

REGENERON
SCIENCE TO MEDICINE®

**ONCOLOGY
INVESTOR EVENT
ASH 2020**

DECEMBER 2020

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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 (collectively, “Regeneron's Products”), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and Regeneron's product candidates and research and clinical programs now underway or planned, including without limitation Libtayo® (cemiplimab), Regeneron's and its collaborators' other oncology programs (including odronextamab (REGN1979), REGN5458, REGN4018, REGN5678, REGN5668, REGN7075, REGN5093, and REGN6569), Regeneron's and its collaborators' other hematology programs (including pozelimab (REGN3918) and REGN7257), Regeneron's and its collaborators' earlier-stage programs, and the use of human genetics in Regeneron's research programs; safety issues resulting from the administration of Regeneron's Products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates and new indications for Regeneron's Products, including without limitation Libtayo, Regeneron's and its collaborators' other oncology programs (including odronextamab (REGN1979), REGN5458, REGN4018, REGN5678, REGN5668, REGN7075, REGN5093, and REGN6569), and Regeneron's and its collaborators' other hematology programs (including pozelimab (REGN3918) and REGN7257); the possible success of Regeneron's oncology strategy and 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 may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; ongoing regulatory obligations and oversight impacting Regeneron's Products (such as Libtayo), research and clinical programs, and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's Products and product candidates; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's Products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's Products and product candidates; 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; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and 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, including, without limitation, capital expenditures, and changes to the assumptions underlying those projections or guidance; risks associated with intellectual property of other parties and pending or future litigation relating thereto, 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; and the potential for any license or collaboration 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. 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 fiscal year ended December 31, 2019 and Form 10-Q for the quarterly period ended September 30, 2020 in each case in the section thereof captioned “Item 1A. Risk Factors.” 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.

REGENERON'S ONCOLOGY/HEMATOLOGY LEADERSHIP TEAM



George D. Yancopoulos, MD, PhD
Co-Founder, President & Chief Scientific Officer



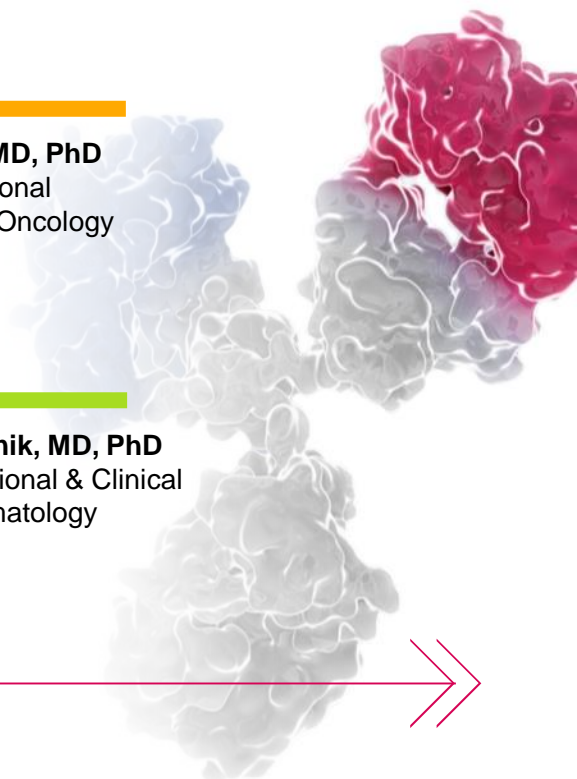
Israel Lowy, MD, PhD
SVP, Translational Sciences and Oncology



David Weinreich, MD
Head, Global Clinical Development



Andres Sirulnik, MD, PhD
SVP, Translational & Clinical Sciences Hematology



AGENDA



Introduction

George D. Yancopoulos, MD, PhD



Oncology Strategy Overview

David Weinreich, MD



Solid Tumors

Israel Lowy, MD, PhD



Hematologic Cancers ASH 2020 Updates

Andres Sirulnik, MD, PhD



Classical Hematology Program Overview

Andres Sirulnik, MD, PhD



Q&A

Panel



2020 ONCOLOGY/HEMATOLOGY ACHIEVEMENTS DESPITE COVID-19

Significant Progress & Developments Across Oncology and Hematology Pipeline

LIBTAYO® (cemiplimab)

- Priority Review in 1L NSCLC (PDUFA 2/28/21)
- Priority Review in 2L+ BCC (PDUFA 3/3/21)
- Completed enrollment in LIBTAYO + Chemo Ph3 in 1L NSCLC
- Completed enrollment in 2L Cervical cancer

CD3 Bispecifics

- Odronextamab (CD20xCD3) – Enrolling pivotal Ph2 in R/R NHL
- REGN5458 (BCMAxCD3) – Advanced to Ph2 in Multiple Myeloma
- REGN4018 (MUC16xCD3) – Ongoing dose escalation in Ovarian cancer

CD28 Costimulatory Bispecifics

- REGN5678 (PSMAxCD28) – (with LIBTAYO) Progressing through dose-escalation cohorts in mCRPC
- REGN5668 (MUC16xCD28) – (with LIBTAYO or MUC16xCD3) Entered clinic
- REGN7075 (EGFRxCD28) – (with LIBTAYO) Entered clinic

Tumor-Targeting Bispecifics / Checkpoints / Non-Oncology

- REGN5093 (METxMET) – Completed dose escalation, moving to dose expansion phase in Met-altered NSCLC
- REGN6569 (GITR) – Entered clinic
- Pozelimab (C5) + cemdisiran (C5 RNAi, Alnylam) – Entered clinic
- REGN7257 (IL2R γ) – Entered clinic for Aplastic Anemia
- NTLA-2001 (TTR gene editing) – entered clinic for ATTR (Intellia)

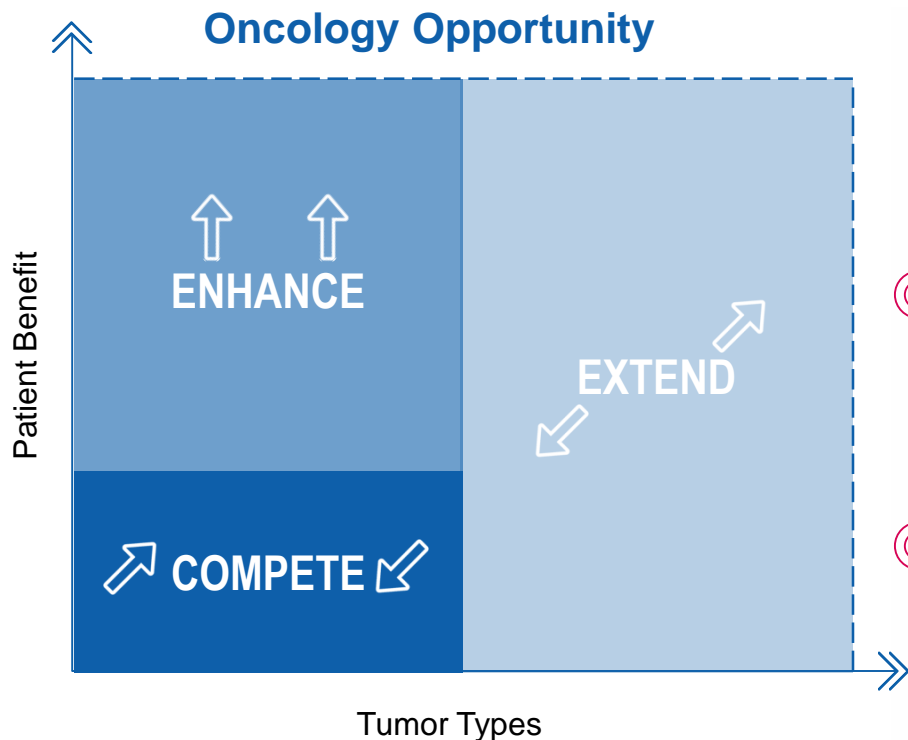


David Weinreich, MD
Head, Global Clinical Development

**Oncology Strategy
Overview**



ONCOLOGY STRATEGY: ASPIRE TO COMPETE, ENHANCE, EXTEND



COMPETE: LIBTAYO delivers potentially ‘best-in-class’ data in tumors “responsive” to PD-1 monotherapy (e.g., skin cancers & NSCLC*)

- “**Compete**” in large PD-(L)1 opportunity:
 - >\$25Bn, +25% YoY growth[^]

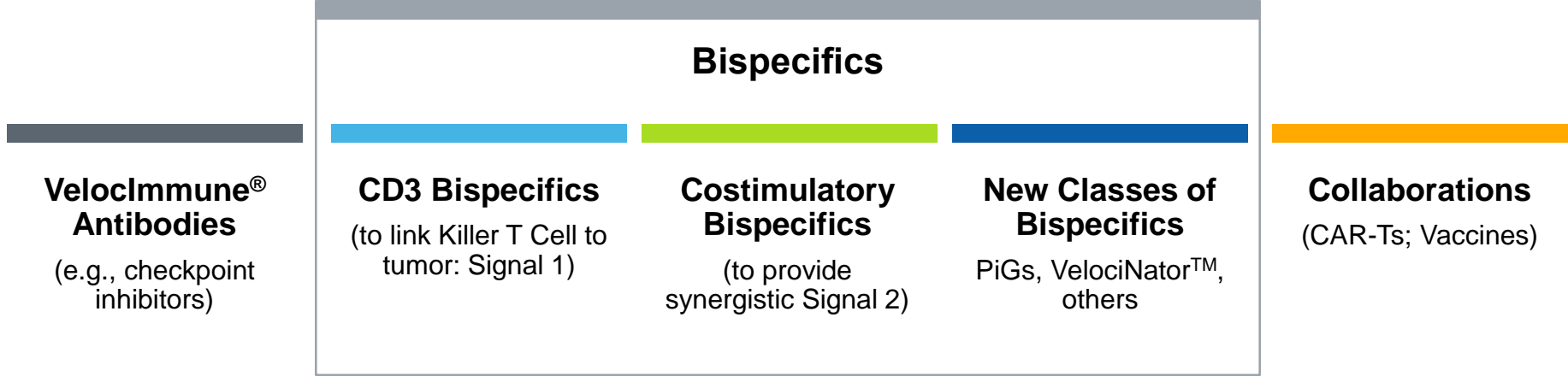
ENHANCE: Even for “PD1 responsive” tumors, more than half of patients do not respond

