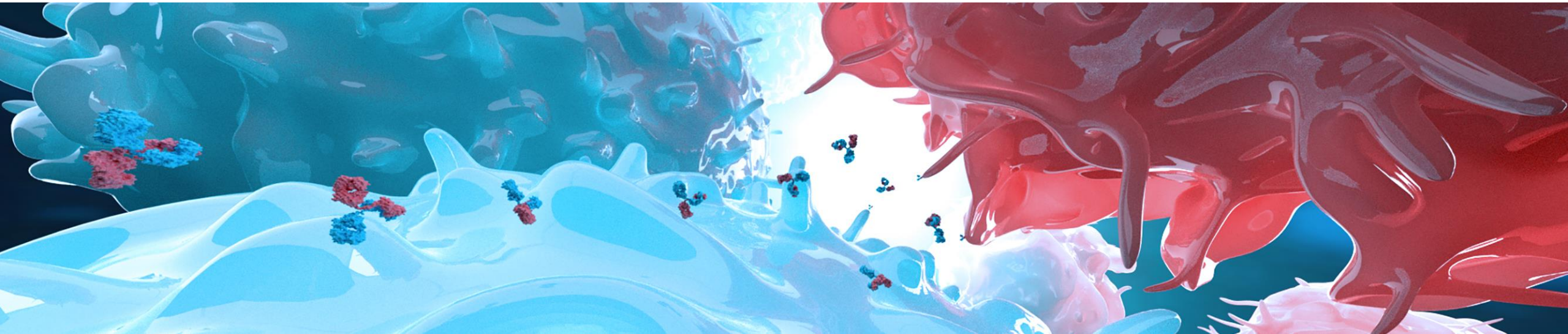
Roche Pharma Day 2021

14 September 2021



Roche Pharma Day 2021

Welcome

Karl Mahler | Head of Investor Relations

Agenda

Welcome
Karl Mahler, Head of Investor Relations

Pharma Strategy: Sustainable growth by delivering more patient benefits at reduced cost to society
Bill Anderson, CEO Roche Pharmaceuticals

Commercial Opportunities: Up-date on ongoing and up-coming launches
Teresa Graham, Head Pharma Global Product Strategy (GPS)

Short break

Late Stage Pipeline Oncology & Non-malignant Hematology
Levi Garraway, Chief Medical Officer and Head Global Product Development

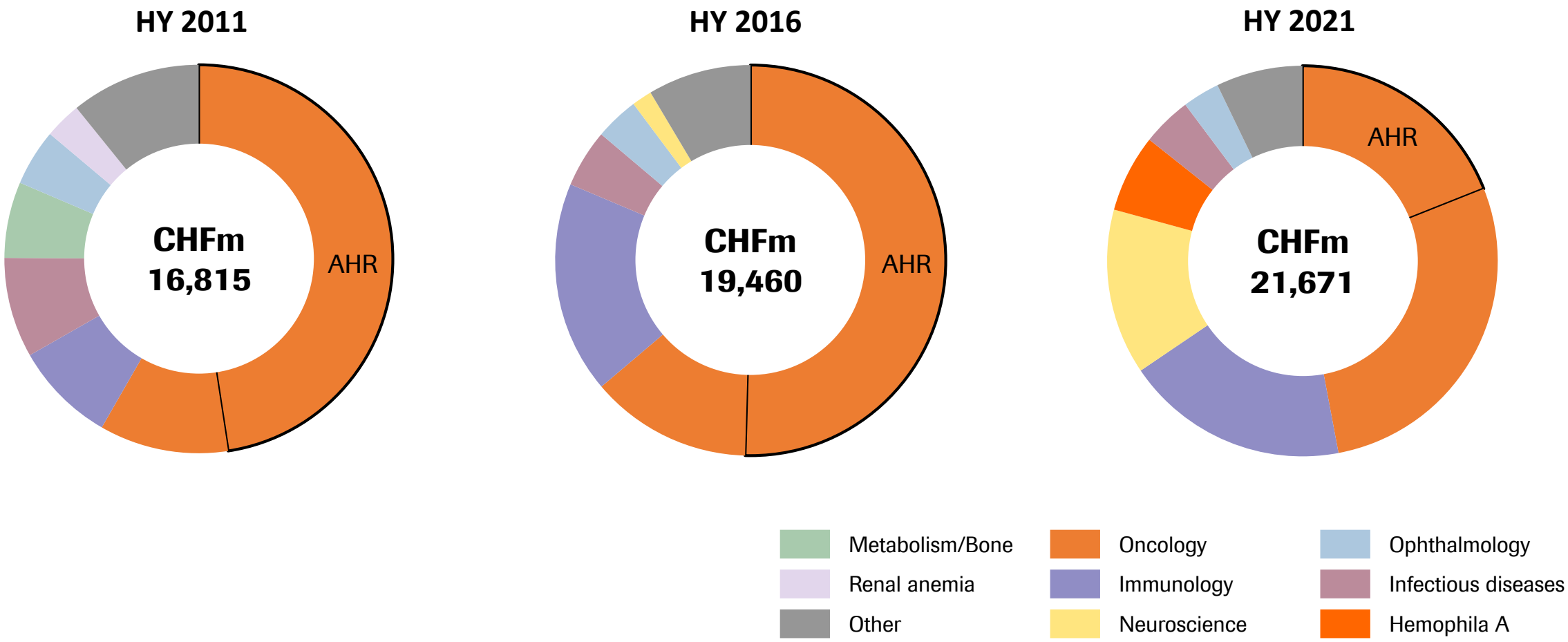
Late Stage Pipeline Neuroscience
Global Head Neuroscience, Immunology, Ophthalmology, Infectious and Rare Diseases, Clinical Development

Late Stage Pipeline Ophthalmology
Nilesh Metha, Lifecycle Leader faricimab, GPS

Infectious Diseases: Influenza & SARS-CoV-2
Barry Clinch, Global Head Infectious Diseases, Clinical Development

Q&A

Strong portfolio rejuvenation and diversification



Source: Pharma HY sales as reported in HY reports; AHR=Avastin, Herceptin, MabThera/Rituxan
Note: HY 2011 – Inflammation/Autoimmune/Transplantation shown as Immunology and Virology shown as Infectious diseases

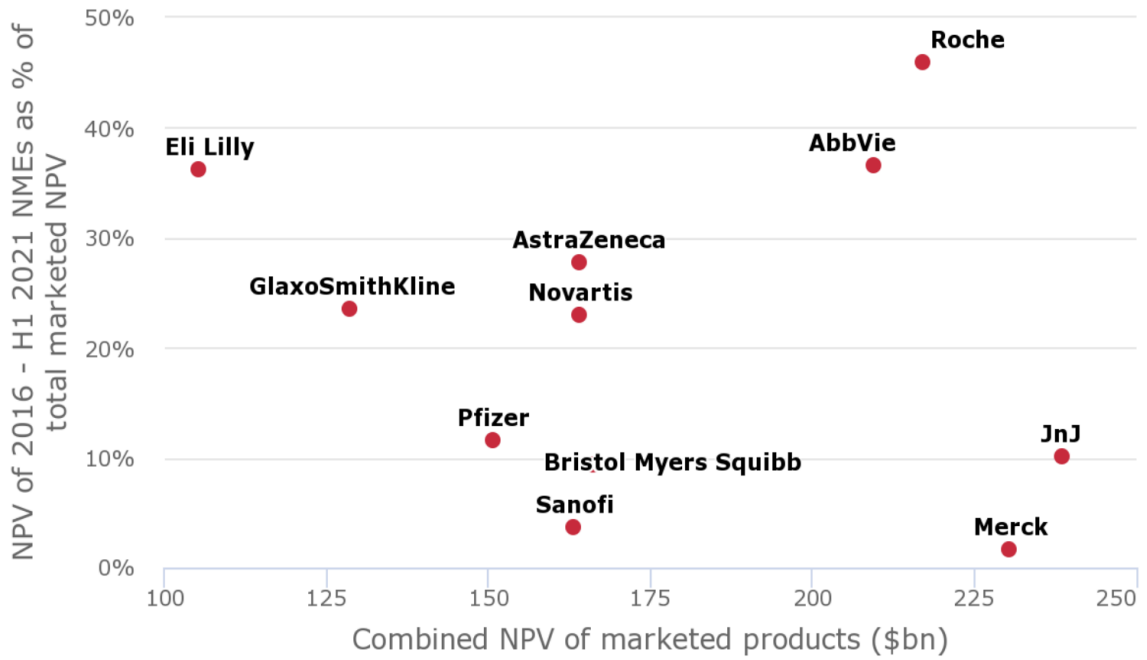
38 Breakthrough Therapy Designations received since 2013

Innovation driving portfolio value

Year	Molecule	Indication
2021	***Venclexta + azacitidine***	*higher-risk MDS*
2020	***tiragolumab +Tecentriq***	*1L PD-L1+ NSCLC*
	mosunetuzumab	*3L+ FL*
	Tecentriq	*unresectable or metastatic ASPS*
	Esbriet	*uILD*
2019	***Gavreto***	*RET fusion-positive NSCLC*
	Gavreto	*RET mutation-positive MTC*
	Cotellic	*Histiocytic neoplasms*
	Gazyva	*Lupus nephritis*
	rhPentraxin-2 (PRM-151)	*IPF*
	Venclexta + Gazyva	*1L unfit CLL*
	Kadcyla	*Adjuvant HER2+ BC*
2018	***SPK-8011***	*Hemophilia A*
	Enspryng	*NMOSD*
	Xolair	*Food allergies*
	Tecentriq + Avastin	*1L HCC*
	Hemlibra	*Hemophilia A non-inhibitors*
	Rozlytrek	*NTRK+ solid tumors*
2017	***Polivy + BR***	*R/R DLBCL*
	Venclexta + LDAC	*1L unfit AML*
	Zelboraf	*BRAF-mutated ECD*
	Rituxan	*Pemphigus vulgaris*

Source: Evaluate Vantage; July 14, 2021

Making a novel contribution (external view)



Roche Pharma Day 2021

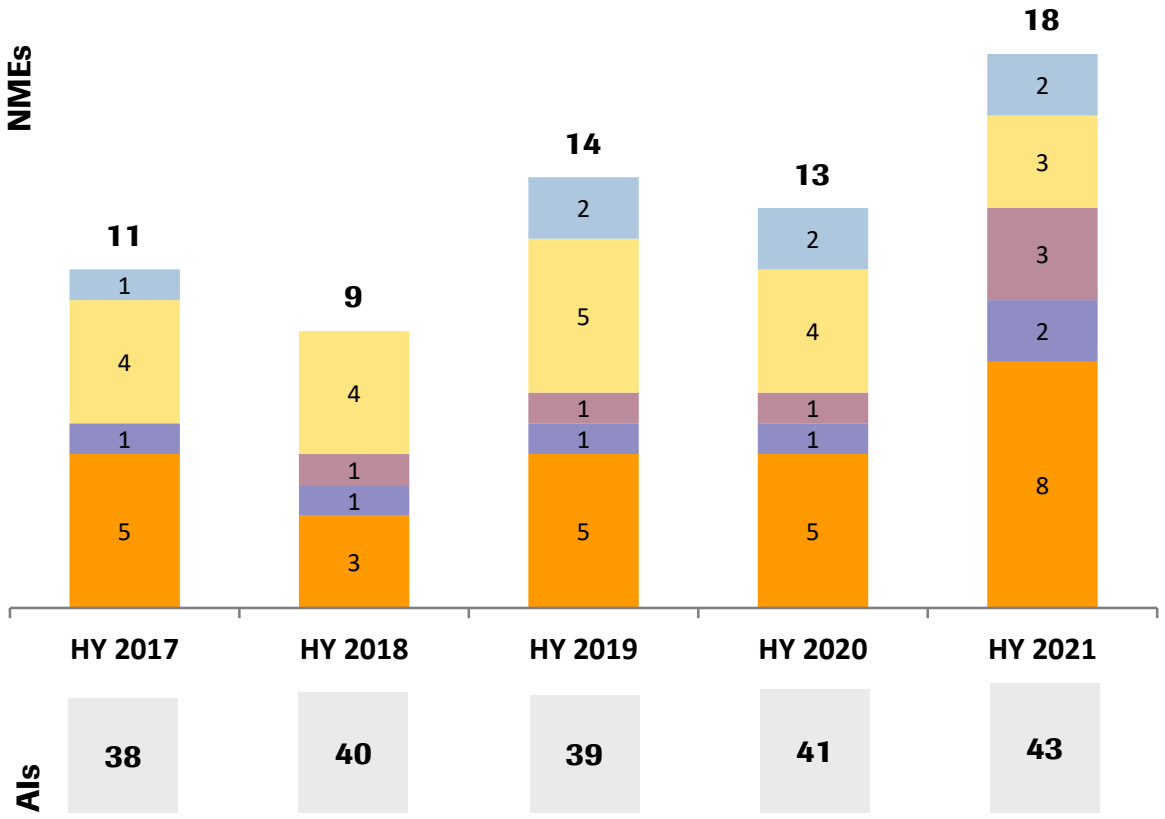
Pharma Strategy: Sustainable growth by delivering more patient benefits at reduced cost to society

Bill Anderson | CEO Roche Pharmaceuticals

What has changed since Pharma Day 2020?

Pipeline at all times high: Assets in Ph III & registration

Continued momentum in the second half



Outlook H2 2021: 10 new Ph III studies planned

- **Tecentriq + lurbinectedin** in 1L maintenance ES-SCLC
- **Venclexta** in adults with AML in first remission after chemo
- **Gavreto** in RET-mutant medullary thyroid cancer
- **mosunetuzumab** in 2L+ FL
- **giredestrant** in ER+ adj BC
- **Enspryng** in generalised Myasthenia Gravis
- **SRP-9001** in DMD (collaboration with Sarepta)
- **Gazyva** in systemic lupus erythematosus
- **crovalimab** in adults with aHUS
- **crovalimab** in pediatrics with aHUS

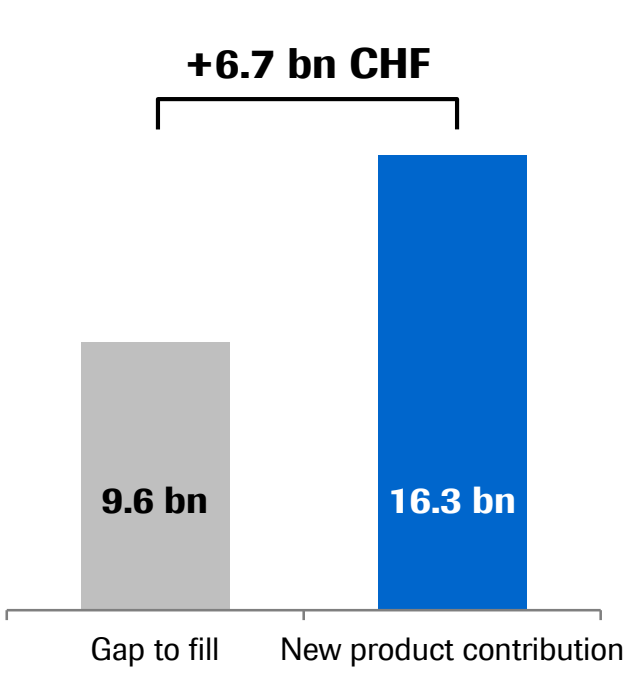
Neuroscience · Infectious Diseases · Immunology · Oncology/Hematology · Ophthalmology

NME=new molecular entity; AI=additional indication; ES-SCLC=extensive stage small cell lung cancer; AML=acute myeloid leukemia; FL=follicular lymphoma; BC=breast cancer; DMD=duchenne muscular dystrophy; aHUS=atypical hemolytic uremic syndrome

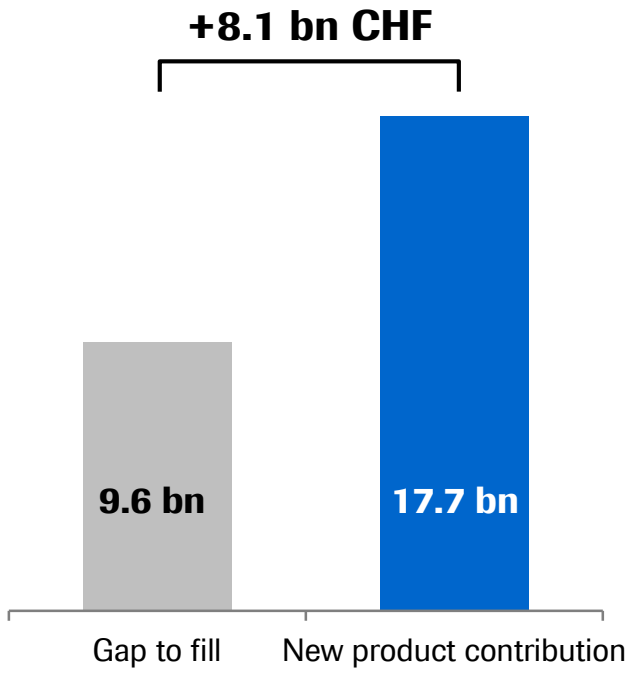
What has changed since our Pharma day a year ago?

