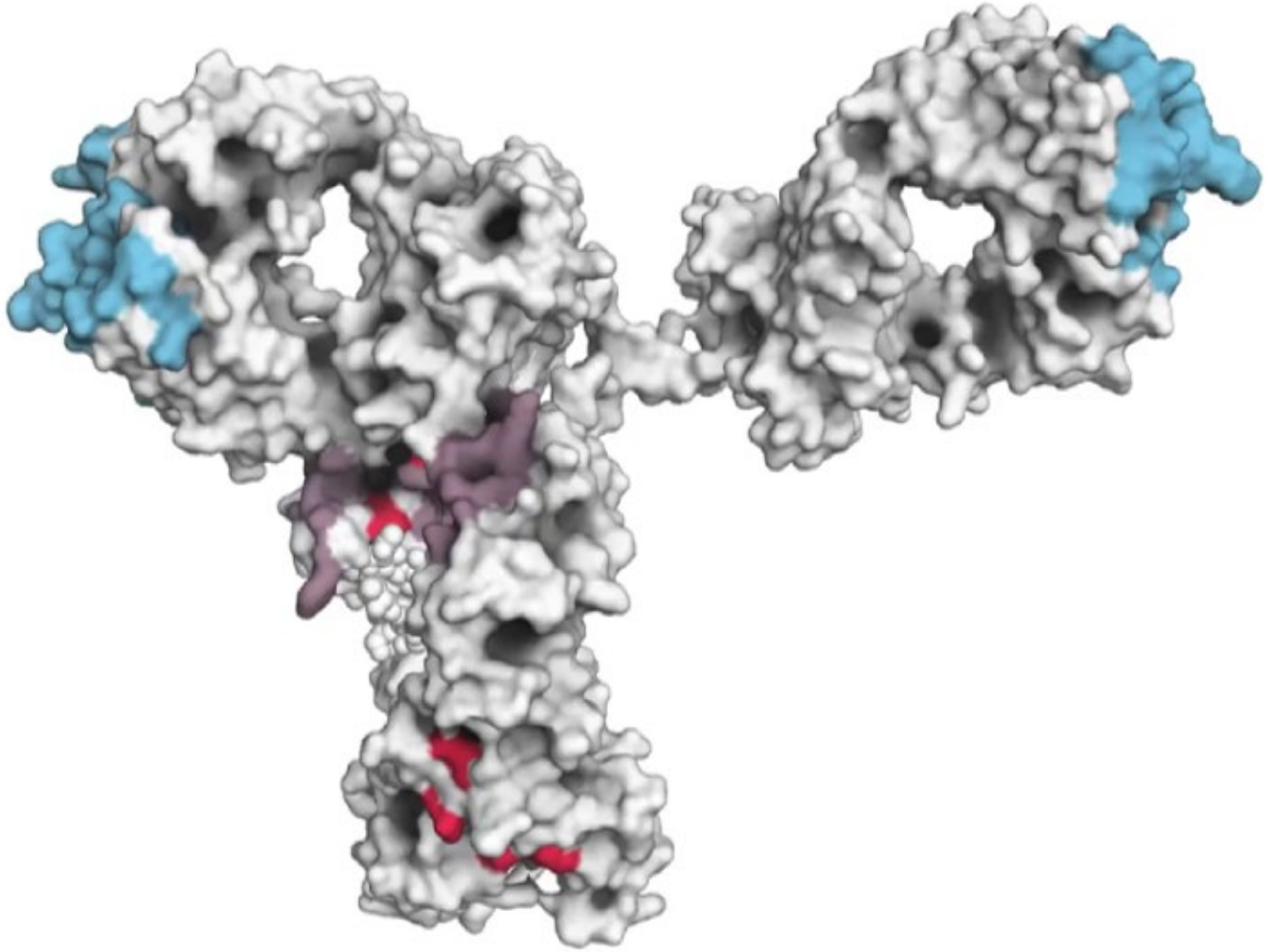
Proprietary Next-Generation Antibody Technology Platforms

Dr. Janine Schuurman
Senior Vice President, Head of Antibody Research & Technology



Natural Immunity Inspires Innovative Technologies and Products



The power of our immune system inspires us

We are curious to understand basic immunological principles

We translate this to innovative technologies

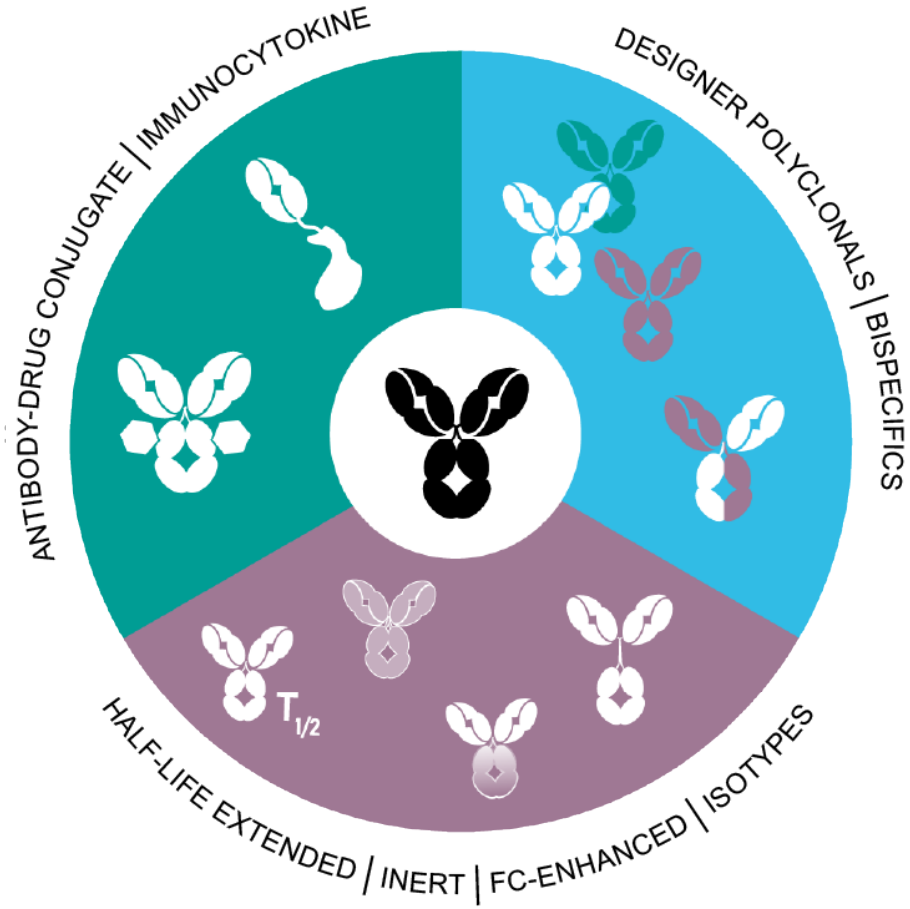
We create differentiated antibody products

Our Approach to a Pipeline of Knock-Your-Socks-Off Antibodies

Antibody Product Ideation: Technology Platform as Critical Ingredient

Knock-Your-Socks-Off Product

Target + Indication + Antibody + Format



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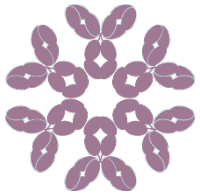
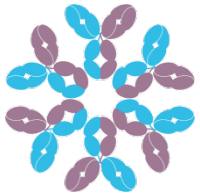
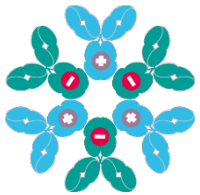
Technology Platform Suite Boosting Our Product Pipeline

		Principle	Applications
DuoBody		Bispecific antibodies	Dual targeting: • Recruitment (e.g. T cells) • Tumor heterogeneity
HexaBody		Target-mediated enhanced hexamerization	Enhanced potency: • CDC • Target clustering, outside-in signaling, apoptosis
DuoHexaBody		Bispecific antibodies with target-mediated enhanced hexamerization	Dual targeting + enhanced potency • CDC • Target clustering, outside-in signaling, apoptosis
HexElect		Two co-dependent antibodies with target-mediated enhanced hexamerization	Dual targeting + enhanced potency & selectivity: • Co-dependent unlocking of potency • New target space, previously inaccessible

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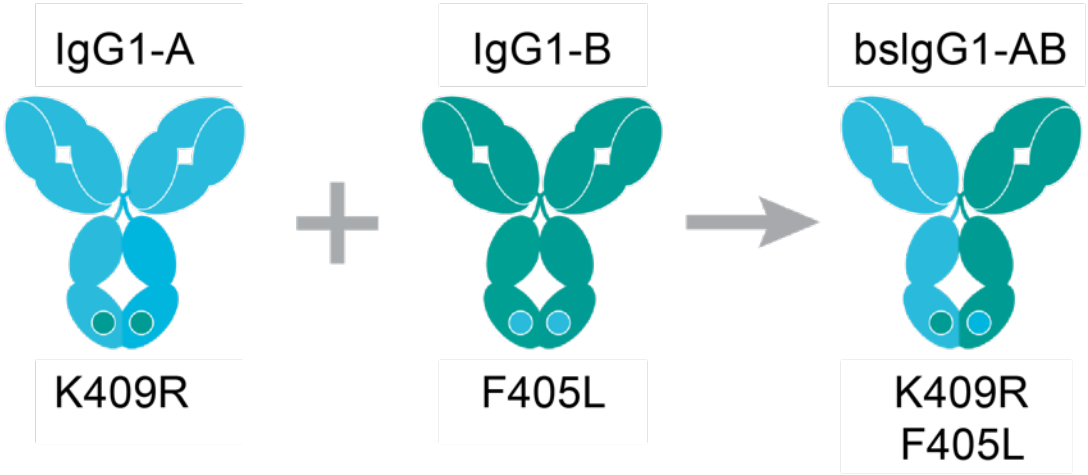
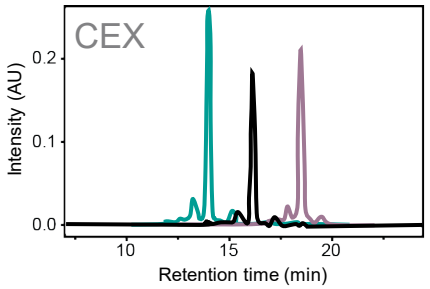
DuoBody Platform: The Principle

