

REGENERON
SCIENCE TO MEDICINE®

**ASCO 2020
INVESTOR EVENT**

JUNE 2020



NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. (“Regeneron” or the “Company”), and actual events or results may differ materially from these forward-looking statements. Words such as “anticipate,” “expect,” “intend,” “plan,” “believe,” “seek,” “estimate,” variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron’s business and its employees, collaborators, 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 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 EYLEA® (afibercept) Injection, Dupixent® (dupilumab), Libtayo® (cemiplimab), Praluent® (alirocumab), Kevzara® (sarilumab), fasinumab, evinacumab, garetosmab, pozelimab, Regeneron’s oncology programs (including its costimulatory bispecific portfolio and other therapeutic approaches discussed in this presentation), Regeneron’s COVID-19 antibody program and other earlier-stage product candidates, and the use of human genetics in Regeneron’s research programs; the extent to which the results from the research and development programs or preclinical testing conducted by Regeneron or its collaborators (including the research and development programs and preclinical testing discussed in this presentation) may be replicated in other studies and may lead to advancement of product candidates to clinical trials or therapeutic applications; unforeseen 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 product candidates in clinical trials; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron’s late-stage product candidates and new indications for Regeneron’s Products, including without limitation EYLEA, Dupixent, Libtayo, Praluent, Kevzara, fasinumab, evinacumab, REGN-EB3, garetosmab, pozelimab, and REGN1979; the likelihood and timing of achieving any of the anticipated milestones described in this presentation; ongoing regulatory obligations and oversight impacting Regeneron’s Products (such as EYLEA, Dupixent, Libtayo, Praluent, and Kevzara), 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 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 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 (including without limitation the patent litigation and other related proceedings relating to Dupixent and Praluent), 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 without any further product success. 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 March 31, 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 any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.



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



AGENDA



Strategy Overview

George D. Yancopoulos,
MD, PhD



LIBTAYO[®] Update

Israel Lowy, MD, PhD



Powerful Pipeline for Rational Combinations

Andres Sirulnik, MD, PhD

Israel Lowy, MD, PhD

George D. Yancopoulos,
MD, PhD



Commercial Excellence

Marion McCourt



REGENERON-INVENTED TECHNOLOGIES REPEATEDLY DELIVER IMPORTANT NEW THERAPEUTICS

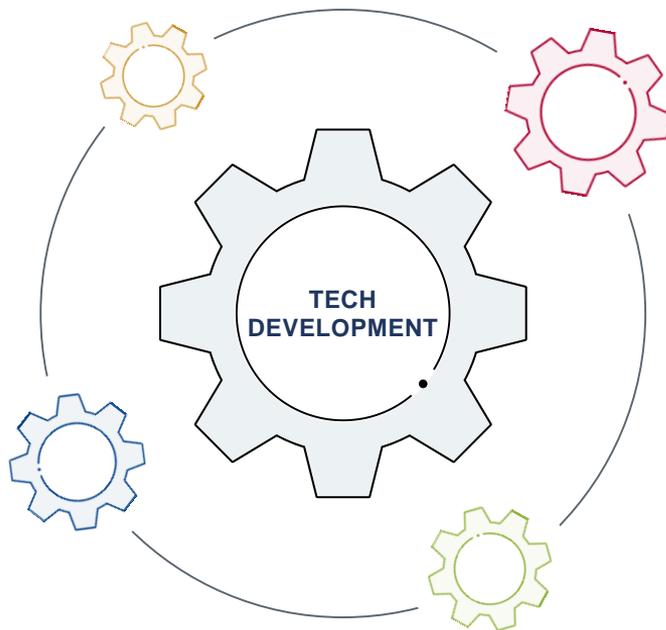
TARGET DISCOVERY & VALIDATION

Human & Mouse Genetics

- *VelociGene*®
- *VelociMouse*®



World leading human sequencing
over 1MM humans sequenced
linked to EHRs
BIG DATA



TURNKEY THERAPEUTICS: TRAPs & ANTIBODIES

- *TRAPs*
- *VelociImmune*®
- *VelociMab*®

NEW THERAPEUTICS APPROACHES:

BiSpecifics: CD3, CoStims, PiGs

siRNA: with Alnylam
Cell & Viral Gene Therapy, Others

2010-2020

EYLEA® PRALUENT®
 DUPIXENT® LIBTAYO®

2020+

Garetosmab CD20xCD3
 Evinacumab BCMAXCD3
 REGN-EB3 MUC16xCD3
 REGN-CoV2 PSMAxCD28...

CLINICAL DEVELOPMENT

MEDICINES

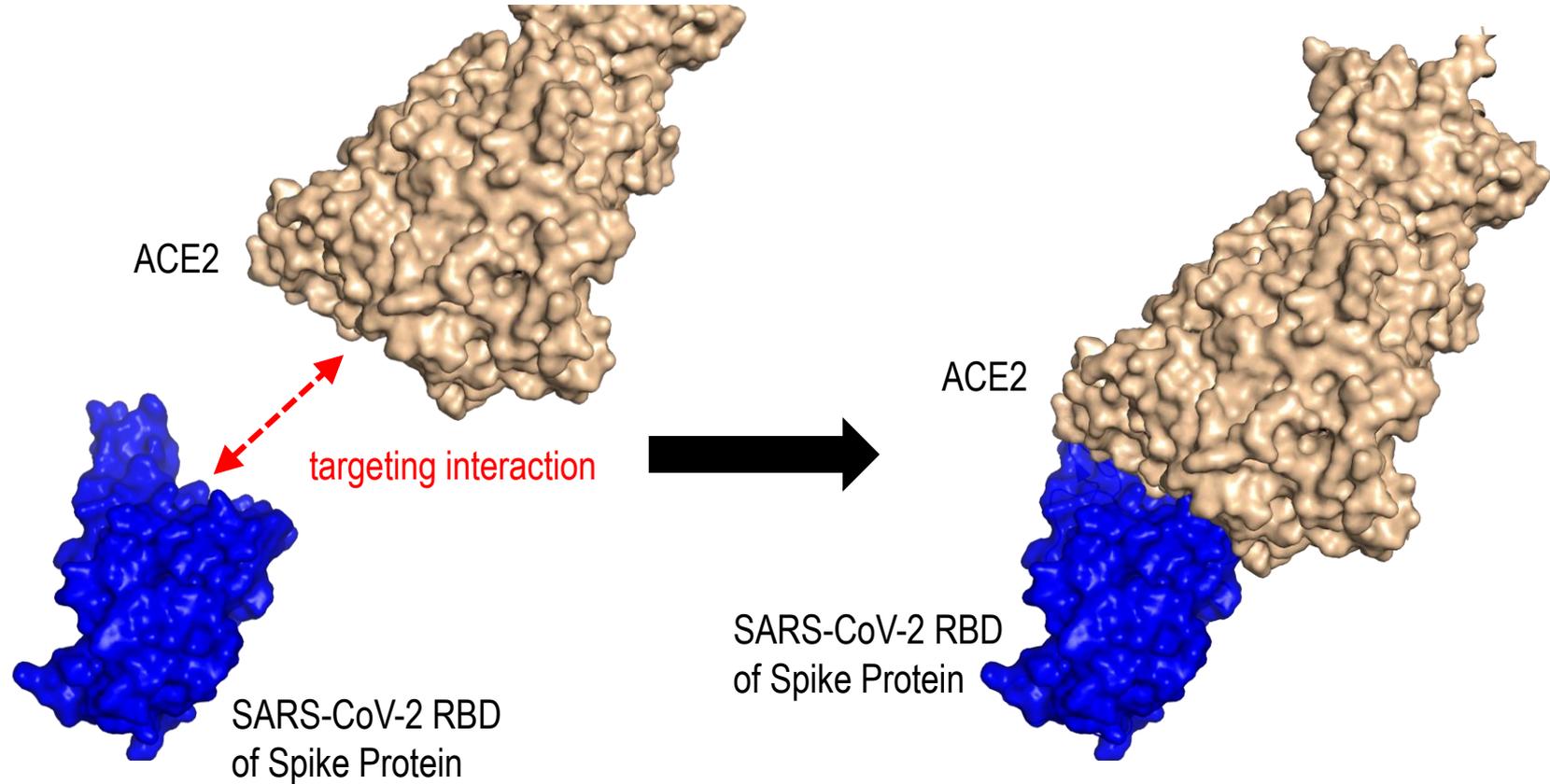
MANUFACTURING

REGENERON technologies *deliver repeated breakthroughs*

by addressing limitations and bottlenecks in every step of the drug discovery.

Regeneron rises to address urgent challenges of emerging diseases – from Ebola to **COVID-19**

SARS2 SPIKE 'RBD' BINDING TO ACE2 RECEPTORS INITIATES INFECTION OF HUMAN LUNG CELLS: CAN REGN TECHNOLOGIES BLOCK THIS INTERACTION?