- “**Enhance**” responsiveness for these tumors via addition of novel therapeutics (e.g., xCD3 & xCD28 BiSpecifics)

EXTEND: Most tumor settings have limited responses to checkpoint inhibition

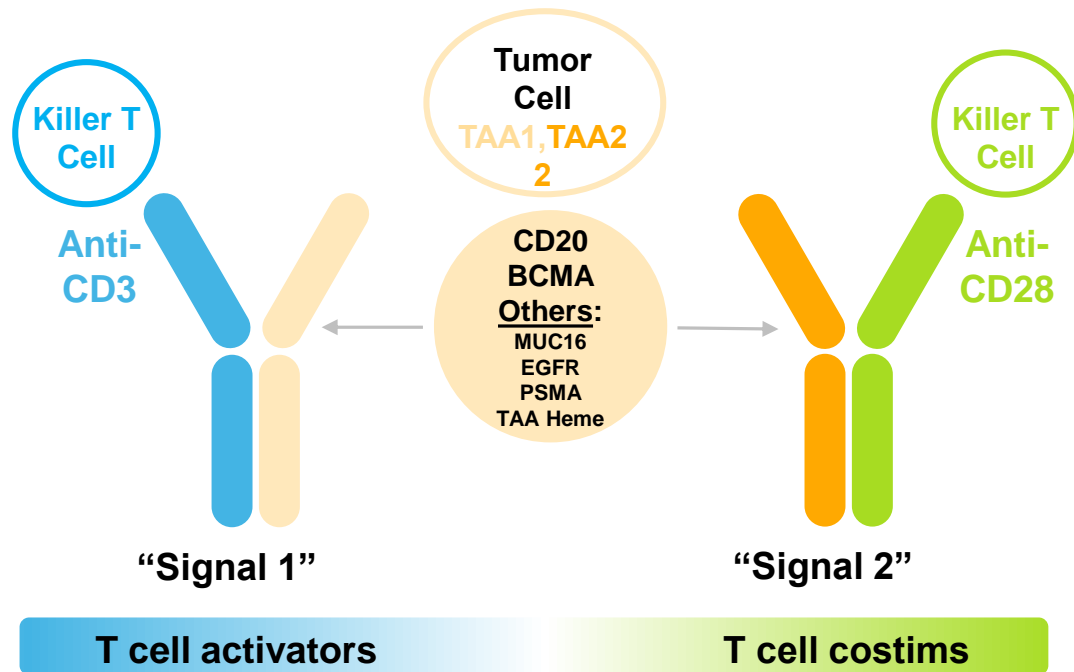
- “**Extend**” responsiveness for these tumors via addition of novel therapeutics (e.g., xCD3 & xCD28 BiSpecifics)

REGENERON ONCOLOGY TOOLKIT LEVERAGES MULTIPLE PLATFORMS TO CREATE COMBINATORIAL FLEXIBILITY



PD-1 (LIBTAYO)

REGENERON'S VELOCI-BI® APPROACH CAN CREATE, MANUFACTURE, AND DEVELOP HIGH-QUALITY BISPECIFICS OF ANY DESIRED SPECIFICITY



VELOCI-BI®

VelociGene® and VelocImmune® technologies are fundamental

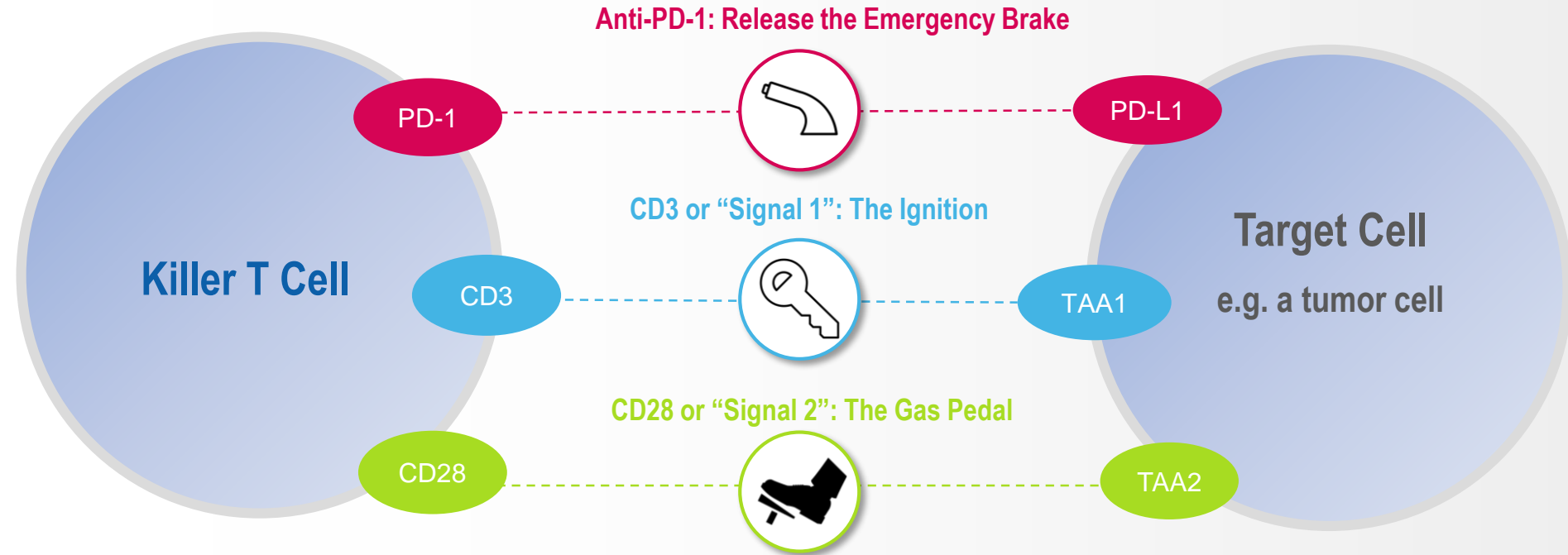
- Foundation for DUPIXENT, PRALUENT, LIBTAYO, REGN-EB3 (INMAZEB), COVID-19 Ab cocktail and other Regeneron-discovered medicines

Next-generation VelocImmune® used to create several distinct classes of bispecifics, with varying specificity and affinity

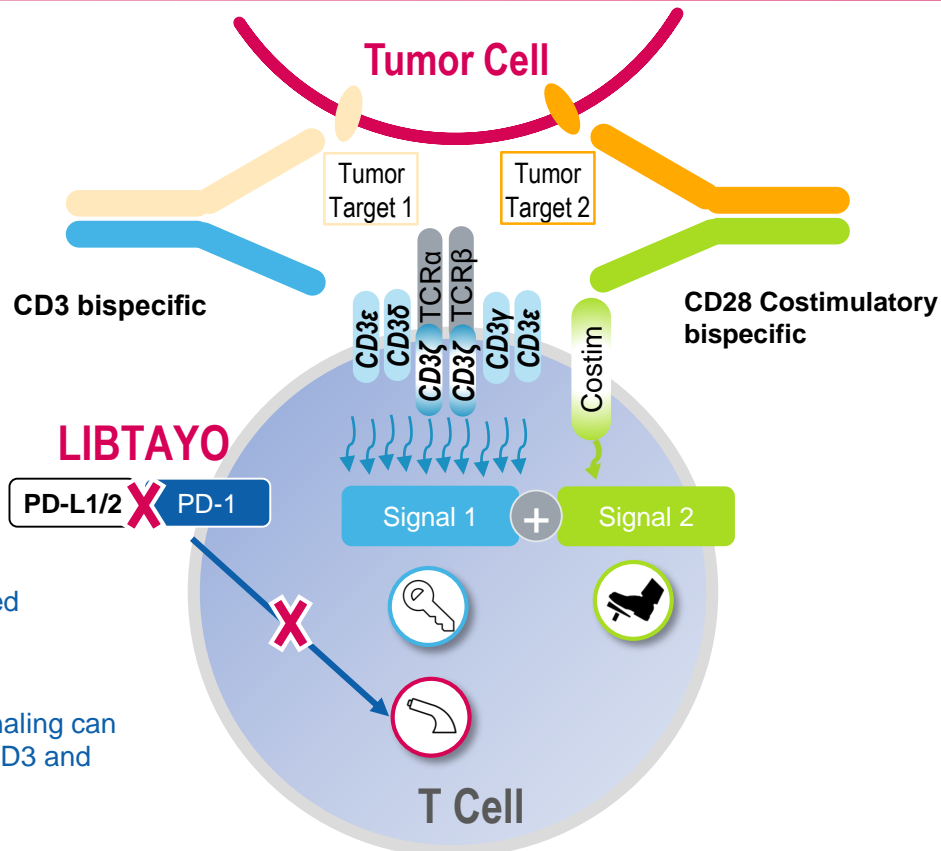
Regeneron bispecific approach is unique

- No linkers or artificial sequences
- Ease of manufacturing using same process as regular antibodies
- Similar PK to regular antibodies