Further increased confidence in delivering growth

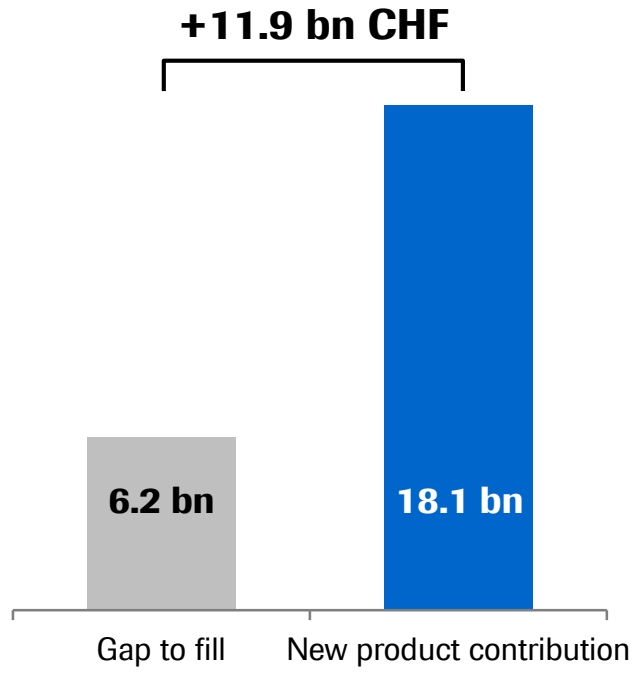
2018–2023 consensus view[1]



2019–2024 consensus view[2]



2020–2025 consensus view[3]



Strong new product contribution and ongoing launches driving growth

[1] Roche Post-HY 2019 consensus survey; [2] Roche Post-HY 2020 consensus survey; [3] Roche Post-HY 2021 consensus survey

Transformation is a key enabler of our Pharma Vision

Guiding principles & decentralized execution for maximum impact

Decentralised execution

- Pharma Development
- Pharma Technical
- Global Product Strategy
- Pharma US
- Pharma International

Following common principles

- **VACC Leadership approach**
- **Pharma Operating Principles**
- **VITAL Resource Allocation**
- **Outcomes Based Planning**

Resulting in

- Improving patients lives
- Serving societal needs
- More fulfilling careers

Pharma Vision 2030

Providing more patient benefit at less cost to society

VACC=Visionary, Architect, Catalyst, and Coach; VITAL=Vision, Improve performance, Talent flow, Accountable to peers, Lucid to all

Adjusting to the new environment: HY 2021 vs. HY 2016

Making a greater impact: Increasing financial flexibility

Pharma Technical	Pharma US	Pharma International	Pharma China	Pharma Development
Sales volume growth +68%	Sales growth +23%	Sales growth +18%	Sales growth +117%	NMEs at pivotal stage[1] +44% Number of projects[2] +24%
Direct spend -1% and Headcount -18%	OPEX -2% and Headcount -19%	OPEX +1% and Headcount -15%	OPEX +9% and Headcount -3%	PD spend +55% and Headcount +27%

[1] Defined as per First Patient In (FPI) at pivotal stage clinical trial, and does not include NMEs already in registration/filing; [2] Late-stage projects

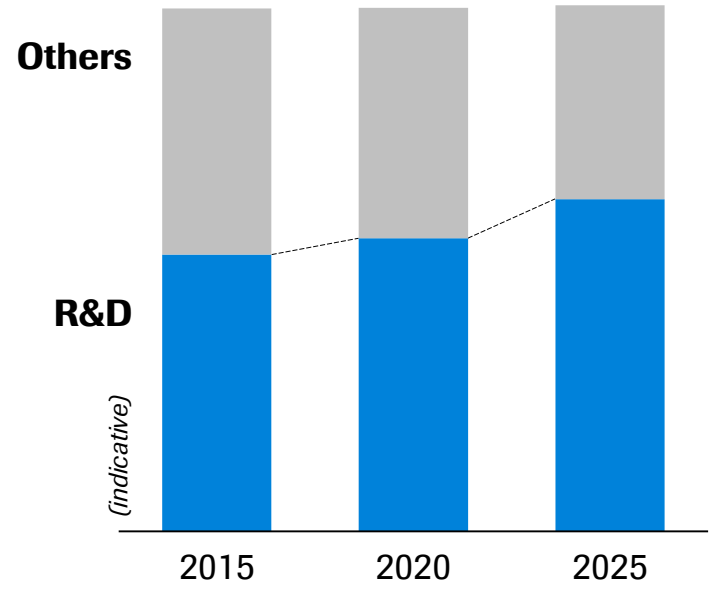
Half-Year 2021: Pharma Division performance

Continued investments into R&D to drive future growth & medical advances

HY 2021 – Pharma Division

	CHFm	CER growth vs PY
Sales	**21,671**	**-3%**
R&OOI	1,372	+34%
Cost of sales	-3,882	-4%
M&D	-2,962	-6%
R&D	-5,883	+19%
G&A	-754	-2%
Core operating profit	**9,562**	**-8%**
Core OP, % of sales	*44.1%*	

R&D investment allocation (% of OPEX)



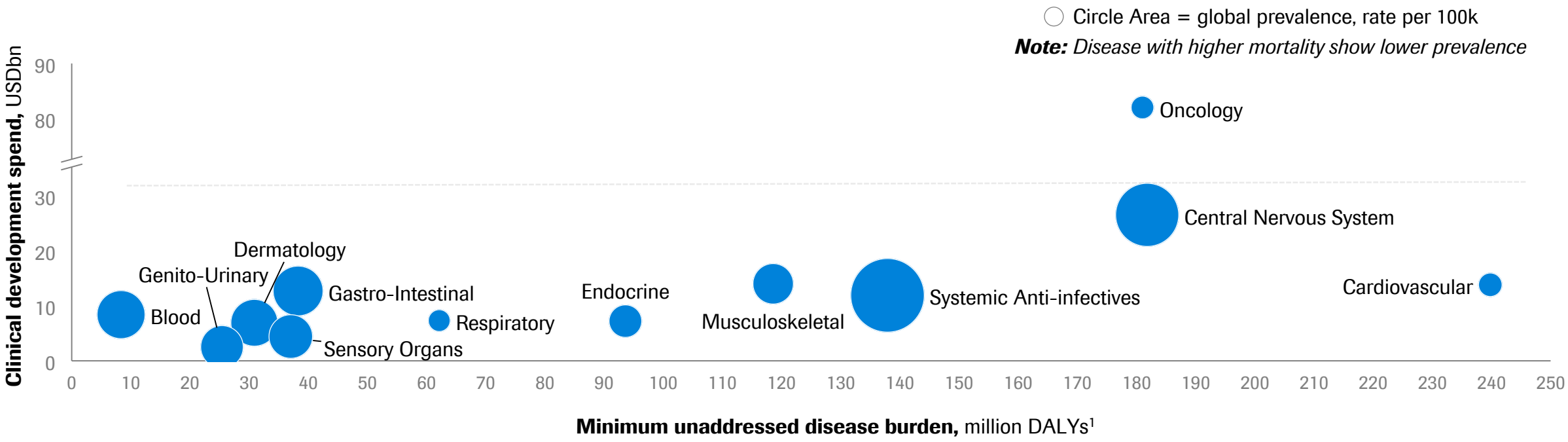
Principles for resource allocation

- Re-allocate resources into R&D while working on and protecting profitability
- All departments of Roche aligned on supporting innovation: transformation ongoing in G&A, M&D, Finance, R&D, etc.

Broad investment in early stage pipeline and new technologies

Many serious conditions lack adequate treatment

Total clinical development spend by therapeutic area vs. global disease burden

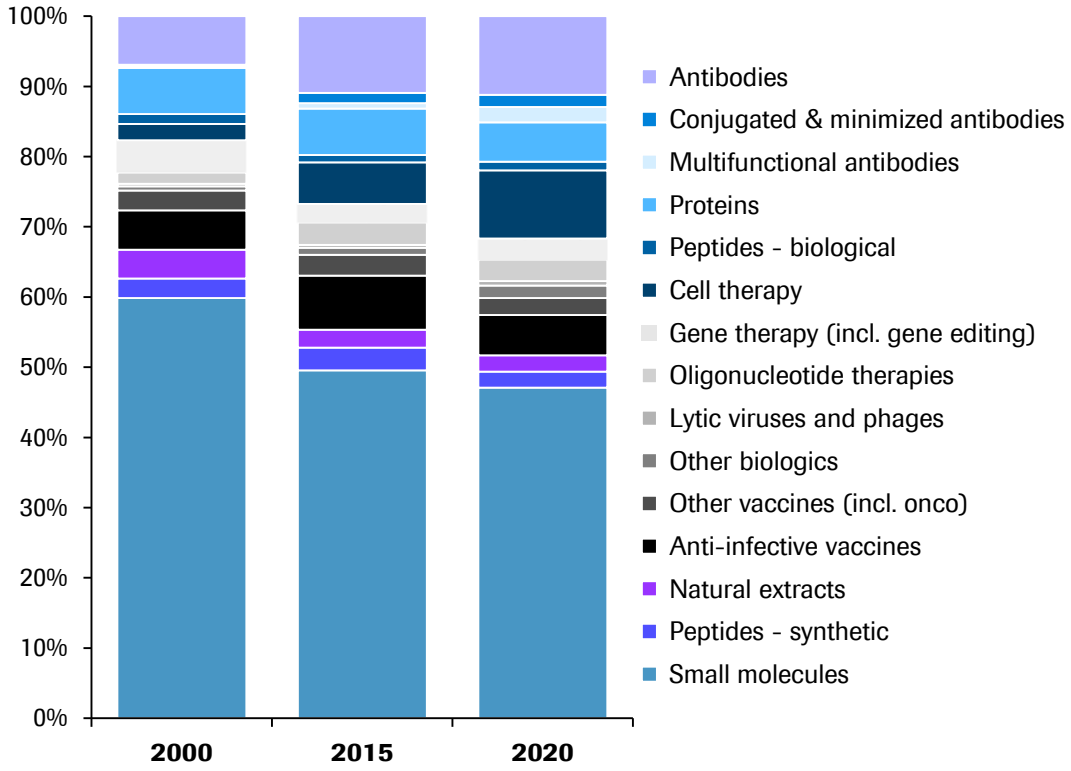


Source: Development spend and first in class ratio based on Evaluate Pharma World Preview 2020; Diseases burden based on Institute for Health Metrics and Evaluation 2021 (DALY in 2019);
[1] Disease burden in DALY in 2019 reduced by the potential reduction in disease burden from existing interventions; DALY=disability-adjusted life year

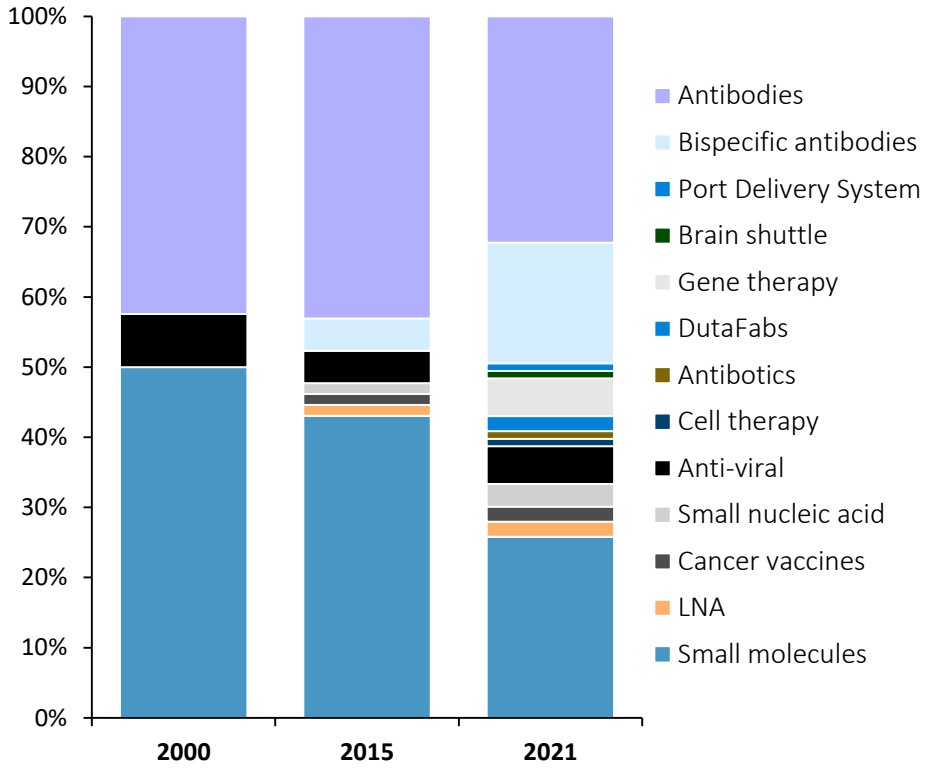
Roche pipeline evolution, increasing leverage of multiple modalities

Diversify the portfolio for future growth

Industry: Pipeline by therapeutic modality[1]

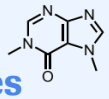
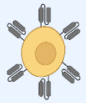


Roche: Pipeline by therapeutic modality[2]



[1] Evaluate & Pharmaprojects 2020: Ph1-3 innovative drugs only, excluding reformulations and biosimilars; snapshot as of June each year with missing phases not approximated; development status based on most progressed indication; [2] Roche disclosed pipeline half year results 2000, 2015 and 2021

Roche with leading portfolio of multiple modalities

	Small molecules	Large molecules		Nucleic acid based medicines		Cell therapies	Vaccines
	Small molecules 	Antibodies & protein engineering 	Protein conjugates 	RNA based technologies 	Gene therapy 	Cell therapies 	Vaccines 
Modalities	Active site inhibitors; allosteric inhibitors; RNA modulators; protein degraders; macrocycles, etc.	Monoclonal antibodies; antibody fragments; bispecific antibodies; T cell directed antibodies; fusion proteins; targeted cytokines etc.	Antibody conjugates etc.	Antisense oligonucleotides; short interfering RNA; locked nucleic acids etc.	Technologies based on adenovirus vectors	Reprogrammed T cells with neo-antigen specificity	RNA vaccines, DNA vaccines against neo-antigens in oncology
Examples	**giredestrant belvarafenib SHP2i KRAS G12C**	**glofitamab, mosunetuzumab, tiragolumab, faricimab, DutaFabs, MAGE-A4 ImmTAC PD1xTIM3, PD1xLAG3, cevostamab, gantenerumab brain shuttle, PD1-IL2v**		**Factor B ASO, HBV siRNA, UBE3A LNA**	**SPK-8011 SRP-9001**	**NEO-T cells**	**autogene cevumeran**
Strategy	*Target currently "undruggable" targets; modify RNA splicing*	*Innovative protein engineering to improve multi-specificity and targeting and allow new mechanisms of action*		*Switching off a disease causing gene on the RNA level*	*Introducing back the wild-type gene to compensate for a disease causing gene mutation*	*Introduction of modified cells to induce a potent immune response or a regenerative effect*	*Using RNA or DNA based vaccines to induce a potent anti-tumor immune response*

Recent deals and partnerships[1]