REGN TECHNOLOGIES DELIVER MAB1 & MAB2 ‘ANTIBODY COCKTAIL’ THAT NOT ONLY POTENTLY BLOCKS INFECTION, BUT AVOIDS “MUTANT ESCAPE”

- REGN VG & VI technologies created Ebola “antibody cocktail” in just 9 months from initiation to clinical trials, and was proven highly effective in World Health Organization’s PALM trial in the Congo
- Now we used our technologies to create COVID19 antibody cocktail ready for trials in ~5 months:
 - Largest collection (1000’s) of highly-potent Abs from both VI mice and convalescent humans
 - Selected highly-potent (picomolar) Abs that are resistant to all naturally-occurring viral mutants described to date
 - But individual Abs are not enough – we demonstrate ‘rapid viral escape mutants’ to all single Abs tested
 - However – using a ‘selected antibody cocktail’ consisting of two Abs that bind and block at same time – we can prevent ‘viral escape’

Our prospectively-designed approach was based on the fundamental realization that – as previously demonstrated for HIV and other viruses – “combination drug therapies” could prevent viral drug-resistance by requiring simultaneous mutation at multiple genetic positions. We reasoned that the same approach might be required to prevent escape to “anti-viral antibodies”.

Thus while others have focused on the potential of single antibody treatments, we have pioneered and demonstrated the value of “antibody cocktails”, and how they are necessary to avoid rapid viral escape.

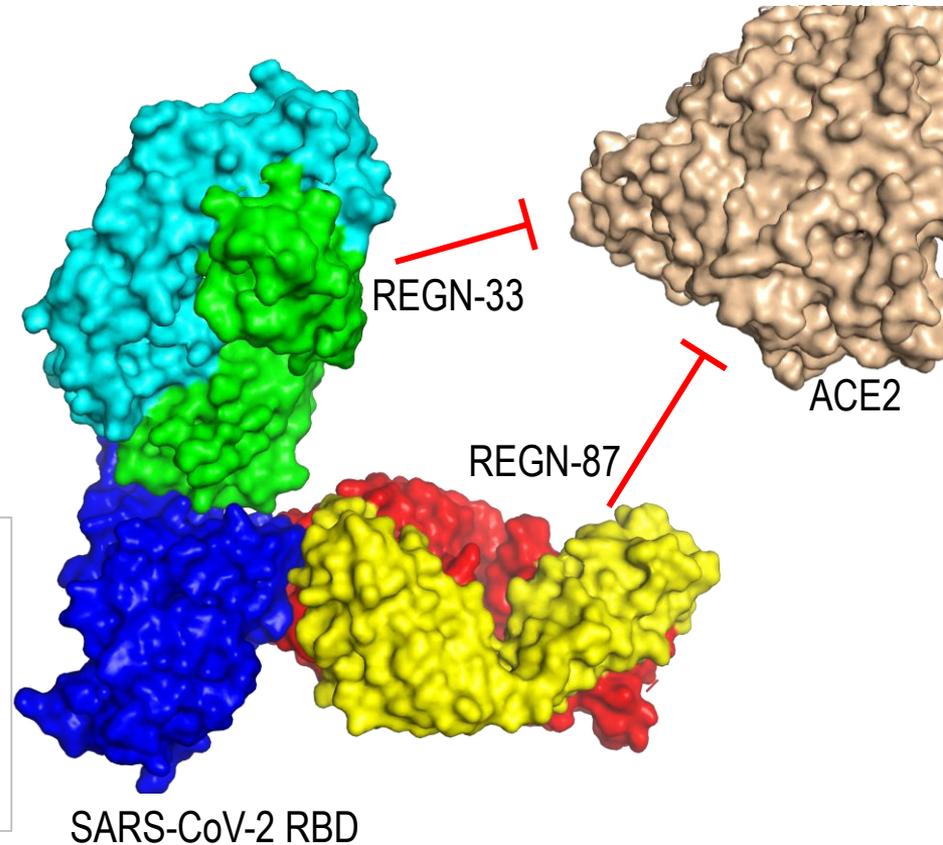


Figure is derived from a 3.9 Å cryo-electron microscopy structure of recombinant SARS-CoV-2 RBD bound to the Fab (fragment antigen-binding) portions of mAb1 and mAb2. Submitted to Science.

ROADMAP TO LEADERSHIP IN ONCOLOGY

Leadership in dermatology

LIBTAYO, first approved anti-PD-1 in **CSCC**



First-in-class potentially approvable data in **BCC**

Potential expansion to **adjuvant /neo-adjuvant CSCC**

Compete in lung

Monotherapy OS benefit in **NSCLC***

Chemo-combination study to be fully enrolled

Execute on novel pipeline & combinations

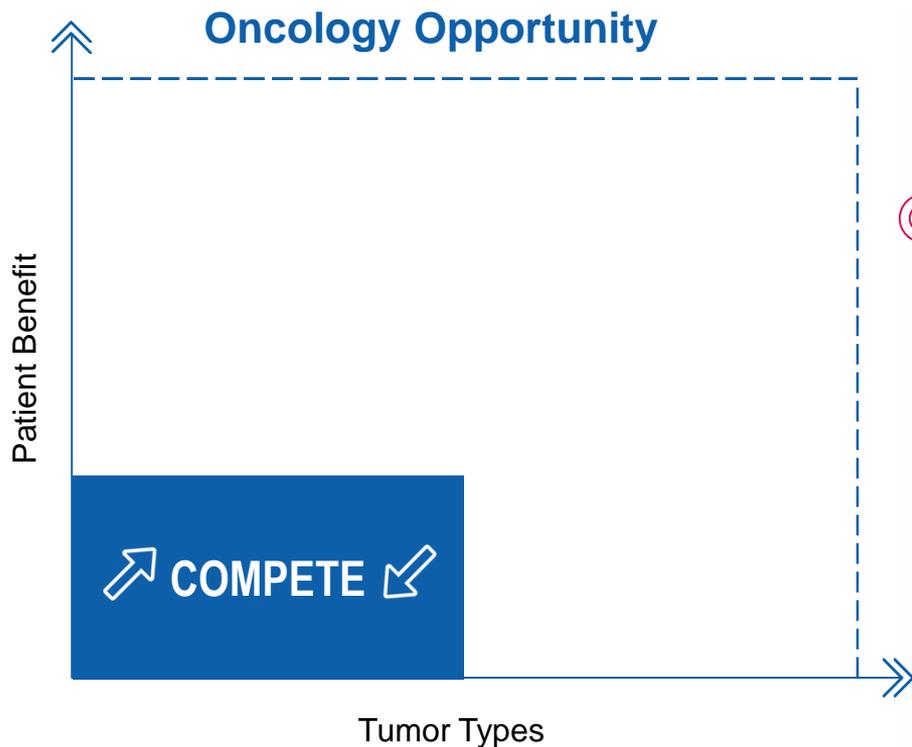
10+ therapies in development for multiple cancer types:

- **Libtayo as foundation** for one set of combination opportunities
- **xCD3 Bispecifics** as foundation for another set of combination opportunities
- **Both can be combined** with each other or '**CoStim BiSpecs**'

Proof-of-concept achieved in two CD3 **BiSpecific programs**

- '**CoStim BiSpecs**' now in clinic

ONCOLOGY STRATEGY: ASPIRE TO COMPETE, ENHANCE, EXTEND



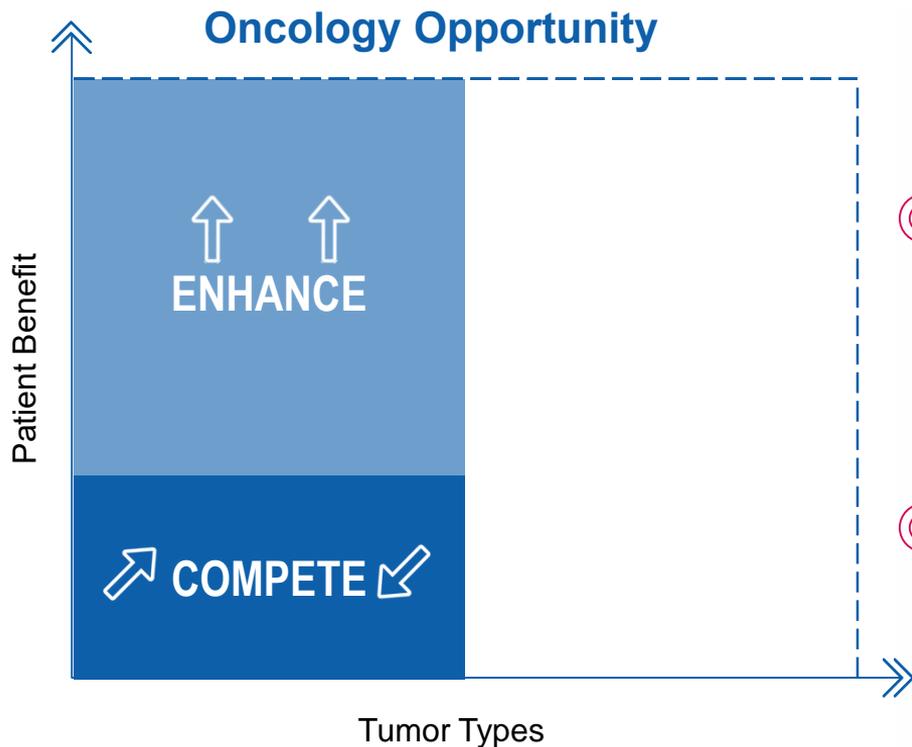
COMPETE: LIBTAYO in tumors “responsive” to PD-1 monotherapy (e.g., skin & NCSLC)

- PD-(L)1 market: >\$21Bn, +42% YoY growth*



*Based on annual sales data for approved PD-(L)1 agents in 2019 and 2018
The use of Libtayo in any indication other than advanced CSCC is investigational and has not been fully evaluated by regulatory authorities

