Roche

Roche Pharma Day 2021

Late Stage Pipeline Oncology & Non-malignant Hematology

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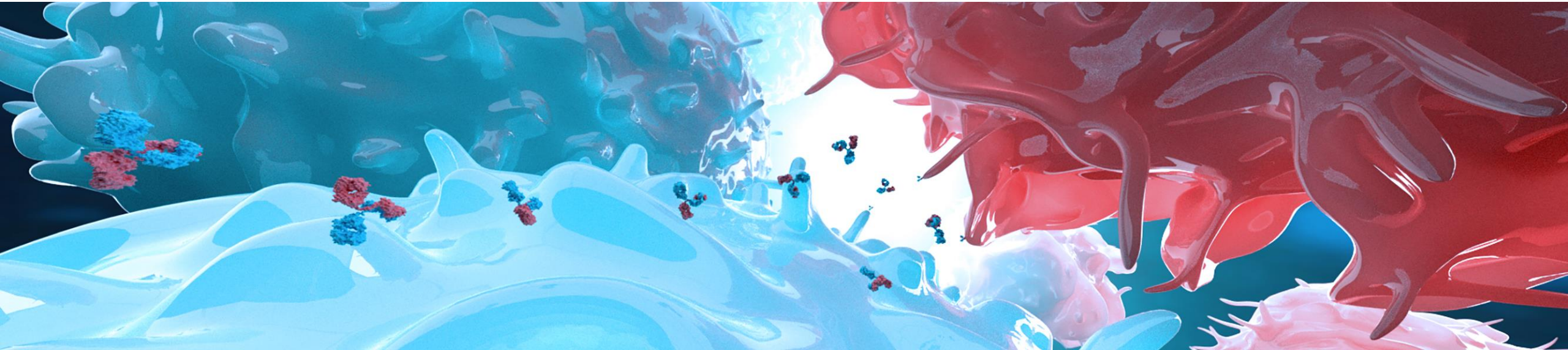
Chief Medical Officer and Head Global Product Development



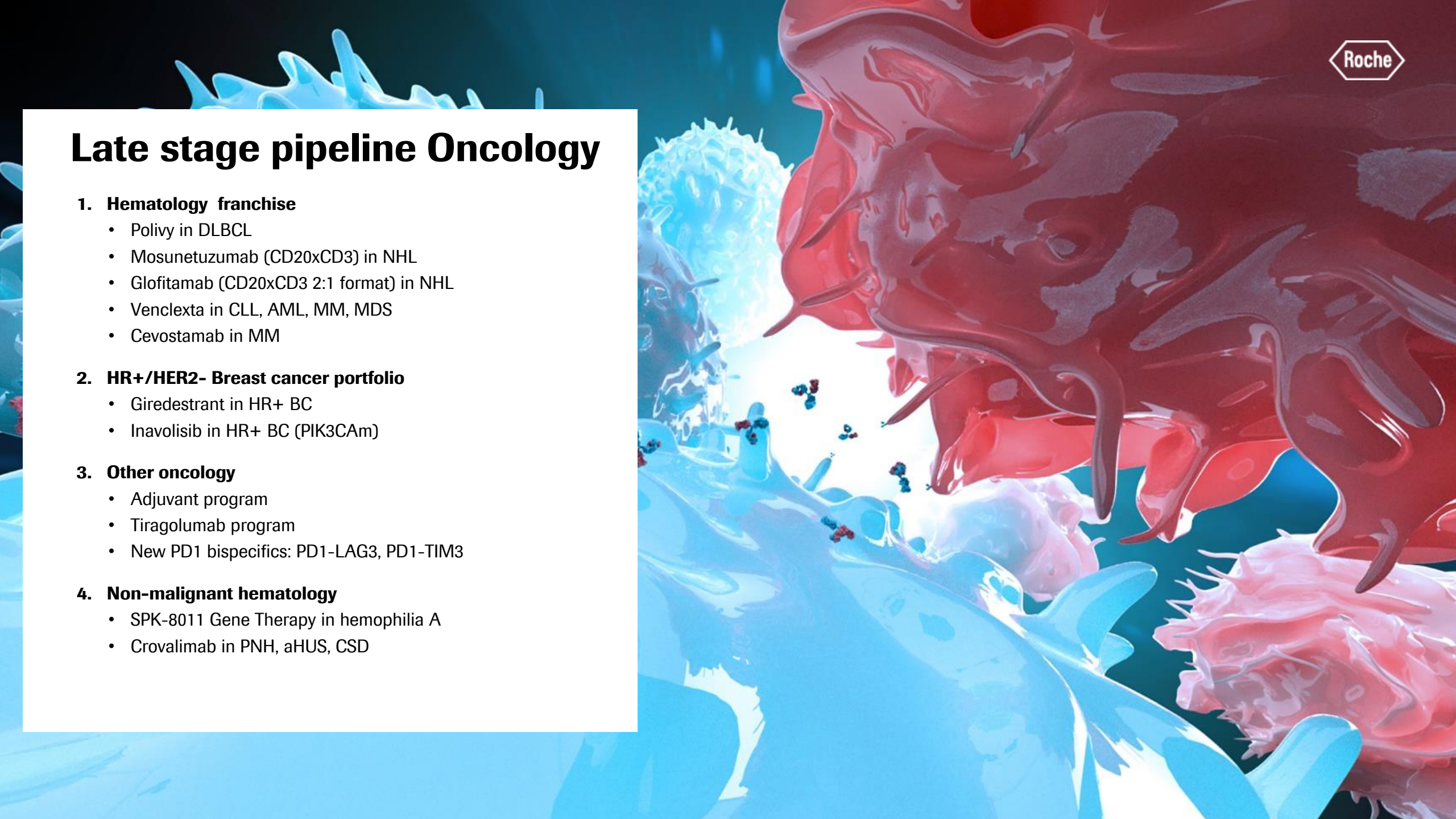
Late stage pipeline Oncology

1. **Hematology franchise**
   - Polivy in DLBCL
   - Mosunetuzumab (CD20xCD3) in NHL
   - Glofitamab (CD20xCD3 2:1 format) in NHL
   - Venclexta in CLL, AML, MM, MDS
   - Cevostamab in MM

2. **HR+/HER2- Breast cancer portfolio**
   - Giredestrant in HR+ BC
   - Inavolisib in HR+ BC (PIK3CAm)

3. **Other oncology**
   - Adjuvant program
   - Tiragolumab program
   - New PD1 bispecifics: PD1-LAG3, PD1-TIM3

4. **Non-malignant hematology**
   - SPK-8011 Gene Therapy in hemophilia A
   - Crovalimab in PNH, aHUS, CSD



Late stage oncology pipeline (Phase II/III)

6 Oncology NMEs with near-term pivotal data

✓ = positive results

= NMEs

= Line extensions

2021

RG7828	**mosunetuzumab** 3L+ FL
RG6013	**Hemlibra** Mild to moderate hemophilia A (EU) ✓
RG6268	**Rozlytrek (BFAST)** 1L NSCLC ROS1+
RG7446	**Tecentriq** adjuvant NSCLC ✓
RG7596	**Polivy** 1L DLBCL ✓

2022

RG6026	**glofitamab** 3L+ DLBCL
RG6058	**tiragolumab + Tecentriq** 1L SCLC
RG6107	**crovalimab** PNH*
RG6171	**giredestrant** 2L/3L ER+/HER2- mBC
RG7440	**ipatasertib + abiraterone** 1L CRPC
RG7446	**Tecentriq** adjuvant RCC
RG7446	**Tecentriq ± chemo** 1L mUC
RG7853	**Alecensa** adjuvant ALK+ NSCLC

2023

RG6058	**tiragolumab + Tecentriq** 1L PD-L1+ NSCLC
RG6114	**inavolisib** 1L HR+ BC
RG7446	**Tecentriq** SC NSCLC
RG7446	**Tecentriq + cabozantinib** 2L NSCLC
RG7446	**Tecentriq + cabozantinib** advanced RCC
RG7446	**Tecentriq + Avastin** adjuvant HCC
RG7446	**Tecentriq** neoadjuvant NSCLC
RG7601	**Venclexta** R/R MM t(11:14)
RG7601	**Venclexta + azacitidine** 1L MDS

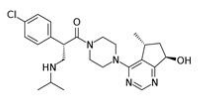
2024 and beyond

RG6354	**rhPTX-2** myelofibrosis
RG7769	**PD1xTIM3** solid tumors
RG7828	**mosunetuzumab + lenalidomide** 2L FL
RG3502	**Kadcyla + Tecentriq** 2L+ HER-2+ PD-L1+ mBC
RG3502	**Kadcyla + Tecentriq** HER-2+ eBC high-risk
RG7446	**Tecentriq + paclitaxel** adjuvant TNBC
RG7446	**Tecentriq** high risk NMIBC
RG7446	**Tecentriq + chemo** adjuvant SCCHN
RG7446	**Tecentriq + capecitabine or carbo/gem** TNBC
RG7446	**Tecentriq** ctDNA+ high-risk MIBC
RG6180	**autogene cevumeran** 1L melanoma
RG6026	**glofitamab + chemo** 2L DLBCL
RG6058	**tiragolumab + Tecentriq** 1L PD-L1+ CC
RG6058	**tiragolumab + Tecentriq** locally advanced esophageal cancer
RG6058	**tiragolumab + Tecentriq** stage III unresectable 1L NSCLC
RG6058	**tiragolumab + Tecentriq** 1L non-sq NSCLC
RG6058	**tiragolumab + Tecentriq** 1L PD-L1+ mSCCHN
RG6058	**tiragolumab+Tecentriq+/- chemo** neoadjuvant/adjuvant NSCLC
RG6139	**PD1xLAG3** solid tumors
RG6171	**giredestrant** 1L ER+/HER2- mBC