Accelerate drug discovery and driving personalized healthcare

Technology stage at the time of licensing

92 new agreements in 2020

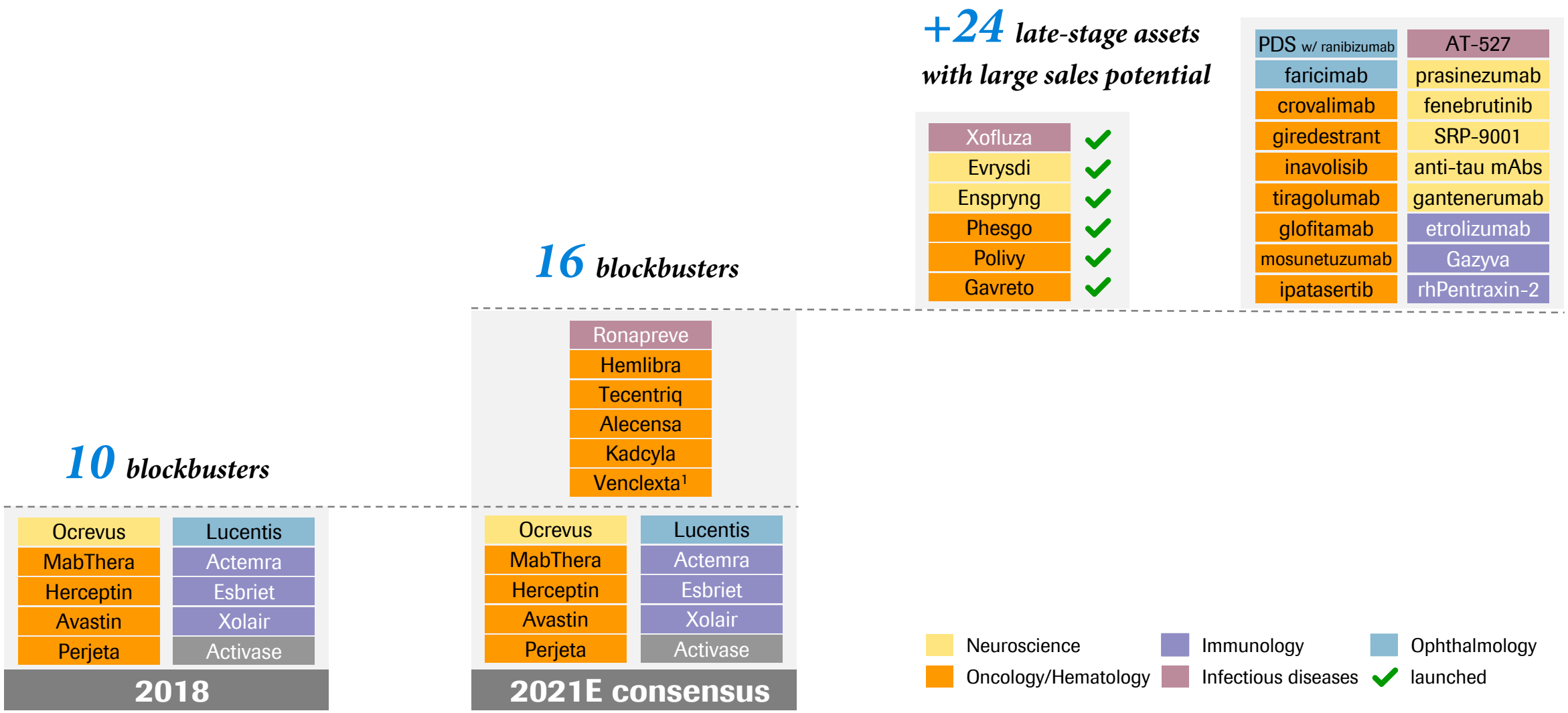
focused on

High disease burden / Promising targets / Novel enabling techologies / Decision support

[1] Non-exhaustive and illustrative overview of deals and partnerships signed over recent years; [2] subject to regulatory clearance

Diversifying and deepening our portfolio

Strong commercial potential throughout late stage portfolio

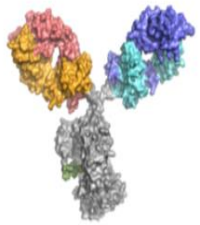


[1] Venclexta sales are booked by partner AbbVie; mAb=monoclonal antibody; Note: based on Post HY 2021 consensus

Broadening and deepening the ophthalmology portfolio

Core focus area for Roche

Faricimab

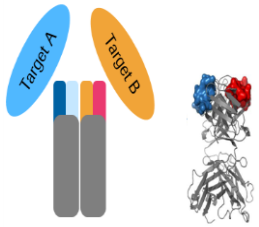


- Anti-VEGF/Ang2 bispecific mAb
- Positive readouts across DME & nAMD, trials in RVO in US/EU
- Expected US/EU launch in 2022

PDS with ranibizumab

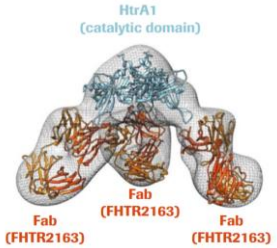
- First Roche intravitreal implant
- Positive readout in nAMD[1], DME and DR in 2022, Q9M extension initiated
- Potential approval in 2021 (US)

PDS with DutaFabs



- DutaMab technology enables creation of a novel bispecific Fab[2]
- Significantly smaller than bispecific antibodies
- Compatible with PDS

Geographic Atrophy



- Chronic progressive degeneration of the macula
- Leading to central scotomas and permanent loss of visual acuity
- Early collaborations ongoing

Improved patient outcome and reduced treatment burden

[1] Non-inferior and equivalent to monthly Lucentis; [2] Fab is the region of an antibody that binds to antigens ; Anti-VEGF=anti-vascular endothelial growth factor; Ang2=angiopoietin-2; DME=diabetic macular edema; mAb=monoclonal antibody; nAMD=neovascular age related macular degeneration; PDS=Port delivery system; DR=diabetic retinopathy; Q9M=every 9 months

Committed to advancing the understanding of CNS diseases

Leveraging digital approaches to improve research & disease management

	Smarter, more efficient R&D	Patient care & access
 **NeuroImmunology**	**MULTIPLE SCLEROSIS** **Internal decision endpoints** Digital, MRI, PET, EEG, Genomics	**MULTIPLE SCLEROSIS** **Patient care tools** Floodlight app
 **NeuroMuscular diseases**	**DUCHENNE MUSCULAR DYSTROPHY** **Regulator enabling endpoints**	**SPINAL MUSCULAR ATROPHY** **Patient care tools** Digital measure bulbar & motor function
 **NeuroDevelopment & psychiatry**	**ANGELMAN SYNDROME** **Prognostic & diagnostic tools** EEG, Gen **Internal decision endpoints** Digital, EEG, MRI, CSF, Genomics	**ANGELMAN SYNDROME** **Patient care tools, diagnostic tool** Digital, Genomics
 **NeuroDegenerative diseases**	**PARKINSON'S DISEASE** **Internal decision endpoints** Digital; imaging and fluid BMs, Genomics	**ALZHEIMER'S DISEASE** **Patient care tools** Digital, imaging and fluid BMs. Smart device and clinical decision support tools in consideration

Digital tools Imaging tools Wet biomarkers Genomics

Investing in early disease in Oncology

Presenting the opportunity for cure

Lung / Rare

Molecule	Indication	Ph 1	Ph 2	Ph 3	
Tecentriq	Adjuvant NSCLC			*IMpower010*	✓
	Neoadjuvant NSCLC			*IMpower030*	
	Adjuvant SCCHN			*IMvoke010*	
tiragolumab[1]	Stage III unres. NSCLC			*SKYSCRAPER-03*	
	Neoadj/Adj NSCLC			*SKYSCRAPER-05*	
Alecensa	Adjuvant ALK+ NSCLC			*ALINA*	

Breast / Gyn

Molecule	Indication	Ph 1	Ph 2	Ph 3	
Tecentriq	Neoadj. TNBC [2]			*IMpassion031*	✓
	Adj TNBC			*IMpassion030*	
giredestrant	Neoadj. HR+ BC			*coopERA*	
	Adjuvant HR+ BC[4]			*lidERA*	

GI / GU

Molecule	Indication	Ph 1	Ph 2	Ph 3
Tecentriq	Adjuvant RCC			*IMmotion010*
	Adjuvant HCC			*IMbrave050*
	HR NMIBC			*ALBAN*
	ctDNA+ HR MIBC			*IMvigor011*
	MSI-H CRC			*ATOMIC*
	BCG unresp. NMIBC			*SWOG S1605*
tiragolumab[1]	Locally adv. ESCC			*SKYSCRAPER-07*

Heme

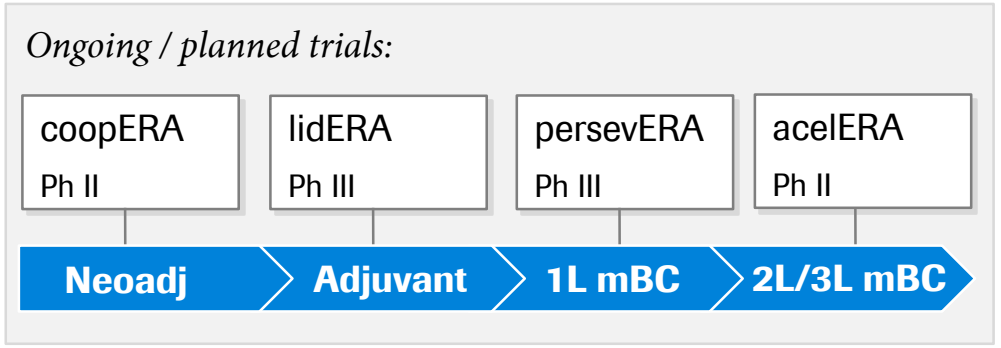
Molecule	Indication	Ph 1	Ph 2	Ph 3	
Polivy	1L DLBCL			*POLARIX*	✓
Venclexta	1L fit AML			*VIALE-M*	
Glofit/Mosun[3]	1L DLBCL			*Ph 1b*	

✓ = met primary endpoint

[1] with Tecentriq; [2] Positive for PCR; [3] +/- Polivy; [4] Planned trial; NSCLC=non-small cell lung cancer; SCCHN=squamous cell carcinoma head & neck; TNBC=triple negative breast cancer; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma; NMIBC=non-muscle invasive bladder cancer; CRC=colorectal carcinoma; ESCC=esophageal squamous cell carcinoma; DLBCL=diffuse large b-cell lymphoma; AML=acute myeloid leukemia

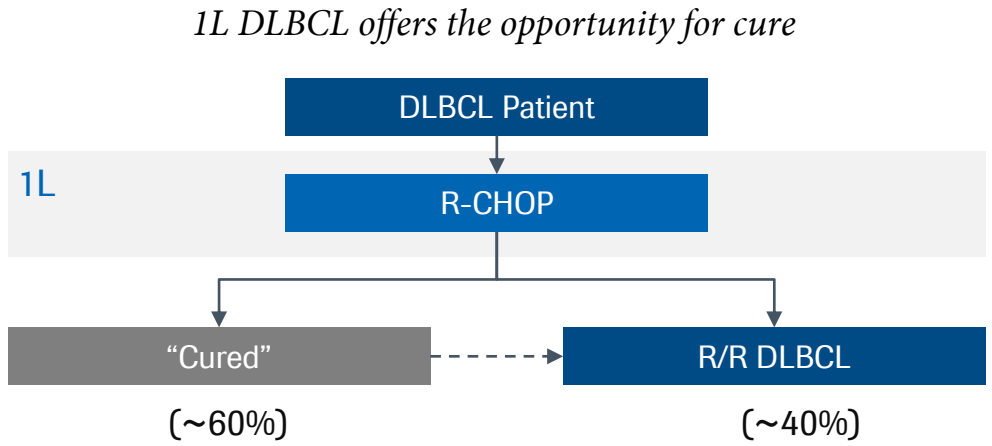
Examples of addressing high unmet need in earlier lines

Giredestrant in HR+ BC: Potential best in class profile



- Differentiated MOA: immobilizes ER in the nucleus prior to degradation
- High potency: 7-15x more potent than other SERDs
- Well tolerated: alone and in combination with CDK4/6i
- Standardized dose: once-daily selected for monotherapy/combo

Polivy in DLBCL: Addressing high unmet need in 1L



- Cure: ~40% of patients not cured with R-CHOP in 1L setting
- Patients with R/R DLBCL have poor prognosis: mOS <2yrs
- No new 1L therapies approved since R-CHOP

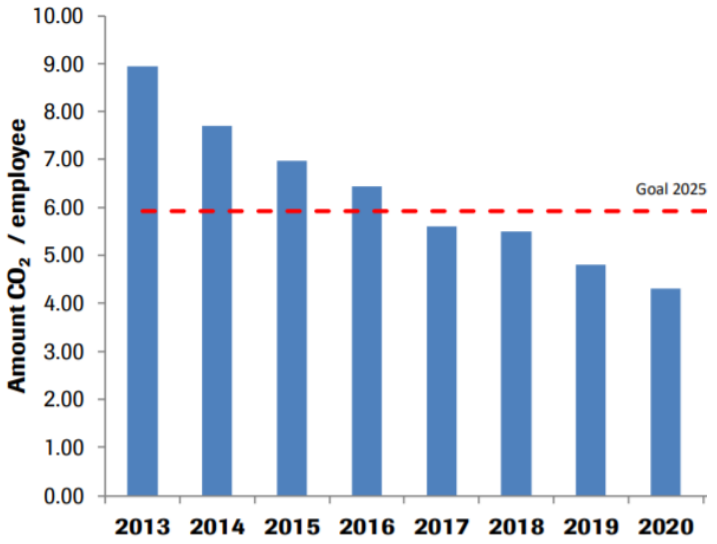
HR+ BC=hormone receptor positive breast cancer; mBC=metastatic breast cancer; MOA=mechanism of action; ER=estrogen receptor; DLBCL=diffuse large B-cell lymphoma; R/R=relapsed/refractory; R-CHOP=Rituxan + cyclophosphamide + hydroxydaunorubicin + vincristine+ prednisone; mOS=median overall survival; Polivy in collaboration with Seagen

Making a sustainable impact

Our impact on society

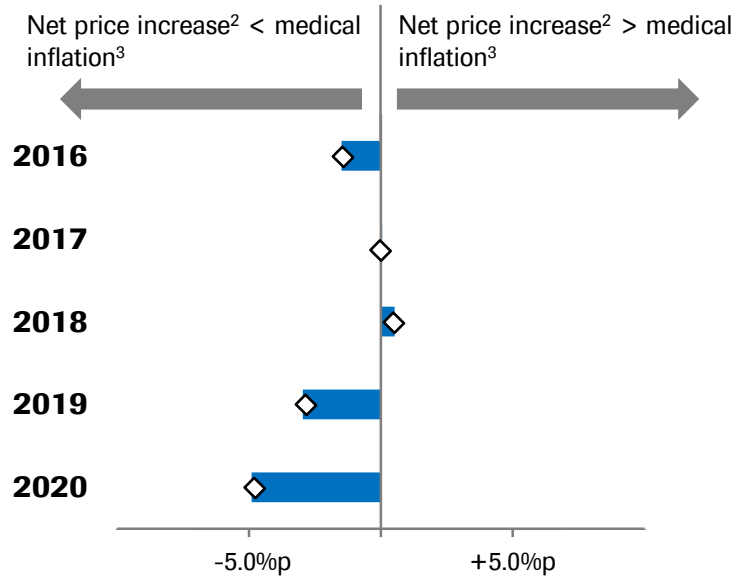
Ranked most sustainable healthcare company by DJSI for the 11th time

Environment



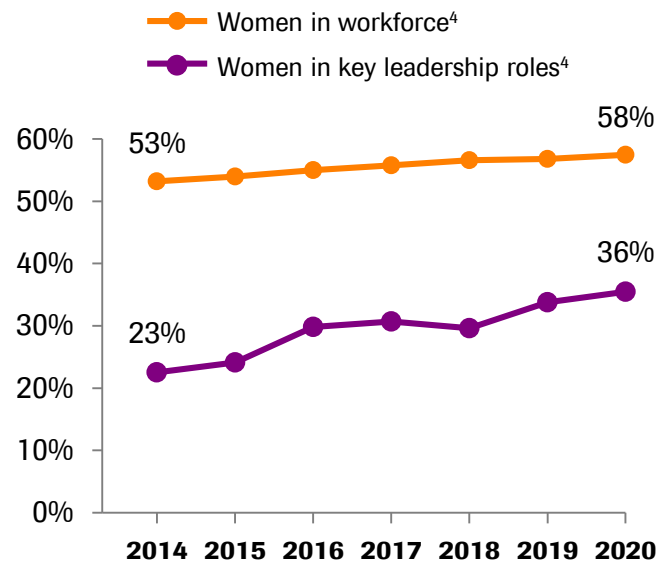
Goal: Scope 1&2 greenhouse gas emissions to real zero by 2050[1]