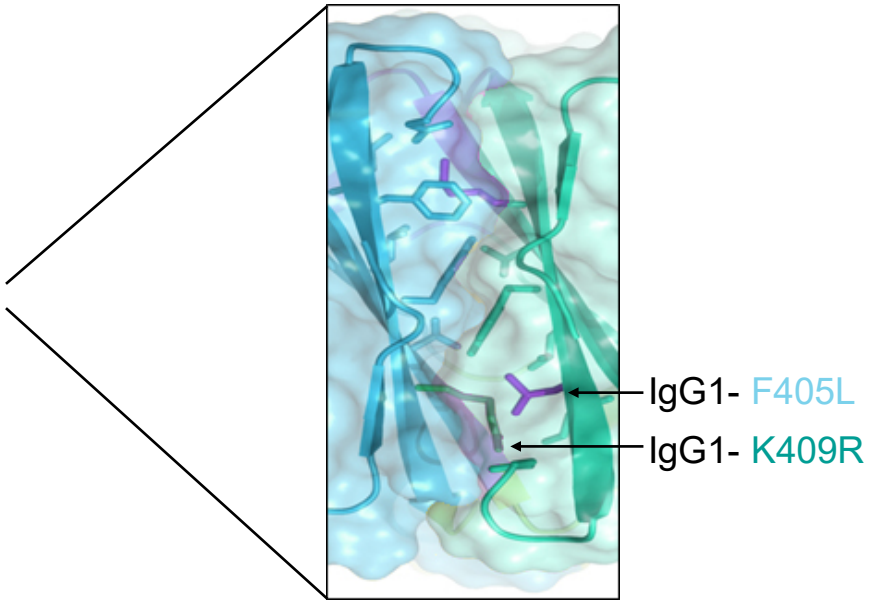
Versatile Platform for Creation & Development of Stable Bispecific Antibodies in Human IgG Format





IgG1 structure and function are fully retained: identical to regular IgG1 (biochemical analysis)

High bispecific yield (and protein yield)



Matched CH3 mutations
Allow dissociation of homodimers
Favor heterodimerization

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Labrijn et al. PNAS 2013, 110: 5145-50

DuoBody Platform - Bispecific Antibody Discovery

Generation and Screening in Final Format

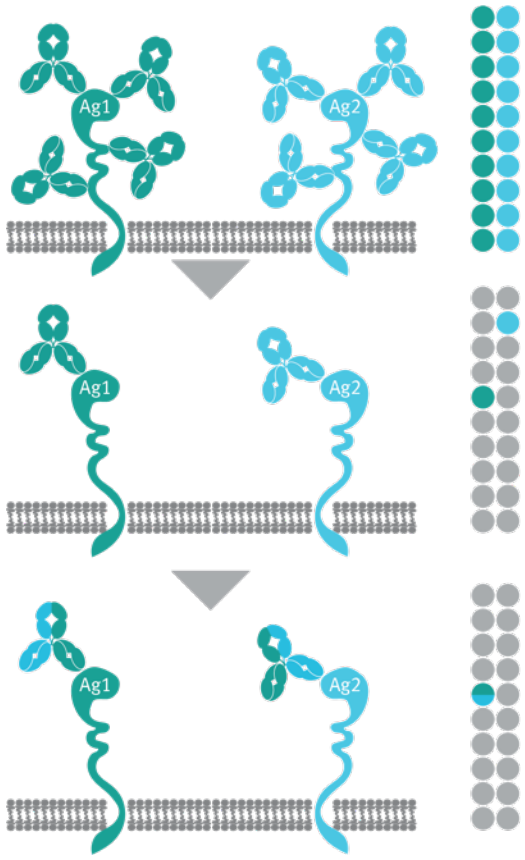
Standard BsAb discovery process

With standard bispecific discovery processes…

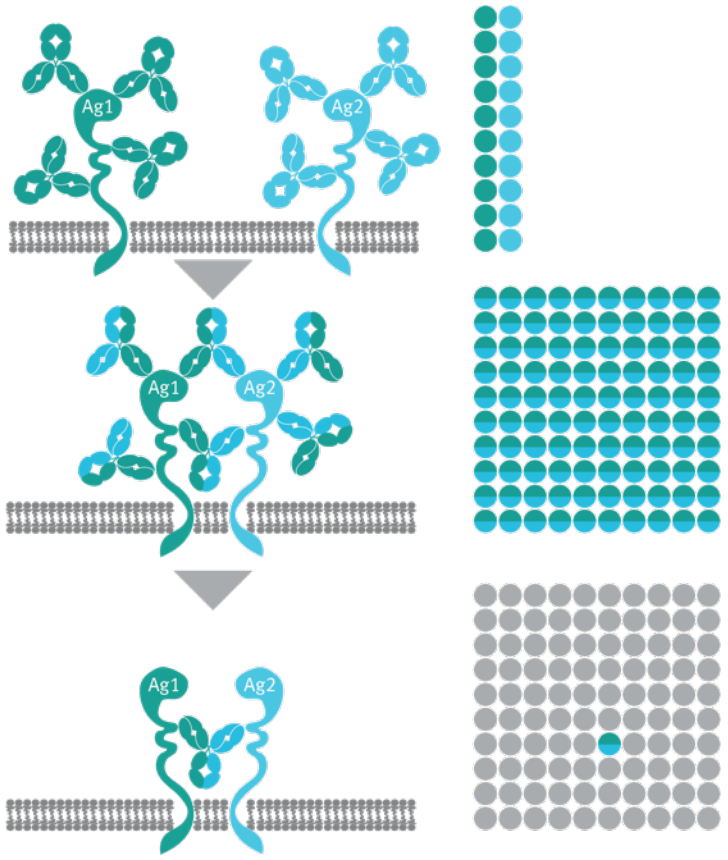
…the antibody with the best characteristics as monoclonal antibody is picked….

… for the generation of the bispecific lead.

This might not be the most optimal candidate.



DuoBody discovery process



The DuoBody platform enables the generation of large libraries of bispecific antibodies….

…screening in an unbiased & empirical approach and in final format.

This enables the selection of the best bispecific lead candidate….

... based upon functional criteria.

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DuoBody Technology: Bispecific Antibodies

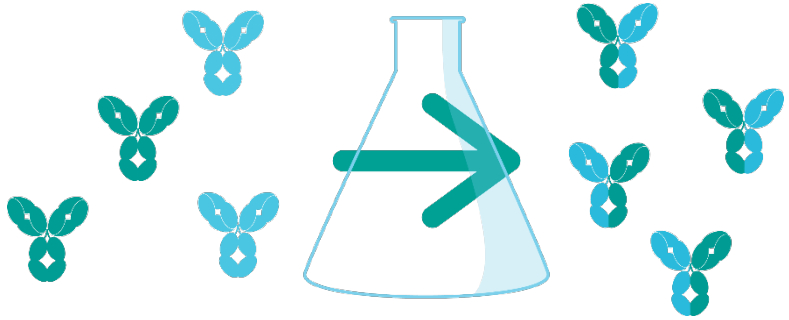
Inspired by Nature – Designed for Success

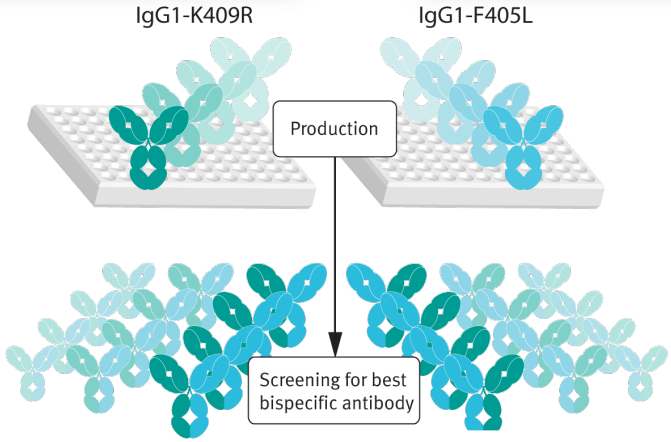
DuoBody Discovery

- Bispecific IgG antibodies compatible with any IgG antibody sequence and subclass
- CD3 arm and inert backbone available
- Enables creation of huge combinatorial DuoBody lead panels in the therapeutically applied format
- DuoBody molecules retain prized IgG1-like stability

DuoBody Development

- >10 clinical programs active
- Ample large scale manufacturing experience
- Technology transferred to multiple CMO's
- Adopted by multiple collaboration partners





HexaBody Technology: Potentiated Antibodies

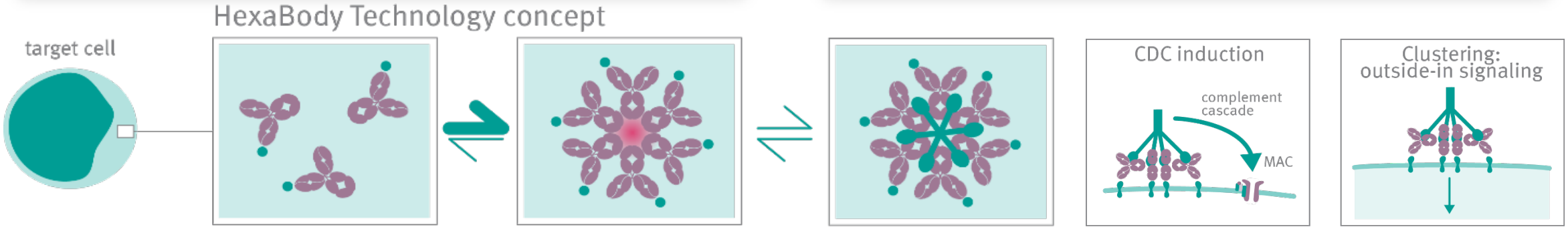
Antibodies Designed to Work as a Team

HexaBody Product Design

- IgG1 antibodies that self-organize at the cell surface only after target binding
- IgG hexamerization can elicit agonistic target signaling or potentiate immune effector functions
- Target signaling does not depend on crosslinking by the recruitment of immune cells

HexaBody Development

- Clinical experience available
- Large scale manufacturing experience was gathered at multiple CMO's
- Compatible with standard IgG manufacturing processes