ONCOLOGY STRATEGY: ASPIRE TO COMPETE, ENHANCE, EXTEND



COMPETE: LIBTAYO in tumors “responsive” to PD-1 monotherapy (e.g., skin & NCSLC)

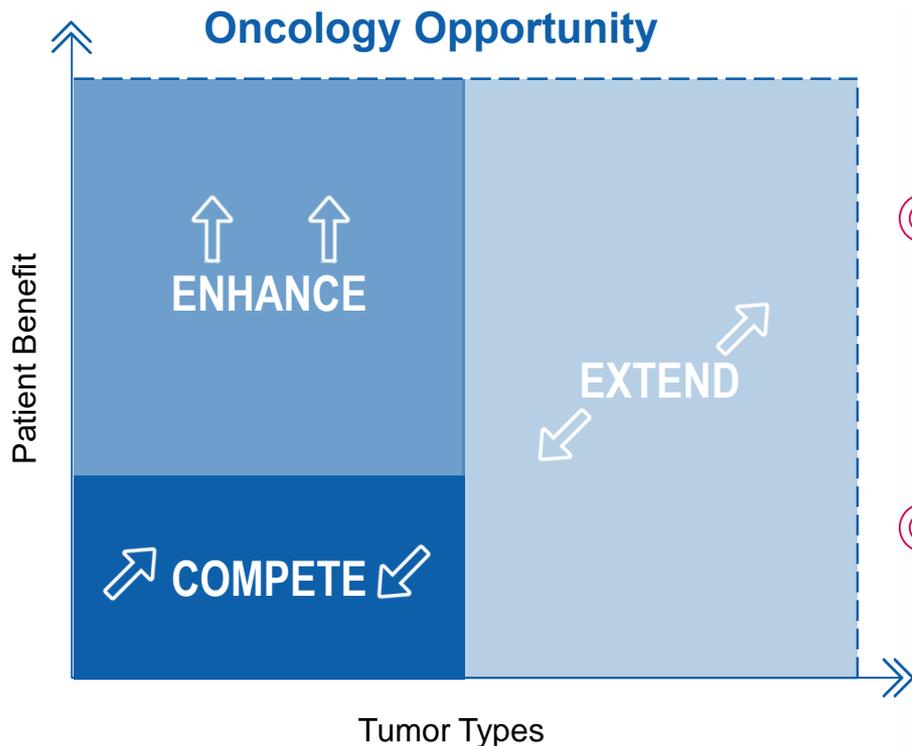
- PD-(L)1 market: >\$21Bn, +42% YoY growth*

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

- Studying addition of novel therapeutics to LIBTAYO to “enhance” responsiveness for these tumors
...e.g., other Checkpoints, xCD3 BiSpecs, CoStims, peptide/RNA/DNA/viral ‘vaccine adjuvants’, etc...

*Based on annual sales data for approved PD-(L)1 agents in 2019 and 2018
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ONCOLOGY STRATEGY: ASPIRE TO COMPETE, ENHANCE, EXTEND



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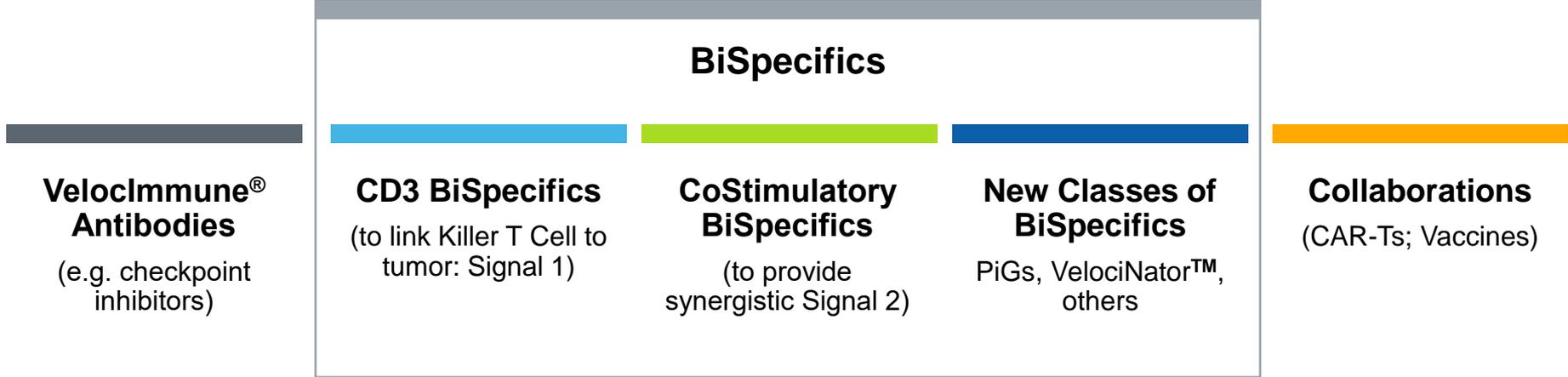
EXTEND: For tumor settings with limited response to checkpoint inhibition

- Studying addition of novel therapeutics to LIBTAYO to “extend” responsiveness to these tumors
...e.g., other Checkpoints, xCD3 BiSpecs, CoStims, peptide/RNA/DNA/viral ‘vaccine adjuvants’, etc...
- Can also combine CD3 BiSpecs and CoStim BiSpecs in these settings to “extend” responsiveness to these tumors

*Based on annual sales data for approved PD-(L)1 agents in 2019 and 2018
The use of Libtayo in any indication other than advanced CSCC is investigational and has not been fully evaluated by regulatory authorities

REGN ONCOLOGY BUILDING BLOCKS CREATE COMBINATORIAL FLEXIBILITY:

LIBTAYO as foundation for one set of combos, **CD3 BiSpecs** as foundation for other set of combos



PD-1 (LIBTAYO)

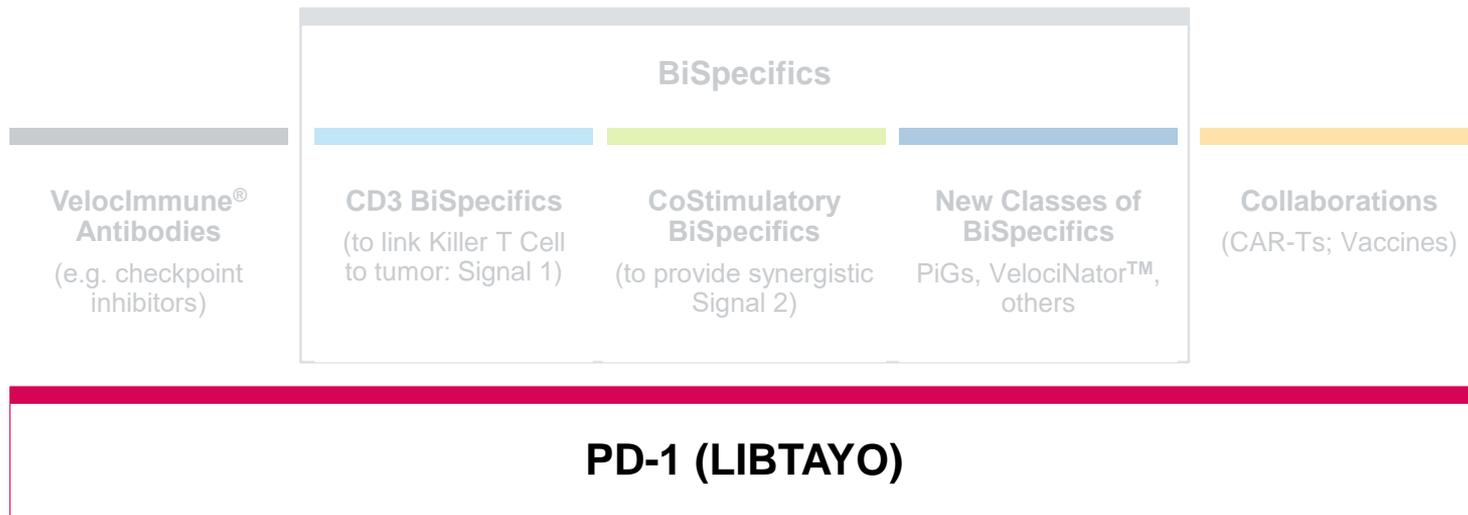


LIBTAYO Update

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



AGENDA



ESTABLISH LIBTAYO AS A FOUNDATION IN ONCOLOGY

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

LEAD in dermato-oncology

CSCC: FIRST-IN-CLASS

- First PD-(L)1 approval for **advanced CSCC**:

- ORR: 51%*
- CR: 20%*

From Ph1 trial initiation to FDA approval: ~3.5 years

- **Neoadjuvant CSCC**:

Pilot study[^]:

- ORR: 70%
- CR: 55%

Ongoing Ph2 in neoadjuvant CSCC and Ph3 in adjuvant CSCC

BCC: FIRST-IN-CLASS

- **Advanced BCC**:

- ORR: 21-29%
- ~85% of responses ongoing after 12 months

Regulatory submission planned for 2H20

COMPETE

NSCLC

- Monotherapy in **PD-L1-high 1L NSCLC** vs. SOC chemotherapy:

- Overall ITT: **HR: 0.676**
- Modified ITT: **HR: 0.566**

Regulatory submission planned for 2H20

- Chemotherapy combination in **all PD-L1 1L NSCLC**:
 - full enrollment in 2H20

ENHANCE & EXTEND

Investigational Combinations

Enhance and Extend responsiveness to anti-PD-1 class:

- Combinations with CD3 and CD28 BiSpecifics as well as other immunomodulatory antibodies
- Novel combinations with vaccines, oncolytic viruses and other modalities

CSCC – Cutaneous Squamous Cell Carcinoma; BCC – Basal Cell Carcinoma; NSCLC – Non-Small Cell Lung Cancer; ORR – Objective Response Rate; CR – Complete Response; SOC – Standard Of Care; ITT – Intention to treat; HR – Hazard Ratio

The use of Libtayo in any indication other than advanced CSCC is investigational and has not been fully evaluated by regulatory authorities

* Updated ASCO 2020 data: Metastatic CSCC, Group 1 with longest available follow-up
[^] Gross et al., ESMO 2019

CSCC ASCO DATA: LONGER FOLLOW-UP DEMONSTRATES IMPROVEMENT IN COMPLETE RESPONSE RATE AND DURABILITY OF RESPONSES

Continuing to build a robust data set in CSCC

ASCO Update

Advanced CSCC*:

- ORR: 51%
- CR: 20%

Increase in CRs over time

mDOR still not reached

Est. mPFS: 18.3 mo[^]

mOS has not been reached
Est. OS at 24 mo: 73.3%

Earlier lines (pilot study)

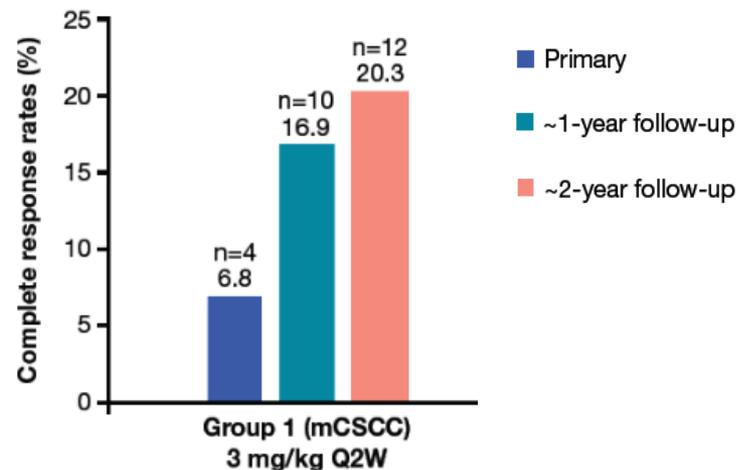
Neoadjuvant CSCC†:

- ORR: 70%
- CR: 55%

Ongoing trials:

- Ph2 neoadjuvant CSCC
- Ph3 adjuvant CSCC

Complete response rates in mCSCC



ASCO 2020 Poster Discussion 10018
ASCO 2020 CSCC Press Release

CSCC – Cutaneous Squamous Cell Carcinoma; mCSCC – metastatic CSCC;
ORR – Objective Response Rate; CR – Complete Response; mDOR – median
duration of response; mPFS – median Progression Free Survival; mOS – median
Overall Survival

* Metastatic CSCC, Group 1 with longest available follow-up; ^ All patients

† Gross et al., ESMO 2019

The use of Libtayo in any indication other than advanced CSCC is investigational and has not
been fully evaluated by regulatory authorities

LIBTAYO IS THE FIRST AGENT TO DEMONSTRATE CLINICALLY MEANINGFUL RESPONSES IN 2L ADVANCED BASAL CELL CARCINOMA (BCC)

Expanding the footprint of LIBTAYO in dermatology

Significant unmet medical need in 2L advanced BCC patients post HHI (hedgehog inhibitors)

Regulatory submission 2H20

Advanced BCC – Ph2 registration intent results:

	N	ORR	Est. DOR >1 year	Durable DCR (≥6 months)
Locally advanced	84	29%	in 85% responders	60%
Metastatic*	28	21%	in 83% responders	46%

Screening

15 Jan 2018



12 Apr 2018



3 Feb 2020



79 year old man with locally advanced disease progression on prior Vismodegib (HHI)

1L NSCLC: LIBTAYO MONOTHERAPY DEMONSTRATED A CLINICALLY MEANINGFUL AND SIGNIFICANT SURVIVAL BENEFIT OVER CHEMOTHERAPY

Goal: become competitive in the major anti-PD-1 opportunity – Lung Cancer

LIBTAYO monotherapy in PD-L1-high 1L NSCLC:

OS in-line with market leading anti-PD-1

LIBTAYO in combination with chemotherapy: full enrollment in 2H20

If positive, LIBTAYO would have the potential to benefit all 1L NSCLC patients regardless of PD-L1 status and histology

Interim analysis in 2021

Overall ITT analysis

N=710

OS HR: **0.676** (p=0.002)

mITT* analysis (PD-L1 ≥50%)

N=563

OS HR: **0.566** (p=0.0002)

Regulatory submission 2H20

EXTERNAL CLINICAL-STAGE COMBINATIONS WITH LIBTAYO

Collaborator	MOA	Indication	Status/Phase	ASCO 2020
 VYRIAD	VSV based oncolytic virus	NSCLC, melanoma, HCC or endometrial carcinoma	Initiating/ Ph2	<u>TPS3161</u>
 ISA Pharmaceuticals	HPV16 long peptide vaccine	Squamous Cell Carcinoma of the Head and Neck; Cervical Cancer	Ongoing/Initiating/ Ph2	
 Replimune [®]	HSV based oncolytic virus	Cutaneous Squamous Cell Carcinoma	Ongoing/ Ph2	
 BIONTECH	mRNA immunotherapy	Prostate (high risk localized)	Ongoing/ Ph1/2	
 inovio PHARMACEUTICALS	DNA immunotherapy	Glioblastoma	Ongoing/ Ph2	Poster Discussion <u>2514</u> LIBTAYO combination: improved OS12, awaiting OS18
 Ziopharm ONCOLOGY	Adenoviral vector expressing IL-12	Glioblastoma	Ongoing/ Ph2	
 SILLAJEN	Vaccinia based oncolytic virus	Metastatic / unresectable Renal Cell Carcinoma	Ongoing/ Ph1b	



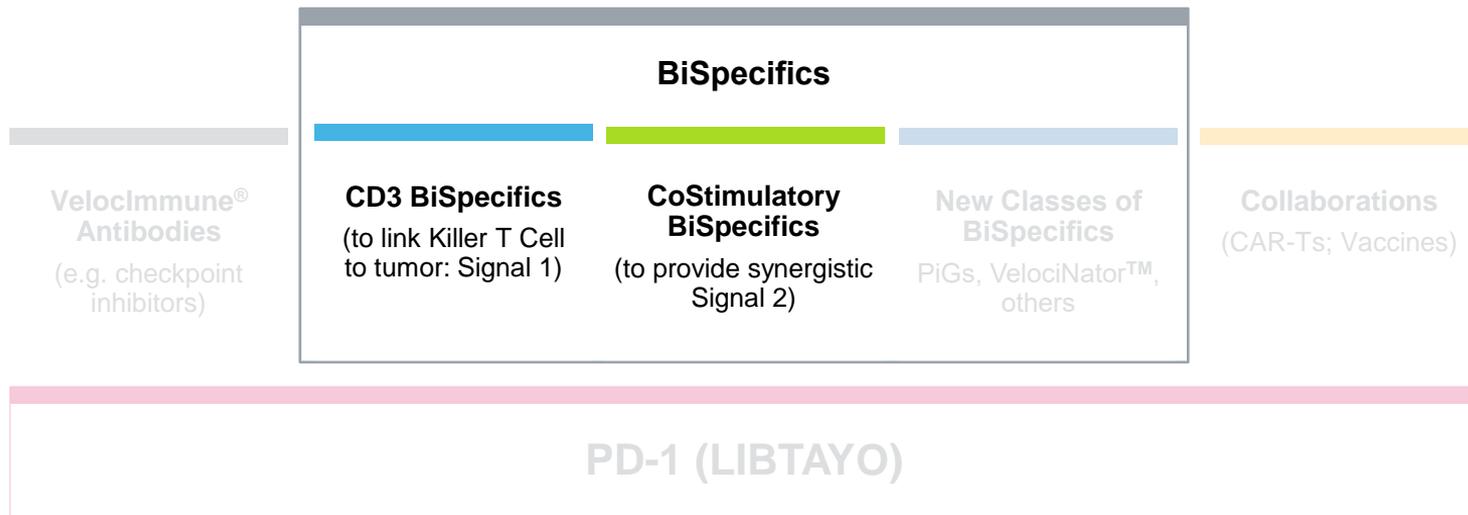
**Powerful Pipeline for
Rational Combinations**