Access to our products



Net price increases in line with medical inflation in the US

Providing a great workplace



2020: 36% of women in key leadership roles

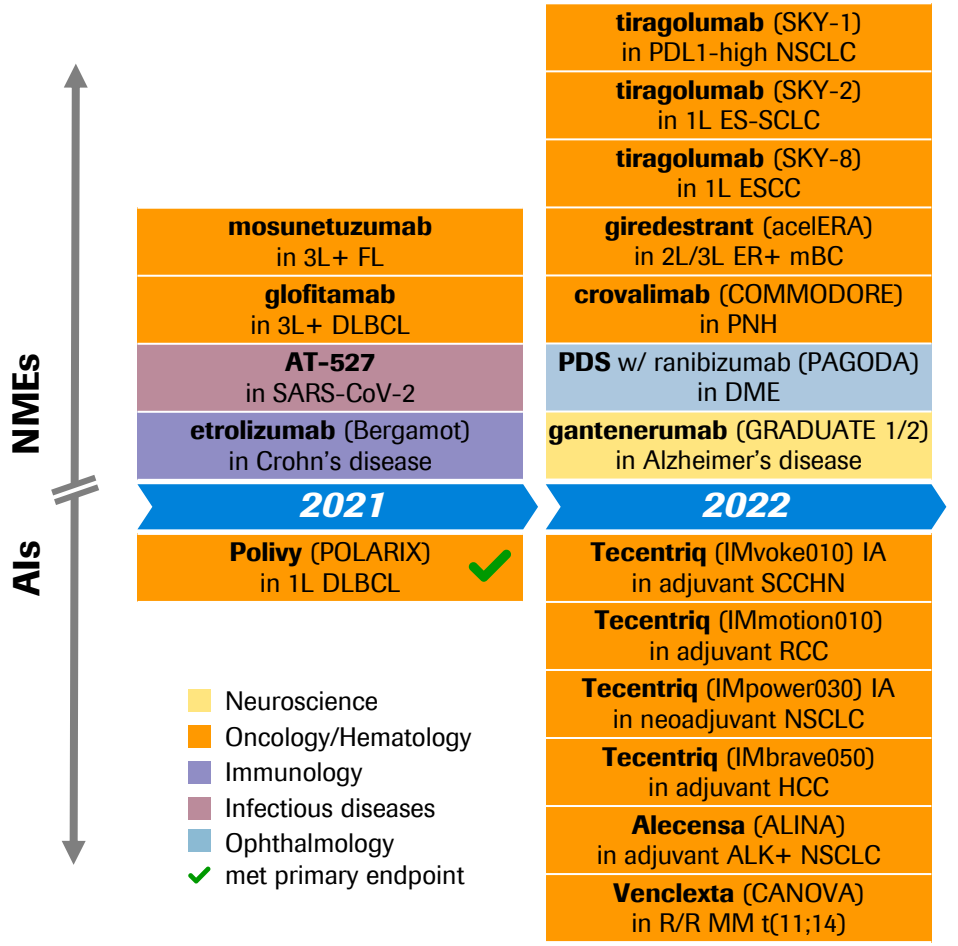
[1] Without buying CO2 certificates; [2] Genentech's annual average net price increase in the U.S., weighted by sales; [3] for inflation CPI-U Medical Care is used for all medical care expenditures (incl. prescription and non-prescription drugs, medical supplies, physicians' services, hospital services, and health insurance) – source: U.S. Bureau of Labor Statistics (US BLS); [4] for Roche Pharma

What can you expect from us?

Our replace and extend strategy is progressing well

Replace ongoing franchises		Entering new franchises
MabThera/Rituxan	Gazyva, Venclexta, Polivy, mosunetuzumab, glofitamab	**Oncology:** Tecentriq (mUC, SCLC, HCC, mM), ipatasertib (mCRPC), giredestrant (HR+ BC)
Herceptin	Perjeta, Kadcyla, Phesgo	**Non-malignant hem:** Hemlibra, SPK-8011, crovalimab (PNH, aHUS)
Avastin	Tecentriq, Alecensa, Rozlytrek, tiragolumab	**Neuroscience:** Ocrevus (RMS, PPMS), fenebrutinib (RMS, PPMS) Enspryng (NMOSD, gMG), Evrysdi (SMA), gantenerumab (AD), SRP-9001 (DMD)
Lucentis	Port delivery system (PDS) faricimab	**Infectious diseases:** Ronapreve (COVID-19), AT-527 (COVID-19)
Tamiflu	Xofluza	**Immunology:** etrolizumab (CD), Gazyva (LN, MN, SLE)
Esbriet	rhPentraxin-2	

Strong news flow ahead (data readout)

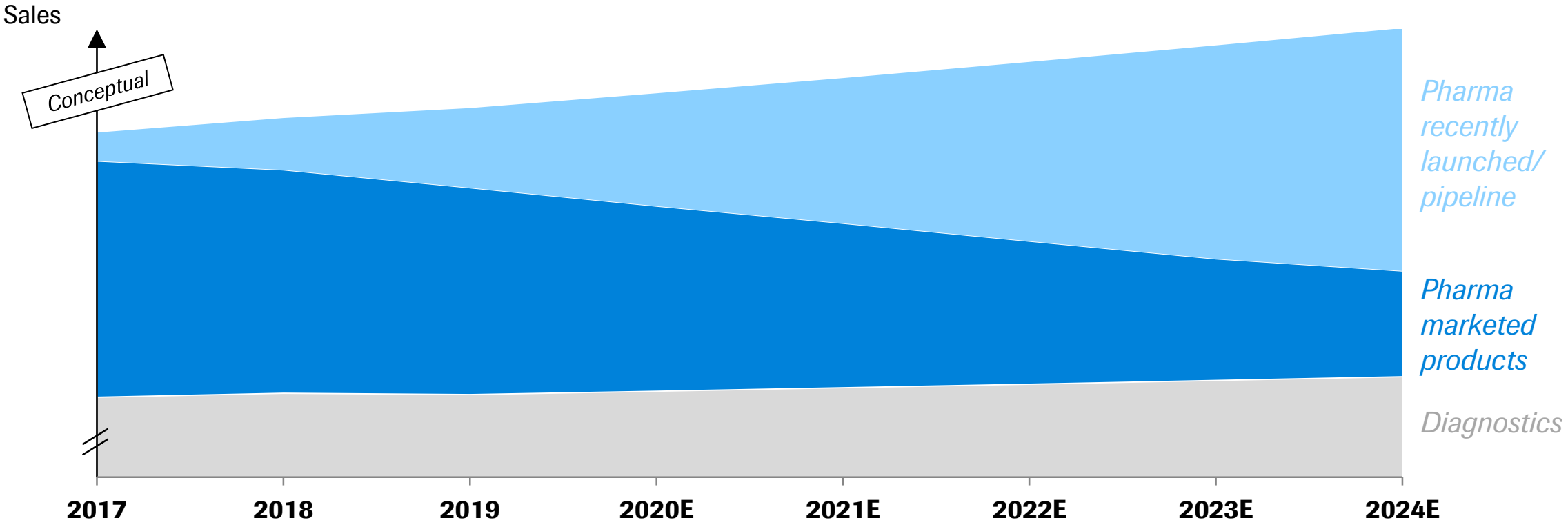


mUC=metastatic urothelial carcinoma; SCLC=small cell lung cancer; HCC=hepatocellular carcinoma; mM=metastatic melanoma; mCRPC=metastatic castration resistant prostate cancer; BC=breast cancer; PNH=paroxysmal nocturnal hemoglobinuria; aHUS=atypical hemolytic uremic syndrome; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; NMOSD=neuromyelitis optica spectrum disorder; SMA=spinal muscular atrophy; AD=Alzheimer's disease; DMD=duchenne muscular dystrophy; CD=Crohn's disease; SLE=systemic lupus erythematosus; FL=follicular lymphoma; DLBCL= diffuse large B cell lymphoma; NSCLC=non-small cell lung cancer; ESCC=esophageal squamous cell carcinoma; DME=diabetic macular edema; IA=interim analysis; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma

Positive outlook re-iterated

Pharma NME and Dia launches
Ocrevus, Perjeta, Hemlibra, Tecentriq, Venclexta, Gazyva, Alecensa, Xofluza, Polivy, Rozlytrek, Evrysdi, Enspryng, PHESGO, Gavreto, PDS, faricimab, etrolizumab, tiragolumab, gantenerumab, giredestrant, etc.

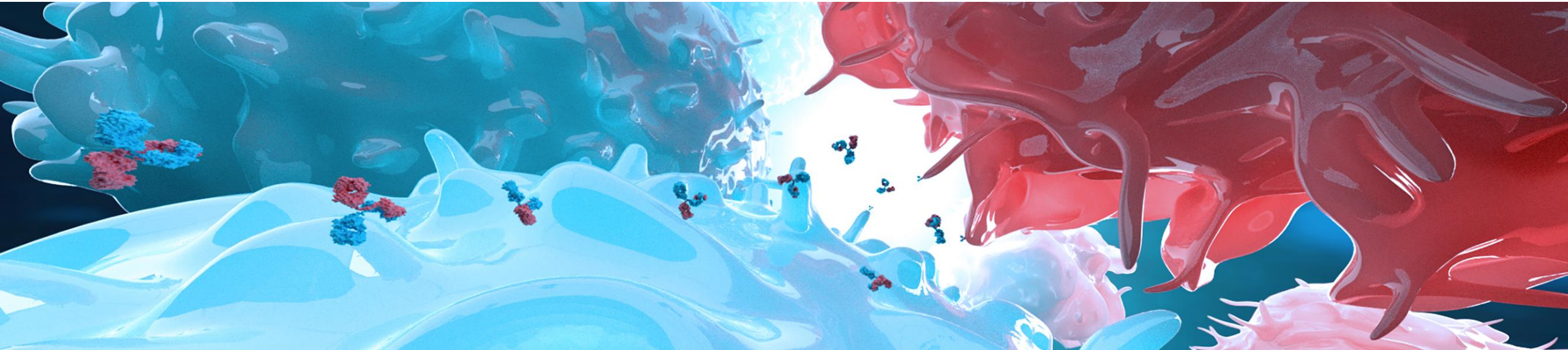
cobas 6800/8800, cobas 5800, cobas pure, cobas pro (high throughput), cobas Mass Spec, cobas Liat, etc.



Roche Late Stage Pipeline Event 2021

Near-term growth drivers

Teresa Graham | Head of Global Product Strategy

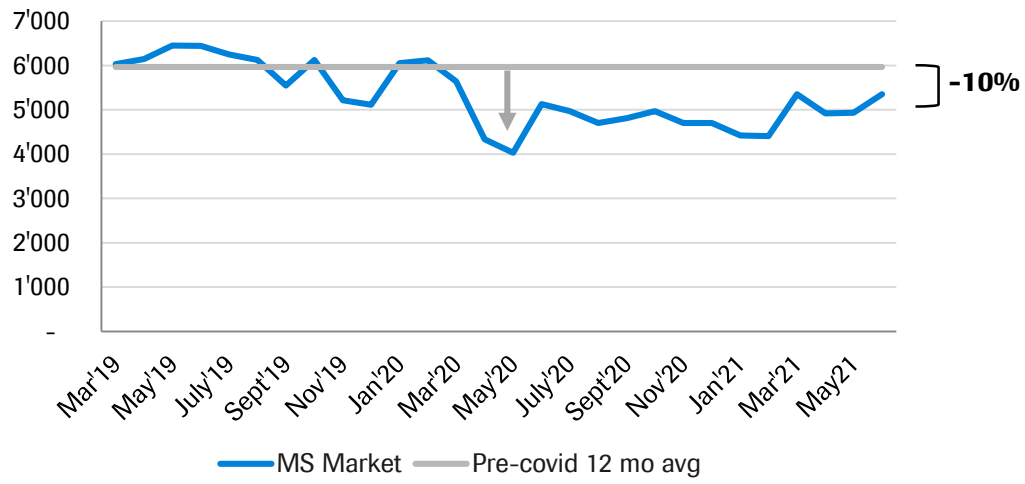


COVID-19 impact: normalization of healthcare systems ongoing

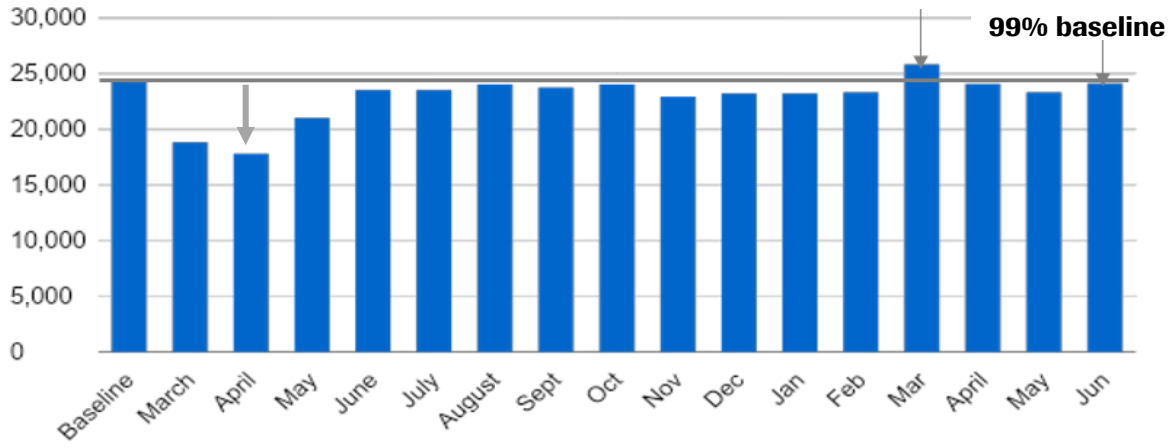
Pandemic continues to impact business dynamics

Some normalization, but not yet back to pre COVID-19 levels in certain indications and geographies

Multiple Sclerosis: US new-to-brand market[1]



Oncology US total patient visits[2]



[1] Source: IQVIA Apr Claims, IQVIA NSP (2-month rolling average); [2] Source: IQVIA U.S. Pharmaceutical Market Trend Report 2021

Significant short term news flow driving near term growth

2021 pivotal trial readouts

Molecule	Trial	Indication	Pts (US/EU5)	
Tecentriq	IMpower010	Adjuvant NSCLC	~101K[1]	✓
Polivy	POLARIX	1L DLBCL	~52K	✓
mosunetuzumab	Ph Ib GO29781	3L+ FL	~4k	
glofitamab	Ph Ib NP30179	3L+ DLBCL	~9K	
Hemlibra	HAVEN6	Mild/Moderate PwHA	~15k	
faricimab	TENAYA/LUCERNE	nAMD	~4,250K	✓
etrolizumab	BERGAMOT	Crohn's Disease	~580k[2]	
Evrysdi	JEWELFISH	SMA type 1/2/3 (switch)	~16K[3]	✓
Ronapreve	Study 2067	COVID-19 outpatient	N/A	✓
Ronapreve	Study 2069	COVID-19 prophylaxis		✓
AT-527		COVID-19		

Oncology/Hematology · Ophthalmology · Immunology · Infectious diseases · Neuroscience

2022 pivotal trial readouts

Molecule	Trial	Indication	Pts (US/EU5)
Tecentriq	IMvoke010	Adjuvant SCCHN	~40K[4]
Tecentriq	IMmotion010	Adjuvant RCC	~34K
Tecentriq	IMpower030	Neoadjuvant NSCLC	~10K[5]
Tecentriq	IMbrave050	Adjuvant HCC	~2K[6]
tiragolumab	SKYSCRAPER-01	1L PD-L1 high NSCLC	~44K
tiragolumab	SKYSCRAPER-02	1L SCLC	~40K
tiragolumab	SKYSCRAPER-08	1L ESCC	~16K
giredestrant	acelERA	2L/3L HR+ BC	~83K
Alecensa	ALINA	Adjuvant ALK+ NSCLC	~5k[7]
Venclexta	CANOVA	R/R MM t(11;14)	~9k
crovalimab	COMMODORE II/III	PNH	~4k
PDS	PAGODA	DME	~6,085k
gantenerumab	GRADUATE I/II	Alzheimer's Disease	~11,564k[8]