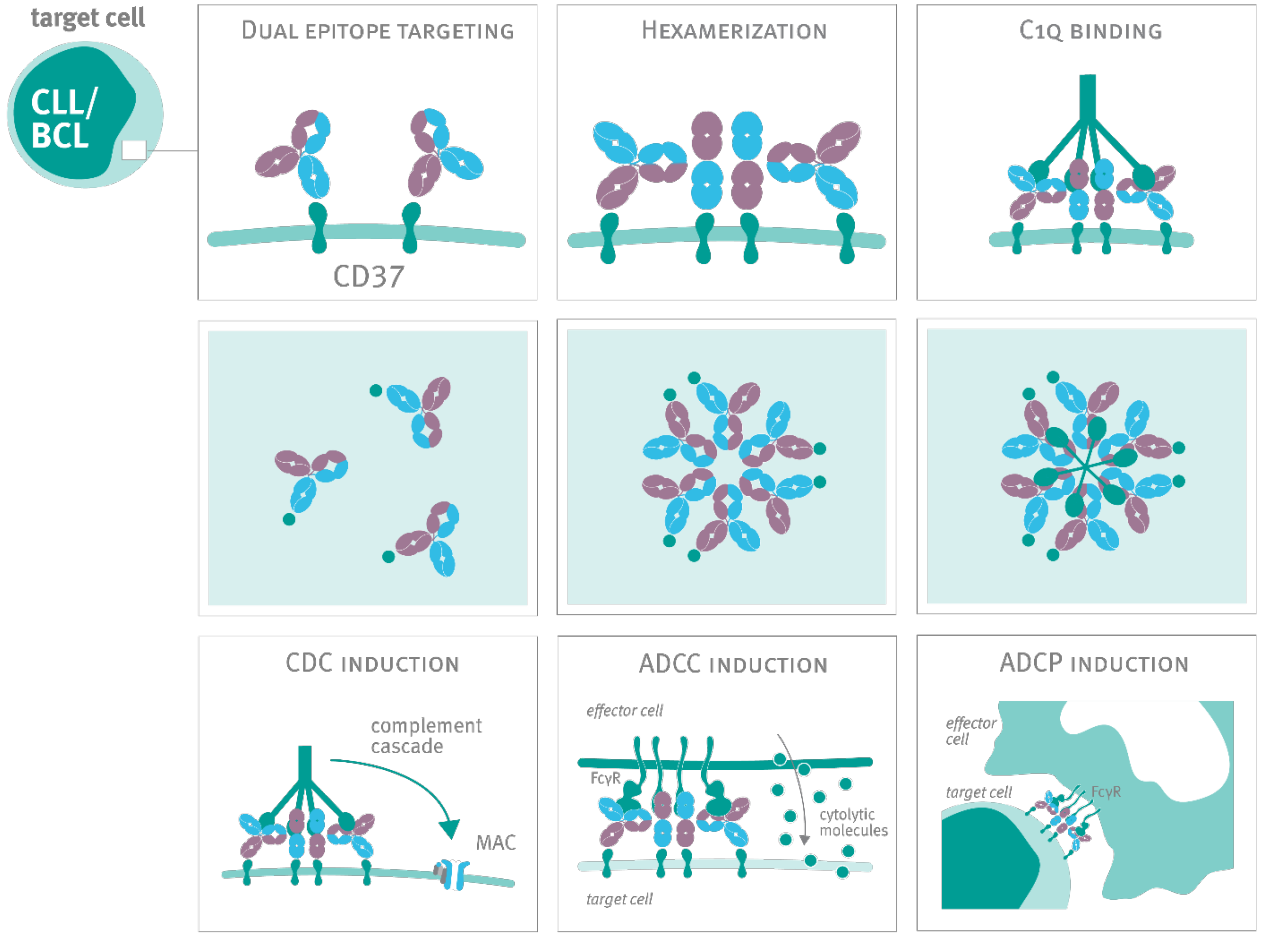


DuoHexaBody Technology: Potentiated Bispecific Antibodies

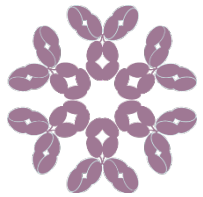
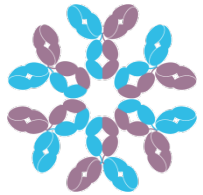
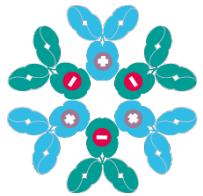
Bispecific Antibodies Designed to Work as a Team

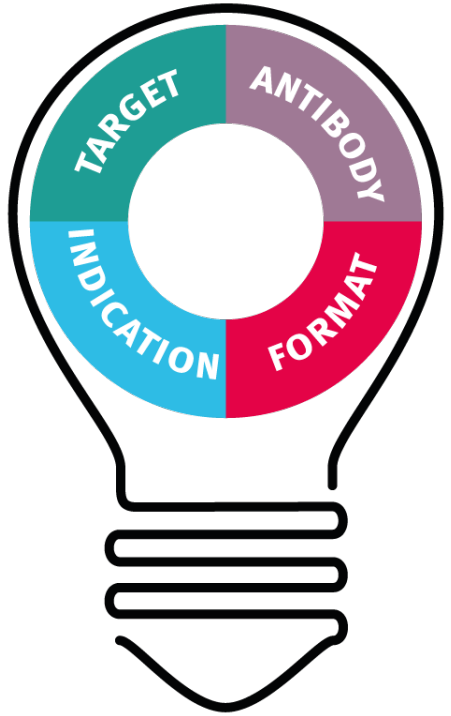
DuoHexaBody Product Design

- DuoHexaBody technology combines the dual targeting of bispecific antibodies with the potentiation of IgG hexamerization
- DuoHexaBody enables multiple mechanisms of action to contribute to maximize the potency of therapeutic compounds
- Clinical and manufacturing experience is gathered within the DuoHexaBody-CD37 development program



Platform Technology Suite Boosting Our Product Pipeline

	Principle
DuoBody 	Bispecific antibodies
HexaBody 	Target-mediated enhanced hexamerization
DuoHexaBody 	Bispecific antibodies with target-mediated enhanced hexamerization
HexElect 	Two co-dependent antibodies with target-mediated enhanced hexamerization



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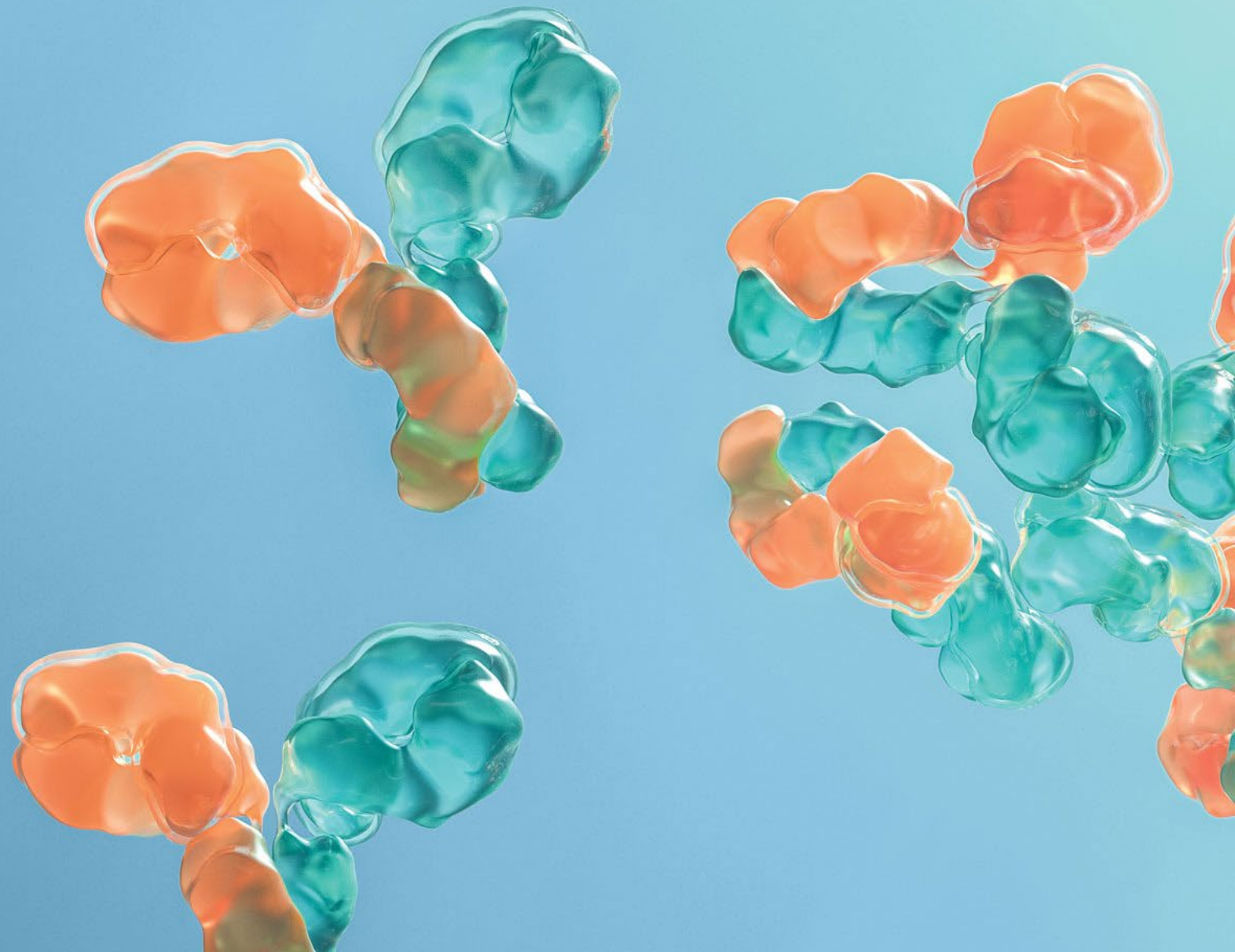
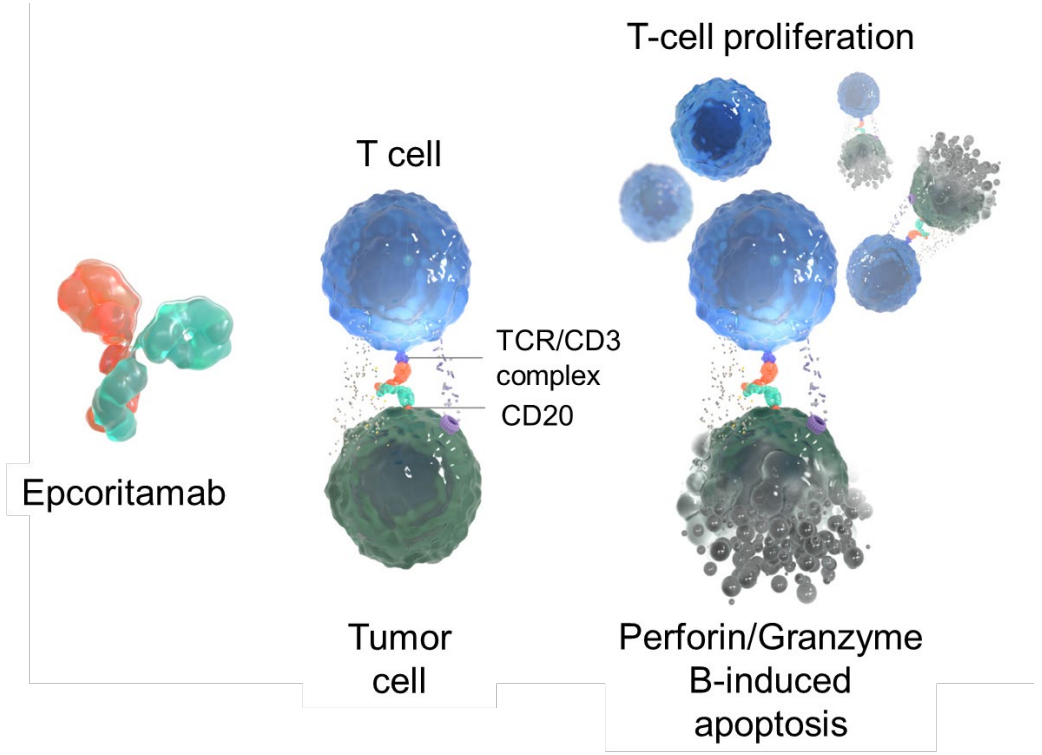
Epcoritamab at ASH