HARNESSING T CELLS WITH THE POTENTIAL TO ENHANCE & EXTEND TREATMENT BENEFITS TO MORE PATIENTS



REGENERON'S CD3 & CD28 COSTIMULATORY BISPECIFICS ARE OFF-THE-SHELF DRUGS WITH POTENTIAL TO TURN PATIENTS' T CELLS INTO TUMOR CELL KILLERS



T cell activation can be inhibited by PD-1 signaling

Using **LIBTAYO** to block PD-1 signaling can further enhance the efficacy of CD3 and costimulatory bispecifics

POWERFUL AND DIVERSE ONCOLOGY PORTFOLIO FOR RATIONAL COMBINATIONS

	VelocImmune® Antibodies	Bispecifics		Other
		CD3 Bispecifics	Costims	
EARLY DEVELOPMENT	REGN3767 (LAG-3) Solid/hematologic cancers	REGN5458* (BCMAxCD3) Multiple myeloma	REGN5678 (PSMAxCD28) Prostate cancer	REGN5093 (METxMET) MET-altered NSCLC
	REGN6569 (GITR) Solid tumors	REGN5459* (BCMAxCD3) Multiple myeloma	REGN5668 (MUC16xCD28) Ovarian cancer	PiG (Peptide in HLA Groove)† Solid tumors
		REGN4018* (MUC16xCD3) Ovarian cancer	REGN7075 (EGFRxCD28) Solid tumors	ISA101b + LIBTAYO (ISA) HNSCC
POTENTIALLY PIVOTAL				Voyager-V1 + LIBTAYO (Vyriad) Solid tumors
		odronextamab (CD20xCD3) B cell NHL		RP1 + LIBTAYO (Replimune) CSCC
APPROVED	LIBTAYO* NSCLC	LIBTAYO* BCC	LIBTAYO* Cervical	LIBTAYO* Adjuvant CSCC
	LIBTAYO* CSCC			

Additional bispecifics and combinations expected to enter the clinic in coming months

BROAD COMBINATIONS PIPELINE CONTINUES TO ADVANCE AND GROW

	COMBINATIONS		INDICATIONS	STATUS	
ONGOING	odronextamab (CD20xCD3)	+	LIBTAYO*	Lymphoma	Resubmit modified study design to FDA [^]
	REGN4018* (MUC16xCD3)	+	LIBTAYO*	Ovarian cancer	Dose escalation ongoing
	REGN5678 (PSMAxCD28)	+	LIBTAYO*	Prostate cancer	Dose escalation ongoing
	REGN3767 (LAG-3)	+	LIBTAYO*	Advanced cancers	Expansion cohort enrolling
	REGN5668 (MUC16xCD28)	+	REGN4018* / LIBTAYO*	Ovarian Cancer	IND open
	REGN6569 (GITR)	+	LIBTAYO*	Solid tumors	Enrolling
	REGN7075 (EGFRxCD28)	+	LIBTAYO*	Solid tumors	IND open
	UPCOMING	odronextamab (CD20xCD3)	+	B cell/CD28 costim	B-NHL
REGN5458/9* (BCMAxCD3)		+	Plasma cell/CD28 costim	Multiple myeloma	IND filing in 2021
TAAxCD3		+	LIBTAYO*	Prostate cancer	IND filing in 2021
odronextamab (CD20xCD3)		+	Standard of Care	B-NHL	Initiating in 2021
REGN5458/9* (BCMAxCD3)		+	Standard of Care	Multiple myeloma	Initiating in 2021

VelocImmune[®] Antibodies

Costim BiSpecifics

CD3 BiSpecifics

Anti-PD-1



Solid Tumors

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



ROADMAP TO LEADERSHIP IN ONCOLOGY

COMPETE, ENHANCE, and EXTEND treatment benefits in monotherapy and in combination settings

COMPETE

LEAD in dermato-oncology



Squamous Cell Carcinoma of the Skin (CSCC)

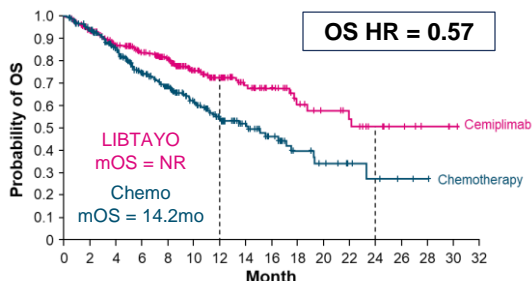
- **LIBTAYO** is first approved anti-PD1 in advanced CSCC with best-in-class data
 - ORR 46%; CR 16%; OS 73% at 2yr *
- **Neoadjuvant CSCC**[^]: pCR or MPR 70%

Basal Cell Carcinoma of the Skin (BCC)

- **LIBTAYO** has first-in-class data
 - 2L+/LA: ORR 31%; CR 6%; OS 92% at 1yr
- Granted Priority Review (PDUFA 3/3/21)

Compete in Non-Small Cell Lung Cancer (NSCLC)[#]

Granted priority review as monotherapy in 1L NSCLC (≥50% PD-L1) (PDUFA 2/28/21)



Chemo-combo NSCLC study fully enrolled; data anticipated in 2021

Additional Cancer Settings

2L **Cervical** cancer study fully enrolled; data anticipated in 2021

ENHANCE & EXTEND

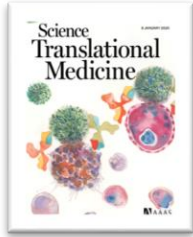
12+ candidates in clinical development for multiple cancer types:

- **LIBTAYO** as foundation for a set of combination opportunities
- **Proof-of-concept** achieved in two CD3 bispecific programs
 - Potentially pivotal studies ongoing (Hem/Onc)
- Three **CD28 costimulatory bispecifics** in clinical development; more to follow

We have the potential to **explore** many new **combinations** with our in-house toolkit

- **CD3** and **CD28** costims in multiple trials in our Solid Tumor Program
 - **LIBTAYO** with PSMA costim in Prostate Cancer
 - **CD3 & CD28** BiSpecifics in Ovarian Cancer

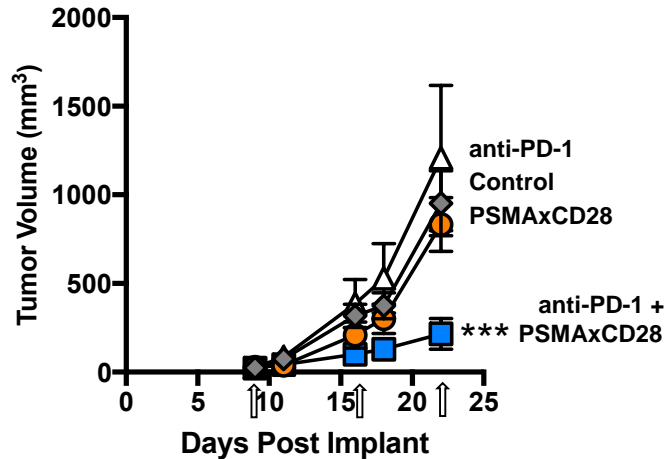
COSTIMS: COMBINATORIAL POTENTIAL WITH ANTI-PD-1 OR CD3 BISPECIFICS SHOWS ENHANCEMENT IN PRECLINICAL SOLID TUMOR MODELS



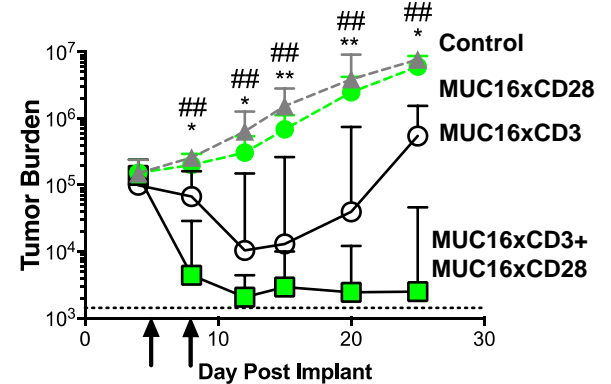
Our CD28 costimulatory bispecifics activate T cells only when they are bridged to cancer cells and after having received the first “recognition” signal from the CD3 engagement

Unlike CD28 superagonists, CD28 costims did not induce cytokine storm as monotherapy or in combination in our animal models

anti-PD-1 + PSMAxCD28
humanized prostate cancer mouse model



MUC16xCD3 + MUC16xCD28
ovarian tumor mouse model



COSTIM COMBINATIONS: ENHANCE AND EXTEND BENEFITS OF CHECKPOINT INHIBITORS

COSTIMS IN THE CLINIC (SOLID TUMORS)

PSMAxCD28 (REGN5678)



Evaluating combination with
LIBTAYO



Prostate Cancer
(metastatic castration-resistant)

MUC16xCD28 (REGN5668)



Evaluating combination with either
MUC16xCD3 or **LIBTAYO**



Ovarian Cancer (recurrent)



EGFRxCD28 (REGN7075)



Evaluating combination with
LIBTAYO



Solid tumors, including:
Non-Small Cell Lung Cancer
Cutaneous Squamous Cell Carcinoma
Colorectal Cancer (microsatellite stable)
Triple Negative Breast Cancer

**Combinations of our bispecific antibodies and checkpoint inhibitors
offer advantage of simultaneously providing multiple signals for activating T cells to kill tumors**



**Hematologic Cancers
ASH 2020 Updates**

Andres Sirulnik, MD, PhD
SVP, Translational & Clinical Sciences Hematology



**Odronextamab
(REGN1979)**

CD20xCD3



ODRONEXTAMAB (CD20xCD3): POTENTIALLY PIVOTAL PROGRAM IN MULTIPLE B-NHL SUBTYPES

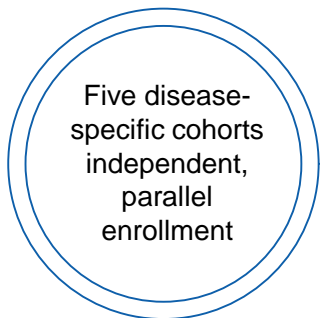
Phase 1 cohort (NCT02290951)