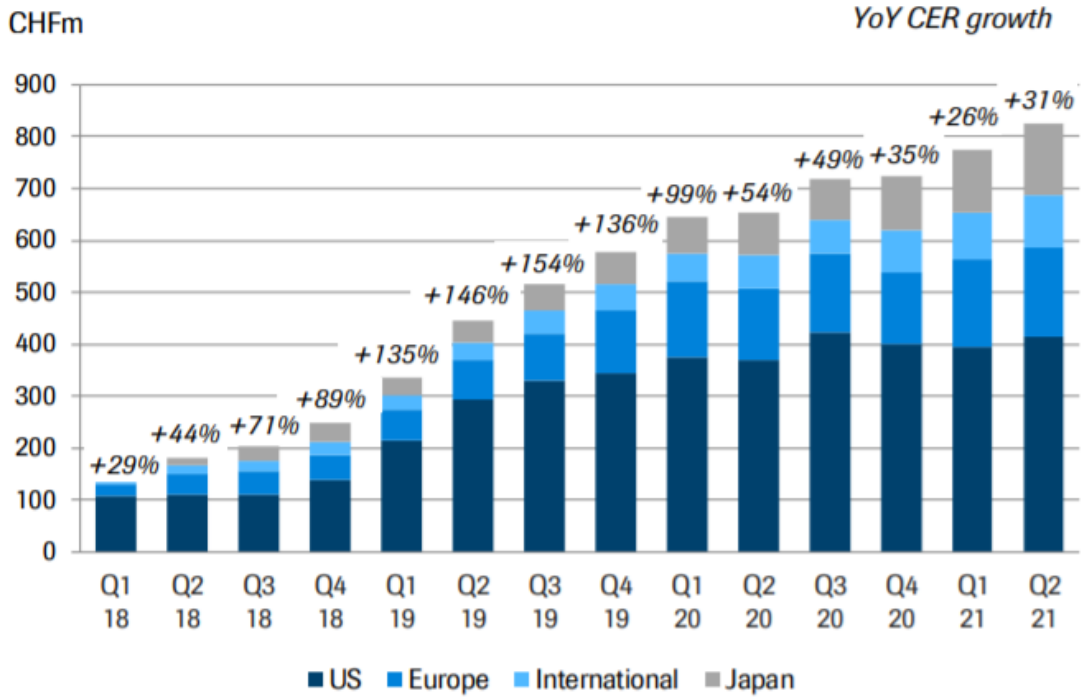
Source: Roche/Genentech Internal Epidemiology Data, all figures represent prevalence; [1] Stage I-III (operable) adjuvant treatment; [2] Moderated to severe; [3] Type 1/2/3 total prevalence; [4] Early stage patients; [5] Stage II-IIIB neoadjuvant treatment; [6] Adjuvant stage 0/A and B; [7] Stage I-III (operable) adjuvant treatment ALK+; [8] Prodromal and mild prevalent population

Commercial opportunities

1. **Oncology / Hematology**
   - Tecentriq
   - Tiragolumab
   - HER2-franchise (Kadcyla, Perjeta/Phesgo)
   - Giredestrant
   - Polivy
   - CD20xCD3 bispecifics (mosunetuzumab, glofitamab)
   - Hemlibra
2. **Ophthalmology / Immunology / Infectious Disease**
   - Faricimab
   - Port Delivery System
3. **Neuroscience / Rare Disease**
   - Ocrevus
   - Evrysdi
   - Gantenerumab

Tecentriq

Annualized sales >3b CHF with significant near term catalysts



Neoadjuvant / adjuvant

- Positive data in adjuvant NSCLC (IMpower010)
- Ph 3 readouts for Adj SCCHN, Adj RCC, Neoadj NSCLC, and Adj HCC all in 2022

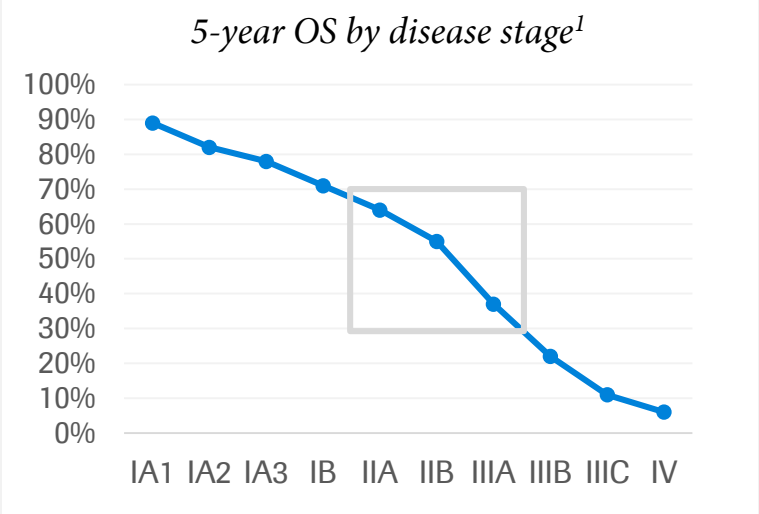
CIT combinations

- Tecentriq + Tiragolumab has the potential to reset the standard of care in markets where PD-1/PD-L1 already established

SCLC=Small Cell Lung Cancer; NSCLC=Non-Small Cell Lung Cancer; HCC=Hepatocellular Carcinoma; mUC=metastatic urothelial carcinoma; SCCHN=head and neck squamous cell carcinoma; RCC=renal cell carcinoma; CIT=cancer immunotherapy

Tecentriq: adjuvant NSCLC
Filed with FDA under RTOR (Priority Review)

High unmet need in early NSCLC



- Many patients with Stage I-III NSCLC continue to have disease recurrence/progression post-surgery

TECENTRIQ atezolizumab

Adjuvant NSCLC treatment is still evolving

Screening: Early detection technologies expected to increase diagnosis at early stage

Testing: Increasing with adjuvant development for EGFR+, PD-L1+, ALK+ patients

Systemic therapy: Adjuvant treatment rates expected to increase with new therapeutic options

[1] Chansky, et al Journal of Thoracic Oncology (2017); NSCLC=non-small cell lung cancer; RTOR=real time oncology review

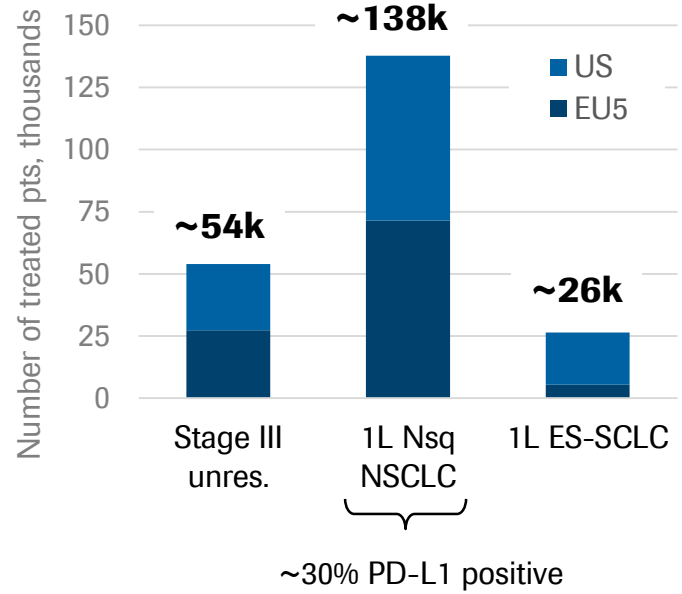
Tiragolumab (aTIGIT)

Nine Ph II/III trials initiated, with four readouts in 2022

	Indication	Ph 1 / Ph 2 / Ph 3	
Lung Cancer	1L NSCLC: PD-L1 high	SKYSCRAPER-01	2022
	1L ES-SCLC	SKYSCRAPER-02	2022
	Stage III unres. NSCLC	SKYSCRAPER-03	
	Neoadj / Adj NSCLC	SKYSCRAPER-05	
	1L NSq NSCLC	SKYSCRAPER-06	
Additional solid tumors	Locally advanced ESCC	SKYSCRAPER-07	
	1L ESCC	SKYSCRAPER-08	2022
	2L+ PD-L1+ Cervical Cancer	SKYSCRAPER-04	2022
	1L SCCHN	SKYSCRAPER-09	

- **Build on Tecentriq:** Improve on Tecentriq benefit in SCLC
- **Expand into early disease:** Trials initiated in ESCC and early NSCLC
- **Compete in new indications:** H2H trials in NSCLC vs. durva (St III), pembro + chemo (1L)

Lung Cancer: treated patients (US/EU5)



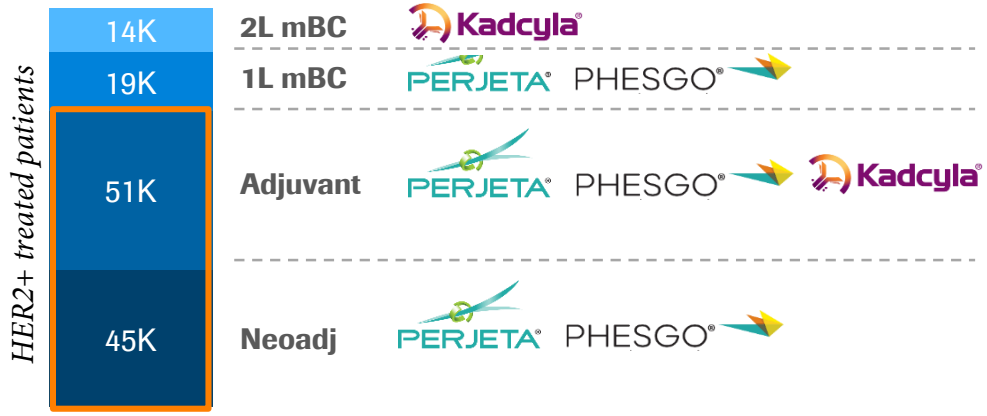
Current market size for PD-1/L1 in Lung Cancer is >$10B[1]

SCLC=Small Cell Lung Cancer; NSCLC=Non-Small Cell Lung Cancer; SCCHN=head and neck squamous cell carcinoma; ESCC=esophageal squamous cell carcinoma

HER2 Franchise

Continuing to innovate for patients with HER2+ BC

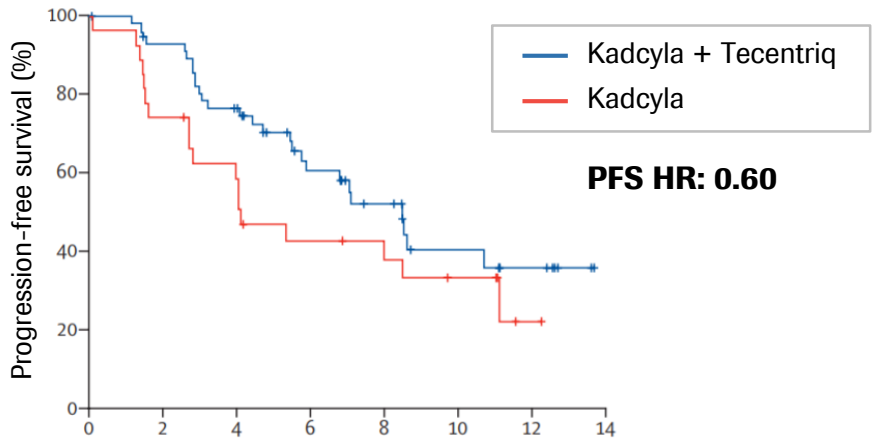
Near term growth driven by eBC, Phesgo uptake



- High bar established in eBC in terms of safety and efficacy (long-term iDFS data)
- >50% of Kadcyla sales in adjuvant setting
- Phesgo: seeing strong early uptake in US, in particular in academic institutions; strong conversion UK with reimbursement in other key markets ongoing

Continuing to build on existing standard of care

KATE-2 (2L+ HER2-positive mBC): PD-L1+ subset



- Combinations with Tecentriq initiated in PD-L1+/HER2+ BC
  - ASTEFANIA [Kadcyla+Tecentriq in high risk adj eBC]
  - NRG-BR004 [H+P+Tecentriq in 1L mBC]
  - KATE-3 [Kadcyla+Tecentriq in 2L+ mBC]

Phesgo in collaboration with Halozyme; eBC=early breast cancer; iDFS=invasive disease free survival; adj=adjuvant; mBC=metastatic breast cancer

Giredestrant (SERD)

Large addressable population, with best-in-class potential

	Endocrine Therapy Given until resistance or visceral disease present	**giredestrant** Replace ET as standard of care in all settings	HR+/HER2- treated population (US/EU5)
eBC	**ET**	**giredestrant**	**385K**
1L mBC	**ET** +/- CDK4/6i	**giredestrant** + CDK4/6i	**62K**
2L mBC	**ET** +/- targeted therapy	**giredestrant**	**44K**

First pivotal readout in 2L/3L mBC in 2022

High unmet need remains in HR+/HER2- BC

- Up to 50% of eBC pts stop treatment early due to tolerability[1]
- 30% of patients develop metastatic disease[2]
- Need for new therapies to overcome resistance

Potential for best-in-class SERD

- **Differentiated MOA**: immobilizes ER in the nucleus prior to degradation
- **High potency**: 7-15x more potent than other SERDs in development
- **Well tolerated** alone and in combination with CDK4/6i
- **Standardized dose**, 30mg once-daily selected for monotherapy/combo
- **Broadest clinical program:** only SERD with adjuvant trial vs. SOC

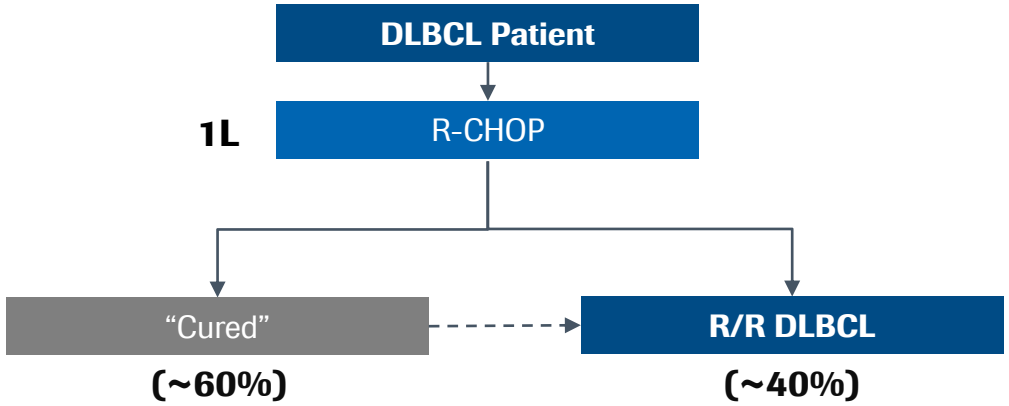
[1] Bowels A, et al *J Oncol Pract* 2012; [2] Ruhstaller, T. *J Clin Oncol* 2018; ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer; SERD=selective estrogen receptor degrader; SOC=standard of care

Polivy + R-CHP

First positive trial in 1L DLBCL in >20 years

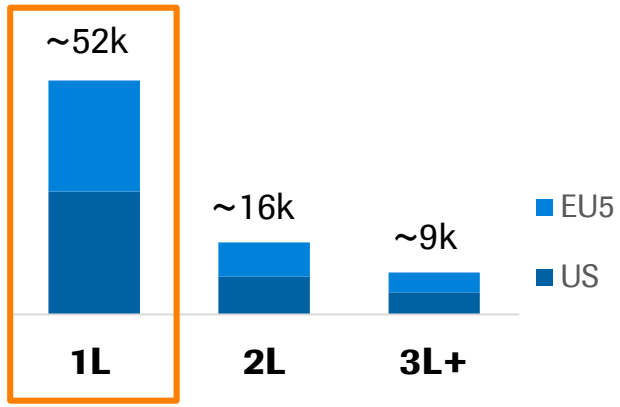
POLIVY® polatuzumab vedotin

1L DLBCL can be curative, but high unmet need remains



- ~40% of patients are not cured with R-CHOP in 1L
- Patients with R/R DLBCL have poor prognosis: mOS <2yrs