Status of planned submissions as of July 22, 2021; * First filing in China

Broadest set of technology platforms applied in Oncology

Small molecules

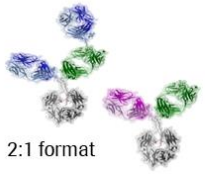


- ipatasertib
- inavolisib
- giredestrant
- KRAS G12C
- TLR7 agonist
- belvarafenib
- SHP2i

Target oncogenes, induce apoptosis, supress tumor growth

- fenebrutinib
- ralmitaront
- GABA Aa5 PAM
- PTH1R agonist
- NLRP3 inhibitor
- Abx MCP
- CpAM
- AT-527

Bi-specifics

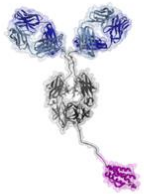


- mosunetuzumab
- glofitamab
- cibisatamab
- Her2 x CD3
- glypican-3 x CD3
- cevostamab
- PD1 x TIM3
- PD1 x LAG3
- TYRP1-CD3

Engage and activate T cells to kill tumour cells

- faricimab
- FIXa x FX
- FGFR1 x KLB
- VEGF x Ang2 Duta

Fusion protein



- PD1-IL2v
- CD19-4-1BBL
- FAP-4-1BBL
- MAGE-A4 ImmTAC
- IL15/IL15Ra-Fc
- FAP-CD40

Amplify immune response

- brain shuttle gantenerumab
- efmarodocokin alfa
- IgG-IL2

mAb

- tiragolumab
- CD25 mAb
- codrituzumab
- CD137

Amplify immune response

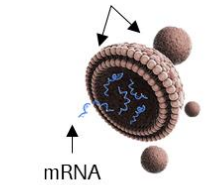
- crovalimab
- gantenerumab
- prasinezumab
- semorinemab
- etrolizumab
- TLR4 mAb
- HtrA1 mAb
- anti-tryptase

Antibody drug conjugate

- preclinic

Targeted toxic payload

Neoantigen vaccines

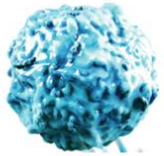


- autogene cevumeran

Patient's neo-antigens for anti-tumour immune response

= Oncology pipeline

Personalized T cells

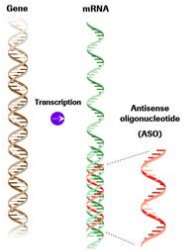


- programmed T cells

Patient's neo-antigens for anti-tumour immune response

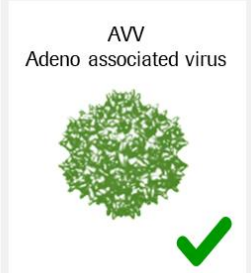
= Products approved

Antisense RNA



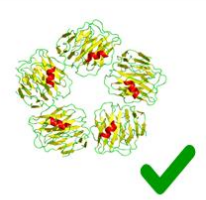
- Factor B ASO
- HBV siRNA
- PDL1 LNA
- UBE3A LNA

Gene therapy



- SPK-8011
- SPK-8016
- SPK-3006
- SPK-7001
- SRP-9001

Recombinant proteins



- rh pentraxin-2

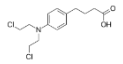
Oncolytic adenovirus

- Type 5 adenovirus

* List of pipeline molecules shown below is not complete; Molecules in the orange box are developed in Oncology

Hematology: Evolving the standard of care in CLL, DLBCL and FL

chemotherapy



1997 Rituxan Rituximab

2013 GAZYVA obinutuzumab injection

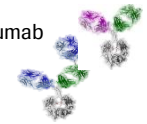
2019 POLIVY polatuzumab vedotin

VENCLEXTA venetoclax tablets

2021/22 filing

mosunetuzumab

glofitamab



Chronic Lymphocytic Leukemia (CLL)

Venclexta chemo free combinations induce deep responses and long treatment-free remissions

SOC	1L	R/R
chemo	clb	benda
R+chemo	R+clb	R+benda
G+chemo	G+clb	
New MOAs	G+Venclexta (FDA BTD)	R+Venclexta (FDA BTD)
CD20x CD3		Ph I/II on-going

Diffuse Large B cell Lymphoma (DLBCL)

Polivy drives higher CR rates with durable responses

1L	R/R	3L+
CHOP	benda	
R-CHOP	R+benda	
Polivy+ R-CHP (FDA BTD)	Polivy+ R+benda (FDA BTD)	
Polivy+ CD20 x CD3	Polivy+ mosunetuzumab	glofitamab
	glofitamab+ GemOx	

Follicular Lymphoma (FL)

Gazyva established as SOC in 1L iNHL with estimated 3 yrs longer mPFS than Rituxan

1L	2L+	3L+
chemo	benda	
R+chemo	R+benda	
G+chemo	G+benda	
	mosunetuzumab +lenalidomide	mosunetuzumab (FDA BTD)

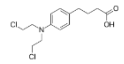
Total CLL, DLBCL, FL market growing to 9bn & 15bn, respectively by 2024[1]

✓ = approved or positive read-out

R/R=relapsed refractory; R=Rituxan; G=Gazyva; clb=chlorambucil; benda=bendamustine; [1] Evaluate Pharma; Venclexta in collaboration with AbbVie

Hematology: Expanding into AML, MM and MDS

chemotherapy



1997 Rituxan Rituximab

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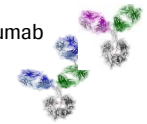
VENCLEXTA venetoclax tablets

2021/22 filing

mosunetuzumab

glofitamab



	Acute Myeloid Leukemia (AML)	Multiple Myeloma (MM)		Myelodysplastic Syndrome (MDS)
	Setting new SOC in a market which has been historically difficult to treat Ph III (VIALE-M) in 1L fit AML maintenance initiated	Ph III (CANOVA) in t(11;14) R/R MM initiated Ph I cevostamab monotherapy data presented at ASH 2020		Ph I interim data presented at ASH 2020; Ph III (VERONA) started in 2020
	1L unfit (50% of 1L patients)	***R/R t(11;14)***	***R/R***	***1L***
Historical SOC	LDAC low dose cytarabine	bortezomib+ dexamethasone	bortezomib+ dexamethasone	azacitidine
Current/ Potential future SOC	**Venclexta+ LDAC** (FDA BTD) ✓	Venclexta+ dexamethasone	cevostamab	Venclexta+/- azacitidine (FDA BTD)
	Venclexta+ HMA ✓			

Total MM & AML market growing to USD 25bn & 7bn, respectively by 2024[1]

✓ = approved

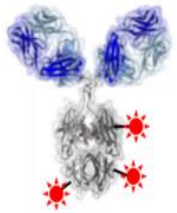
R/R=relapsed refractory; LDAC=low dose aracytarabine; HMA=hypomethylating agent; [1] Datamonitor and Evaluate Pharma; Venclexta in collaboration with AbbVie