Hematological tumors

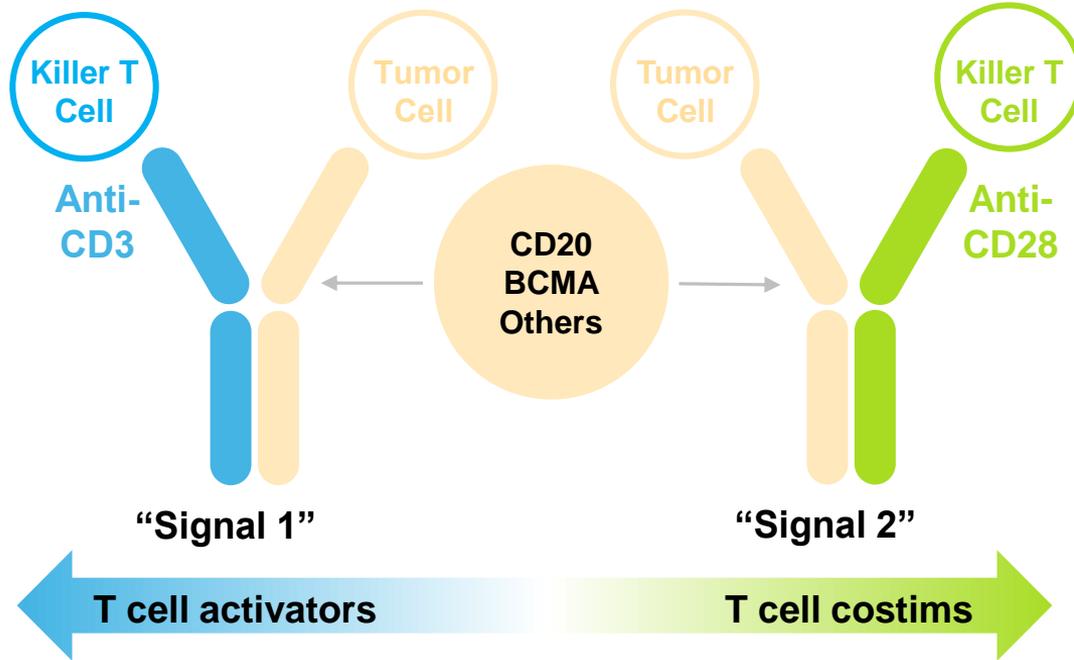
Andres Sirulnik, MD, PhD
SVP, Translational & Clinical Sciences Hematology



AGENDA



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, 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

REGN1979: FIRST REGN CD3 BISPEC DEMONSTRATES SUBSTANTIAL CLINICAL ACTIVITY

REGN1979 is currently in phase 1 and potentially pivotal phase 2 studies

FIH results are encouraging

American Society of Hematology (ASH) – December 2019 Data

R/R Follicular Lymphoma

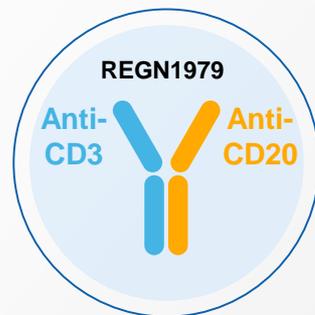
- **ORR=95%, CR=77%**
- N=22, doses 5-320 mg
- mPFS est: 11.4 mo (6.7-NE)

R/R DLBCL (CAR-T naïve)

- **ORR=71%, CR=71%**
- N=7, doses 80-320 mg

R/R DLBCL (post-CAR-T)

- **ORR=50%, CR=25%**
- N=12, doses 80-320 mg



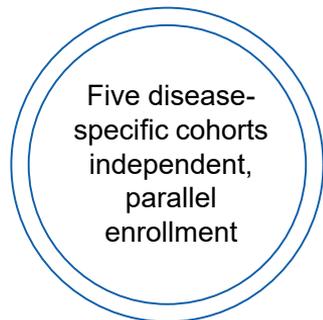
- Encouraging durability of responses
- *Ongoing potentially pivotal program in each of these settings*

REGN1979 – POTENTIALLY PIVOTAL PROGRAM IN MULTIPLE B-NHL SUBTYPES

Phase 1 cohort (NCT02290951)

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

Phase 2 cohorts (NCT03888105)



Five disease-specific cohorts independent, parallel enrollment

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

U.S. est. annual treatment eligible patients*:

~1K

~4K

~3.5K

~1.6K

~3K

REGN1979 – FUTURE DEVELOPMENT PLAN; MILESTONES

- ✓ First patients dosed in multiple pivotal cohorts, including FL and DLBCL

UPCOMING

Continue Ph1 REGN1979 + LIBTAYO combination*

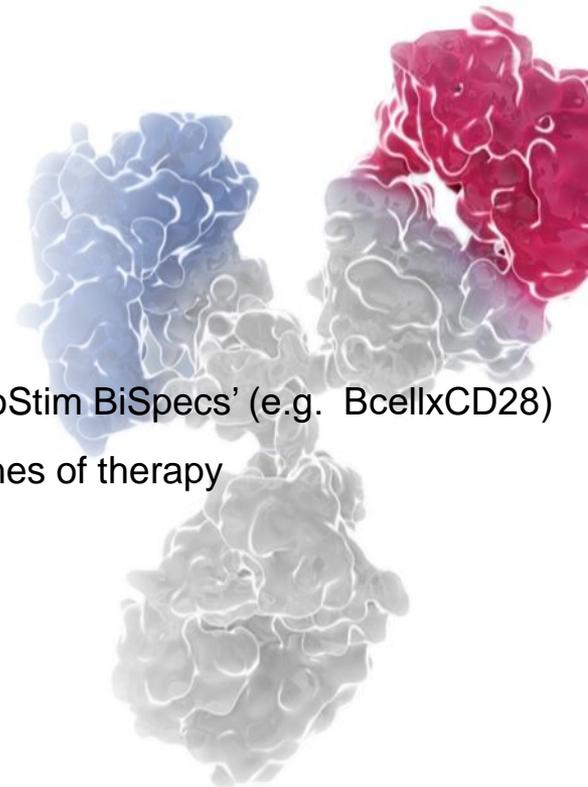
Explore combinations with SOC and novel internal agents, including 'CoStim BiSpecs' (e.g. BcellxCD28)

Broaden pivotal development program in DLBCL/FL, including earlier lines of therapy

Test subcutaneous formulation

Complete enrollment for Ph2 trial (2021)

Potential BLA submission (2022)

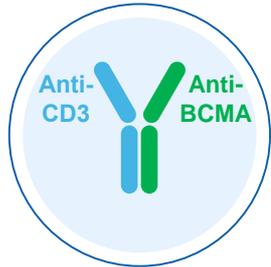


* Currently on partial clinical hold
SOC – Standard of Care; TAA – Tumor Associated Antigen; BLA – Biologic License Application (US FDA)

BCMAxCD3 – ENCOURAGING INITIAL ANTI-TUMOR ACTIVITY; ANSWERING IMPORTANT CLINICAL QUESTIONS

REGN5458 our first BCMAxCD3 bispecific to enter clinic

Ph1 update from ASH – Dec 2019



R/R Multiple Myeloma

N=7*, doses 3-6 mg

At 6mg dose (n=4):

- ORR=3/4 patients (75%)
- MRD-neg=2/4 patients (50%)

Dose escalation ongoing; MTD not reached

Very encouraged by safety, depth & sustained activity

REGN5459 our second BCMAxCD3; lower CD3 arm affinity

Early in Ph1 dose escalation, encouraged by emerging data

Evaluating if different CD3 affinity results in different clinical outcomes – to our knowledge, no such data are available

*Median of 7 lines of prior systemic therapy, including anti-CD38; Patients with primarily medullary and secretory disease
R/R – Relapsed/ Refractory (heavily pre-treated); MRD – Minimal Residual Disease; MTD – Maximal Tolerated Dose

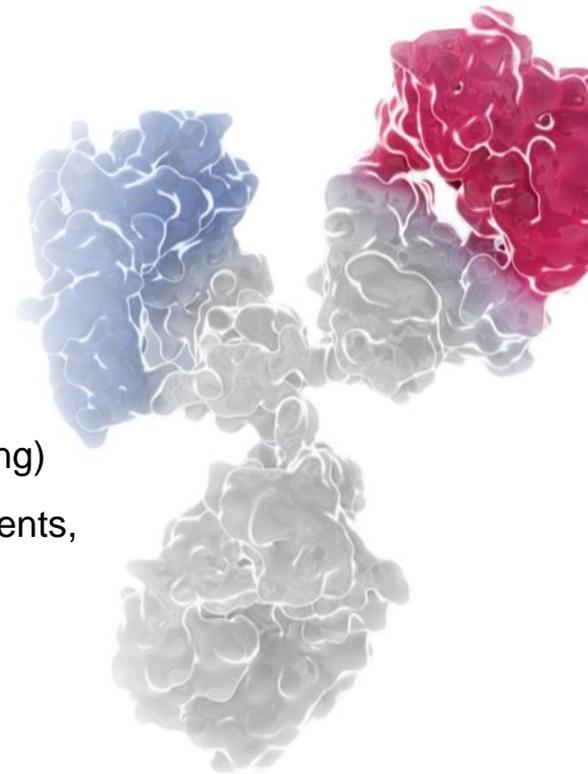
BCMAxCD3 – FUTURE DEVELOPMENT PLAN; MILESTONES

UPCOMING

Provide updates on Ph1s dose escalation (ASH 2020)

Initiate potentially pivotal studies in various MM stages (planning ongoing)

Explore combinations with SOC (e.g., anti-CD38) and novel internal agents, including 'CoStim BiSpecs', PlasmaCellxCD28 (planning ongoing)