Presented by Dr. Martin Hutchings,
Department of Hematology
Rigshospitalet, Copenhagen University Hospital

Epcoritamab

- Epcoritamab (DuoBody®-CD3xCD20) is a subcutaneously administered bispecific antibody that simultaneously binds to CD3 on T-cells and CD20 on B-cells and induces T-cell–mediated killing of CD20+ malignant B cells[1,2]
- At ASH 2020 we presented data from the dose escalation trial of single-agent epcoritamab in patients with heavily pretreated B-cell NHL [3]
- In this patient population epcoritamab demonstrated promising antitumor activity with a manageable safety profile[3]



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TCR, T-cell receptor.

1. Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. 2. van der Horst HJ, et al. *Blood Cancer J*. 2021;11:38. 3. Hutchings M, et al. *Lancet*. 2021;398:1157-69.

Key Epcoritamab Disclosures at ASH 2021

EPCORE NHL-2 Arm 1

POSTER

Subcutaneous Epcoritamab in Combination with R-CHOP in Patients with Previously Untreated High-Risk Diffuse Large B-cell Lymphoma: Preliminary Results from a Phase 1/2 Trial

David Belada, MD, PhD

Abstract #1413

EPCORE NHL-2 Arm 2

POSTER

Subcutaneous Epcoritamab in Combination with R2 (Rituximab and Lenalidomide) in Patients with Relapsed or Refractory Follicular Lymphoma: Preliminary Results from a Phase 1/2 Trial

Kim M Linton, MBChB, PhD

Abstract #3535

EPCORE CLL-1

POSTER

Subcutaneous Epcoritamab in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia: Preliminary Results from the EPCORE CLL-1 Trial

Arnon P Kater, MD, PhD

Abstract #2627

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DLBCL/FL

CLL

EPCORE NHL-2 Arm 1

Subcutaneous Epcoritamab in Combination with R-CHOP in Patients with Previously Untreated High-Risk Diffuse Large B-cell Lymphoma: Preliminary Results From a Phase 1/2 Trial

David Belada, MD, PhD[1], Jacob Haaber Christensen, MD, PhD[2], Kristina Drott, MD, PhD[3], Sylvia Snauwaert, MD, PhD[4], Joshua Brody, MD[5], Mayur Narkhede, MD[6], Fritz Offner, MD, PhD[7], Brian Elliott, MD[8], Tracy Liu, MS[8], Mariana Cota Stirner, MD, PhD[9], Aqeel Abbas, MS[8], Lorenzo Falchi, MD[10], Michael Roost Clausen, MD, PhD[11]

- The targeted mechanism of action of epcoritamab differs considerably from the broader, cell-cycle–dependent activity of the components of CHOP, and T cells pretreated with individual CHOP components were capable of mediating epcoritamab-induced cytotoxicity[1]
- Preclinical data has indicated that epcoritamab does not interfere with the activity of rituximab,[2] supporting the exploration of adding epcoritamab to R-CHOP
- The EPCORE NHL-2 phase 1/2 trial (NCT04663347) is evaluating epcoritamab in combination with multiple standard-of-care therapies in patients with B-cell NHL
  - Arm 1 is exploring epco + R-CHOP in newly diagnosed patients with high risk (IPI 3-5) DLBCL, a population that represents a high unmet medical need

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1. Engelberts PJ, et al. *EBioMedicine.* 2020;52:102625. 2. Chiu CW, et al. AACR 2021. Abstract 1574.

Study Design: EPCORE NHL-2 Arm 1

Arm 1 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + standard R-CHOP for 6 cycles of 21 days, followed by epcoritamab monotherapy for a total of 1 year, in adults with previously untreated DLBCL with high-risk features[a]

Key inclusion criteria

- Newly diagnosed CD20+ DLBCL[b]
  - DLBCL, NOS
  - "Double-" or "triple-hit" DLBCL[c]
  - FL grade 3B
- IPI score ≥3
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Dose escalation

Dose level 1:
Epcoritamab 24 mg
QW C1–4,
Q3W C5–6,
Q4W C7+
+ R-CHOP
C1–6

n=4 enrolled

Dose level 2:
Epcoritamab 48 mg
QW C1–4,
Q3W C5–6,
Q4W C7+
+ R-CHOP
C1–6

n=7 enrolled

Primary objectives: DLT/Safety and tolerability
Key secondary objective: Antitumor activity[d]

Expansion

Epcoritamab 48 mg
QW C1–4, Q3W C5–6, Q4W C7+
+ R-CHOP
C1–6

n=13 enrolled
n≈20 planned

Primary objective: Antitumor activity[d]

Data cutoff: September 16, 2021

C, cycle; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; HGBCL, high-grade B-cell lymphoma; IV, intravenous; LYRIC, Lymphoma Response to Immunomodulatory Therapy Criteria; NOS, not otherwise specified.
[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[1] to mitigate CRS. R-CHOP regimen in C1–6, 21 d each: rituximab 375 mg/m^2 IV Q3W; cyclophosphamide 750 mg/m^2 IV Q3W; doxorubicin 50 mg/m^2 IV Q3W; vincristine 1.4 mg/m^2 IV (with a recommended maximum of 2 mg) Q3W; and prednisone 100 mg/d IV or orally on days 1–5. Subsequent cycles of epcoritamab were 28 d. [b]De novo or histologically transformed from FL or nodal marginal zone lymphoma; based on World Health Organization 2016 classification.[2] [c]Classified as HGBCL, with *MYC* and *BCL2* and/or *BCL6* translocations. [d]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. Lugano criteria and LYRIC were used to assess response.
AEs were graded by CTCAE, v5.0; CRS was evaluated by Lee et al[9] criteria. ClinicalTrials.gov Identifier: NCT04663347.
1. Hutchings M, et al. *Lancet*. 2021;398:1157-69. **2.** Swerdlow SH, et al. *Blood*. 2016;127:2375-90.

Baseline Demographics and Characteristics

Characteristic	Total N=24
Median age, y (range)	65 (30–82)
Male, n (%)	13 (54)
ECOG PS, n (%)	
0	6 (25)
1	14 (58)
2	4 (17)
Stage, n (%)	
III	6 (25)
IV	18 (75)
DLBCL subtype, n (%)	
De novo	19 (79)
Transformed	3 (13)
Unknown	2 (8)
Molecular classification, n (%)	
GCB	15 (63)
Non-GCB	7 (29)
Unknown	2 (8)
Median time from diagnosis to first dose, wk (range)	3.6 (1.3–8.6)

Data cutoff: September 16, 2021.

Data for all patients across both full dose levels assessed; 24 mg and 48 mg

ECOG PS, Eastern Cooperative Oncology Group performance status; GCB, germinal center B cell.

Follow-up

Median (range) follow-up was 1.3 (0.2–7.9) mo

Treatment Exposure

Median (range) number of cycles initiated was 9.5 (6–11) for 24 mg, 2 (1–7) for 48 mg, and 2 (1–11) overall

Safety Data - Treatment-Emergent Adverse

TEAE ≥15%, n (%)	Total N=24			
	Grade 1–2	Grade 3	Grade 4	Any grade
Anemia	7 (29)	2 (8)	0	9 (38)
CRS	8 (33)	1 (4)	0	9 (38)
All infections[a]	6 (25)	3 (13)	0	9 (38)
Neutropenia[b]	1 (4)	1 (4)	6 (25)	8 (33)
Constipation	7 (29)	0	0	7 (29)
Dyspnea	5 (21)	0	0	5 (21)
Injection-site reaction[c]	5 (21)	0	0	5 (21)
Nausea	5 (21)	0	0	5 (21)
Fatigue	4 (17)	0	0	4 (17)
Peripheral sensory neuropathy	4 (17)	0	0	4 (17)
Pyrexia[d]	3 (13)	0	0	4 (17)

Data cutoff: September 16, 2021. [a]Includes all events under the System Organ Class of infections and infestations; oral candidiasis (n=3 [13%]), urinary tract infection (n=3 [13%]), and bacteriuria, bronchopulmonary aspergillosis, COVID-19, *Escherichia*-related urinary tract infection, and rhinovirus infection (each n=1 [4%]). [b]Combined term includes neutropenia and neutrophil count decreased; 2 patients (8%) had febrile neutropenia (grade 3). [c]Combined term includes injection-site pain, reaction, pruritis, and swelling. [d]Confirmed that the investigator did not consider the pyrexia to be related to CRS. Pyrexia was not graded for 1 patient.