Hematology: Polivy in DLBCL

First positive Ph III (POLARIX) in a curative setting in the last 20 years

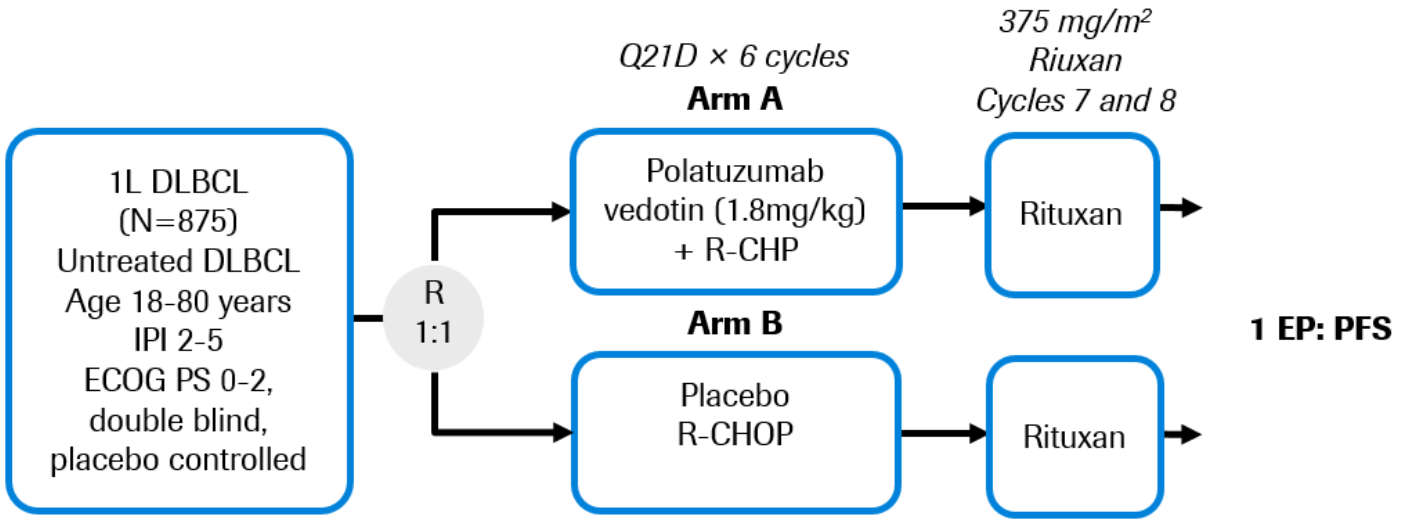
Polivy program

Anti-CD79b ADC



Combination	Indication	Ph1	Ph2	Ph3	
Polivy+R+CHP	1L DLBCL				✓
Polivy+R+GemOx	R/R DLBCL				
Polivy+/-BR	R/R DLBCL/FL				✓
Polivy+G	R/R DLBCL/FL				
Polivy+mosun	R/R DLBCL				
Polivy+mosun+CHP	1L DLBCL				
Polivy + glofit	R/R NHL				
Polivy + mosun SC	1L unfit DLBCL				

Ph III (POLARIX) in 1L DLBCL



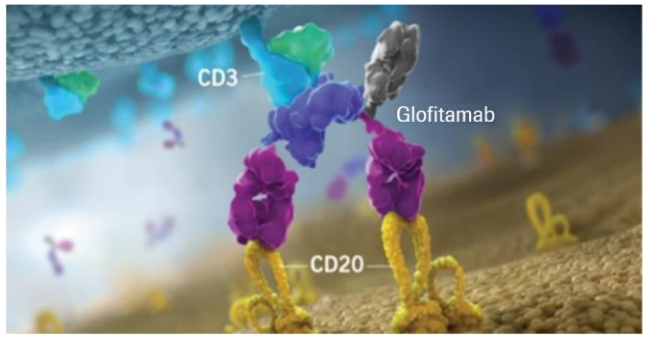
- Positive Ph III (POLARIX) results for Polivy + R-CHP in 1L DLBCL to be presented at upcoming conference
- Ph III (SUNMO) in 2L+ DLBCL for Polivy + mosunetuzumab to be initiated

ADC=antibody drug conjugate; DLBCL=diffuse large B-cell lymphoma; PFS=progression free survival; R=Rituxan; CHP=cyclophosphamide, doxorubicin, prednisone; GemOx=gemcitabine, oxaliplatin; G=Gazyva; BR=bendamustine+Rituxan; mosun=mosunetuzumab; glofit=glofitamab; Polivy in collaboration with Seagen

Hematology: Glofitamab in NHL

On track for early 3L+ DLBCL filing in 2022

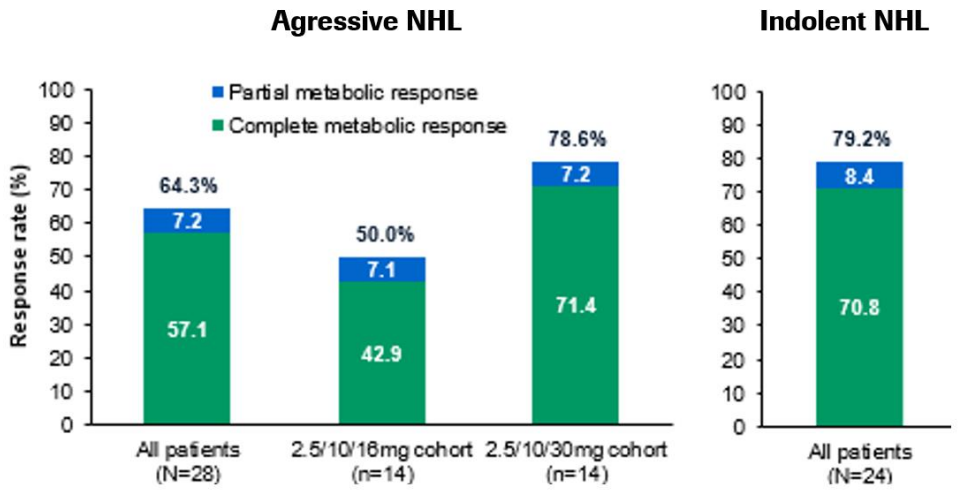
Glofitamab program



Combination	Indication	Ph1	Ph2	Ph3
glofit+GemOx	2L+ DLBCL			
glofit	R/R DLBCL/FL			
glofit+Gazyva/R+CHOP	1L DLBCL			
glofit+Polivy+R-CHP	1L DLBCL			
glofit+Tecentriq	R/R DLBCL/FL			
glofit+Gazyva	R/R FL			
glofit+Polivy	R/R DLBCL			

Ph I glofitamab step up dosing in heavily pretreated R/R NHL

Response rates (2.5/10/16mg or 2.5/10/30mg)



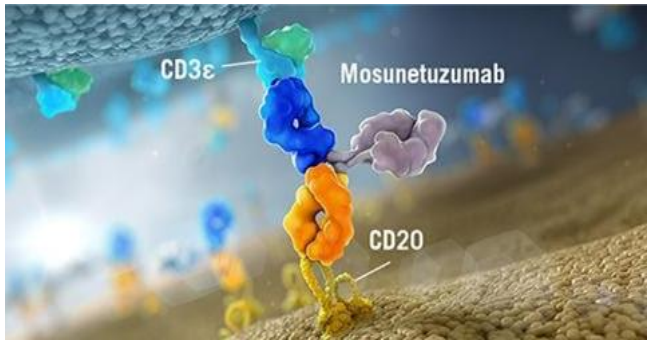
- High and durable response rates in patients who have failed multiple lines of treatment
- Good safety profile with manageable CRS largely confined to cycle 1
- Ph III (STARGLO) for glofitamab + GemOx in 2L+ DLBCL started in Q1 2021
- Combination development with G/R-CHOP and Polivy+/- R-CHP in DLBCL on-going

Carlo-Stella C. et al, ASCO 2021; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; glofi=glofitamab; GemOx=gemcitabine, oxaliplatin; R=Rituxan; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; CHP=cyclophosphamide, doxorubicin, prednisone; CRS=cytokine release syndrome

Hematology: Mosunetuzumab in NHL

On track for early 3L+ FL filing in 2021

Mosunetuzumab program

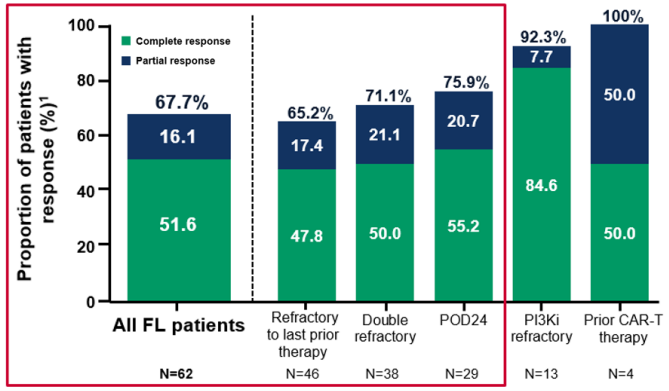


Combination	Indication	Ph1 Ph2 Ph3
mosun+len	R/R FL	
mosun+CHOP	1L DLBCL	
mosun+CHP+Polivy	1L DLBCL	
mosun	R/R DLBCL/FL/MCL	
mosun	1L unfit DLBCL	
mosun SC+Polivy	1L unfit DLBCL	
mosun	3L+ DLBCL/FL	
mosun+Polivy	R/R DLBCL	
mosun+Tecentriq	R/R DLBCL/FL	
mosun SC	R/R DLBCL/FL	

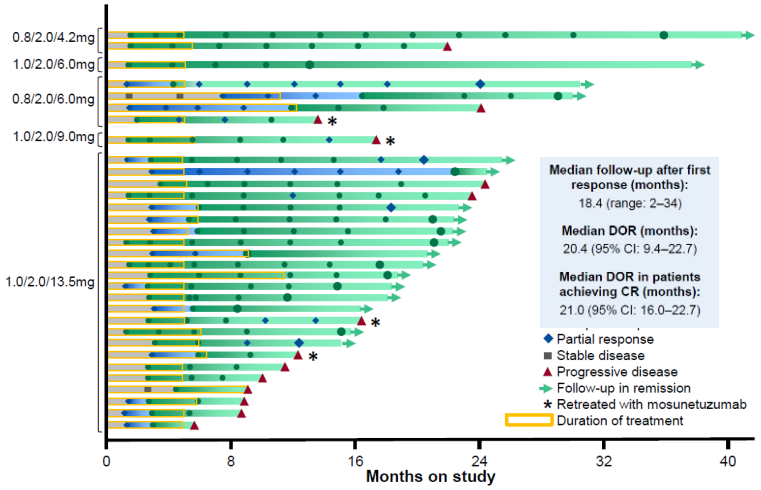
Ph I mosunetuzumab step up dosing in heavily pretreated R/R FL