SUMMARY OF HEMATOLOGICAL TUMOR THERAPIES IN THE CLINIC, AND ONES TO COME

	MONOTHERAPY		INDICATIONS	STATUS
ONGOING	REGN1979 (CD20xCD3)		R/R Follicular Lymphoma	Enrollment ongoing
	REGN1979 (CD20xCD3)		R/R DLBCL	Enrollment ongoing
	REGN1979 (CD20xCD3)		R/R DLBCL: post-CAR-T	Enrollment ongoing
	REGN5458/9* (BCMAxCD3)		Multiple myeloma	Dose escalation ongoing
	COMBINATIONS			
	REGN1979 (CD20xCD3)	LIBTAYO*	Lymphoma	Resubmit modified study design to FDA in 2H20 [^]
UPCOMING	REGN1979 (CD20xCD3)	+	B cell/CD28 costim	IND filing in 2H20
	REGN5458/9* (BCMAxCD3)	+	Plasma cell/CD28 costim	Multiple myeloma
	REGN1979 (CD20xCD3)	+	Standard of Care	B-NHL
	REGN5458/9* (BCMAxCD3)	+	Standard of Care	Multiple myeloma

VelocImmune® Antibodies

Costim BiSpecifics

CD3 BiSpecifics

Anti-PD-1



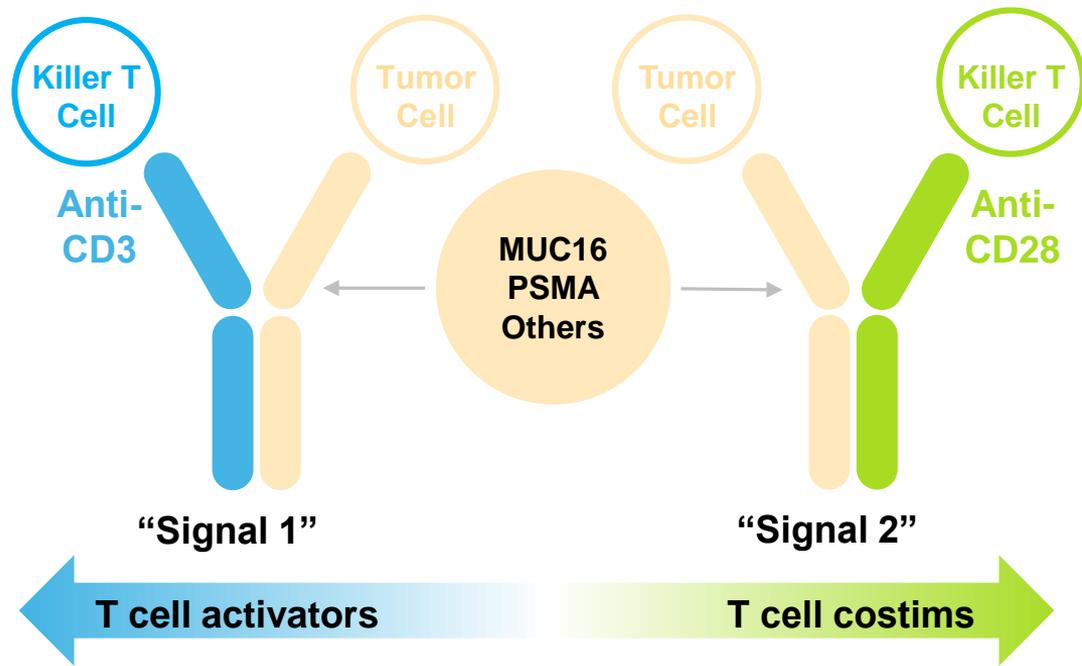
Israel Lowy, MD, PhD
SVP, Translational Sciences and Oncology

**Powerful Pipeline for
Rational Combinations**

Solid tumors



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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

REGN4018 (MUC16xCD3) – OUR FIRST CD3 BISPECIFIC IN SOLID TUMORS

Biologic Rationale:
PD-1 monotherapy is not effective in ovarian cancer, therefore our strategy is to “extend” beyond checkpoint blockade

MUC16 is widely expressed on the majority of ovarian tumors, as well as others (pancreatic, endometrial)

CA-125 levels arise from cleaved MUC16

Our dose escalation in MUC16xCD3 monotherapy is proceeding without any dose-limiting toxicities to date

Our interest in combinations are informed by experiments across our IO portfolio, including published preclinical data on MUC16xCD3

This is an advantage of REGN’s diverse toolkit that allows us to “plug and play” with multiple combinations

Have initiated combination cohorts with LIBTAYO

MUC16xCD28: FIH trial will test combination with either MUC16xCD3 or LIBTAYO

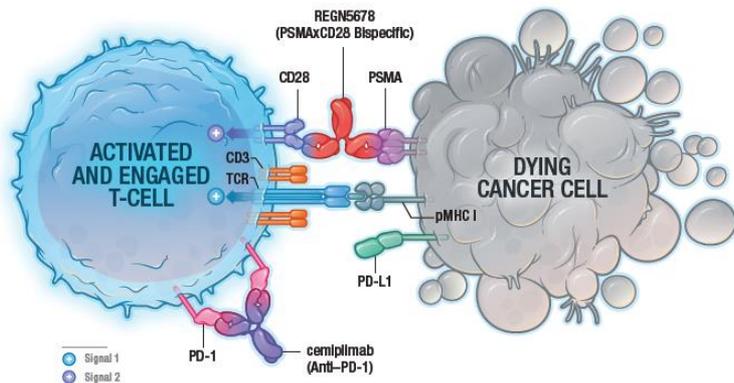


REGN5678 (PSMAxCD28) – OUR FIRST CD28 BISPECIFIC IN SOLID TUMORS

Biologic Rationale:

PD-1 monotherapy is not effective in prostate cancer; our strategy is to “extend” beyond checkpoint blockade

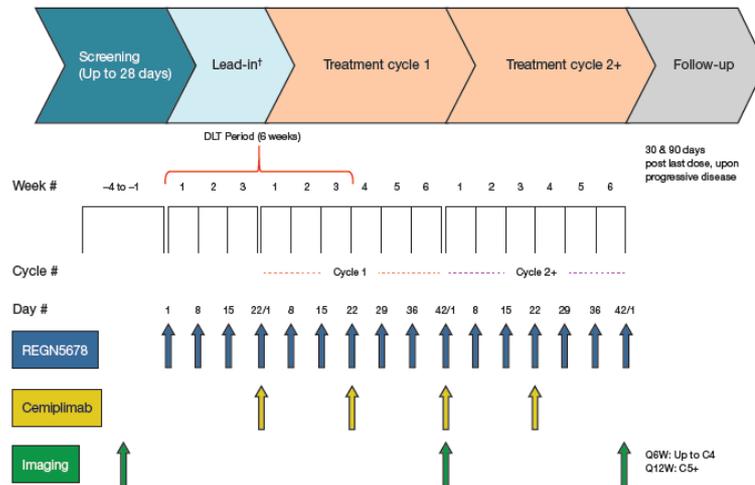
REGN5678 mechanism of action:



PD-1, programmed cell death-1; PD-L1, programmed death-ligand 1; pMHC I, peptide (antigen)-bound major histocompatibility complex class I; TCR, T-cell receptor.

Dose-escalation is underway in combination with LIBTAYO

No evidence of CD28 superagonism

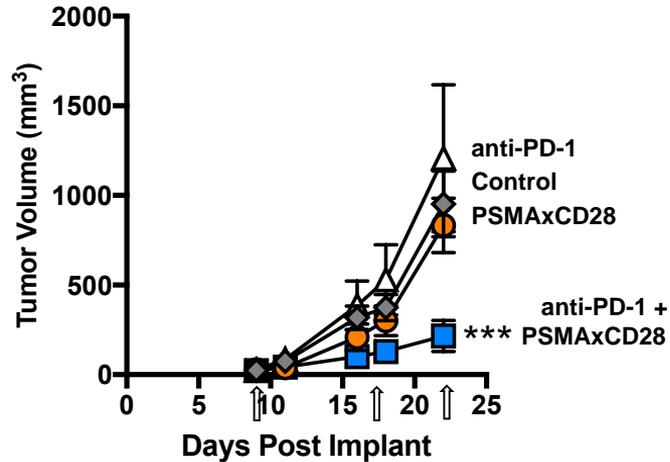


*Dose escalation cohorts will receive a 3-week monotherapy lead-in. Dose expansion cohorts are not expected to receive the 3-week monotherapy lead-in of REGN5678. C, cycle; DLT, dose-limiting toxicity; Q6W, every 6 weeks, Q12W, every 12 weeks.