CRS Graded by Lee et al1 Criteria	Total N=24
CRS, n (%)	9 (38)
Grade 1	4 (17)
Grade 2	4 (17)
Grade 3	1 (4)
CRS onset at study day ≥15, n/n (%)[a]	7/9 (78)
Median time to resolution, d (range)[b]	2 (1–5)

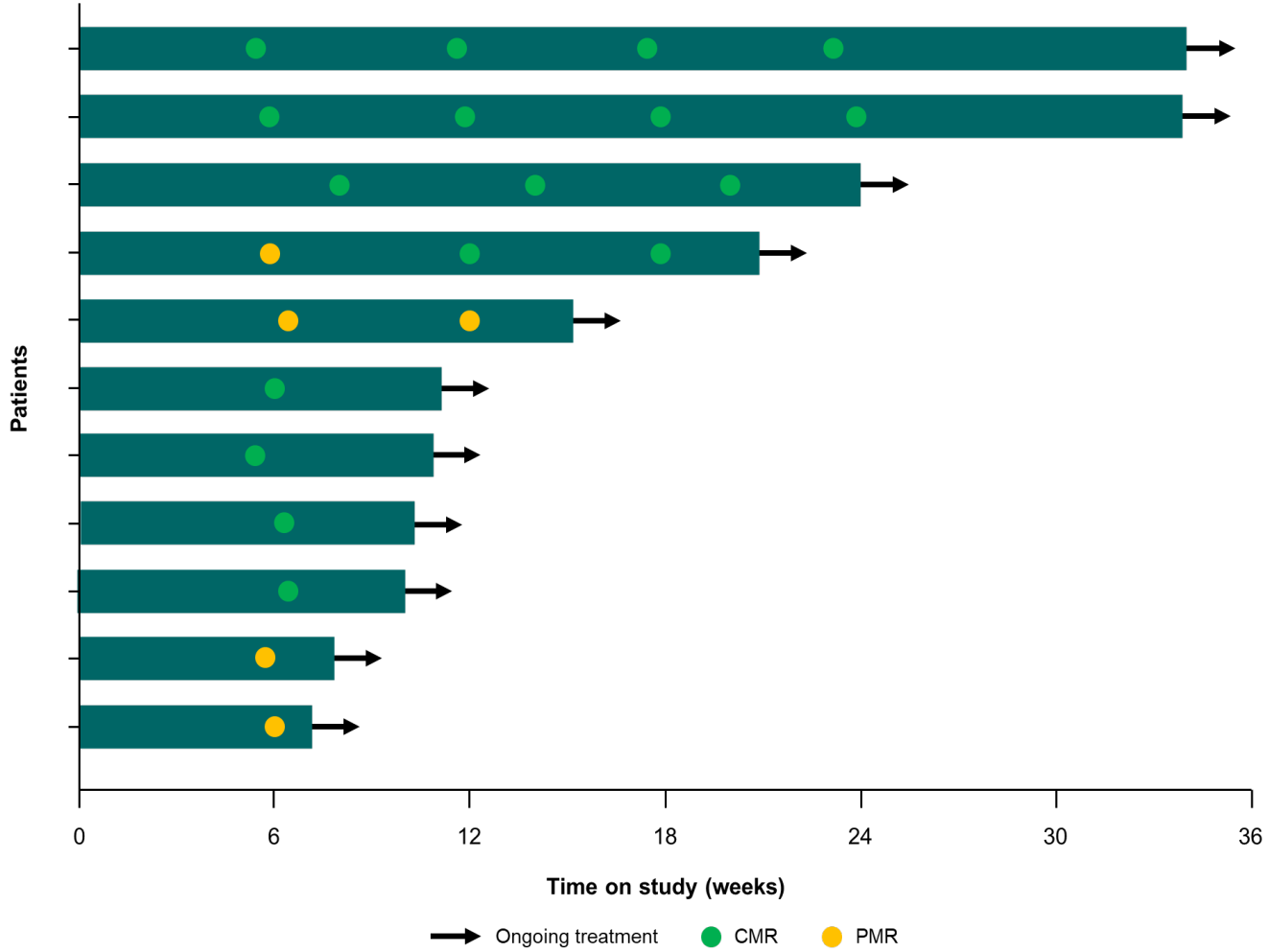
Data cutoff: September 16, 2021. [a]Percent based on number of patients with CRS. The first full dose was administered on C1D15. [b]Median is Kaplan–Meier estimate based on longest CRS duration in patients with CRS; range is defined by shortest and longest CRS duration.

- No DLTs were reported for epcoritamab
- One patient (4%) had tumor lysis syndrome
- No immune effector cell–associated neurotoxicity syndrome (ICANS) was reported
- No fatal TEAEs were reported

- All CRS events resolved within 1–5 days
- Majority of CRS events occurred in Cycle 1
- No patients were discontinued from treatment due to CRS

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; TEAE, treatment-emergent adverse event.

Efficacy Data



Response, n (%)[a]	Total n=11
Overall response	11 (100)
CMR	8 (73)
PMR	3 (27)
Stable disease	0
Progressive disease	0

Data cutoff: September 16, 2021. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose.

- All responders (n=11) remain on study treatment with ongoing responses as of the data cutoff date

CMR, complete metabolic response; PMR, partial metabolic response.

Conclusions

- Preliminary data with subcutaneously administered epcoritamab in combination with R-CHOP in patients with previously untreated high-risk DLBCL demonstrated:
  - **No DLTs** for epcoritamab
  - **Manageable safety profile** with no unexpected safety findings
  - No ICANS events; 1 tumor lysis syndrome event
- Encouraging responses were seen in all patients **(ORR: 100%)**
  - CMR (73%); PMR (27%)
- These data support further exploration of epcoritamab + R-CHOP in this population

CMR, complete metabolic response; DLTs, dose-limiting toxicities; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, overall response rate; PMR, partial metabolic response.

EPCORE NHL-2 Arm 2

Subcutaneous Epcoritamab in Combination with R^2 (Rituximab and Lenalidomide) in Patients with Relapsed or Refractory Follicular Lymphoma: Preliminary Results from a Phase 1/2 Trial

Kim M Linton, MBChB, PhD[1], Björn Wahlin, MD, PhD[2], Sirpa Leppä, MD[3], Franck Morschhauser, MD, PhD[4], Brian Elliott, MD[5], Tracy Liu, MS[5], Mariana Cota Stirner, MD, PhD[6], Aqeel Abbas, MS[5], Lorenzo Falchi, MD[7]

- R^2 has immunomodulatory properties that may potentiate the activity of epcoritamab, suggesting that combining R^2 with epcoritamab may be beneficial
  - In preclinical studies, potent inhibition of tumor growth was observed in the presence of an Fc-silenced rituximab analogue at the tested concentrations[1]
  - Preclinical data suggest that lenalidomide may enhance epcoritamab-induced T-cell–mediated killing[2]
- The EPCORE NHL-2 phase 1/2 trial (NCT04663347) is evaluating epcoritamab in combination with different standard-of-care therapies in patients with B-cell NHL
  - Arm 2 is exploring epcoritamab + R2 in patients with R/R FL

1. Engelberts PJ, et al. *EBioMedicine*. 2020;52:102625. 2. Chiu CW, et al. AACR 2021. Abstract 1574

Study Design: EPCORE NHL-2 Arm 2

Arm 2 of EPCORE NHL-2, a phase 1b/2, open-label, multicenter trial, is evaluating the safety and antitumor activity of SC epcoritamab + standard R² for 12 cycles of 28 days, followed by epcoritamab monotherapy for a total of 2 years, in adults with R/R FL[a]

Key inclusion criteria

- R/R CD20⁺ FL
  - Grade 1, 2, or 3A
  - Stage II–IV
- Need for treatment based on symptoms or disease burden, as determined by GELF criteria[1]
- ECOG PS 0–2
- Measurable disease by CT or MRI
- Adequate organ function

Dose escalation → **Expansion**

Dose escalation		Expansion	
Dose level 1: Epcoritamab 24 mg QW C1–3, Q2W C4–9, Q4W C10+ **+ R²** C1–12	**Dose level 2: Epcoritamab 48 mg** QW C1–3, Q2W C4–9, Q4W C10+ **+ R²** C1–12	**Cohort 2a: Epcoritamab 48 mg** QW C1–3, Q2W C4–9, Q4W C10+ **+ R²** C1–12	**Cohort 2b: Epcoritamab 48 mg** QW C1–2, Q4W C3–26 **+ R²** C1–12
n=3 enrolled	n=3 enrolled	n=23 enrolled	n≈80 planned
Primary objectives: DLT/Safety and tolerability **Key secondary objective:** Antitumor activity[b]		**Primary objective:** Antitumor activity[b]	

Data cutoff: September 16, 2021

C, cycle; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; GELF, Groupe d'Etude des Lymphomes Folliculaires; IV, intravenous; LYRIC, Lymphoma Response to Immunomodulatory Therapy Criteria.
[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[2] to mitigate CRS. Epcoritamab was administered in 28-d cycles as shown. Rituximab regimen: 375 mg/m² IV QW in C1 and Q4W in C2–5; lenalidomide regimen: 20 mg QD (oral administration) for 21 d in C1–12. [b]Tumor response was evaluated by PET-CT obtained at 6, 12, 18, 24, 36, and 48 wk, and every 24 wk thereafter, until disease progression. Lugano criteria and LYRIC were used to assess response. AEs were graded by CTCAE, v5.0; CRS was evaluated by Lee et al[3] criteria. ClinicalTrials.gov Identifier: NCT04663347.

1. Brice P, et al. *J Clin Oncol*. 1997;15:1110-7. 2. Hutchings M, et al. *Lancet*. 2021;398:1157-69. 3. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-38

Baseline Demographics and Characteristics

Characteristic	Total N=29
Median age, y (range)	67 (42–80)
Female, n (%)	17 (59)
ECOG PS, n (%)	
0	22 (76)
1	7 (24)
Stage, n (%)	
II	3 (10)
III	6 (21)
IV	20 (69)
Histologic grade, n (%)	
1	4 (14)
2	18 (62)
3A	5 (17)
Unknown[a]	2 (7)
Median time from diagnosis to first dose, mo (range)	92 (6–281)
FLIPI score, n (%)	
0–2	8 (28)
3–5	18 (62)
Unknown[b]	3 (10)

Data cutoff: September 16, 2021. [a]Unknown histologic grade was confirmed low grade, not grade 3B. [b]FLIPI scores were calculated based on baseline data. Unknown FLIPI scores were due to missing baseline laboratory values.
- Median (range) follow-up was 2.8 (0.2–8.5) mo

Prior Therapies and Timing

Characteristic	Total N=29
Median number of prior lines of therapy, n (range)	1 (1–5)
Prior lines of therapy, n (%)	
1	19 (66)
2	4 (14)
≥3	6 (21)
Prior lines of anti-CD20–containing therapy, n (%)	
1	23 (79)
2	3 (10)
≥3	3 (10)
Primary refractory disease, n (%)	5 (17)
Refractory to last line of therapy, n (%)	5 (17)
Progressed within 24 mo of initial therapy, n (%)	11 (38)
Progressed within 24 mo of first immunochemotherapy, n (%)	8 (28)
Median time from end of last line of therapy to first dose, mo (range)	30 (1–182)
Median time from end of last anti-CD20–containing therapy, mo (range)	35 (1–182)
Prior radiotherapy, n (%)	5 (17)
Prior stem cell transplant, n (%)	5 (17)

Data cutoff: September 16, 2021.