FDA BTD

Response rates in high risk patients



DOR in patients who achieved CR



- Fixed duration treatment induced strong and durable responses in multiple high-risk subgroups; outpatient regimen
- Ph III (CELESTIMO) mosunetuzumab + lenalidomide in 2L+ FL initiated
- Ph III (SUNMO) mosunetuzumab + Polivy in 2L+ DLBCL initiated
- Combination development with CHOP, Polivy+CHP, Tecentriq and as SC formulation on-going

Assouline S. et al,, ASH 2020; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; CHP=cyclophosphamide, doxorubicin, prednisone; mosun=mosunetuzumab; ORR=overall response rate; CR=complete response; AE=adverse event; CRS=cytokine release syndrome; R/R=relapsed/refractory; DOR=duration of response; SC=subcutaneous

Hematology: Venclexta in CLL, AML, MM, MDS

6th BTD for Venclexta in MDS obtained

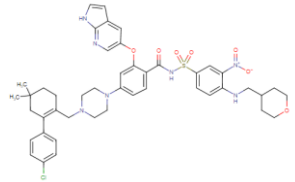
VENCLEXTA venetoclax tablets 10mg, 50mg, 100mg

Roche

ASH 2020

Venclexta progam

Bcl-2 inhibitor

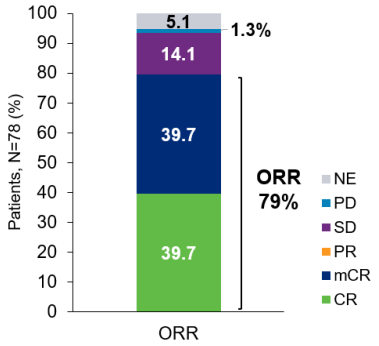


	Combination	Indication	Ph1	Ph2	Ph3
NHL	*V+P+G/R*	R/R DLBCL/FL			
CLL	*V+G*	1L unfit CLL			✓
	V+R	R/R CLL			✓
	V	R/R CLL 17p			✓
	V	R/R CLL after ibru/idel			
	V+G	1L fit CLL			
MM	*V+dex*	t(11;14) R/R MM			
	V+carfilzomib +dex	t(11;14) R/R MM			
AML	*V+aza*	1L unfit AML			✓
	V+LDAC	1L unfit AML			✓
	V+aza	1L fit AML maintenance			
	V+chemo	1L fit AML			
	V+AMG176	R/R AML			
	V+gilteritinib	R/R AML			
MDS	*V+aza*	1L MDS			
	V+/-aza	R/R MDS			

Ph I dose escalation Venclexta + azacitidine in 1L high-risk MDS

FDA BTD

Response rate



Historical azacitidine ORR: 38%[1]

Overall survival (OS)

	N	mOS	12m OS	24 mOS
Venclexta + azacitidine	78	27.5m	77%	60%
All Venclexta + azacitidine patients receiving 400mg	51	NR		

Median time on study 16.4m

Historical azacitidine mOS estimated ~15 months[1]

- Ph I results for Venclexta + azacitidine in 1L MDS showed strong efficacy, durability and acceptable safety; Ph III (VERONA) in 1L MDS started in Q4 2020
- Ph III (Viale-M) in 1L fit AML maintenance and Ph III (HOVON) in 1L fit AML initiated
- Ph III (CristaLLo) in 1L fit CLL (primary endpoint MRD) ongoing; read-out expected in 2023
- Ph III (CANOVA) in t(11;14) MM ongoing; results expected in 2022

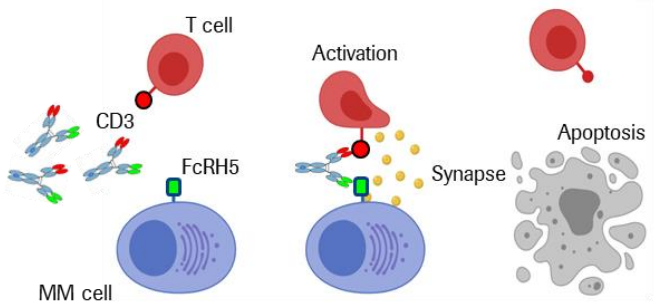
Garcia et al, ASH 2020; [1] Sekeres MA, et al. *J Clin Oncol*. 2017;35(24):2745–53; BTD=break through designation; CLL=chronic lymphoid leukemia; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; mOS=median overall survival; V=Venclexta; P=Polivy; G=Gazyva; R=Rituxan; dex=dexamethasone; aza=azacitidine; LDAC=low dose cytarabine; Venclexta in collaboration with AbbVie

Hematology: Cevostamab in R/R MM with unique MOA

Promising activity in heavily pretreated patients

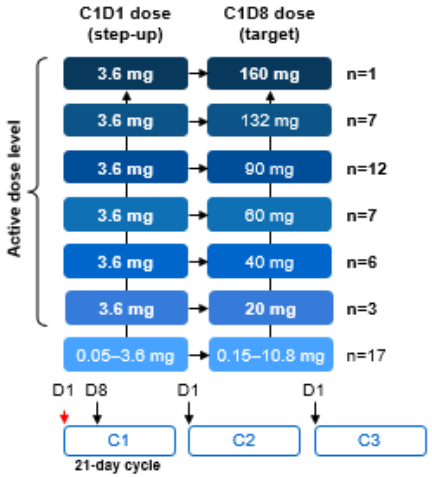
ASH 2020

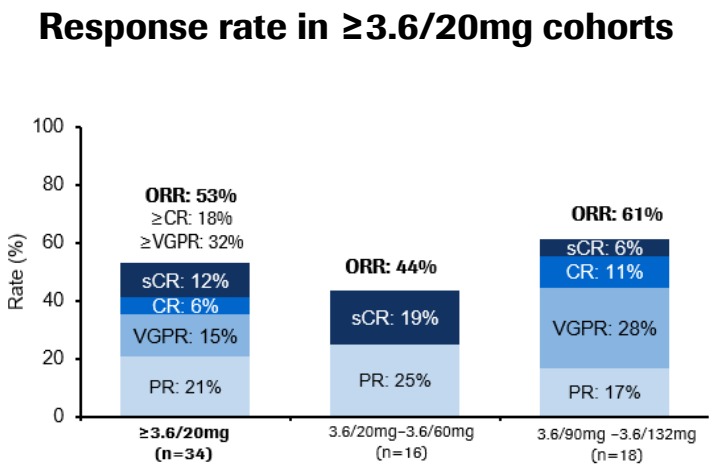
FcRH5 x CD3 bispecific mAb



- Bispecific T-cell engaging antibody
- FcRH5 expressed exclusively in the B-cell lineage and across all maturation stages (elevated in myeloma cells and normal plasma cells vs normal B cells)[1]
- Expressed on 100% of myeloma cells

Ph I dose escalation interim results





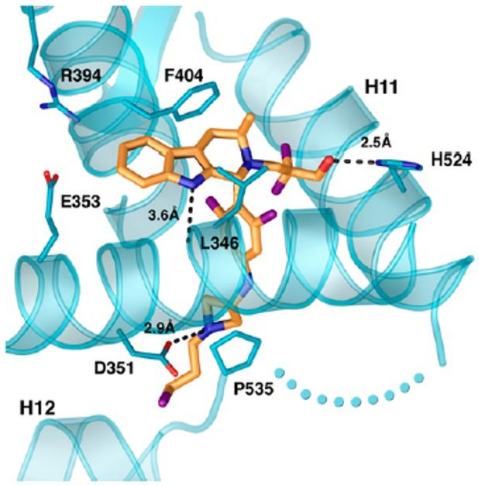
- Preliminary Ph I dose escalation data: Strong response rates in refractory patients (7/17, ORR: 41%) and patients with prior BCMA (5/8, ORR: 63%); Responses observed across all FcRH5 expression levels (FcRH5 expression on myeloma cells detected in all patients)
- Manageable toxicities with step-up dosing (CRS most common in C1; nearly all grade 1-2; one patient with grade 3 CRS)
- Ph I update expected later in 2021

[1] Li et al. Cancer Cell 2017;31:383–95; Cohen A.D. et al., ASH 2020; MM=multiple myeloma; mAb=monoclonal antibody; MOA=mechanism of action; CR=complete response; sCR=stringent CR; PR=partial response; VGPR=very good partial response; ORR=overall response rate; CRS=cytokine release syndrome

HR+/HER2- breast cancer: Giredestrant a next generation SERD

Well differentiated with outstanding efficacy/safety profile

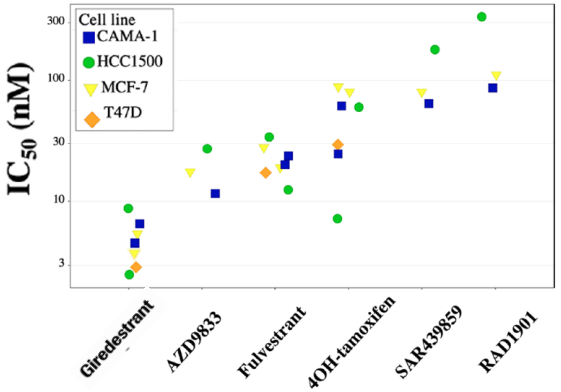
Selective ER degrader (SERD)