Data Updated ASH 2020

3L+, post-CAR-T **DLBCL**, N≈60
160 mg QW; 320 mg Q2W

Phase 2 cohorts (NCT03888105)

Enrolling



3L **FL** Grade 1–3a, N=112
80 mg QW; 160 mg Q2W

3L CAR-T naïve **DLBCL**, N≈112
160 mg QW; 320 mg Q2W

MCL after BTKi therapy, N=78*
160 mg QW; 320 mg Q2W

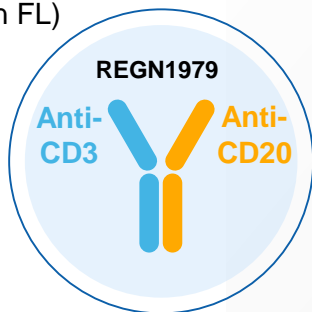
2L **MZL**, N=78
80 mg QW; 160 mg Q2W

Other B-NHLs (excluding FL Grade 1–3a, DLBCL, MCL, MZL, WM), N=67
160 mg QW; 320 mg Q2W

ODRONEXTAMAB ASH 2020 UPDATE: DEEP AND DURABLE RESPONSES

American Society of Hematology (ASH) Dec 2020 update:

- A **single bispecific**, effective in both indolent and aggressive lymphomas, including patients who failed CAR-Ts
- **Off-the-shelf** agent, administered in outpatient setting*
- Pivotal Phase 2 enrolling rapidly – robust development plan ahead
- Over 350 patients dosed to date across program
- **Durable responses** (~3.5 years in FL)
- Acceptable safety profile



R/R Follicular Lymphoma

- **ORR=90%, CR=70%**
- N=30, doses 5-320 mg
- CRs ongoing for up to ~3.5 years

R/R DLBCL (CAR-T naïve)

- **ORR=55%, CR=55%**
- N=11, doses 80-320 mg
- CRs ongoing for up to 21 months

R/R DLBCL (post-CAR-T)

- **ORR=33%, CR=21%**
- N=24, doses 80-320 mg
- All CRs ongoing for up to 20 months

Durable CRs: mDoCR not reached for any indication

Safety:

Acceptable safety profile with manageable CRS observed mainly during the step-up dosing

- In FL and DLBCL, no CRS higher than Gr3
- No discontinuations due to CRS or neurotoxicity (3 FL and 3 DLBCL patients discontinued due to TEAEs)

ODRONEXTAMAB ASH 2020: SAFETY

Safety summary 0.5–320 mg odronextamab	Number of patients, n (%) (N=136)	
	All events	Treatment-related
TEAE	135 (99.3)	126 (92.6)
Serious TEAE	84 (61.8)	61 (44.9)
Gr ≥3 TEAE	110 (80.9)	87 (64.0)
Gr 5 (fatal) TEAE*	6 (4.4)	5 (3.7)
TEAE leading to treatment discontinuation	9 (6.6)	8 (5.9)

- Most frequent Gr ≥3 TEAEs (>10% of patients) included anemia (24.3%; Gr 1–3 at baseline in 22%), lymphopenia (20.6%; transient), neutropenia (18.4%; febrile in 2.2%), and hypophosphatemia (18.4%; transient)
- Nine patients (6.6%) had to discontinue odronextamab due to a TEAE, including:
 - Gr 1 cytomegalovirus infection (n=1), Gr 1 fatigue (n=1)
 - Gr 2 pneumonia (n=1)
 - Gr 3 hemolysis, fatigue, pneumonia, toxoplasmosis, and TLS (all n=1), plus abscess (n=1; unrelated to study treatment)
- No patients discontinued odronextamab due to CRS or neurotoxicity
- Odronextamab was administered up to 320 mg weekly without DLTs or reaching MTD; no dose-dependent increase in toxicity was observed (data not shown)

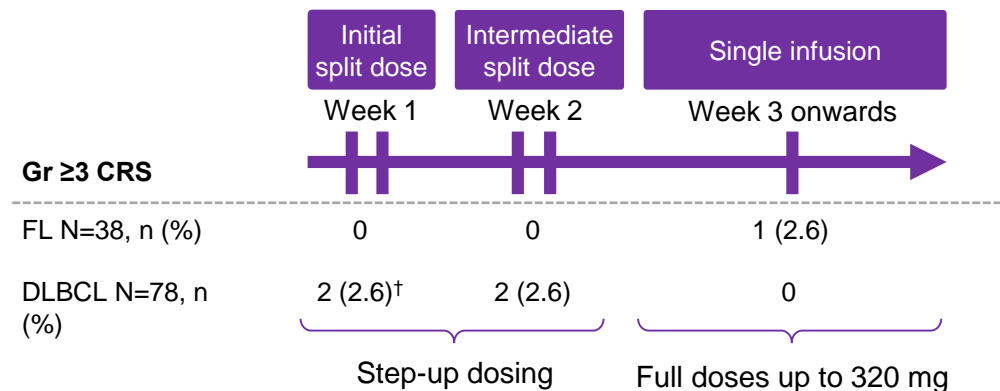
Data cut-off: Sep 18, 2020.

*Related to treatment: gastric perforation, pneumonia, pneumocystis pneumonia, TLS (in a patient with MCL), toxoplasmosis (n=1 each); not related: cardiac arrest (n=1).

CRS, cytokine release syndrome; DLT, dose-limiting toxicity; Gr, grade; MCL, mantle cell lymphoma; MTD, maximum tolerated dose; TEAE, treatment-emergent adverse event; TLS, tumor lysis syndrome.

ODRONEXTAMAB ASH 2020: CYTOKINE RELEASE SYNDROME

CRS, n (%)	DLBCL, n=78	FL Gr 1–3a, n=38	Other B-NHL,* n=20	Total, N=136
Gr 1	31 (39.7)	13 (34.2)	4 (20.0)	48 (35.3)
Gr 2	14 (17.9)	11 (28.9)	0 (0)	25 (18.4)
Gr 3	4 (5.1)	1 (2.6)	4 (20.0)	9 (6.6)
Gr 4	0 (0)	0 (0)	1 (5.0)	1 (0.7)
Total	49 (62.8)	25 (65.8)	9 (45.0)	83 (61.0)



- Majority of CRS events were mild or moderate in severity
- Majority of Gr ≥3 CRS events occurred with initial or intermediate odronextamab step-up doses
- Highest grade of CRS observed in patients with FL or DLBCL was Gr 3
- One episode of Gr 3 CRS occurred in FL patients
- CRS events resolved within a median of 2 days (range 1–41), with supportive care measures

Data cut-off: Sep 18, 2020.

*Other B-NHL includes mantle cell lymphoma, marginal zone lymphoma, FL Grade 3b, and Waldenström macroglobulinemia; [†]One patient had Gr 3 CRS after an initial dose of 1 mg on day 29.

CRS was graded according to modified Lee et al. 2014 or Lee et al. 2019 criteria.

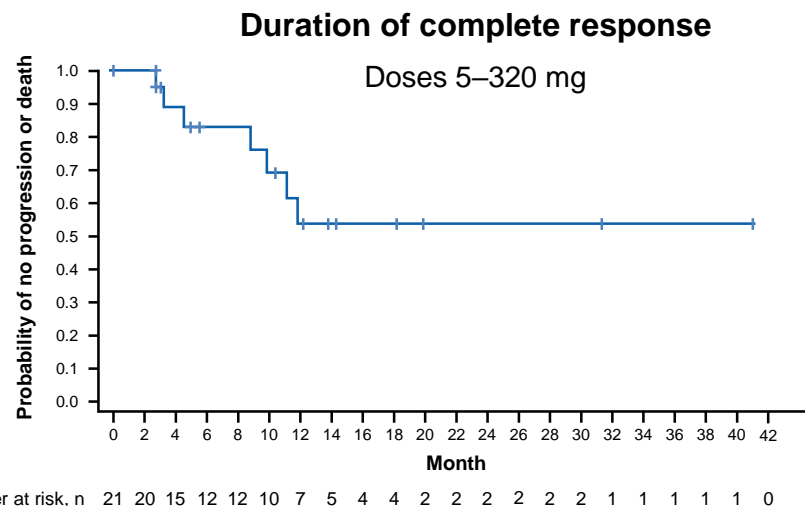
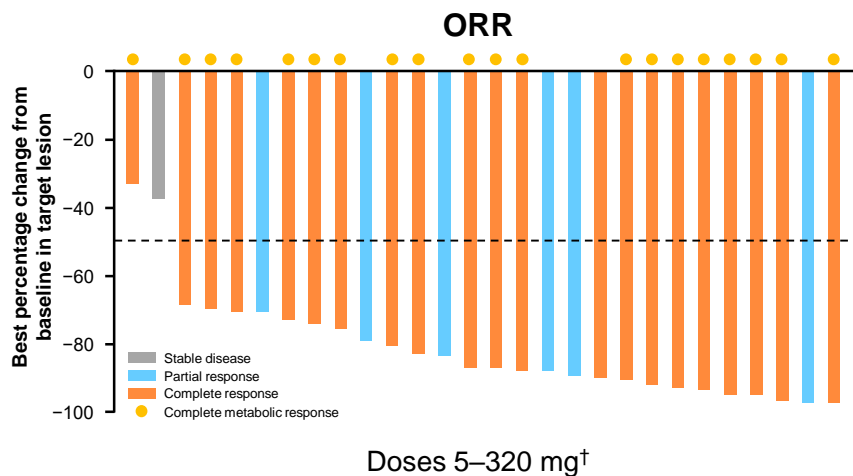
B-NHL, B-cell non-Hodgkin lymphoma; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; Gr, grade.