ECOG PS, Eastern Cooperative Oncology Group performance status; FLIPI, Follicular Lymphoma International Prognostic Index. Data for all patients across both full dose levels assessed; 24 mg and 48 mg

Safety Data

TEAE ≥15%, n (%)	Total N=29			
	Grade 1–2	Grade 3	Grade 4	Any grade
CRS	12 (41)	2 (7)	0	14 (48)
Injection-site reaction[a]	12 (41)	0	0	12 (41)
All infections[b]	9 (31)	2 (7)	0	11 (38)
Constipation	8 (28)	0	0	8 (28)
Cough	8 (28)	0	0	8 (28)
Fatigue	6 (21)	1 (3)	0	7 (24)
Nausea	7 (24)	0	0	7 (24)
Muscle spasms	6 (21)	0	0	6 (21)
Neutropenia[c]	1 (3)	4 (14)	1 (3)	6 (21)
Tremor	5 (17)	0	0	5 (17)

Data cutoff: September 16, 2021. [a]Combined term includes injection-site reaction, erythema, pain, and rash. [b]Includes all events under the System Organ Class of infections and infestations; cellulitis, conjunctivitis, device-related infection, infection, mucosal infection, nasopharyngitis, neuroborreliosis, oral fungal infection, oral herpes, pneumonia, rhinovirus infection, sinusitis, staphylococcal infection, tinea pedis, and urinary tract infection (each n=1 [3%]). Three grade 3 infections were observed in a total of 2 patients overall: cellulitis, neuroborreliosis, and pneumonia. [c]Combined term includes neutropenia and neutrophil count decreased; 1 patient (3%) had febrile neutropenia.

CRS Graded by Lee et al1 Criteria	Total N=29
CRS, n (%)	14 (48)
Grade 1	8 (28)
Grade 2	4 (14)
Grade 3	2 (7)
CRS onset at study day ≥15, n/n (%)[a]	9/14 (64)

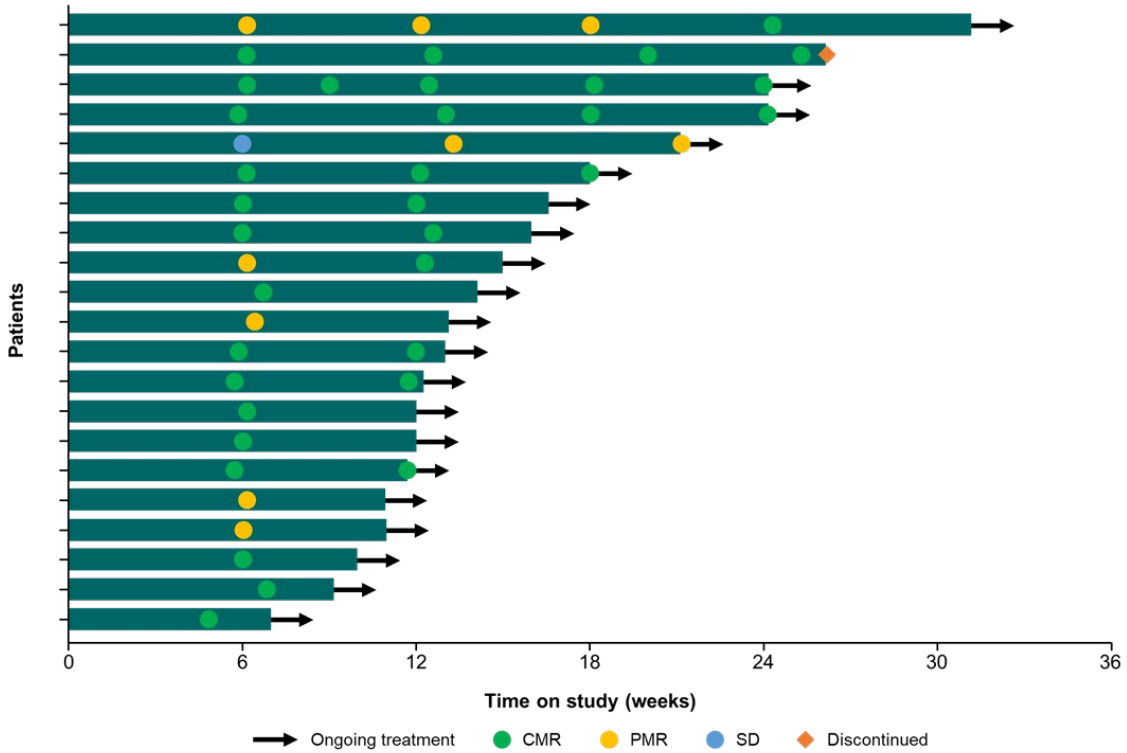
Data cutoff: September 16, 2021. [a]Percent based on number of patients with CRS. The first full dose was administered on C1D15.

- No DLTs were reported for epcoritamab
- No ICANS or clinical tumor lysis syndrome events were reported
- No fatal TEAEs were observed

- Majority of CRS events occurred in Cycle 1
- All CRS events resolved with standard management

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event.

Efficacy Data



Data cutoff: September 16, 2021. One patient discontinued treatment due to mania; 7 additional patients were receiving treatment but had not yet received their first scan (6 had not reached 6 wk of treatment). Patient with stable disease at first scan had a 6-wk delay between first and second epcoritamab doses due to pneumonia in the setting of underlying severe chronic obstructive pulmonary disease.

- 95% of responders (20/21) remained in response and continued to receive study treatment as of the September 16, 2021, data cutoff date
- As of an updated November 3, 2021, data cutoff date, ORR was 100% (24/24) and CMR rate was 92% (22/24); responses appear durable, although with short follow-up

Response, n (%)[a]	Total n=21
Overall response	21 (100)
CMR	17 (81)
PMR	4 (19)
Stable disease	0
Progressive disease	0

Data cutoff: September 16, 2021. [a]Based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and ≥1 postbaseline response evaluation and patients who died within 60 d of first dose.

CMR, complete metabolic response; PMR, partial metabolic response; SD, stable disease.

Conclusions

- Preliminary data for subcutaneously administered epcoritamab in combination with R^2 in patients with R/R FL demonstrated:
  - **No DLTs** identified for epcoritamab
  - **Manageable safety profile**, with no new safety findings
  - No ICANS or tumor lysis syndrome events
- **Response in 100% of patients**, with nearly all achieving early CMR and no relapses observed
- No cases of progressive disease
- These data support further studies of epcoritamab + R^2 in this population; expansion cohort 2b will enroll up to approximately 80 additional patients

CMR, complete metabolic response; DLT, dose-limiting toxicity; ICANS, immune effector cell-associated neurotoxicity syndrome.

EPCORE CLL-1

Subcutaneous Epcoritamab in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia: Preliminary Results from the EPCORE CLL-1 Trial

Arnon P Kater, MD, PhD[1], Jacob Haaber Christensen, MD, PhD[2], Hans Herluf Bentzen, MD[3], Carsten Utoft Niemann, MD, PhD[4], Martin Hutchings, MD, PhD[4], Jenny Chen, MD, PhD[5], Marcia Rios, MBA[5], Tammy Palenski, PhD[6], Tommy Li, PhD[5], Anthony Mato, MD, MSCE[7]

- In the first-in-human trial in R/R B-cell non-Hodgkin lymphoma, epcoritamab showed manageable safety and encouraging single-agent antitumor activity
- Here we report first results from the dose-escalation part of the EPCORE CLL-1 phase 1b/2 trial (NCT04623541) evaluating epcoritamab in patients with heavily pretreated R/R CLL

Study Design: EPCORE CLL-1

Open-label, multicenter, phase 1b/2 trial of single-agent epcoritamab in adults with R/R CLL

Key inclusion criteria

- Diagnosis of CLL with evidence of CD20^{+}
- Previously treated with ≥2 prior lines of systemic therapy, including treatment with (or intolerance to) a BTK inhibitor
- Measurable disease with ≥5×10^{9}/L B lymphocytes *or* measurable lymphadenopathy, *and/or* organomegaly
- ECOG PS 0–2
- Acceptable laboratory parameters

Epcoritamab[a] in 4-wk (28-d) cycles

QW C1–3, Q2W C4–9, Q4W C10+ until progression or unacceptable toxicity

Phase 1b: Dose escalation
- 2 full-dose levels
  24 mg → 48 mg

Phase 2: Expansion
- 2 arms at RP2D (48 mg)
  – Cohort 1: R/R CLL

Primary objectives:
DLT/Safety and tolerability

Key secondary objective:
Antitumor activity[b]

Primary objective:
Antitumor activity[b]

Data cutoff: October 1, 2021

C, cycle; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; RP2D, recommended phase 2 dose.
[a]Patients received SC epcoritamab with step-up dosing (ie, priming and intermediate doses before first full dose) and corticosteroid prophylaxis as previously described[1] to mitigate CRS.
[b]Tumor response was evaluated by CT/MRI every 8 wk up to wk 24, and then every 24 wk until PD, start of new anticancer therapy, consent withdrawal, or death. ClinicalTrials.gov identifier: NCT04623541.
1. Hutchings M, et al. *Lancet*. 2021;398:1157-69.