- Highly potent with improved efficacy versus previous SERDs
- High potency + minimal safety findings lead to wide nonclinical safety margins

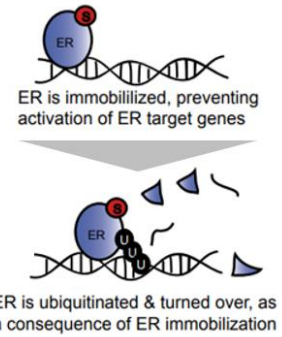
Well differentiated small molecule

In vitro potency comparison



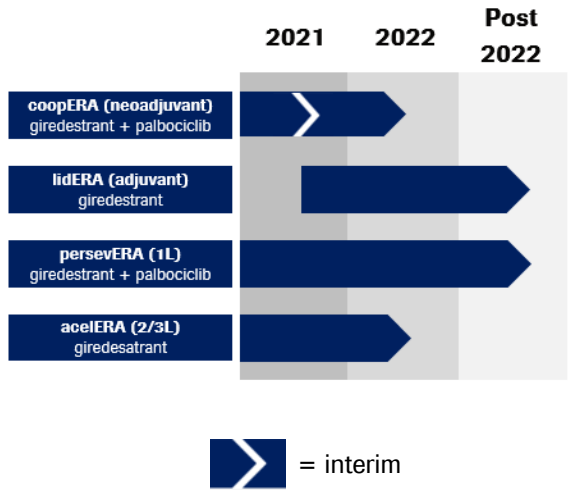
Editorial by Shao P., J.Med.Chem. 2021

Differentiated MOA



Guan J. and Zhou W. et al., Cell 2019

Trial program accelerated



- Potentially best-in-class efficacy being 7-15x more potent than other SERDs in development
- Novel MOA leads to immobilization of the ER prior to its degredation
- Well-tolerated alone or in combination with standardized dose of 30mg once daily; no DDI observed

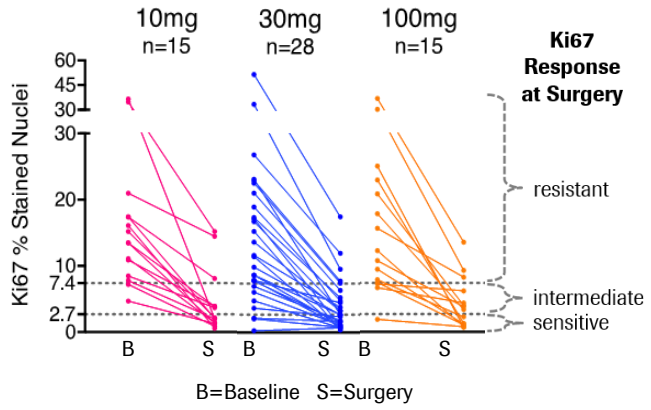
Liang J. et al., J.Med.Chem. 2021; SERD=selective ER degrader; HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; MOA=mechanism of action; DDI=drug drug interaction

HR+/HER2- breast cancer: Giredestrant with early promising data

Strong efficacy/safety data in early and late settings

Stage I-III operable HR+/HER2- BC

Window-of-opportunity study
giredestrant monotherapy (10/30/100mg)



- Encouraging impact on proliferation (78% geomean reduction in Ki67); 55% of tumors with complete cell cycle arrest at 2 weeks*
- Efficacy supportive of 30mg dose
- Ph III (lidERA) adjuvant started
- Ph II (coopERA) neoadj. results at ESMO

Metastatic HR+/HER2- BC (≤2L)

Ph Ib
giredestrant monotherapy (30mg)

Clinical activity	(n=41)
ORR**	20%
CBR	55%
Prior fulvestrant	3/8 (38%)
Prior CDK4/6i	11/26 (42%)
ESR1 mut	13/17 (76%)

- Strong efficacy in all patient subgroups including patients with ESR1 mutations
- Well tolerated at all doses with no DLTs; low treatment discontinuation; no clinically relevant bradycardia or ocular toxicity
- Pivotal Ph II (acceIERA) data in 2/3L in 2022

Metastatic HR+/HER2- BC (≤2L)

Ph Ib
giredestrat (100mg) + palbociclib (125mg)

Clinical activity	(n=48)
ORR	33%
CBR	81%
mPFS	9.3 months

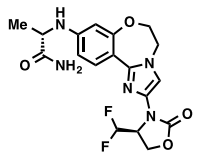
- Potentially best-in-class efficacy in combination with a CDK4/6 inhibitor in pre-treated patients, regardless of ESR1 resistance mutations
- No drug-drug interactions observed
- Well-tolerated up to 100 mg daily
- Expansion cohort at 30 mg daily on-going
- Ph III (persevERA) giredestrant + palbociclib in 1L started in Q4 2020

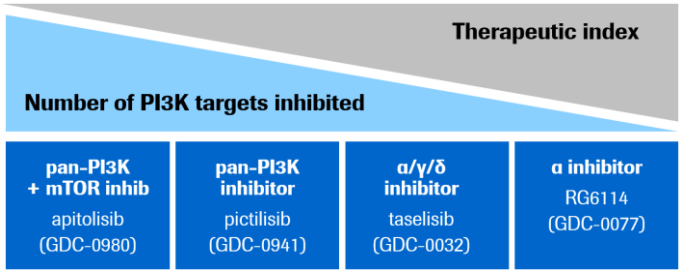
Moore H.M. et al., ASCO 2021; Jhaveri K.L. et al., ASCO 2021; Lim E. et al., ASCO 2020; HR=hormone receptor; BC=metastatic breast cancer; ER=estrogen receptor; * complete cell cycle arrest defined as Ki67 ≤2.7%; ORR=overall response rate; CBR=clinical benefit rate; ** ORR in patients with baseline measurable disease; DLT=dose limiting toxicity

HR+/HER2- breast cancer: Inavolisib in *PIK3CA*-mutant tumors

Ph III for potentially best in class PI3Kα inhibitor started

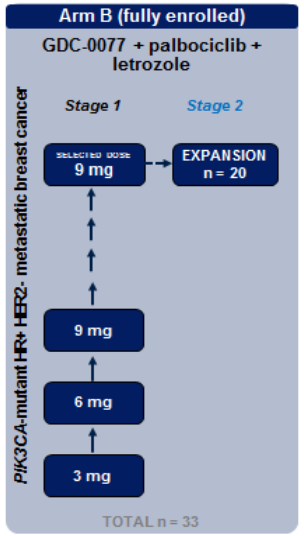
PI3Kα inhibitor/mutant PI3Kα degrader

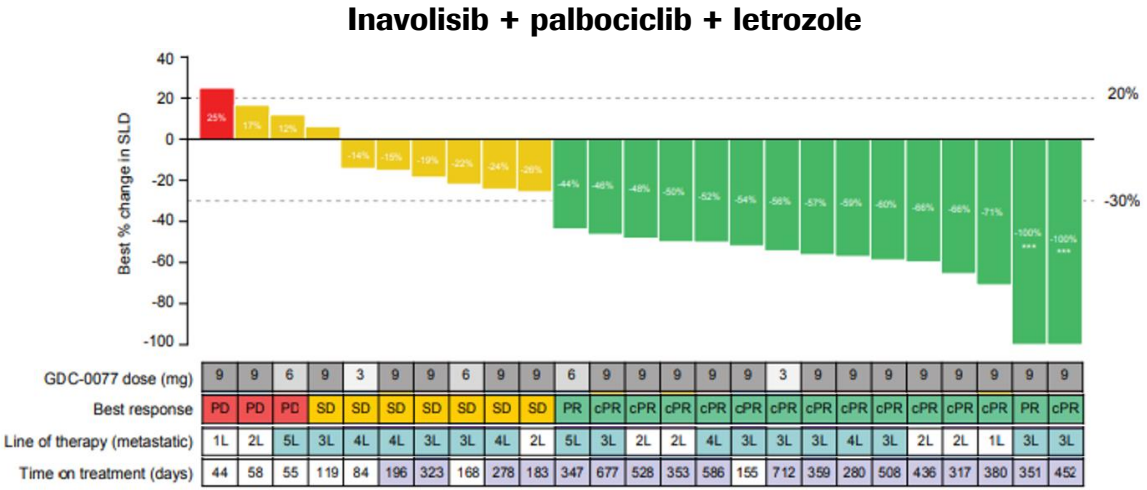




- Differentiation from previous PI3K inhibitors:
  - More selective for PI3Kα subunit
  - Greater safety margins
  - Better in vivo efficacy
- Degrades mutant PI3Kα efficiently
- Combines well with other therapies

Ph I (dose escalation and expansion cohort)