ODRONEXTAMAB ASH 2020: ANTITUMOR ACTIVITY IN R/R FOLLICULAR LYMPHOMA

ORR: 90% (n=27/30); CR rate: 70% (n=21/30)

CRs appear durable; median DoCR not reached

- 81% of CRs were durable,* and are ongoing for up to 41 months



Data cut-off: Oct 14, 2020.

Response per investigator assessment according to Lugano criteria. Median duration of follow up is 9 months (range, 1–44).

*Defined as a CR lasting at least 3 months; [†]Two patients with missing tumor assessments are not presented.

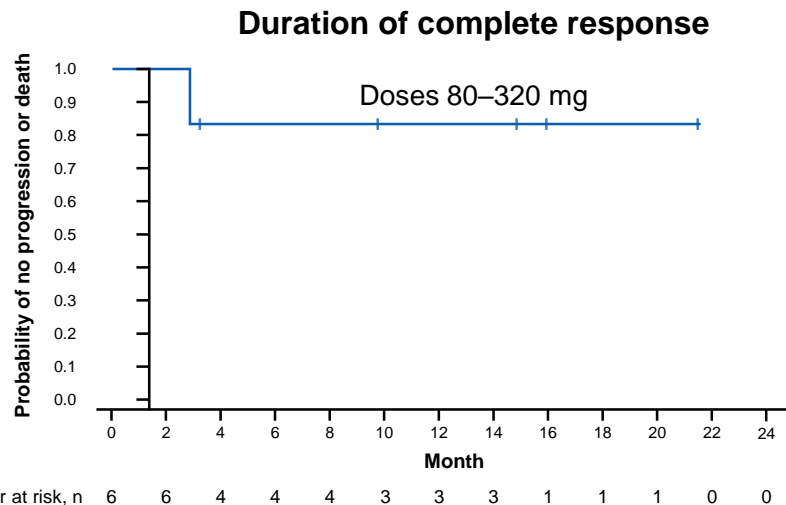
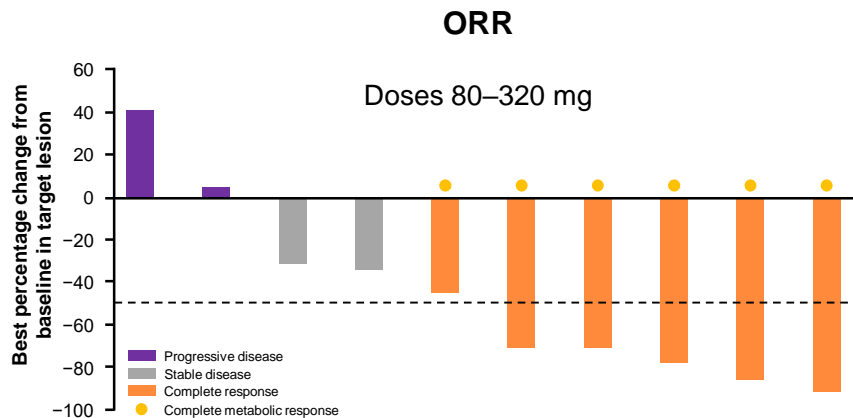
CR, complete response; DoCR, duration of complete response; ORR, objective response rate; R/R, relapsed/refractory.

ODRONEXTAMAB ASH 2020: ANTITUMOR ACTIVITY IN R/R DLBCL: NO PRIOR CAR-T

ORR: 55% (n=6/11); CR rate: 55% (n=6/11)

CRs appear durable; median DoCR not reached

- 83% of CRs were durable,* and are ongoing for up to 21 months



Data cut-off: Oct 14, 2020.

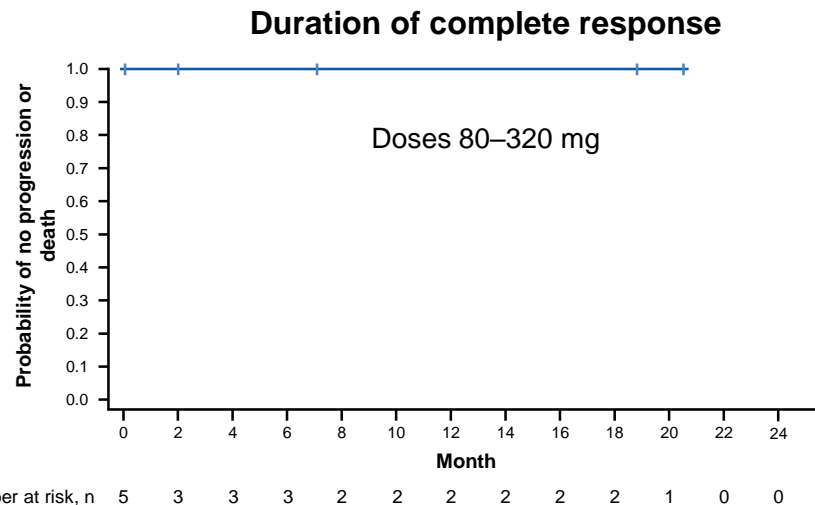
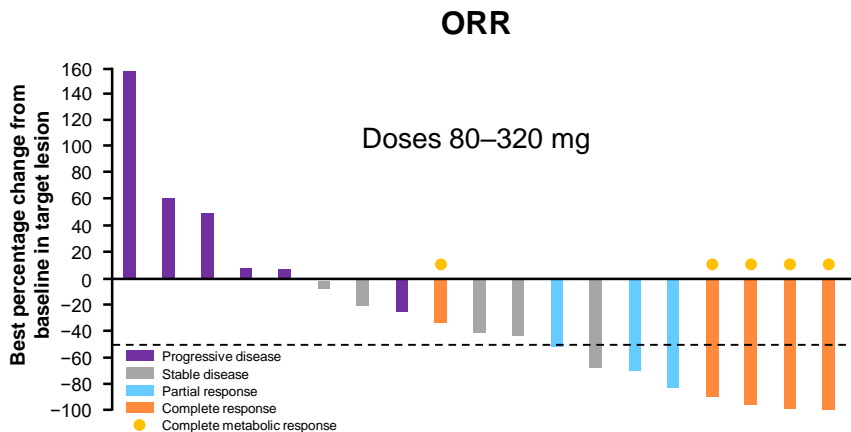
Response per investigator assessment according to Lugano criteria. Median duration of follow up is 6 months (range, 1–24).

*Defined as a CR lasting at least 3 months.

CAR T, chimeric antigen receptor T cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoCR, duration of complete response; ORR, objective response rate; R/R, relapsed/refractory.

ODRONEXTAMAB ASH 2020: ANTITUMOR ACTIVITY IN R/R DLBCL: POST-CAR-T

ORR: 33% (n=8/24); CR rate: 21% (n=5/24)
CRs appear durable; median DoCR not reached
 • **100%** of CRs are ongoing,* for up to **20 months**



Data cut-off: Oct 14, 2020.

Response per investigator assessment according to Lugano criteria. Median duration of follow up is 3 months (range, 0–22).

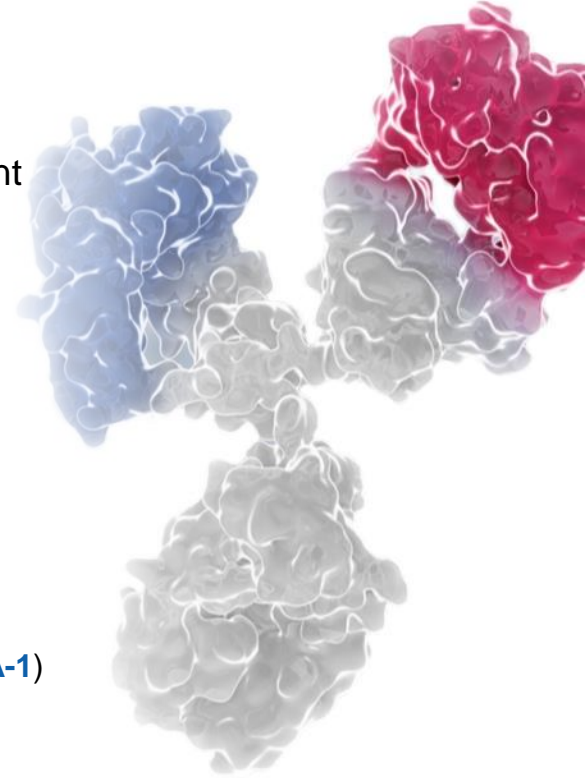
*At time of last tumor assessment.

CAR T, chimeric antigen receptor T cell; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoCR, duration of complete response; ORR, objective response rate; R/R, relapsed/refractory.