Demographics and Disease Characteristics at Baseline

Characteristic		Total N=11
Median age (range), y		63 (50–77)
Male, n (%)		10 (91)
Median time from initial diagnosis (range), mo		157 (57–234)
ECOG PS, n (%)	0	6 (55)
	1	5 (45)
CLL stage,[a] (%)	Rai intermediate risk	2 (18)
	Rai high risk	3 (27)
	Binet A	1 (9)
	Binet B	1 (9)
	Binet C	4 (36)
Median lines of prior therapy (range)		6 (2–9)

Characteristic		Total N=11
Prior treatment, n (%)	BTK inhibitor	11 (100)
	Ibrutinib	9 (82)
	Venetoclax	7 (64)
	CAR-T therapy	2 (18)
Mutation status, n (%)	*TP53*	7 (64)[b]
	IGHV	2 (18)[c]
	SF3B1	2 (18)[d]
	NOTCH1	2 (18)[e]
	BIRC3	1 (9)[f]
Chromosomal alteration, n (%)	del(11q)	5 (45)[g]
	del(13q)	8 (73)
	del(17p)	7 (64)[h]
	Trisomy 12	3 (27)[i]

Data cutoff: October 1, 2021. [a]CLL stage assessed at screening. Method of staging varied by geographic region. [b]*TP53* data were missing for 1 patient. [c]*IGHV* data were missing for 3 patients. [d]*SF3B1* data were missing for 8 patients. [e]*NOTCH1* data were missing for 8 patients. [f]*BIRC3* data were missing for 9 patients. [g]del(11q) data were missing for 1 patient. [h]del(17p) data were missing for 1 patient. [i]Trisomy 12 data were missing for 2 patients.

- Patients were heavily pretreated (median of 6 prior lines of therapy), and the majority had poor-risk features of del(17p) and/or *TP53* mutations

ECOG PS, Eastern Cooperative Oncology Group performance status.

Treatment-Emergent Adverse Events

TEAE ≥15%, n (%)	Total N=11			
	Grade 1–2	Grade 3	Grade 4	Any grade
CRS	8 (73)	0	0	8 (73)
Fatigue	4 (36)	0	0	4 (36)
Injection-site reaction	4 (36)	0	0	4 (36)
Nausea	2 (18)	1 (9)	0	3 (27)
Abdominal pain	1 (9)	1 (9)	0	2 (18)
ALT increased	1 (9)	1 (9)	0	2 (18)
Constipation	2 (18)	0	0	2 (18)
Cough	2 (18)	0	0	2 (18)
Diarrhea	2 (18)	0	0	2 (18)
Dyspnea	2 (18)	0	0	2 (18)
Erythema	2 (18)	0	0	2 (18)
Hypotension	2 (18)	0	0	2 (18)
Hyponatremia	2 (18)	0	0	2 (18)
Hypophosphatemia	2 (18)	0	0	2 (18)
Peripheral edema	2 (18)	0	0	2 (18)
Pyrexia	2 (18)	0	0	2 (18)
Hematologic TEAEs				
Thrombocytopenia	0	1 (9)	4 (36)	5 (45)
Anemia	0	3 (27)	0	3 (27)
Neutropenia	0	1 (9)	2 (18)	3 (27)

Data cutoff: October 1, 2021.

	Total N=11
CRS,[a] n (%)	8 (73)
Grade 1	2 (18)
Grade 2	6 (55)
CRS leading to dose delay	3 (27)
Median time to onset, d (range)	9 (2–23)

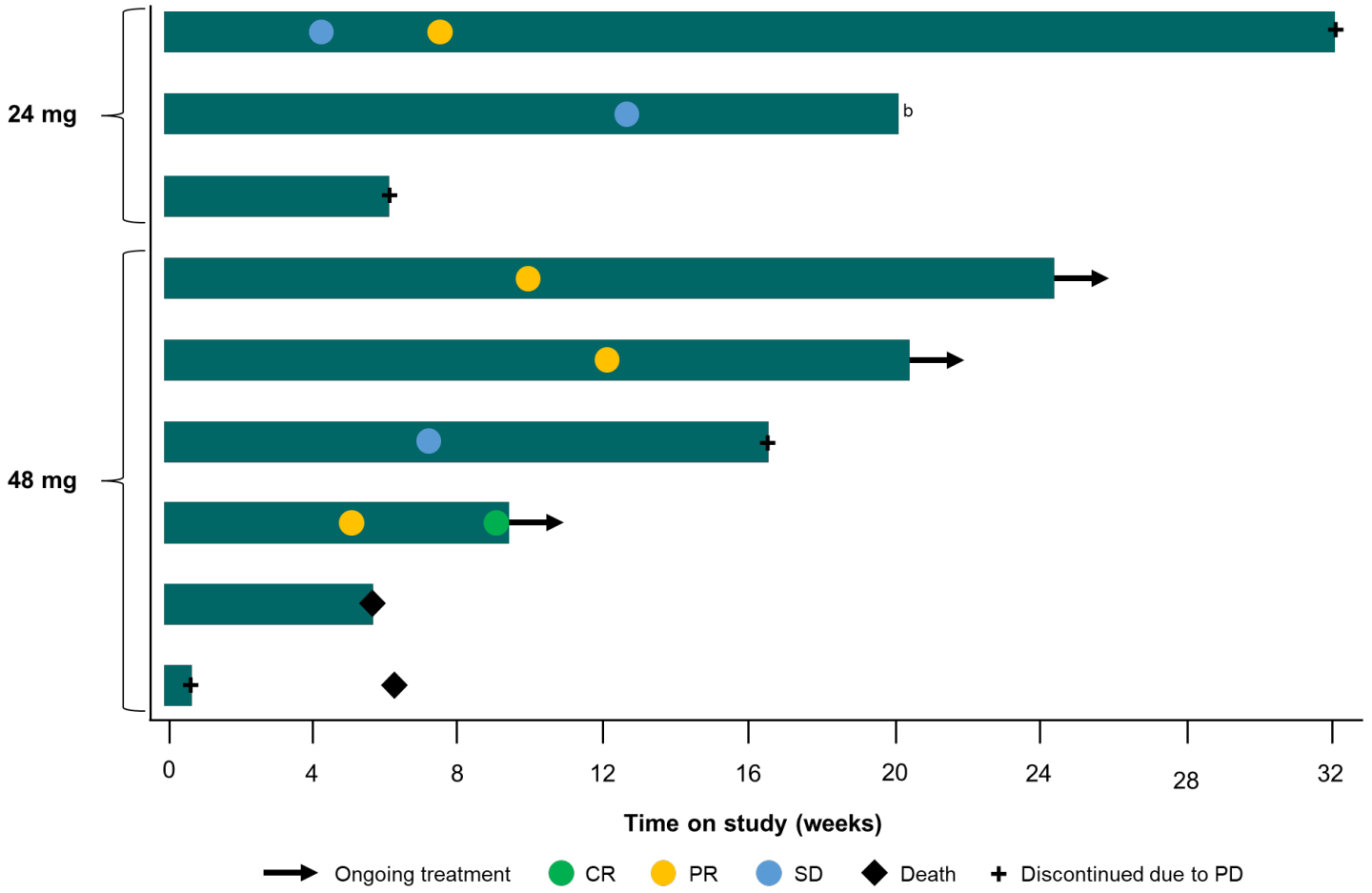
Data cutoff: October 1, 2021. [a]CRS graded by Lee et al[1] criteria.

- No DLTs occurred at 24 or 48 mg
- The most common TEAEs were CRS (73%), thrombocytopenia (45%), fatigue (36%), and injection-site reaction (36%)
- CRS events occurred early in treatment and resolved
- No patient discontinued epcoritamab due to CRS
- No cases of ICANS or tumor lysis syndrome were observed

Data for all patients across both full dose levels assessed; 24 mg and 48 mg

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; TEAE, treatment-emergent adverse event.

Response-Evaluable Population[a] (n=9)



- Responses were observed in 4 patients, including 1 CR and 3 PRs
- Responders had high-risk disease; 3 of 4 responders had *TP53* aberrations

Data cutoff: October 1, 2021. [a]The response-evaluable population includes patients who had evaluable disease at baseline and ≥1 postbaseline response evaluation or died within 60 d of first dose. [b]Patient discontinued due to physician decision.

Conclusions

- These first-reported clinical data for epcoritamab in patients with R/R CLL showed:
  - **No DLTs** at doses up to 48 mg
  - **Manageable safety profile** and no unexpected safety findings
  - CRS events occurred early and resolved
  - No ICANS or tumor lysis syndrome events
- Preliminary efficacy findings show responses in this heavily pretreated population with high-risk disease, including 1 CR and 3 PRs
- Further clinical evaluation in CLL and Richter's syndrome is ongoing

DLT, dose-limiting toxicity; ICANS, Immune effector cell-associated neurotoxicity syndrome.

Data in context

- To summarize, the emerging epcoritamab data as very encouraging for patients
- Data continues to underline the great potential for epco based on the convenience, combinability, efficacy and manageable safety
- The encouraging activity in the combination arms (EPCORE NHL-2 Arms 1 & 2) warrants further clinical investigation in phase 3 studies

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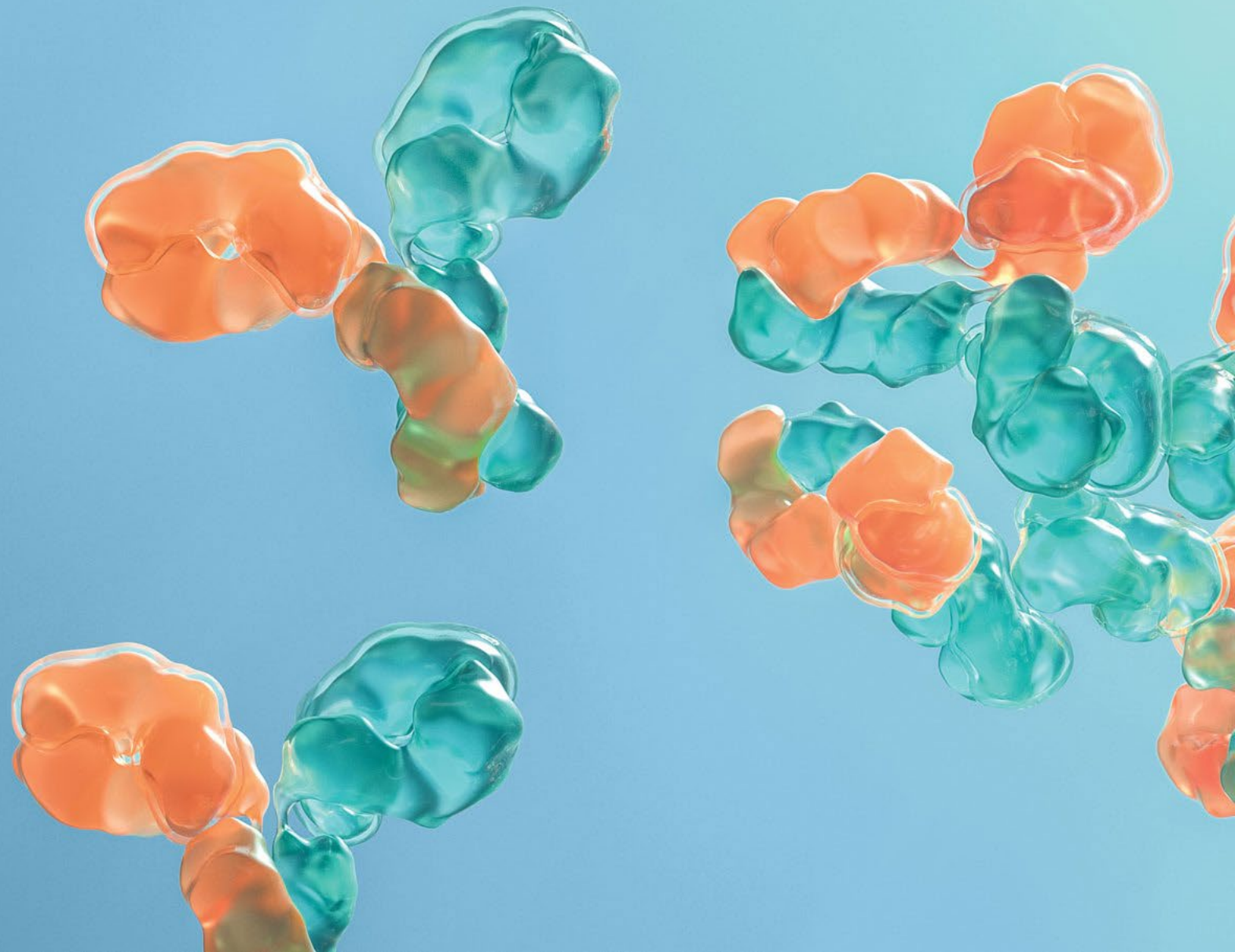
Q&A