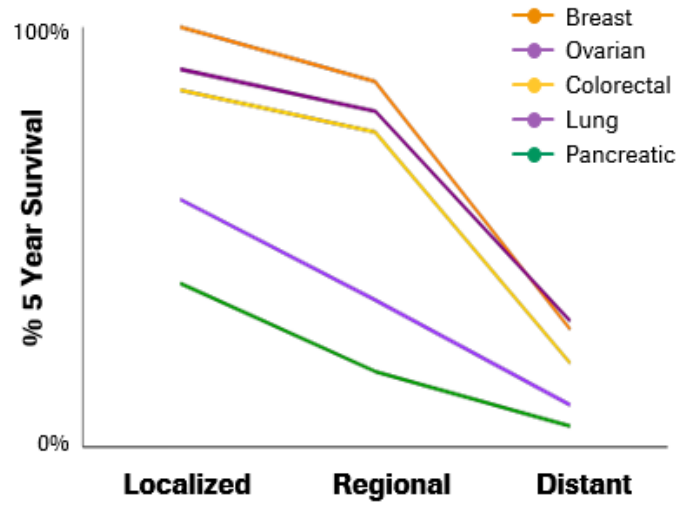
- Strong efficacy in ongoing Ph I/Ib as single agent or as combo with ET (letrozole or fulvestrant) +/- palbociclib in patients with locally advanced or metastatic *PIK3CA*-mutant solid tumors
- Favorable safety as single agent or when combined
- Ph III (INAVO120) inavolisib + palbociclib + letrozole in 1L *PIK3CA*-mutant HR+/HER2- mBC started in Q1 2020

Jhaveri, K., et al, SABCS 2019; Kalinsky K. et al., AACR 2020; * Confirmed ORR in pts with measurable disease; ET=endocrine therapy; HR=hormone receptor; BC=breast cancer; ORR=overall response

Adjuvant program: Pivotal read-outs in 2022

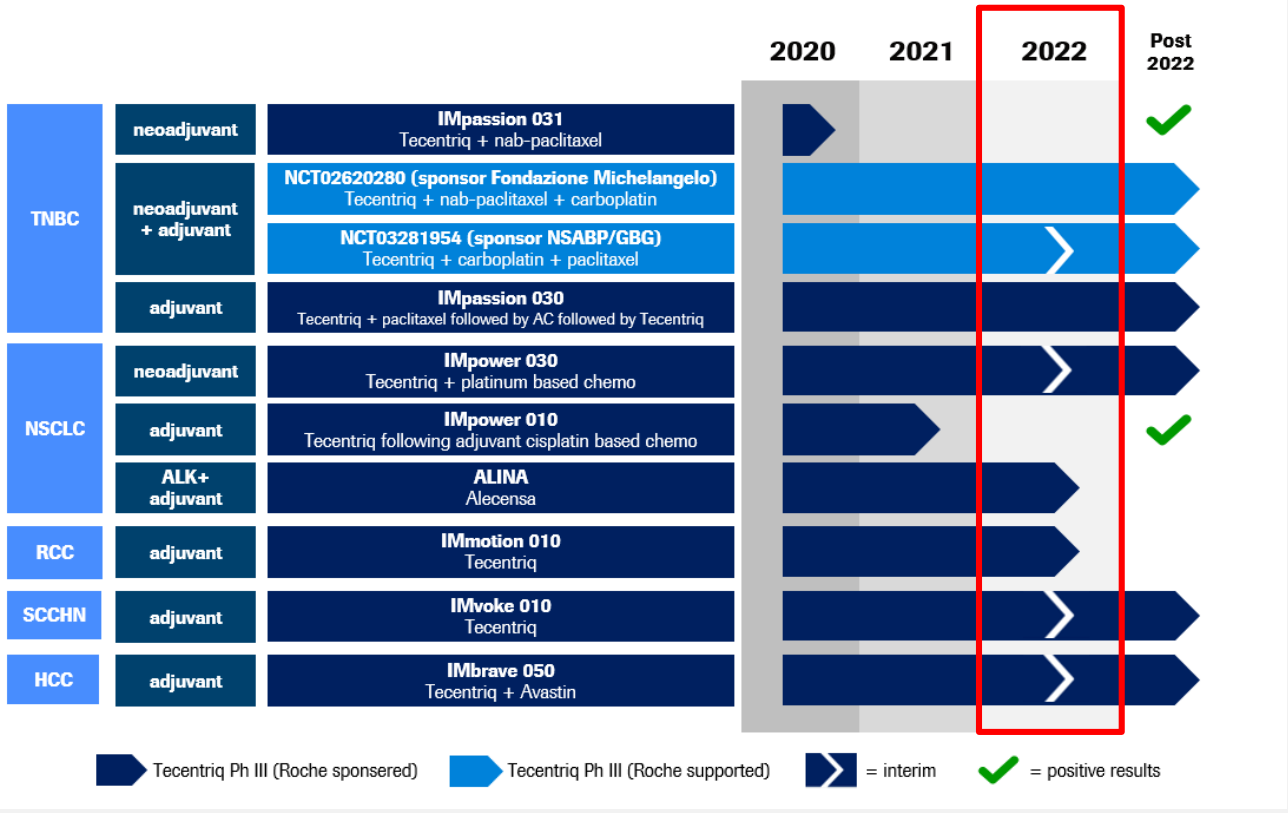
Earlier treatment increases chances for cure

Outcomes by cancer type and stage at diagnosis [1]



- Early detection technologies and increasing screening will allow for earlier treatment
- Early treatment increases cure rates and reduces overall treatment rates

Ph III adjuvant trial program



[1] National Cancer Institute, SEER database, literature review

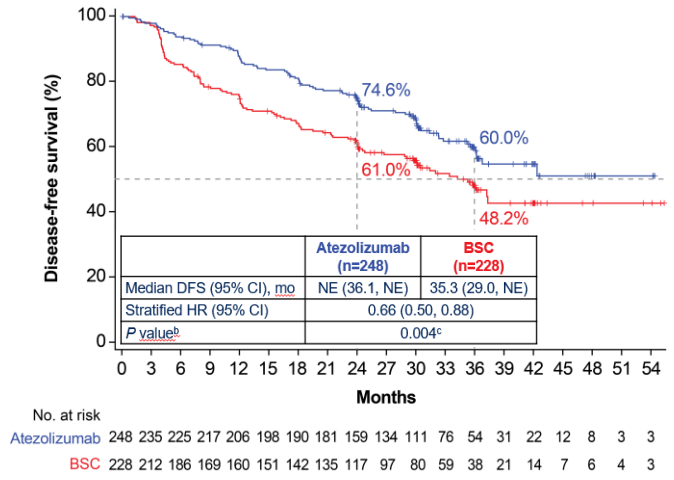
Lung franchise: Tecentriq in adjuvant NSCLC

First positive CIT read-out defining a new standard of care

FDA RTOR review

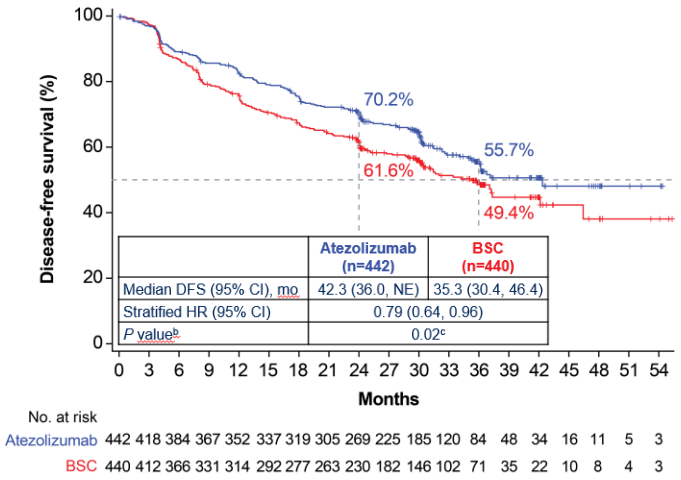
Ph III (IMpower010) interim results in adjuvant NSCLC

DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population



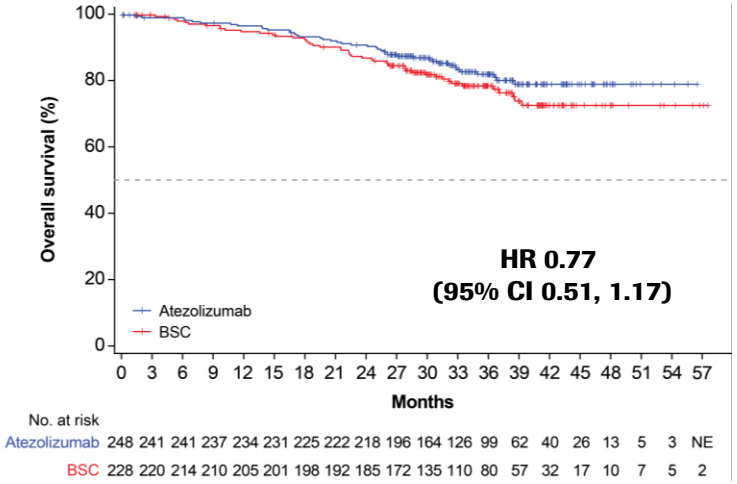
	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