Multibillion CHF market opportunity in 1L DLBCL



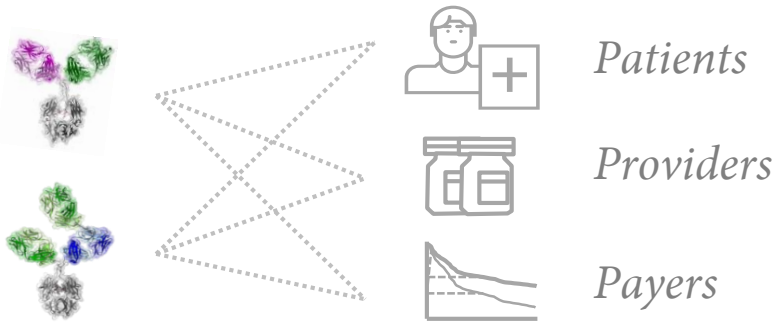
- No new 1L therapies approved since R-CHOP
- 3x more drug treated patients in 1L than 2L DLBCL
- No competitors expected in 1L DLBCL for >3.5 years

Polivy in collaboration with Seagen; R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; R-CHOP=Rituxan + cyclophosphamide + hydroxydaunorubicin + vincristine + prednisone; mOS=median overall survival

Mosunetuzumab and glofitamab (CD20 x CD3 bispecifics)

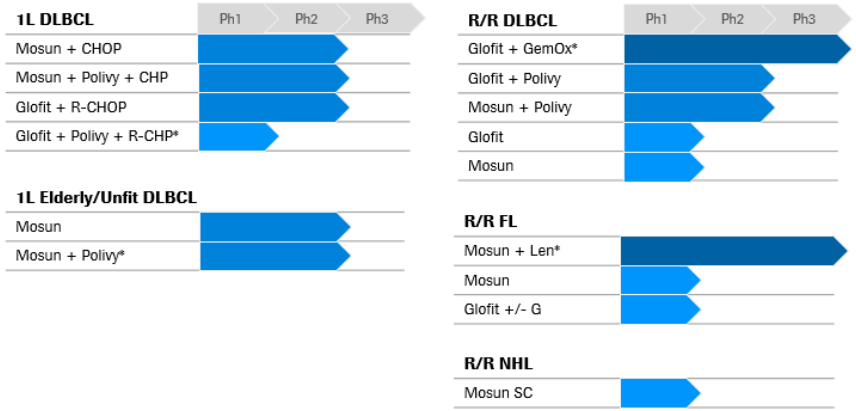
Potential to be first-in-class and best in class in FL and DLBCL

Mosun and Glofit are differentiated and can be tailored to address diverse patient and customer needs



- **Mosun**: attractive profile for the outpatient setting and across a broad range of indications and settings; no required hospitalization
- **Glofit:** best in class efficacy potential with high CR rates, and manageable CRS

Most advanced clinical development plan with pivotal cohorts reading out in 2021



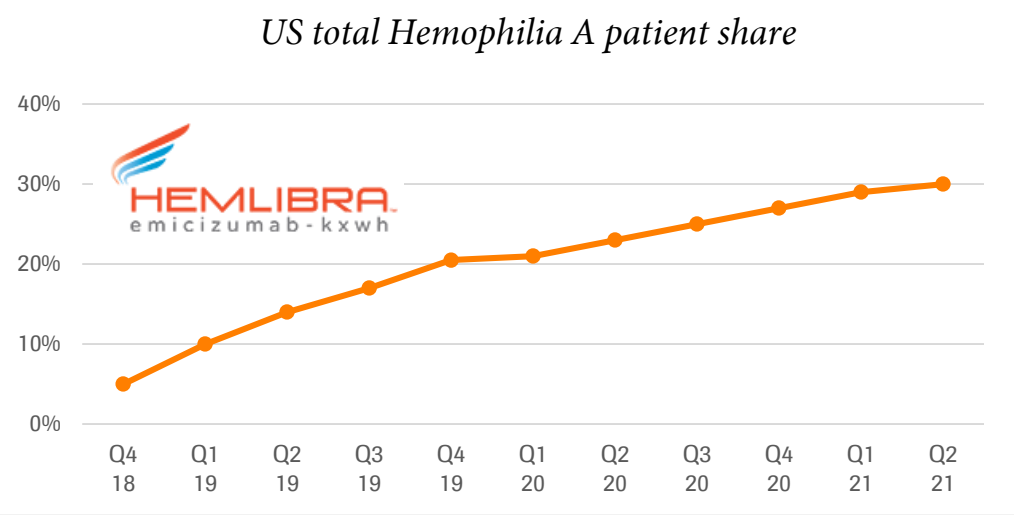
- **Late line monotherapy:** Mosun pivotal cohort (3L+ FL) filing in 2021, glofit pivotal cohort (3L+ DLBCL) filing in 2022
- **R/R NHL combinations:** Randomized Ph 3 trials initiated in R/R FL (mosun+len) and 2L+ DLBCL (glofit + GemOx)
- **1L DLBCL:** Moving into 1L DLBCL in combination with Polivy

R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; len=lenalidomide; gemOx=gemcitabine + oxaliplatin; CR=complete response; CRS=cytokine release syndrome

Hemlibra

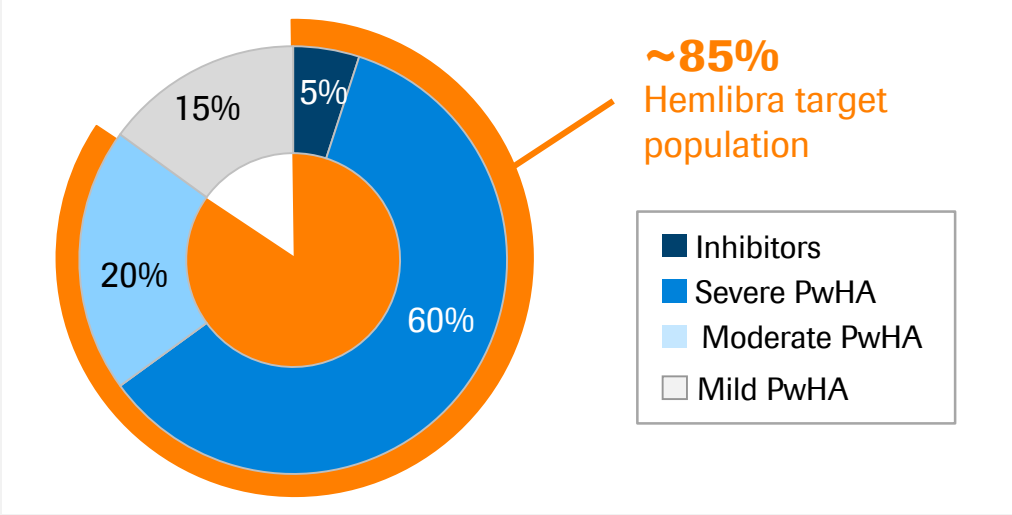
Transformational advance for Hemophilia A patients

Continuing to gain market share in US and globally



- 30% total patient in US (all severities), 28% patient share in EU5 (severe patients only)
- Non-inhibitor approval in >90 countries, reimbursement in >30 countries to-date
- Approved in China in Q2'21

Additional subgroups supported by further data



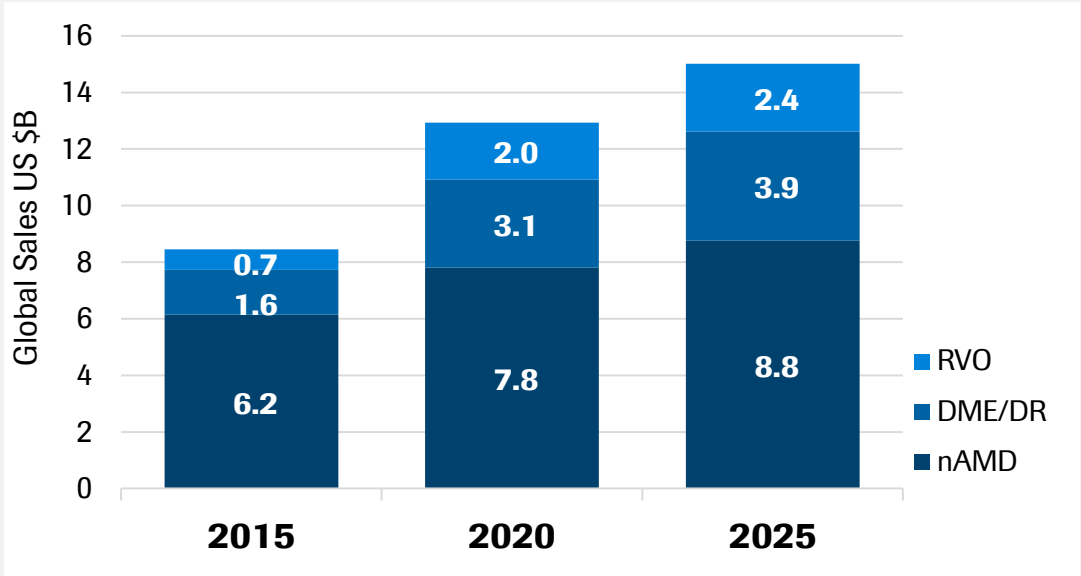
- HAVEN1-4: Five year follow-up (data expected in 2022)
- HAVEN6: Mild-moderate study for EU label; interim data submitted to ASH
- HAVEN7: <1yr; first novel therapy to be studied for prophylaxis in infants (data expected in 2022)

Source: Treated patients, Hemlibra Epidemiology models 2018; PWHA=People with Hemophilia A

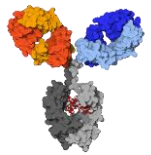
Ophthalmology

*Preparing for first launch of PDS in 2021 and faricimab in 2022**

Global retina market growing to $15b



- Market growth driven by aging population, product innovation
- Potential to further increase market size with increased compliance from less frequent dosing



Faricimab: First new MOA in nAMD/DME >15 yrs. Strong durability, with approximately half of patients able to be maintained on Q16W dosing

Port Delivery System (PDS): Permanent, refillable intraocular implant. Nearly all patients maintained on dosing every 6 months

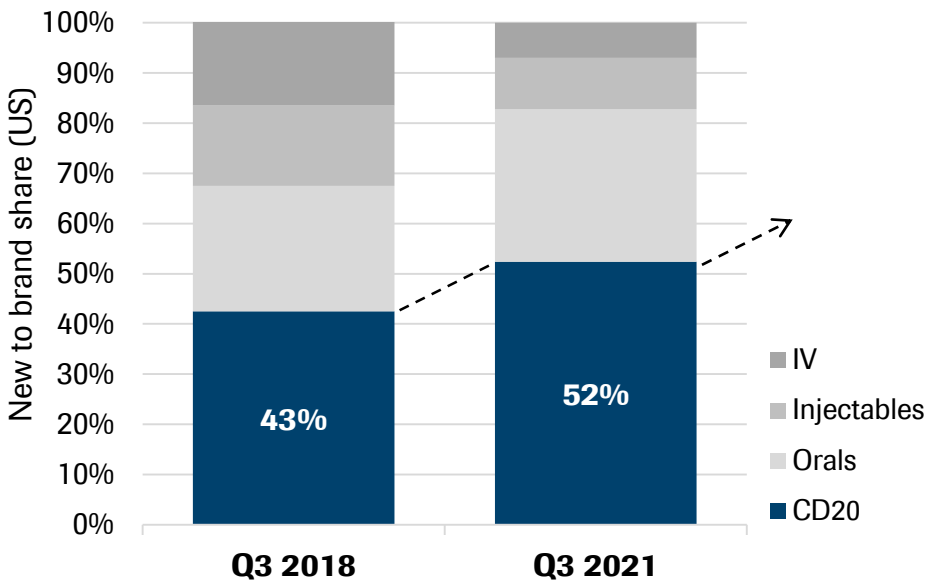
Global rights secured for faricimab and PDS

Source: Evaluate Pharma January 2021; * Timelines reflect first launch in US; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO=retinal vein occlusion

Ocrevus

Ocrevus continues to have a strong growth profile

Continued opportunity to grow CD20 class share



OCREVUS® ocrelizumab

Best in disease efficacy and safety

- Robust, consistent, and sustained delay in disability progression
- Ocrevus is the only therapy approved in PPMS
- >200K patients treated, with consistent benefit-risk profile
- Higher dose Ocrevus studies look to further improve on best-in-disease profile

Twice yearly dosing drives better compliance

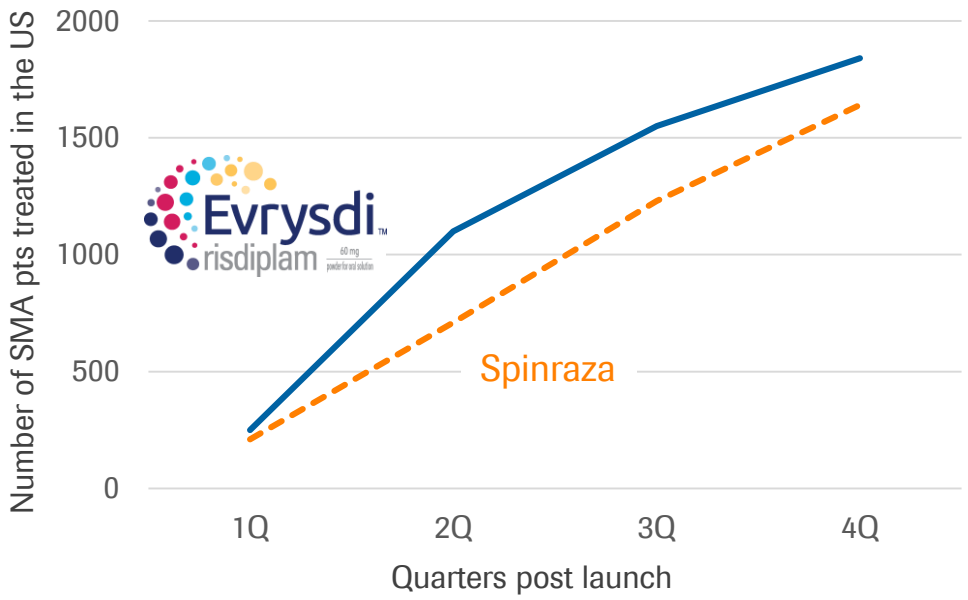
- >90% persistence/adherence after 1 yr; superior to oral & injectable medicines
- Short infusion (2h) further improves convenience
- Ocrevus has been infused in >46K locations in the US (~50% of infusions occur outside of the hospital)

Source: IQVIA; MS=Multiple Sclerosis; PPMS=Primary Progressive

Evrysdi

Growth supported by global expansion, and further share gains

US: fastest uptake for a DMT in SMA[1]



Seeing patients with all SMA types, broad range of ages, and both tx naïve and previously treated

Strong global launch with approval now in all major markets

- 20% market share in Germany within 4 months of launch
- Ongoing dialogue with EU reimbursement bodies
- Japan public reimbursement secured
- Approved in China

Global SMA market expected to grow to >$5b by 2025[2]

- Global expansion (significant untreated populations in many countries)
- Treatment of previously untreated Type 2/3 patients (driven by new options like Evrysdi)

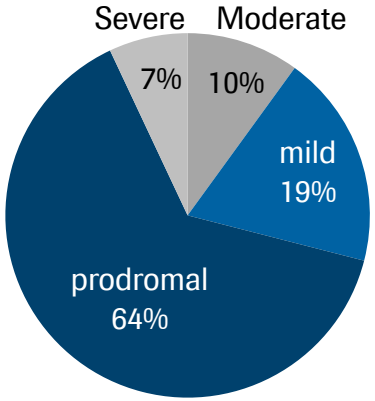
[1] Source: company reported data; [2] Evaluate Pharma; SMA=spinal muscular atrophy