PSMA: COSTIM COMBINATORIAL POTENTIAL WITH LIBTAYO NEW PROMISING PRECLINICAL DATA

anti-PD-1 + PSMAxCD28

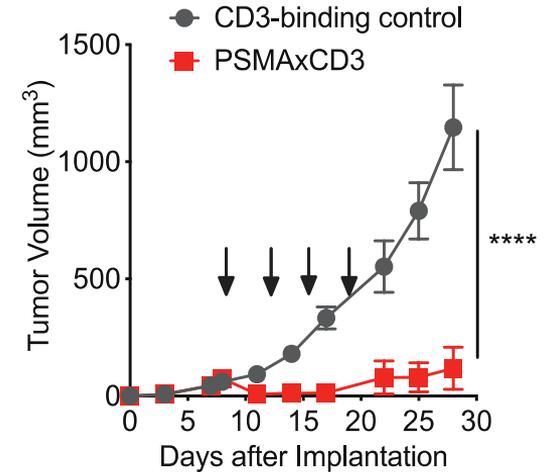
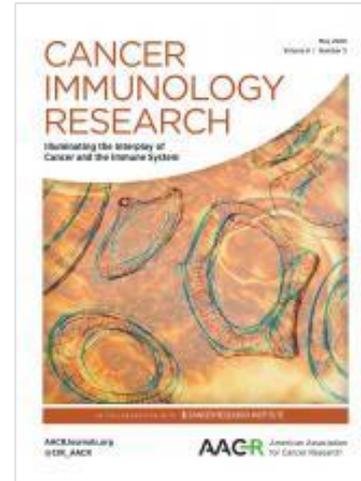
syngeneic humanized prostate cancer mouse model



In 2019, first-in-class costim PSMAxCD28 entered clinical development; planning to advance several other CD28 BiSpecific antibodies into the clinic in 2020

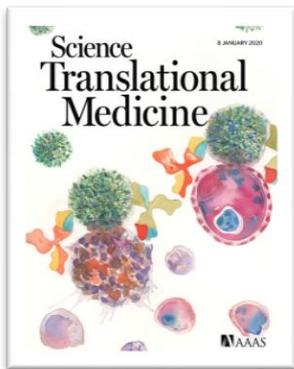
PSMAxCD3

induces tumor regression in a syngeneic humanized prostate cancer mouse model



Chiu, Danica, et al. "A PSMA-targeting CD3 bispecific antibody induces antitumor responses that are enhanced by 4-1BB costimulation." *Cancer Immunology Research* (2020)

COSTIMS: COMBINATORIAL POTENTIAL WITH CD3 BISPECIFICS SHOWS ENHANCEMENT IN PRECLINICAL TUMOR MODELS

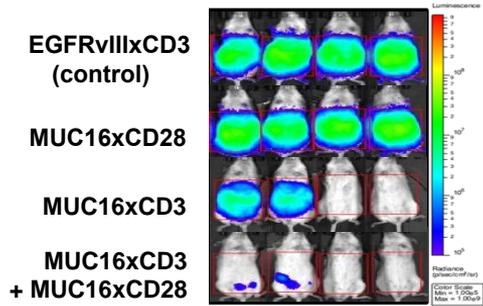
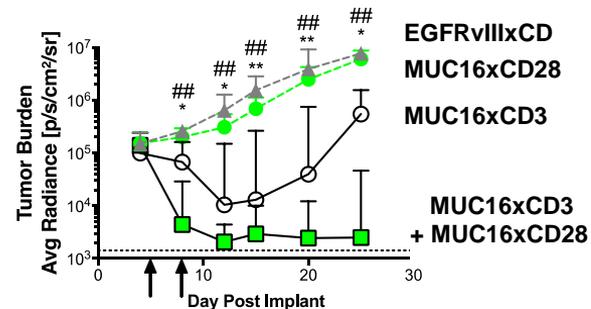


Our CD28 costimulatory BiSpecifics activate T cells only when they are bridged to cancer cells and after having received the first “recognition” signal from the CD3 engagement

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

MUC16xCD28 in the clinic: FIH trial will test combination with either MUC16xCD3 or LIBTAYO

MUC16xCD3 + MUC16xCD28 xenogeneic ovarian tumor mouse model



SUMMARY OF SOLID TUMOR COMBINATIONS IN CLINIC, AND ONES TO COME

	COMBINATIONS			INDICATIONS	STATUS
ONGOING	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
UPCOMING	REGN5668 (MUC16xCD28)	+	REGN4018* / LIBTAYO*	Ovarian Cancer	IND cleared
	REGN6569 (GITR)	+	LIBTAYO*	Solid tumors	IND cleared
	TAAxCD28	+	LIBTAYO*	Solid tumors	IND filing in 2H20
	TAAxCD3	+	LIBTAYO*	Prostate cancer	IND filing in 2021

VelocImmune® Antibodies

Costim BiSpecifics

CD3 BiSpecifics

Anti-PD-1



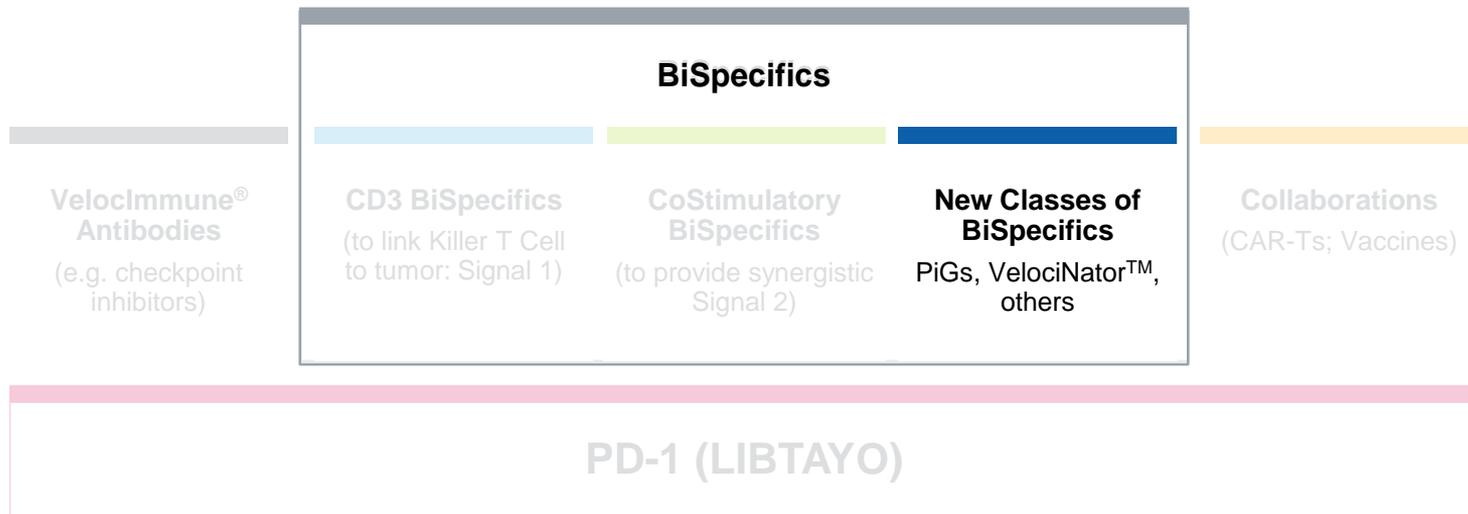
Powerful Pipeline for Rational Combinations

New classes

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



AGENDA

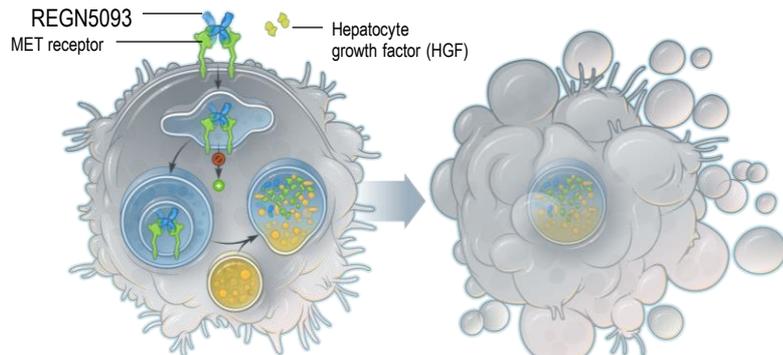


METxMET: A NOVEL MECHANISM OF ACTION IN THE CLINIC

METxMET bispecific induces apoptosis of tumor cells

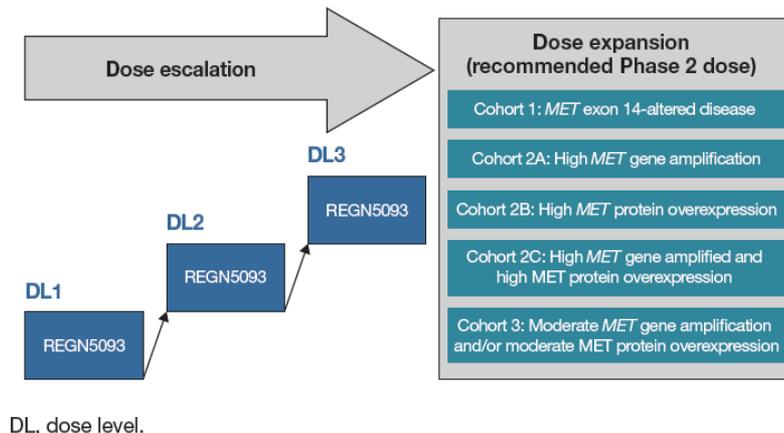
REGN5093 binds to MET receptors and prevents their interaction with HGF, a protein used by cancer cells to regulate cell growth, and then traffics the complex to endosomes for degradation

Cancer cell undergoes apoptosis due to the disruption in cell-survival signaling caused by REGN5093

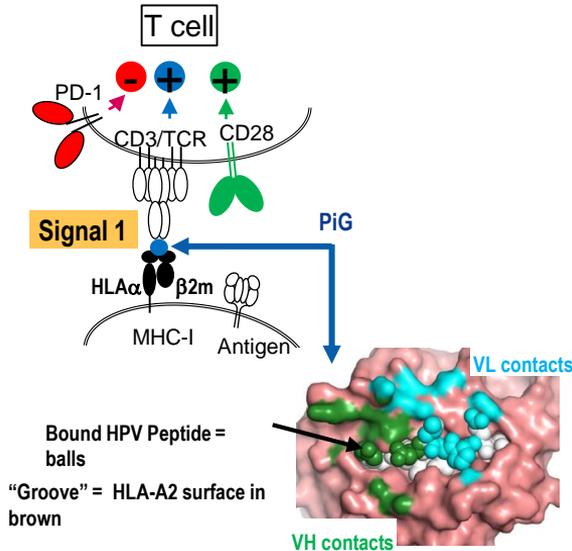


METxMET Ph1 dose-escalation is underway

Figure 3. Dose escalation and dose expansion



PEPTIDE-IN-GROOVE (PIG) TARGETS: T CELL ACTIVATION IS DRIVEN BY HIGHLY SPECIFIC PEPTIDE-HLA/TCR INTERACTIONS THAT CAN BE UTILIZED TO FIGHT CANCER



Bound HPV Peptide = balls
 "Groove" = HLA-A2 surface in brown

Structure of REGN PiG Ab in contact with HPV peptide in HLA-A2
VH and VL Variable domains recognize part peptide and part groove.