DFS in the all-randomized stage II-IIIA population



	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	

Early overall survival PD-L1 TC ≥1% stage II-IIIA



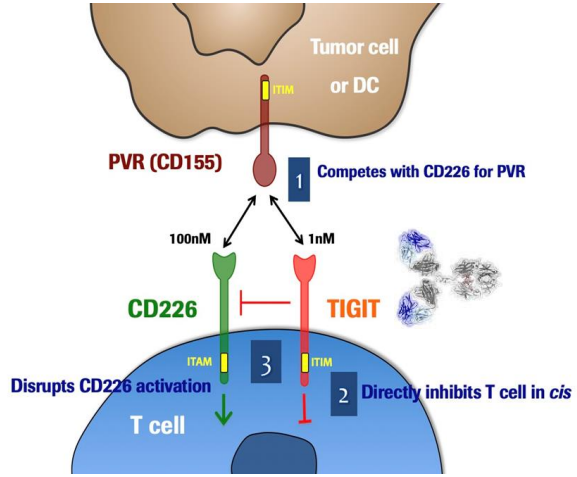
- Improvement in DFS for PD-L1+ Stage II-IIIA (HR=0.66) and all stage II-IIIA patients (HR=0.79); Follow-up will continue for DFS in ITT (Stage IB-IIIA)
- OS data immature at time of DFS interim analysis; next OS interim and DFS final expected in 2022
- Filed with FDA under RTOR and Project Orbis (priority review with PDUFA date set for December 1rst)

Wakelee H.A. et al, ASCO 2021; Clinical cutoff: January 21, 2021; CIT=cancer immunotherapy; DFS=disease free survival; OS=overall survival; CI=confidence interval; HR=hazard ratio; NE=not evaluable; a Per SP263 assay; b Stratified log-rank; c Crossed the significance boundary for DFS; RTOR=real time oncology review

Lung franchise: Tiragolumab + Tecentriq in NSCLC & SCLC

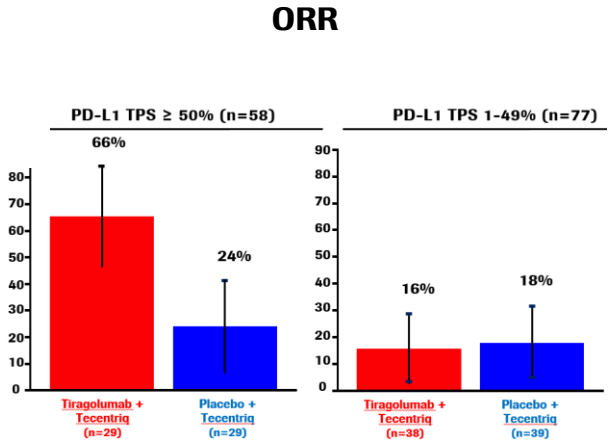
Four Ph II/III tiragolumab studies reading out in 2022

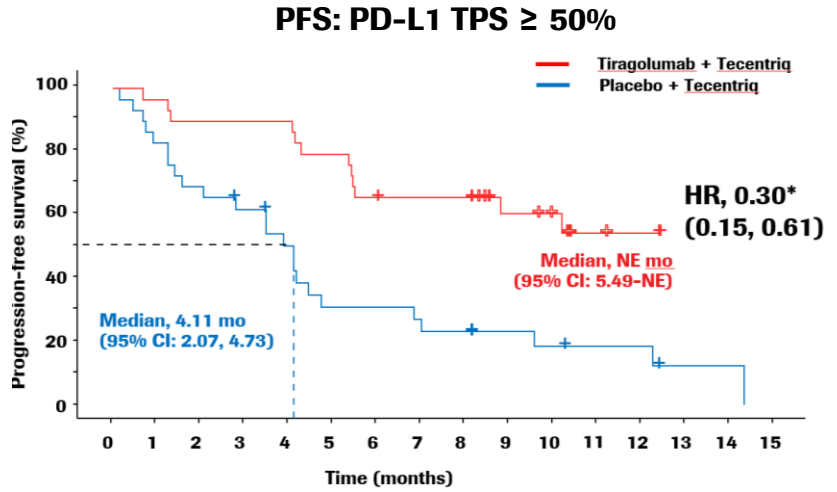
Anti-TIGIT mAb



- Fully human IgG1/kappa Ab with intact Fc region that blocks the binding of TIGIT to its receptor PVR
- Could restore anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

Randomized Ph II (CITYSCAPE) results in 1L NSCLC





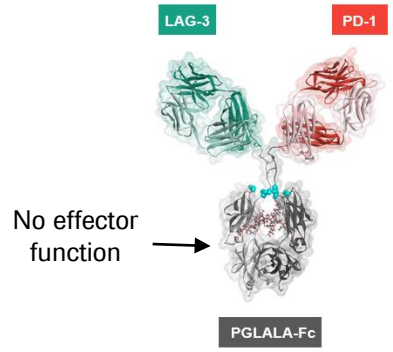
- Tiragolumab + Tecentriq showed clinically meaningful improvement in ORR and PFS in the ITT population with a greater magnitude of improvement in the PD-L1 TPS ≥ 50% subgroup
- Tiragolumab + Tecentriq was well-tolerated with a safety profile similar to the control arm
- Ph III in 1L PDL1+ NSCLC (SKYSCRAPER-01), 1L ES-SCLC (SKYSCRAPER-02) and 1L esophagel cancer (SKYSCRAPER-08) and Ph II in 2L+ PDL1+ CC (SKYSCRAPER-04) to read-out in 2022
- Large Ph II/III program with 7 pivotal studies in 5 indications on-going

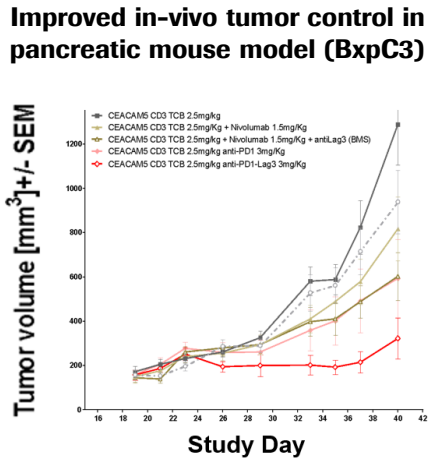
Johnson et al. Cancer Cell 2014; Rodriguez-Abreu D. et al., ASCO 2020; Follow-up data cut-off: 02 December, 2019; mAb=monoclonal antibody; ORR=overall response rate; PFS=progression free survival; HR=hazard ratio; NE=non evaluable; ITT=intention-to-treat; TPS=tumor proportion score; NSCLC=non small cell lung cancer; ES-SCLC=extensive stage SCLC; CC=cervical cancer; * unstratified HR

Different technologies applied to leverage T cell responses

PD1 x LAG3 and PD1 x TIM3 bispecific Abs moved into Ph II

PD1 x LAG3 bispecific Ab

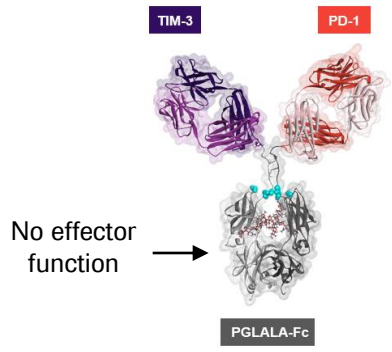


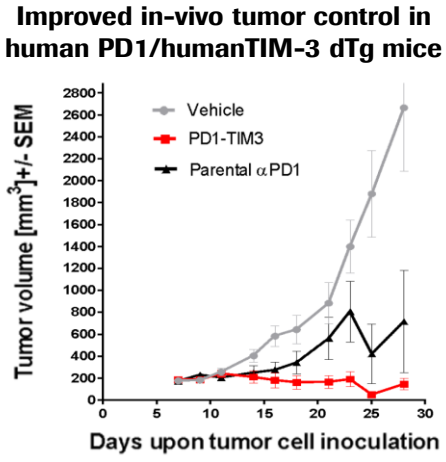


Deak L.C. et al., SITC Meeting 2019

- PD1 x LAG 3 shows improved control of tumor growth and eradication vs. combination of the two parental anti-PD1 and anti-LAG3 mAbs
- Bispecific mAb binding to PD-1 (high affinity) and LAG3 (low affinity)
- May reinvigorate exhausted T cells and potentially targets T resource cells and their progeny by blocking two co-inhibitory checkpoint receptors
- Ph I monotherapy in 2L+ melanoma and 2/3L NSCLC ongoing