Gantenerumab

Pivotal data expected 2H'22; most comprehensive data in AD

Large patient population and high unmet need

AD Continuum Distribution [2]



- 47M patients worldwide and projected to be 76M by 2030[1]
- 6th leading cause of death in the US[1]
- ~10M new cases / year who may be eligible for therapy[2]

Confidence in GRADUATE I/II to deliver clear & robust dataset

- Well powered: two parallel studies with ~1,000 participants each
- Extended trial duration: 27 months
- Maximized exposure: optimized titration scheme & single target dose regardless of APOE genotype
- Demonstrated Aβ plaque reduction (80% of patients below amyloid positivity threshold at 3 years in OLE)

First and only subcutaneous treatment for AD

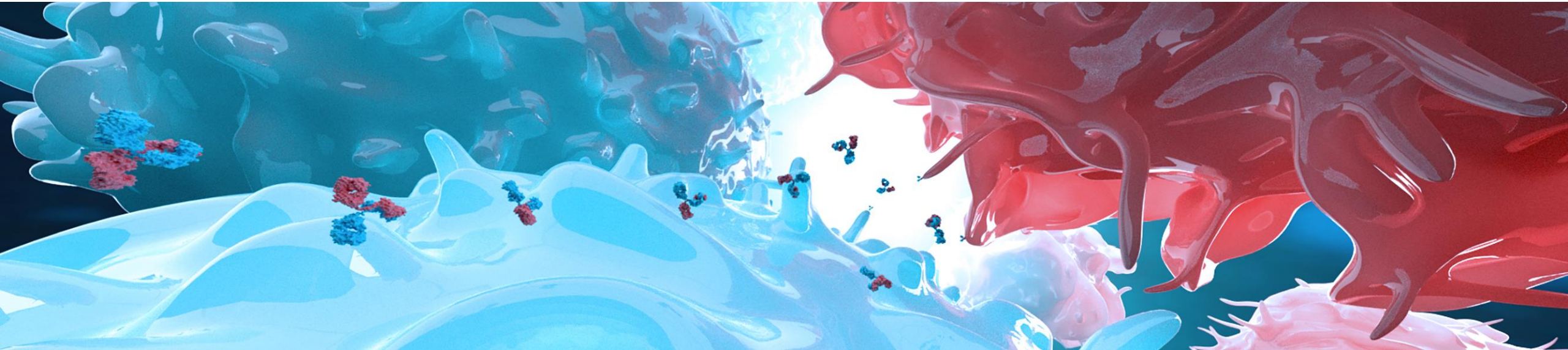
- SC delivery allows flexible care setting incl home-administration by caregiver
- Reduces the burden of IV infusions for AD patients
- Enables broad patient access and reduces health care burden

[1] Alzheimer's Association; [2] Roche/Genentech internal data; AD=Alzheimer's Disease; OLE=open label extension

Roche Pharma Day 2021

Late Stage Pipeline Oncology

Levi Garraway |
Chief Medical Officer and Head Global Product Development



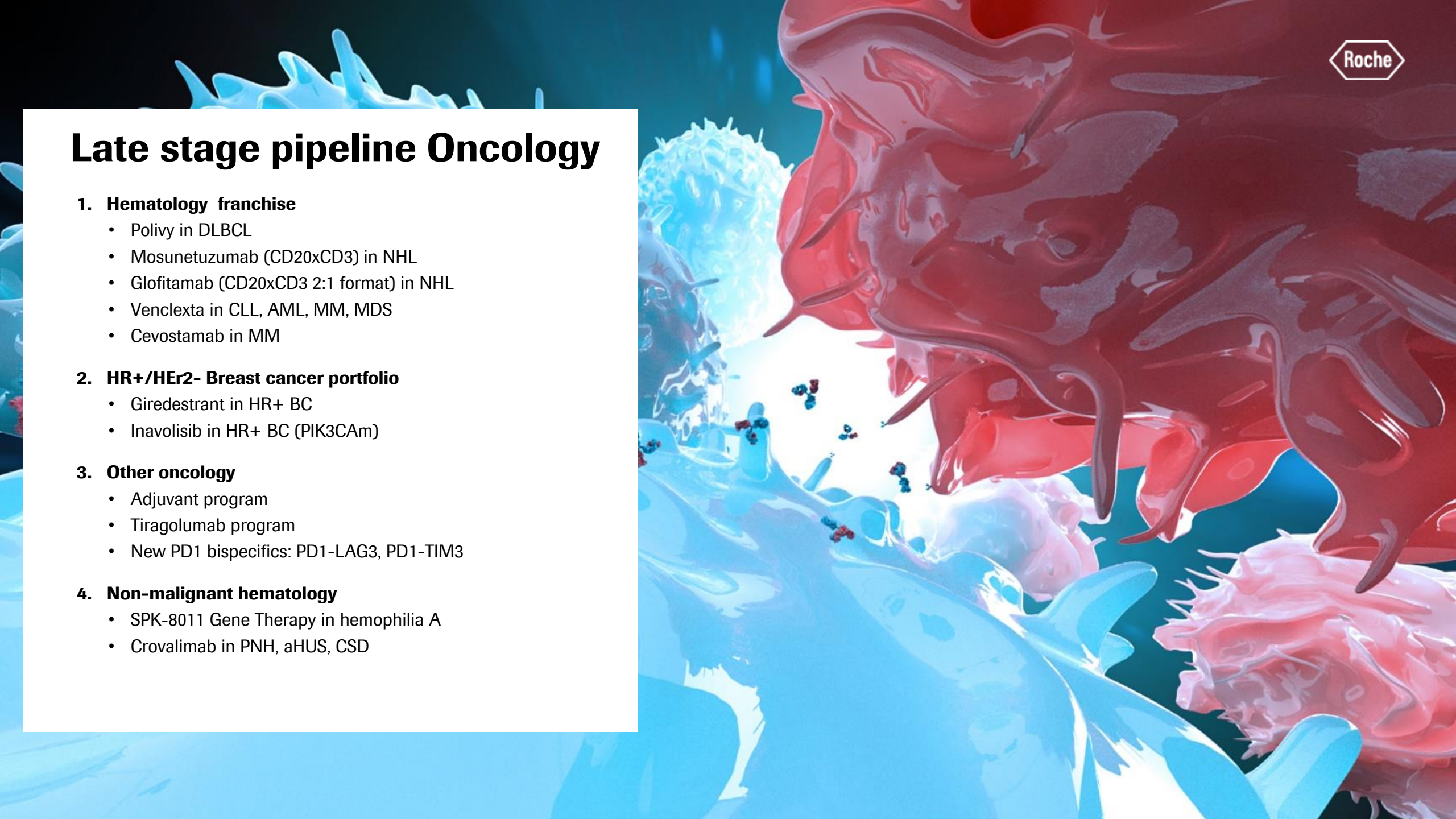
Late stage pipeline Oncology

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

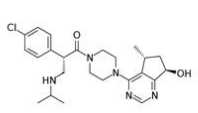
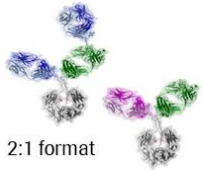
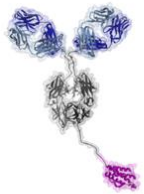
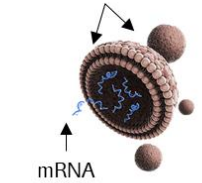
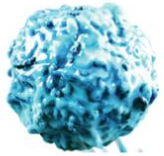
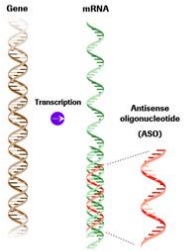
RG6058	**tiragolumab + Tecentriq** 1L PD-L1+ NSCLC
RG6114	**inavolisib** 1L HR+ BC
RG7446	**Tecentriq** SC NSCLC
RG7446	**Tecentriq + cabozantinib** 2L NSCLC
RG7446	**Tecentriq + cabozantinib** advanced RCC
RG7446	**Tecentriq + Avastin** adjuvant HCC
RG7446	**Tecentriq** neoadjuvant NSCLC
RG7601	**Venclexta**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

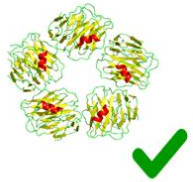
2024 and beyond

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	Bi-specifics	Fusion protein	mAb	Antibody drug conjugate	Neoantigen vaccines	Personalized T cells	Antisense RNA	Gene therapy
								
• ipatasertib • inavolisib • giredestrant • KRAS G12C • TLR7 agonist • belvarafenib • SHP2i	• mosunetuzumab • glofitamab • cibisatamab • Her2 x CD3 • glypican-3 x CD3 • cevostamab • PD1 x TIM3 • PD1 x LAG3 • TYRP1-CD3	• PD1-IL2v • CD19-4-1BBL • FAP-4-1BBL • MAGE-A4 ImmTAC • IL15/IL15Ra-Fc • FAP-CD40	• tiragolumab • CD25 mAb • codrituzumab • CD137	• preclinic	• autogene cevumeran	• programmed T cells	• Factor B ASO • HBV siRNA • PDL1 LNA • UBE3A LNA	• SPK-8011 • SPK-8016 • SPK-3006 • SPK-7001 • SRP-9001
Target oncogenes, induce apoptosis, supress tumor growth	*Engage and activate T cells to kill tumour cells*	*Amplify immune response*	*Amplify immune response*	*Targeted toxic payload*	*Patient's neo-antigens for anti-tumour immune response*	*Patient's neo-antigens for anti-tumour immune response*		
• fenebrutinib • ralmitaront • GABA Aa5 PAM • PTH1R agonist • NLRP3 inhibitor • Abx MCP • CpAM • AT-527	• faricimab • FIXa x FX • FGFR1 x KLB • VEGF x Ang2 Duta	• brain shuttle gantenerumab • efmarodocokin alfa • IgG-IL2	• crovalimab • gantenerumab • prasinezumab • semorinemab • etrolizumab • TLR4 mAb • HtrA1 mAb • anti-tryptase					

Recombinant proteins	Oncolytic adenovirus
	
• rh pentraxin-2	• Type 5 adenovirus

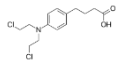
☐ = Oncology pipeline

✓ = Products approved

* 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

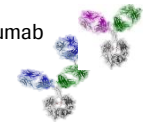
2019 POLIVY polatuzumab vedotin

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 (FDA BTD)	mosunetuzumab (FDA BTD)

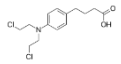
Total CLL, DLBCL, FL market growing to 9bn & 15bn, respectively by 2024[1]

✓ = 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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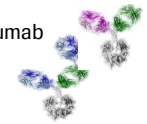
VENCLEXTA venetoclax tablets

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

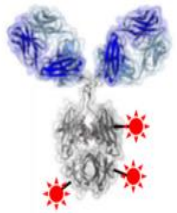
R/R=relapsed refractory; LDAC=low dose aracytarabine; HMA=hypomethylating agent; [1] Datamonitor and Evaluate Pharma; Venclexta in collaboration with AbbVie

Hematology: Polivy in DLBCL

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

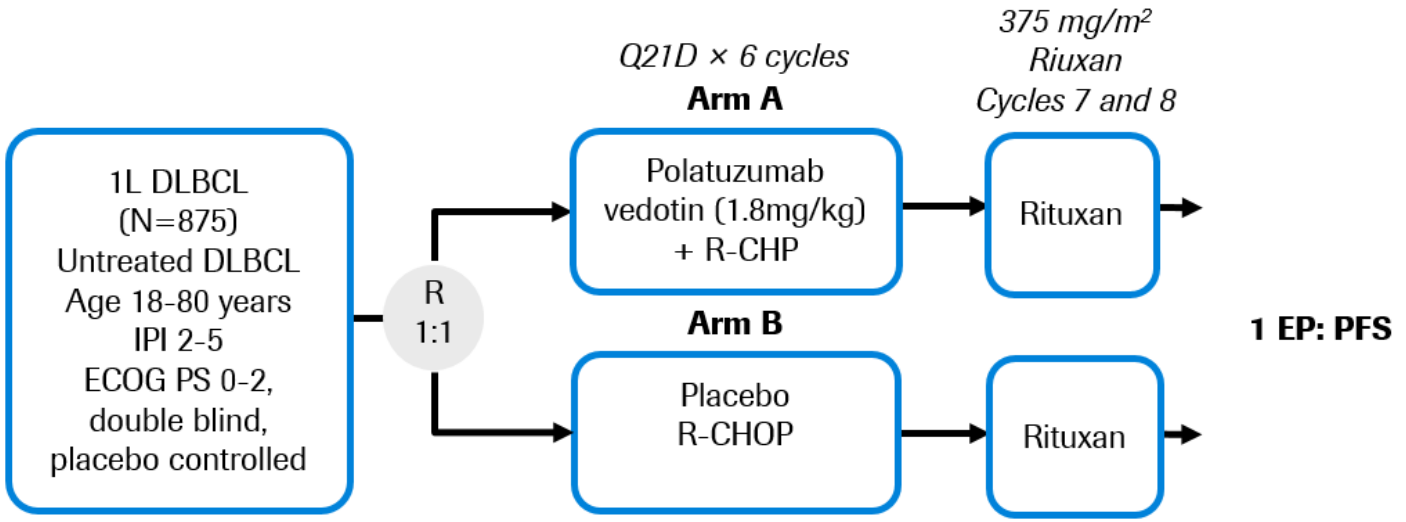
Polivy program

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



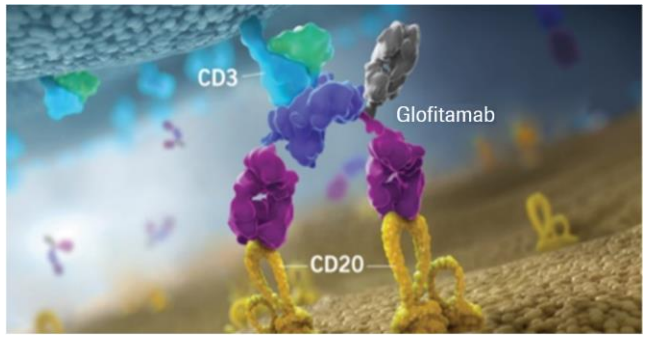
- Positive Ph III (POLARIX) results for Polivy + R-CHP in 1L DLBCL to be presented at upcoming conference
- Ph III (SUNMO) in 2L+ DLBCL for Polivy + mosunetuzumab to be initiated

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

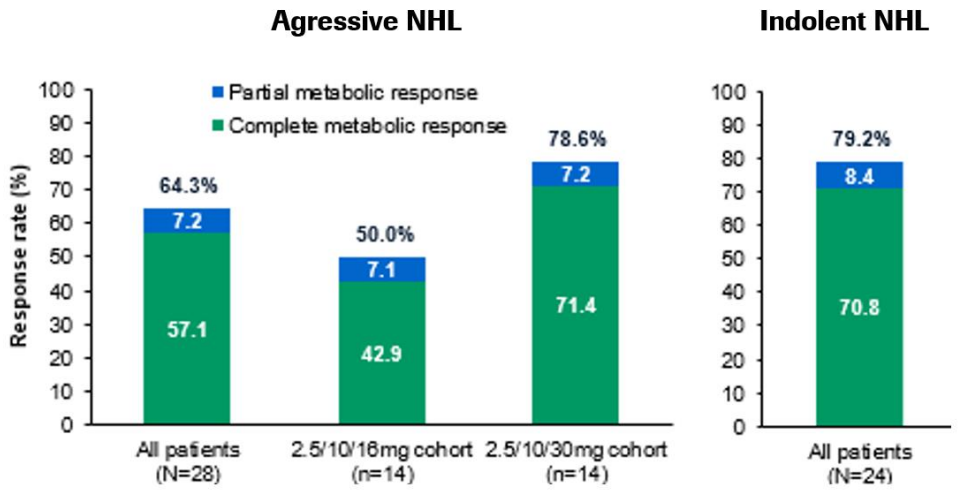
Glofitamab program



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)