ODRONEXTAMAB DEVELOPMENT PLAN: POTENTIAL PATH TO APPROVAL AND LONGER-TERM PLANS OF ADDRESSING LARGE UNMET NEED

UPCOMING MILESTONES

- 1H21: Complete FL and DLBCL potentially pivotal Phase 2 enrollment
- 1H21: Subcutaneous odronextamab in clinic
- 2021: Start confirmatory OLYMPIA Phase 3 trials in FL and DLBCL
 - Phase 3 in 2L+ DLBCL (**OLYMPIA-1**)
 - Phase 3 in FL (**OLYMPIA-2**)
 - Phase 3 in 1L DLBCL (IPI 3-5) (**OLYMPIA-3**)
- 2021: Evaluate chemo-free combinations
 - LIBTAYO combination
 - Phase 1 first dual bispecific combo in DLBCL (with TAAxCD28) (**ATHENA-1**)
- 2022: Potential BLA submission



REGN5458
BCMAxCD3

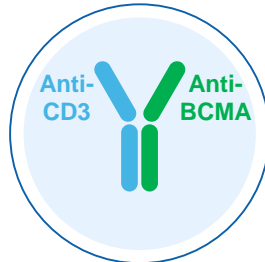


REGN5458 (BCMAxCD3): COMPETITIVE ANTI-TUMOR ACTIVITY; POTENTIALLY REGISTRATIONAL PH2 UNDERWAY IN MULTIPLE MYELOMA

REGN5458

Our first BCMAxCD3 bispecific to enter clinic; now in potentially registrational Ph2 dose expansion

- Competitive efficacy profile in a heavily pretreated, vulnerable patient population:
 - 100% refractory to anti-CD38 and at least triple refractory
 - 67% with prior autologous transplant
 - 31% 70 years or older
- Data shown for all patients at all dose levels explored (intention to treat analysis)
 - Deep responses across all dose levels
- Acceptable safety profile
 - No Grade 3+ neurotoxicity or CRS



Phase 1 ASH Dec 2020 update:

R/R Multiple Myeloma

N=49*, doses 3-96 mg

Efficacy:

3-12mg (n=24): **ORR=29%, VGPR or better= 25%**

24-48mg (n=17): **ORR=41%, VGPR or better= 41%**

96mg (n=8): **ORR=63%, VGPR or better= 63%**

- High and deep response rates: 95% of responders achieved VGPR or better
- Among responding patients with ≥ 6 months of follow-up, 83% have ongoing responses for up to 13 months
- Responses occur early and improve over time
- Acceptable tolerability up to 96mg (dose level 6)

Encouraging depth and durability of responses with acceptable safety profile

REGN5458 ASH 2020: SAFETY

Adverse events, n (%)	Total (N=49)	
	Any grade	Grade ≥3
Hematological, in ≥15% of patients (any grade)		
Anemia	18 (37)	11 (22)
Lymphopenia	9 (18)	6 (12)
Thrombocytopenia	9 (18)	3 (6)
Neutropenia	8 (16)	7 (14)
Non-hematological, in ≥20% of patients (any grade)		
CRS	19 (39)	0
Fatigue	17 (35)	3 (6)
Nausea	15 (31)	0
Pyrexia	15 (31)	1 (2)
Back pain	13 (27)	2 (4)
Total (N=49)		
Infections, n (%)	Any grade	Grade ≥3
Overall	23 (47)	9 (18)
Most common, in ≥10% of patients (any grade)		
Pneumonia	6 (12)	2 (4)
Upper respiratory tract infection	6 (12)	0
<i>No opportunistic infections were reported</i>		

Dose-limiting toxicity (DLT)

- DLTs were reported in 2 patients
 - Acute kidney injury (Grade 4; DL4 = 24 mg): Resolved with supportive care
 - Elevated ALT/AST (Grade 3; DL6 = 96 mg): Resolved with supportive care; REGN5458 treatment ongoing with VGPR

Neurotoxicity

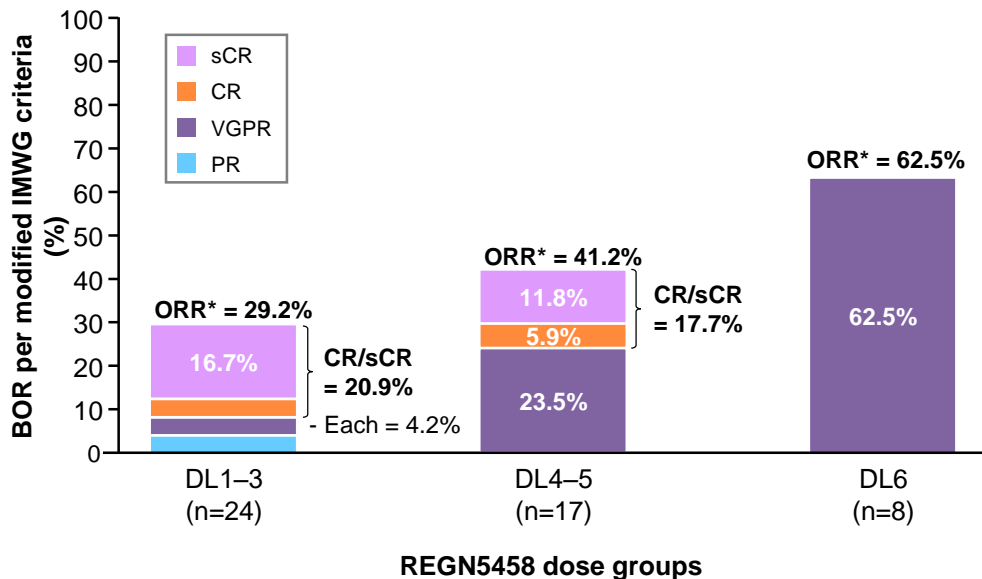
- No Grade ≥3 reported
- Grade 1 and 2: 6 (12%) patients

All adverse events were treatment-emergent adverse events irrespective of causality and were evaluated based on the National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE v5.0) except CRS which was graded per ASTCT (Lee et al. *Biol Blood Marrow Transplant.* 2019;25:625–638). Total patient number represents the total number of patients treated. At baseline, 84% of patients had anemia of any grade; 6% of patients had Grade 3 anemia; no Grade 4 or 5 anemia were reported.

ALT, alanine transaminase; AST, aspartate transaminase; ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; DL, dose level; VGPR, very good partial response.

REGN5458 ASH 2020: EFFICACY – INTENT-TO-TREAT ANALYSIS

Observed median duration of follow-up (range): 2.6 (0.5–13.4) months

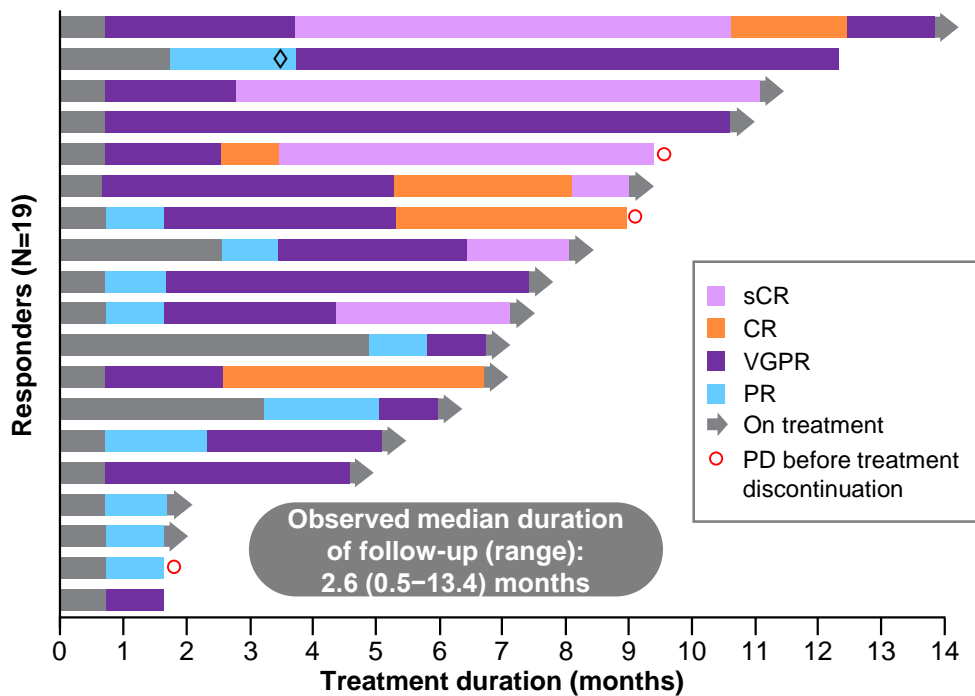


- 95% (18/19) of responders achieved VGPR or better
- 42% (8/19) of responders had a CR or sCR
- 57% (4/7) evaluable patients[†] achieved MRD negative (10^{-5})
- Tumor response was not impacted by level of BCMA expression in core biopsy as assessed by IHC

DL6 patients had been followed for a median of 2 months, and responses may deepen over time

*Includes patients who had opportunity for response assessment at 4 weeks. [†]Includes patients who achieved CR or sCR and received MRD testing. BCMA, B-cell maturation antigen; BOR, best overall response; CR, complete response; DL, dose level; IHC, immunohistochemistry; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, objective response rate; PR, partial response; sCR, stringent CR; VGPR, very good partial response.

REGN5458 ASH 2020: DURATION OF RESPONSE



- Responses occurred early (most by Week 4) and deepened with time
- 74% of responders have ongoing treatment

Among responding patients with ≥ 6 months of follow-up, 83% (10/12) have ongoing responses for up to 13 months

◇ Treatment stopped due to patient decision.
 CR, complete response; DOR, duration of response; PD, progressive disease; PR, partial response; sCR, stringent CR; VGPR, very good partial response.