PD1 x TIM3 bispecific Ab





Deak L.C. Et al., AACR 2020

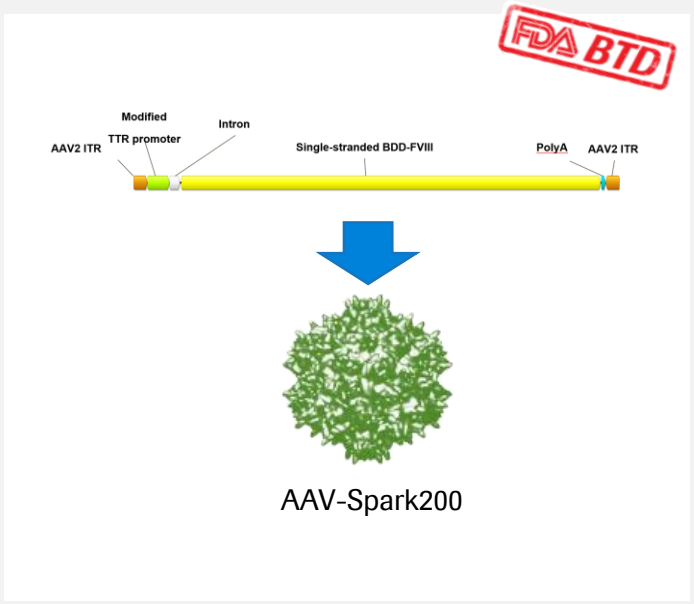
- PD1 x TIM 3 shows improved control of tumor growth and eradication vs. PD1 in animal models
- Bispecific mAb binding to PD-1 (high affinity) and TIM3 (low affinity)
- May reinvigorate exhausted T cells by blocking co-inhibitory checkpoint receptors
- Ph I monotherapy in 2L melanoma, 2/3L NSCLC, 2L ESCC ongoing

mAb=monoclonal antibody; NSCLC=non small cell lung cancer; ESCC=esophageal squamous cell carcinoma

Non-malignant hematology: SPK-8011 in hemophilia A

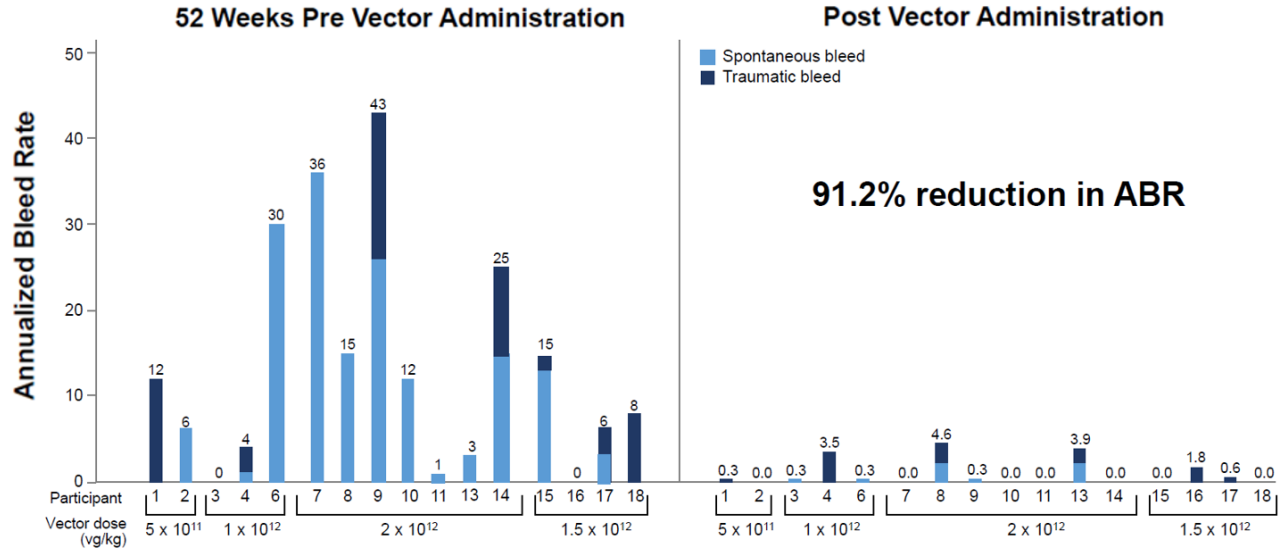
Efficacy and safety data up to 4 years

Hemophilia A gene therapy



- Bio-engineered adeno-associated viral (AAV) vector utilizing the AAV-LK03 capsid (Spark200)
- Contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter

Ph I/II results (SPK-8011-101)



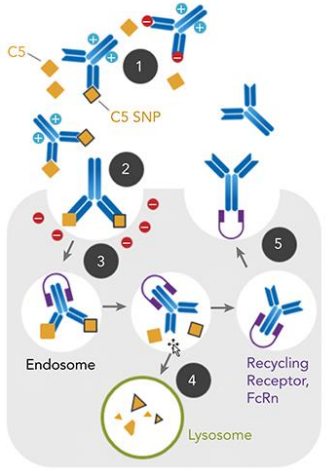
- 15 (out of 17) participants maintained expression with stable, durable Factor VIII activity and a 91% reduction in the ABR and 97% reduction in AIR (median follow up was 2.8 yrs)
- SPK-8011 shows acceptable safety in the ranges of doses studied: $5x10^{11}$–$2x10^{12}$ vg/kg
- Further dose optimization and selection of immunomodulatory regimen ongoing
- Generating data to enable Phase III start

George, L.A. et al, ISTH 2021; * Excludes 2 participants who lost expression; ABR=annualized bleed rate; AIR=annualized infusion rate

Non-malignant hematology: Crovalimab in PNH, aHUS, SCD

Recycling anti-C5 mAb for maximal complement inhibition

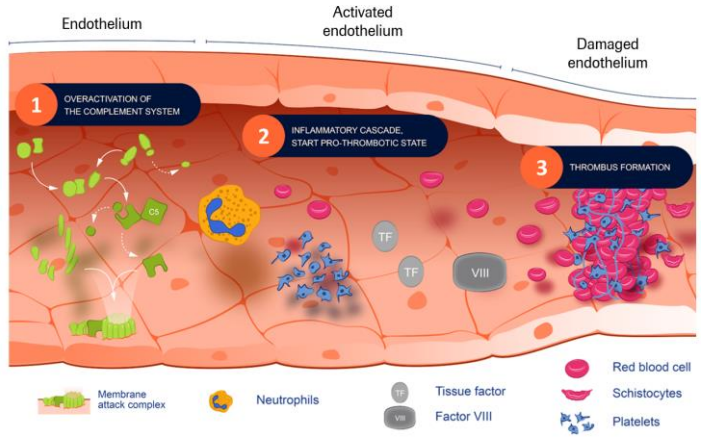
Anti-C5 mAb



1. High affinity binding
2. Preferential Ab uptake of antigen-bound Ab (PI engineering)
3. Acid-sensitive antigen release
4. C5 degradation in the endosome
5. Ab recycling by FcRn engineering, protecting Abs from degradation

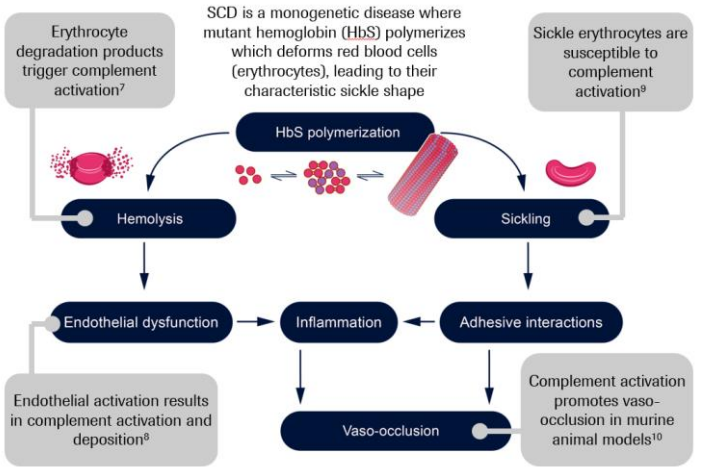
- Chugai engineered, anti complement component 5 (C5) recycling mAb[1–6]
- Engineered to enable maximal, long-lasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

Atypical Hemolytic Uremic Syndrome (aHUS)



Adapted from Feitz WJ et al. Med Genet. 2018;30:400

Sickle Cell Disease (SCD)



- Ph III (COMMODORE 1/2) in PNH (paroxysmal nocturnal hemoglobinuria) achieved first-patient-in in H2 2020; first PNH results expected in 2022
- Ph III in aHUS for adults (COMMUTE-A) initiated in Q2 2021; Ph III for pediatrics (COMMUTE-P) to start in Q4 2021
- Ph I for acute SCD initiated; Ph II in chronic SCD to start in Q4 2021
- Development in additional complement-mediated diseases is being explored

[1] Röth A et al. Blood 2020;135:912–20; [2] Fukuzawa T et al. Sci Rep 2017;7:1080; [3] Sampei Z et al. PLoS One 2018;13:e0209509; [4] Röth A, Nishimura J. Centro Congressi Federico II 2019; [5] Röth A et al. ASH 2018; [6] Sostelly A et al. ASH 2019; [7] Röth A et al. EHA 2019; [8] Peffault de la Tour, R. et al. EHA 2020; PNH=paroxysmal nocturnal hemoglobinuria; [7] Merle NS et al. JCI Insights 2018;3:e96910; [8] Roumenina LT et al. Am J Hematol. 2020;95:456; [9] Chudwin DS et al. Clin Immunol Immunopathol. 1994;71:199; [10] Vercellotti GM et al. Am J Hematol. 2019;94:327.

Doing now what patients need next