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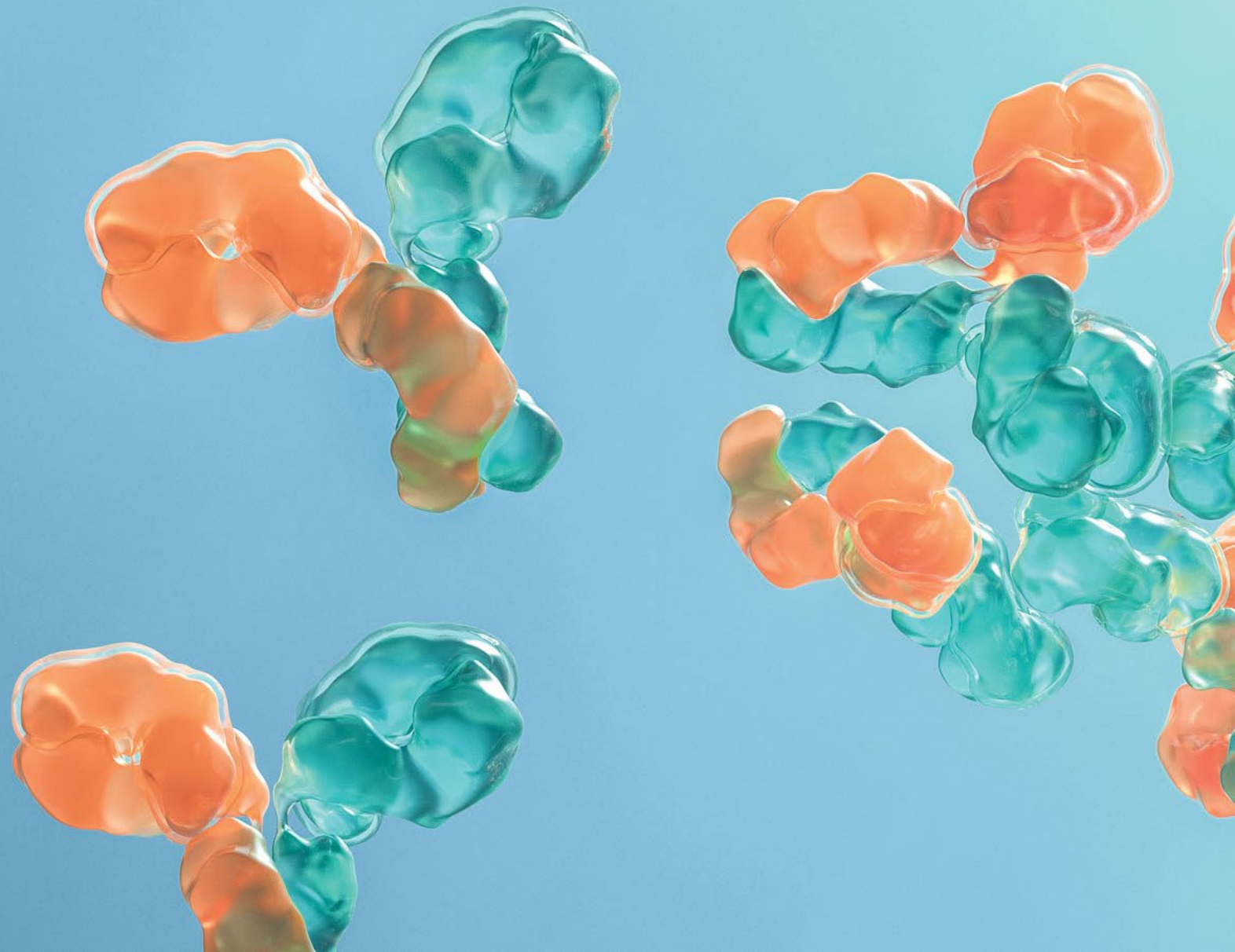
2022 & Beyond: Positioned for Continued Success

Dr. Jan van de Winkel
President & CEO



Key 2022 Priorities
Advancing Differentiated Products Towards the Market

Priority	✓	Targeted Milestones
Broad and rapid development of late-stage clinical pipeline and further build U.S. country organization		➢ Epcoritamab • Expand clinical development program with multiple Phase 3 trials initiated and submission of first BLA (subject to supportive FDA feedback) ➢ TIVDAK • Establish TIVDAK as a clear choice for 2L+ r/m Cervical Cancer patients • Broaden clinical development program including Phase 2 evaluation of combination therapy in earlier line treatment for cervical cancer and other solid tumors
Growth and development of differentiated early-stage product candidates		➢ DuoBody-PD-L1x4-1BB & DuoBody-CD40x4-1BB • Data from clinical expansion cohorts to progress to next steps ➢ Expand and advance proprietary clinical product portfolio
Further scale organization aligned with growing product portfolio and brand needs		➢ Further scale organization aligned with differentiated antibody product portfolio growth and future launches ➢ Use solid financial base to grow and broaden antibody product and technology portfolio

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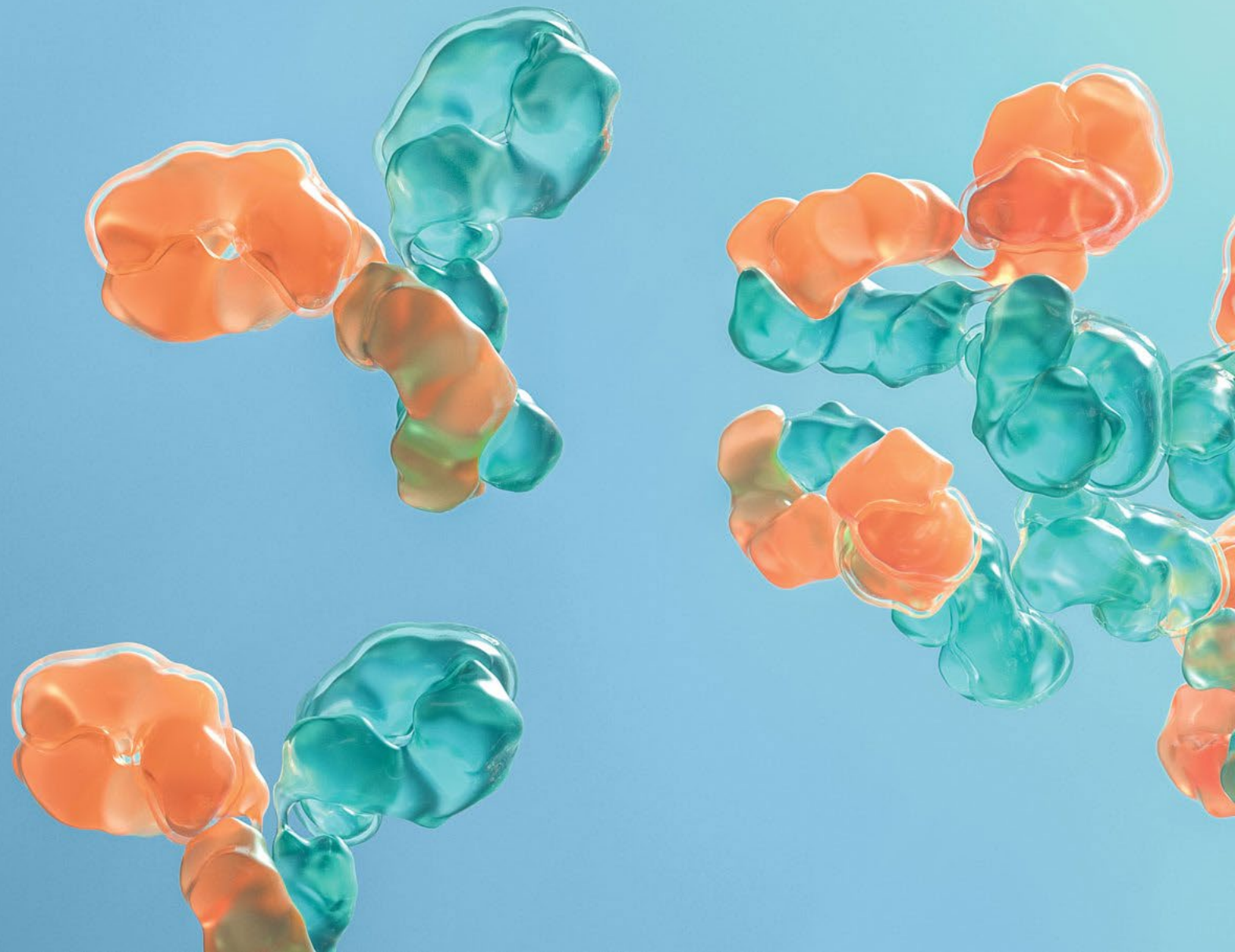
Q&A



Happy Holidays

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