Peptide-in-Groove (PiG)

PiGs are short peptides loaded into HLA and presented on the surface of cells.

Peptides can be from any protein in the cell (cytosolic loaded into MHC I, vesicular loaded into MHC II)

TCRs on T cells recognize specific PiGs (CD8+ T cells recognize MHC I, CD4+ T cells recognize MHC II)

Cancer: The majority of tumor-specific proteins are intracellular and inaccessible to traditional Abs, but presented as PiGs

REGN PiGs:

REGN has developed Mass Spectrometry methods to mine the HLA peptidome and cutting edge tech to generate PiG reagents

We have generated **antibodies, TCRs, CARs, etc.** that **recognize PiGs** to direct T cell killing of target cells.

We have also generated peptide/HLA reagents that **stimulate TCRs**, resulting in PiG-specific T cell activation

POWERFUL PIPELINE FOR RATIONAL COMBINATIONS

		BiSpecifics			
			Costims	New Classes	
	VelocImmune® Antibodies	CD3 BiSpecifics	BiSpecifics		Collaborations
EARLY DEVELOPMENT	REGN3767 (LAG-3) Solid/hematologic cancers	REGN5458* (BCMAxCD3) Multiple myeloma	REGN5678 (PSMAxCD28) Prostate cancer		ISA101b + LIBTAYO (ISA) HNSCC
	REGN6569 (GITR) Solid tumors	REGN5459* (BCMAxCD3) Multiple myeloma	REGN5668 (MUC16xCD28) Ovarian cancer		Voyager-V1 + LIBTAYO (Vyriad) Solid tumors
		REGN4018* (MUC16xCD3) Ovarian cancer	REGN5093 (METxMET) MET-altered NSCLC		
			PiG (Peptide in HLA Groove)† Solid tumors		
POTENTIALLY PIVOTAL		REGN1979 (CD20xCD3) B cell NHL			RP1 + LIBTAYO (Replimune) CSCC
	LIBTAYO* NSCLC	LIBTAYO* BCC	LIBTAYO* Cervical		LIBTAYO* Adjuvant CSCC
APPROVED	LIBTAYO* CSCC				

Additional BiSpecifics and combinations expected to enter the clinic in 2020

SUMMARY OF COMBINATIONS IN THE CLINIC, AND ONES TO COME

	COMBINATIONS		INDICATIONS	STATUS	
ONGOING	REGN1979 (CD20xCD3)	+	LIBTAYO*	Lymphoma	Resubmit modified study design to FDA in 2H20 [^]
	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
UPCOMING	REGN5668 (MUC16xCD28)	+	REGN4018* / LIBTAYO*	Ovarian Cancer	IND cleared
	REGN6569 (GITR)	+	LIBTAYO*	Solid tumors	IND cleared
	TAAxCD28	+	LIBTAYO*	Solid tumors	IND filing in 2H20
	REGN1979 (CD20xCD3)	+	B cell/CD28 costim	B-NHL	IND filing in 2H20
	REGN5458/9* (BCMAxCD3)		Plasma cell/CD28 costim	Multiple myeloma	
	TAAxCD3	+	LIBTAYO*	Prostate cancer	IND filing in 2021
	REGN1979 (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



Marion McCourt
SVP, Head of Commercial

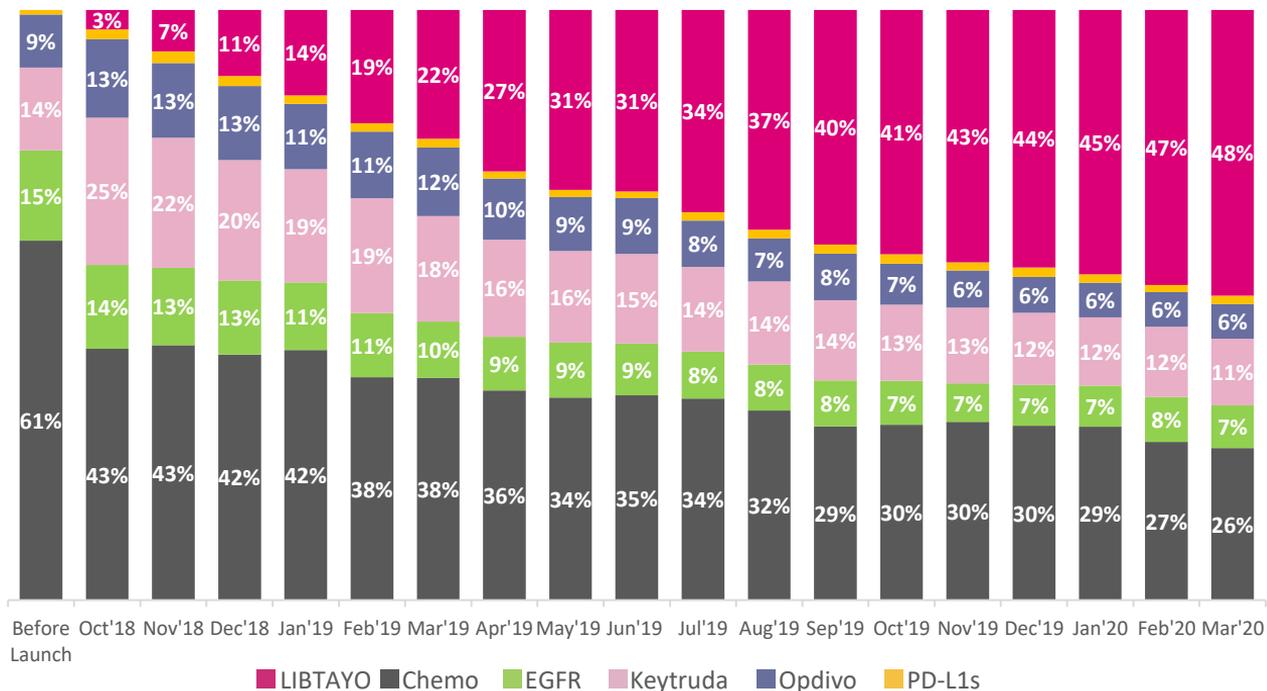
Commercial Excellence



LIBTAYO®: LEADING TREATMENT FOR ADVANCED CSCC IN U.S.



Advanced CSCC – Total U.S. Patient Share by Products†



SIGNIFICANT GROWTH OPPORTUNITIES WITH POTENTIAL NEAR-TERM LAUNCHES

1L NSCLC Monotherapy Opportunity

~20,000 1L advanced NSCLC patients with $\geq 50\%$ PD-L1 expression diagnosed annually in the U.S.

Only one PD-1 antibody has been commercialized as monotherapy in 1L NSCLC

Significant unmet need remains in 1L NSCLC

If approved, LIBTAYO would provide additional product choice for patients, providers and payers

BCC Opportunity

Most common skin cancer in the world; ~3,000 cases of advanced BCC in the U.S.

Potential first-in-class approval

No approved 2L therapies

If approved, demonstrates LIBTAYO's potential in patients with another difficult-to-treat, non-melanoma skin cancer

ONCOLOGY COMMERCIAL ACCOMPLISHMENTS



- ✓ Successfully launched LIBTAYO and built new immuno-oncology advanced CSCC market
- ✓ Created an experienced and competitive commercial organization
- ✓ Well-positioned to apply and extend capabilities for new indications and future products

UPCOMING MILESTONES/CATALYSTS 2020

LIBTAYO: CSCC launch in 6 additional EU countries

Present pivotal NSCLC Data

File for regulatory approval in NSCLC

Present pivotal BCC data

File for regulatory approval in BCC

LIBTAYO + chemo: Complete Ph3 enrollment in 1L NSCLC (2H20)

REGN1979: Complete Ph2 enrollment; initiation of multiple phase 3 trials (next 6-12 months)

BCMMaxCD3: Updated data in multiple myeloma (ASH 2020)

Novel bispecifics to enter clinic (MUC16xCD28, two costims, one CD3)



Q&A PANEL DISCUSSION



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



David Weinreich, MD
SVP, Global Clinical Development



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



Marion McCourt
SVP, Head of Commercial



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