REGN5458: POTENTIAL PATH TO APPROVAL IN R/R MM, ADDRESS LARGER UNMET NEED IN COMBINATION WITH STANDARD OF CARE

ANTICIPATED 2021 MILESTONES

- Enroll potentially pivotal R/R MM Ph2 study
- Evaluate combinations:
 - With MM standard of care
 - With novel agents, including costims (PlasmaCellxCD28)
- Initiate pivotal studies in earlier lines of MM therapy
- Develop REGN5458 subcutaneous administration
- Evaluate application in other plasma cell disorders
- REGN5459 (lower CD3 arm affinity) data



COSTIMS COMBINED WITH CD3 BISPECIFICS SHOW ENHANCEMENT IN PRECLINICAL HEMATOLOGICAL TUMOR MODELS

Our CD28 costimulatory bispecifics activate T cells only when they are bridged to cancer cells and after having received the first “recognition” signal from the CD3 engagement



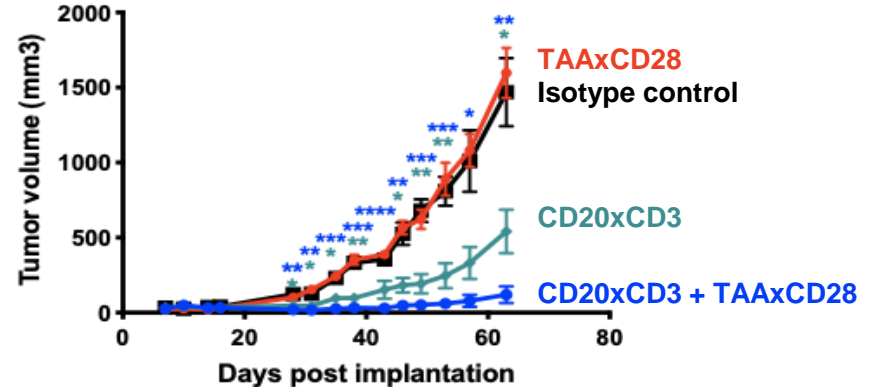
2021: (B cell TAA)xCD28 + odronextamab to enter clinic for B-NHL

2021: (Plasma cell TAA)xCD28 + REGN5458 to enter clinic for Multiple Myeloma

odronextamab + TAAxCD28 costim

odronextamab-resistant DLBCL mouse model

Average tumor growth



Complementary costimulatory bispecifics could further enhance anti-tumor effects of odronextamab and REGN5458

**Classical Hematology
Program Overview**



ESTABLISHING A BROAD HEMATOLOGY PORTFOLIO

COMPLEMENT



COAGULATION

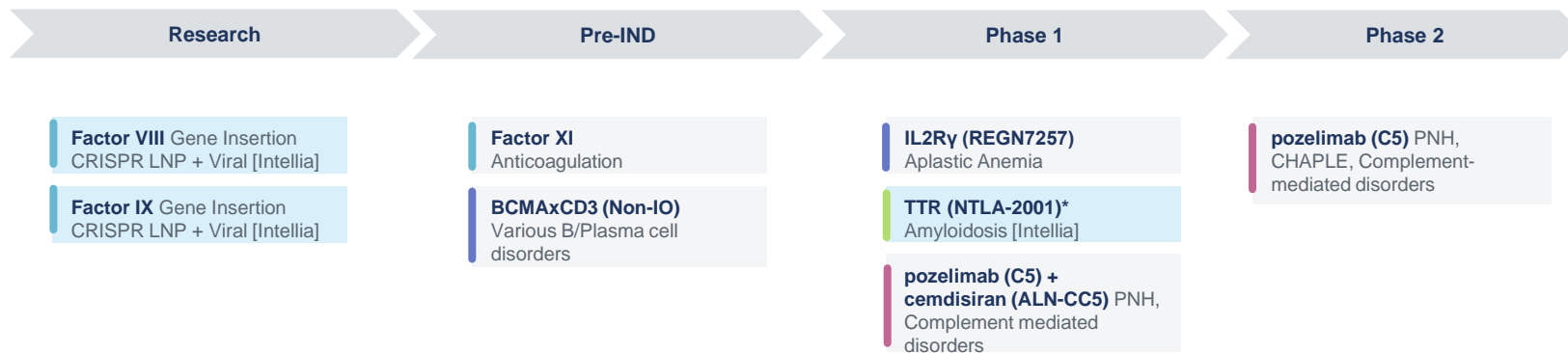


TRANSPLANTATION &
IMMUNOMODULATION

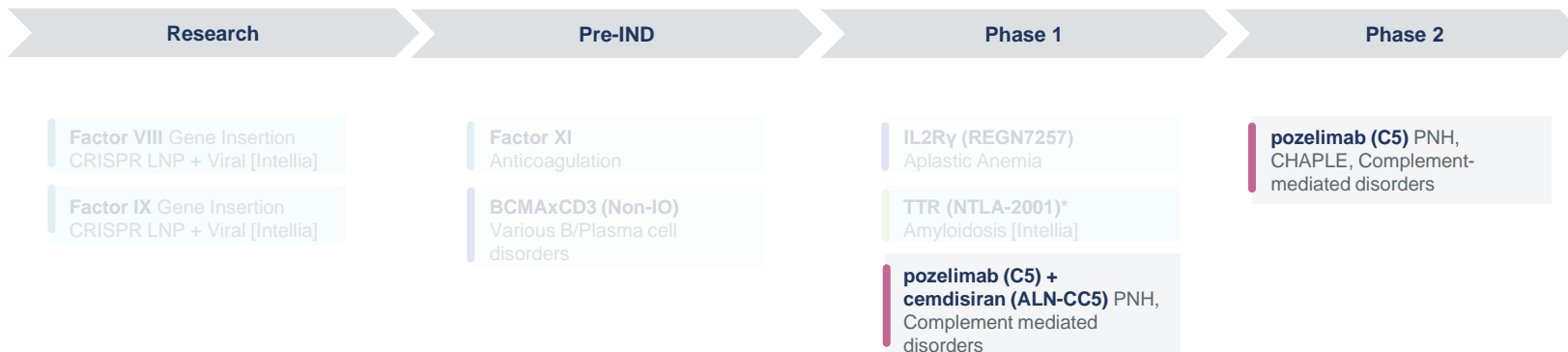
OTHER – hATTR
[TRANSTHYRETIN AMYLOIDOSIS]



CLASSICAL HEMATOLOGY DEVELOPMENT PIPELINE



CLASSICAL HEMATOLOGY DEVELOPMENT PIPELINE



COMPLEMENT
 Pozelimab (anti-C5 antibody) +
 Cemdisiran (C5 RNAi)

PNH, Other
 Complement-Mediated Diseases

- Advantages:
 - Convenient SC self-administration with ALNY's RNAi
 - More complete blockade of inappropriate complement activation in patients with complement-mediated diseases
 - Proof of concept for combining antibodies and RNAi
- Timelines to clinic: Pozelimab monotherapy is tested in Ph2
 - Combination entered first-in-human studies in healthy volunteers
 - Ph3s planned for next 12 months
- Timelines to market: 2022+



CLASSICAL HEMATOLOGY DEVELOPMENT PIPELINE



Factor VIII Gene Insertion
CRISPR LNP + Viral [Intellia]

Factor IX Gene Insertion
CRISPR LNP + Viral [Intellia]

Factor XI
Anticoagulation

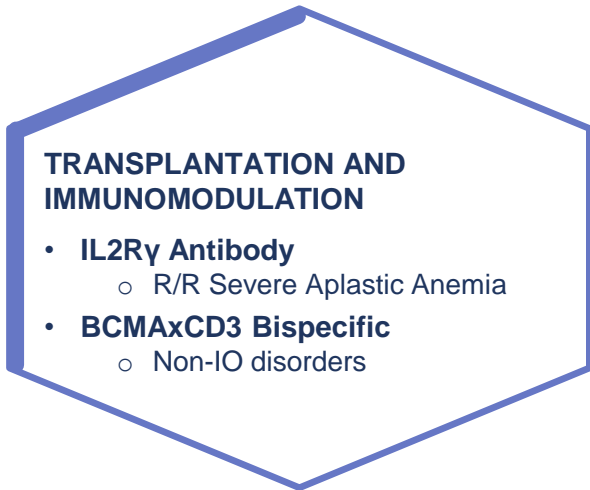
BCMAxCD3 (Non-IO)
Various B/Plasma cell disorders

IL2Ry (REGN7257)
Aplastic Anemia

TTR (NTLA-2001)*
Amyloidosis [Intellia]

pozelimab (C5) +
cemdisiran (ALN-CC5) PNH,
Complement mediated disorders

pozelimab (C5) PNH,
CHAPLE, Complement-mediated disorders



- **IL2Ry**
 - Phase 1 in aplastic anemia enrolling
 - Development planned for multiple indications that require transient suppression of T cell response as an alternative to T cell depleting agents (e.g. ATG) that are associated with serious toxicities and limited response
- **BCMAxCD3**
 - Development planned for various disorders caused by abnormal antibody production by plasma cells



CLASSICAL HEMATOLOGY DEVELOPMENT PIPELINE



Factor VIII Gene Insertion
CRISPR LNP + Viral [Intellia]

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pozelimab (C5) PNH,
CHAPLE, Complement-mediated disorders

OTHER

- **TTR Gene Knockout: CRISPR LNP**
 - hATTR (Transthyretin Amyloidosis)



- **NTLA-2001** (TTR gene knockout, Intellia-led)
 - First patient dosed in Nov 2020 – the first-ever CRISPR genome editing treatment delivered intravenously
 - Single-course therapy that potentially halts and reverses ATTR progression
 - Ph1 is in hereditary ATTR patients with polyneuropathy (hATTR-PN), with plans to evaluate NTLA-2001 in a broader ATTR population of both polyneuropathy and cardiomyopathy patients



CLASSICAL HEMATOLOGY DEVELOPMENT PIPELINE



Factor VIII Gene Insertion
CRISPR LNP + Viral [Intellia]

Factor IX Gene Insertion
CRISPR LNP + Viral [Intellia]

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pozelimab (C5) PNH,
CHAPLE, Complement-mediated disorders

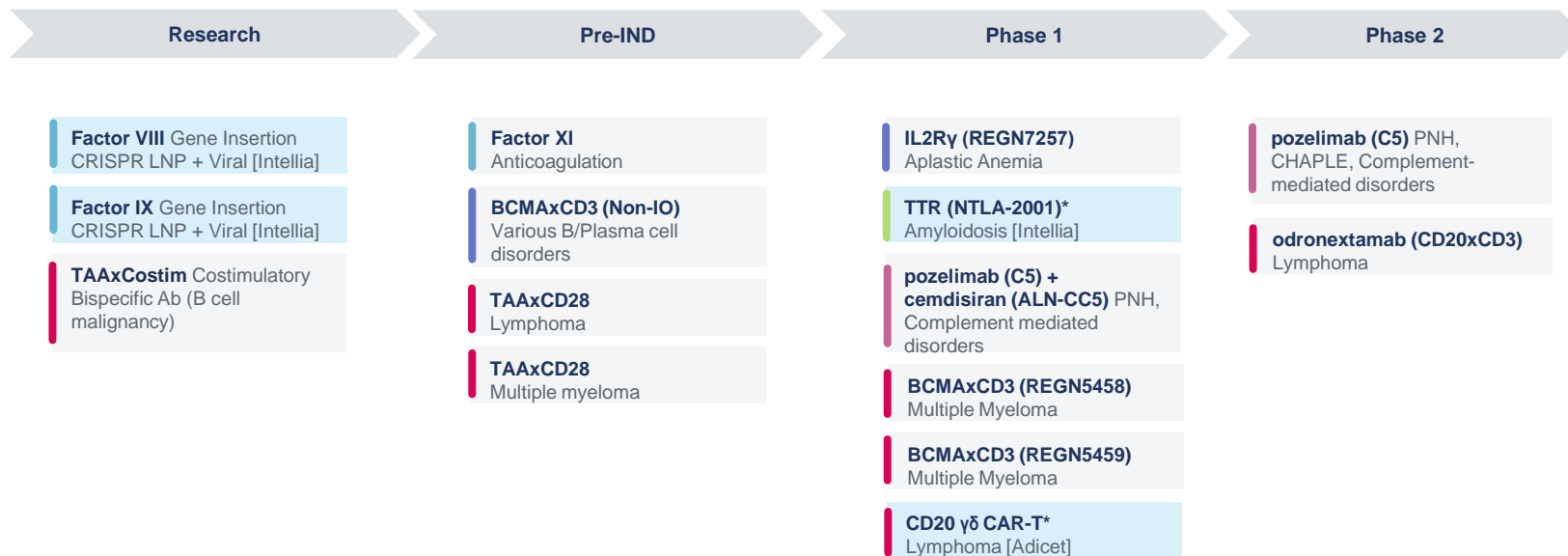
COAGULATION

- **Factor XI Antibody**
 - Anticoagulation in thrombotic disorders
- **Factor VIII Gene Insertion: CRISPR LNP + viral**
 - Hemophilia A 
- **Factor IX Gene Insertion: CRISPR LNP + viral**
 - Hemophilia B 

- **Factor XI**
 - Currently in IND-enabling studies
 - In development for thrombotic disorders with high unmet need
- **Factor VIII and IX** (Intellia collaboration, REGN lead)
 - Moving rapidly to IND-enabling studies
 - Potential single-course gene insertion therapy for hemophilia
 - Preclinical data show potential for more durable Factor IX expression vs. comparable AAV gene therapy approach



HEMATOLOGY DEVELOPMENT PIPELINE



KEY TAKEAWAYS FROM ASH 2020 UPDATE

- Broad **oncology and hematology pipeline** advancing with potential to unlock numerous opportunities
- Odronextamab (**CD20xCD3**): a single bispecific effective in both indolent and aggressive lymphomas, with a broad program and an accelerated path to approval
- REGN5458 (**BCMAxCD3**): continues to show responses in patients with heavily-pretreated Multiple Myeloma, now in potentially pivotal Ph2 trial
- Emerging **classical hematology** portfolio

SELECT UPCOMING 2021 MILESTONES – ONCOLOGY & HEMATOLOGY

LIBTAYO

- Regulatory action in 1L NSCLC (PDUFA 2/28/21)
- Regulatory action in 2L+ BCC (PDUFA 3/3/21)
- 1L NSCLC chemo combo data anticipated
- 2L Cervical cancer data anticipated

Odronextamab (CD20xCD3)

- Complete enrollment in potentially pivotal Phase 2
- Initiate OLYMPIA Phase 3 program and evaluate combinations

BCMAxCD3

- Complete enrollment in potentially pivotal Phase 2
- Evaluate combinations with SOC and novel agents

Other bispecifics

- Potential first data for MUC16xCD3 and PSMAxCD28



Q&A



George D. Yancopoulos, MD, PhD
Co-Founder, President & Chief Scientific Officer



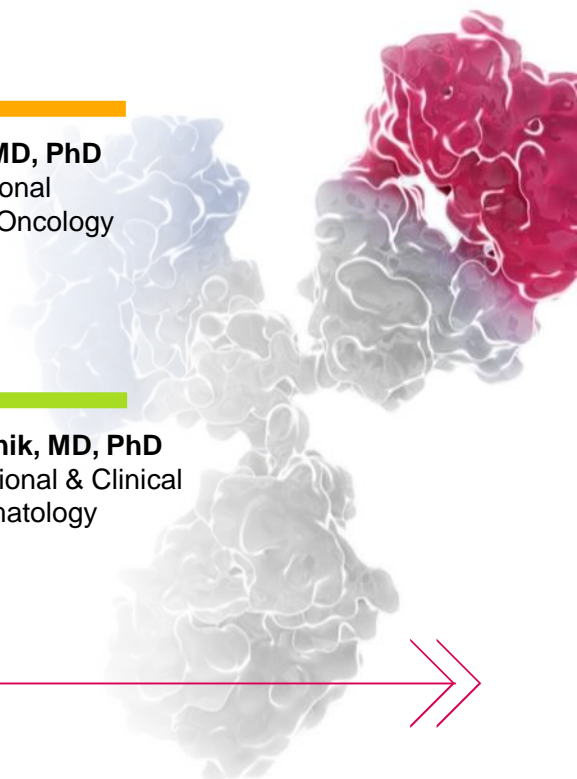
Israel Lowy, MD, PhD
SVP, Translational Sciences and Oncology



David Weinreich, MD
Head, Global Clinical Development



Andres Sirulnik, MD, PhD
SVP, Translational & Clinical Sciences Hematology



Appendix



NOTABLE 2020/2021 ONCOLOGY MILESTONES (1/3)

	CLINICAL PROGRAM	DISEASE AREA	SELECT UPCOMING MILESTONES
Checkpoint Inhibitor Antibodies	Libtayo® (cemiplimab) (PD-1 Inhibitor)	Non-small cell lung cancer	U.S. FDA Priority Review decision expected February 28, 2021 EC approval decision expected by mid 2021
		Basal cell carcinoma	U.S. FDA Priority Review decision expected March 3, 2021 EC approval decision expected by mid 2021
		Cervical cancer	Anticipate first data from pivotal Phase 3 trial (2021)
	Libtayo + Chemotherapy	Non-small cell lung cancer	Anticipate first data from pivotal Phase 3 trial (2021)
	REGN6569 (GITR antibody) + Libtayo	Solid tumors	Continue enrolling Phase 1 first-in-human trial (2020)

NOTABLE 2020/2021 ONCOLOGY MILESTONES (2/3)

	CLINICAL PROGRAM	DISEASE AREA	SELECT UPCOMING MILESTONES
CD3 Bispecific Antibodies	Odronextamab (CD20xCD3)	Follicular lymphoma	Report updated results from Phase 1 trial at the ASH Annual Meeting (2020)
		Diffuse large B-cell non-Hodgkin lymphoma	Complete enrollment of potentially pivotal Phase 2 trial (2021)
		Other B-cell non-Hodgkin lymphomas	Initiate a trial for subcutaneous odronextamab, confirmatory trials in FL and DLBCL, and trials investigating chemotherapy-free combinations with Libtayo® (cemiplimab) and a CD28 bispecific antibody (2021)
	REGN5458 (BCMAxCD3)	Multiple myeloma	<p>Report updated results from Phase 1/2 trial at the ASH Annual Meeting (2020)</p> <p>Continue enrolling patients in potentially pivotal Phase 2 first-in-human trial (2021)</p> <p>Evaluate combinations with Libtayo and novel agents, including a CD28 bispecific antibody (2021)</p> <p>Initiate pivotal trials in earlier lines of multiple myeloma therapy (2021)</p> <p>Develop subcutaneous REGN5458 (2021)</p>
REGN4018 (MUC16xCD3) +/- Libtayo	Platinum-resistant ovarian cancer	Anticipate first data from Phase 1 first-in-human trial (2021)	

NOTABLE 2020/2021 ONCOLOGY MILESTONES (3/3)

	CLINICAL PROGRAM	DISEASE AREA	SELECT UPCOMING MILESTONES
CD28 Costimulatory Bispecific Antibodies	REGN5678 (PSMAxCD28) + Libtayo	Prostate cancer (metastatic castration-resistant)	Continue enrolling Phase 1/2 first-in-human trial (2021)
	REGN5668 (MUC16xCD28) + Libtayo or REGN4018	Ovarian cancer (recurrent)	Initiate Phase 1/2 first-in-human trial (2020)
	REGN7075 (EGFRxCD28) + Libtayo	EGFR-positive cancers, including: <ul style="list-style-type: none"> • colorectal cancer (microsatellite stable) • Triple negative breast cancer • Cutaneous squamous cell carcinoma, • Non-small cell lung cancer 	Initiate Phase 1 first-in-human trial (2020)
Tumor-specific Bispecifics	REGN5093 (METxMET)	MET-altered non-small cell lung cancer	Continue enrolling Phase 1 first-in-human trial (2021)