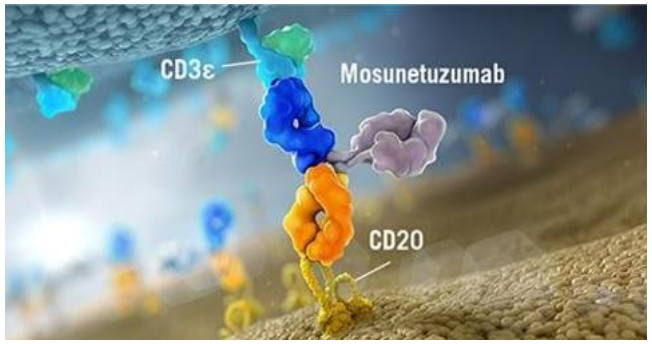
- High and durable response rates in patients who have failed multiple lines of treatment
- Good safety profile with manageable CRS largely confined to cycle 1
- Ph III (STARGLO) for glofitamab + GemOx in 2L+ DLBCL started in Q1 2021
- Combination development with G/R-CHOP and Polivy+/- R-CHP in DLBCL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

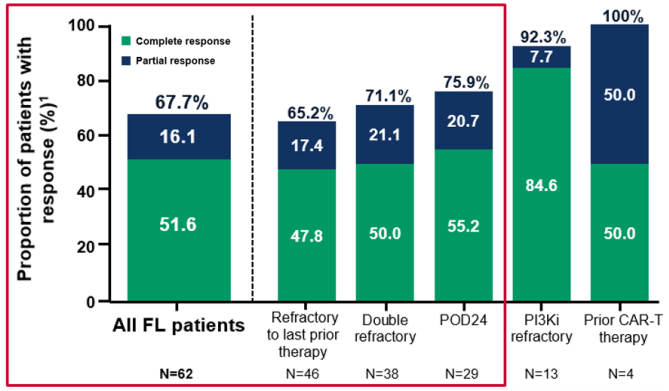


Combination	Indication	Ph1 Ph2 Ph3
mosun+len	R/R FL	
mosun+CHOP	1L DLBCL	
mosun+CHP+Polivy	1L DLBCL	
mosun	R/R DLBCL/FL/MCL	
mosun	1L unfit DLBCL	
mosun SC+Polivy	1L unfit DLBCL	
mosun	3L+ DLBCL/FL	
mosun+Polivy	R/R DLBCL	
mosun+Tecentriq	R/R DLBCL/FL	
mosun SC	R/R DLBCL/FL	

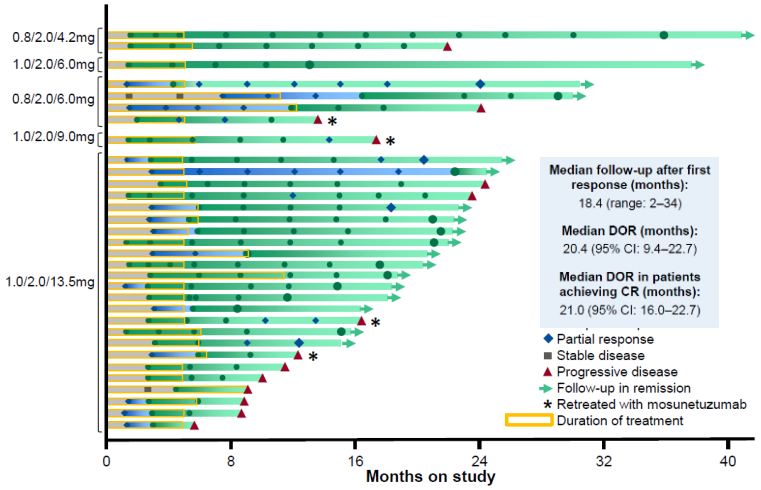
Ph I mosunetuzumab step up dosing in heavily pretreated R/R FL

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

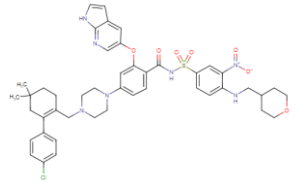
VENCLEXTA venetoclax tablets 10mg, 50mg, 100mg

Roche

ASH 2020

Venclexta progam

Bcl-2 inhibitor

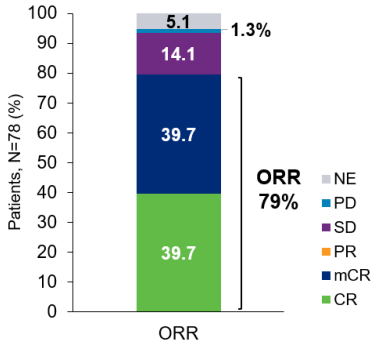


	Combination	Indication	Ph1	Ph2	Ph3
NHL	*V+P+G/R*	R/R DLBCL/FL			
CLL	*V+G*	1L unfit CLL			✓
	V+R	R/R CLL			✓
	V	R/R CLL 17p			✓
	V	R/R CLL after ibru/idel			
	V+G	1L fit CLL			
MM	*V+dex*	t(11;14) R/R MM			
	V+carfilzomib +dex	t(11;14) R/R MM			
AML	*V+aza*	1L unfit AML			✓
	V+LDAC	1L unfit AML			✓
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

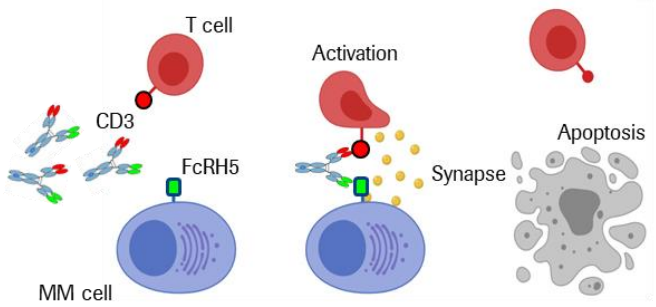
Garcia et al, ASH 2020; [1] Sekeres MA, et al. *J Clin Oncol*. 2017;35(24):2745–53; BTD=break through designation; CLL=chronic lymphoid leukemia; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; mOS=median overall survival; V=Venclexta; P=Polivy; G=Gazyva; R=Rituxan; dex=dexamethasone;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

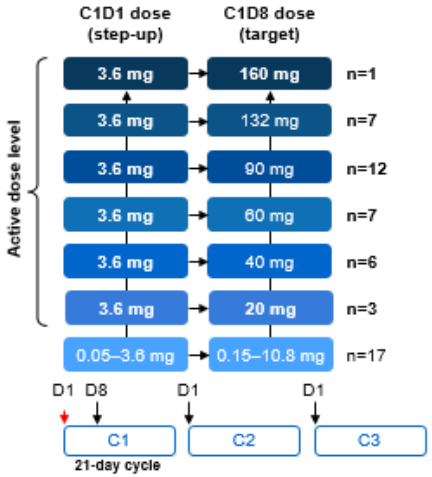
ASH 2020

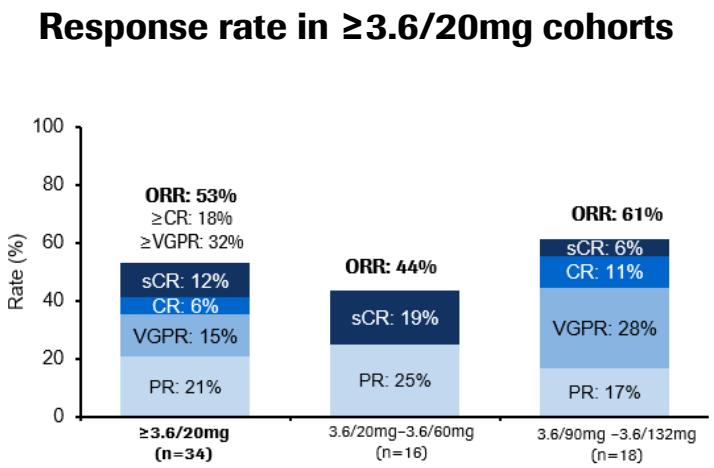
FcRH5 x CD3 bispecific mAb



- 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





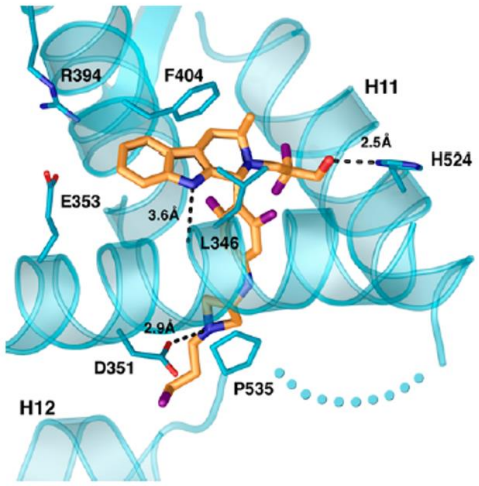
- Preliminary Ph I dose escalation data: Strong response rates in refractory patients (7/17, ORR: 41%) and patients with prior BCMA (5/8, ORR: 63%); Responses observed across all FcRH5 expression levels (FcRH5 expression on myeloma cells detected in all patients)
- Manageable toxicities with step-up 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

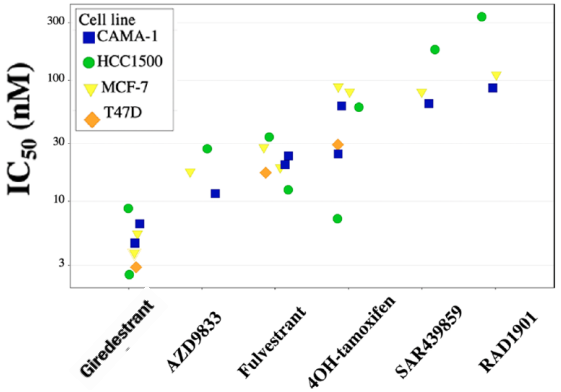
Selective ER degrader (SERD)



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

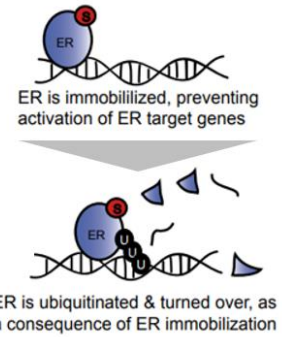
Well differentiated small molecule

In vitro potency comparison



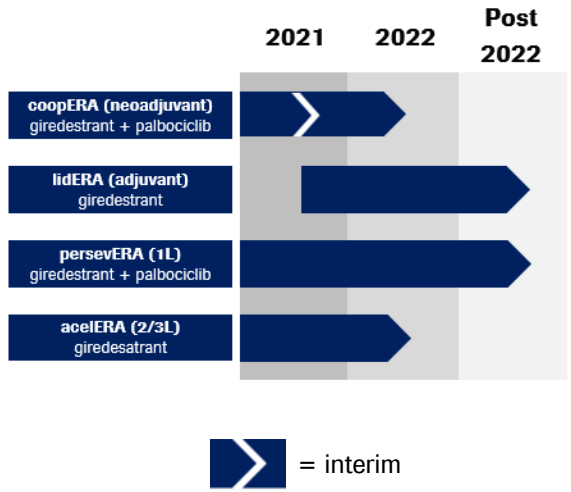
Editorial by Shao P., J.Med.Chem. 2021

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
- Differentiated 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

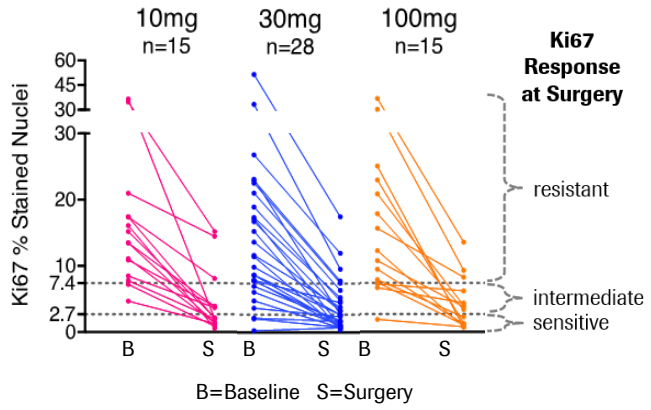
Liang J. et al., J.Med.Chem. 2021; SERD=selective ER degrader; HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; MOA=mechanism of action; DDI=drug drug interaction

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

2021 ESMO congress 16-21 SEPTEMBER 2021

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 (acceleRA) 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

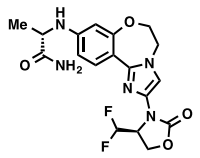
- Potentially best-in-class efficacy in combination with a CDK4/6 inhibitor in pre-treated patients, regardless of ESR1 resistance mutations
- No drug-drug interactions observed
- Well-tolerated up to 100 mg daily
- Expansion cohort at 30 mg daily on-going
- Ph III (persevERA) giredestrant + palbociclib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

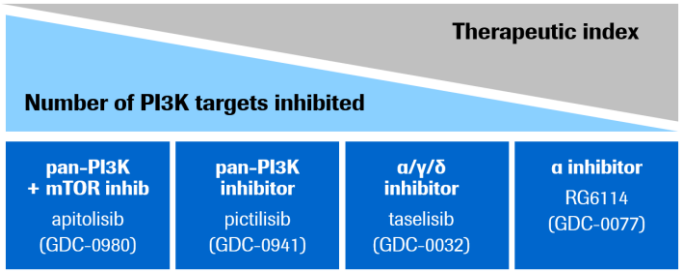
Moore H.M. et al., ASCO 2021; Jhaveri K.L. et al., ASCO 2021; Lim E. et al., ASCO 2020; HR=hormone receptor; BC=metastatic breast cancer; ER=estrogen receptor; * complete cell cycle arrest defined as Ki67 ≤2.7%; ORR=overall response rate; CBR=clinical benefit rate; ** ORR in patients with baseline measurable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

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

Ph III for potentially best in class PI3Kα inhibitor started

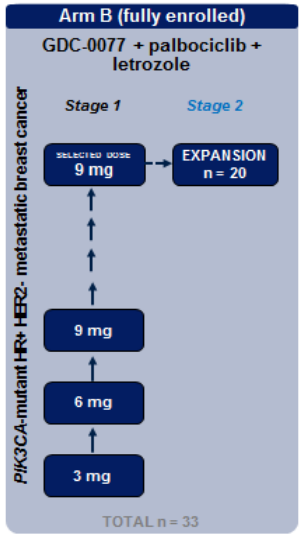
PI3Kα inhibitor/mutant PI3Kα degrader

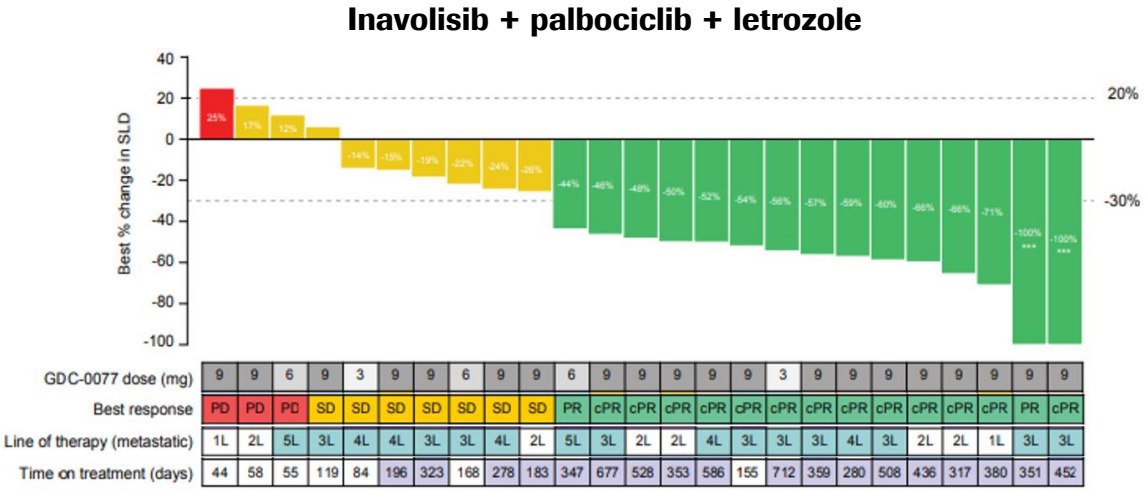




- Differentiation from previous PI3K inhibitors:
  - More selective for PI3Kα subunit
  - Greater safety margins
  - Better in vivo efficacy
- Degrades mutant PI3Kα efficiently
- Combines well with other therapies

Ph I (dose escalation and expansion cohort)





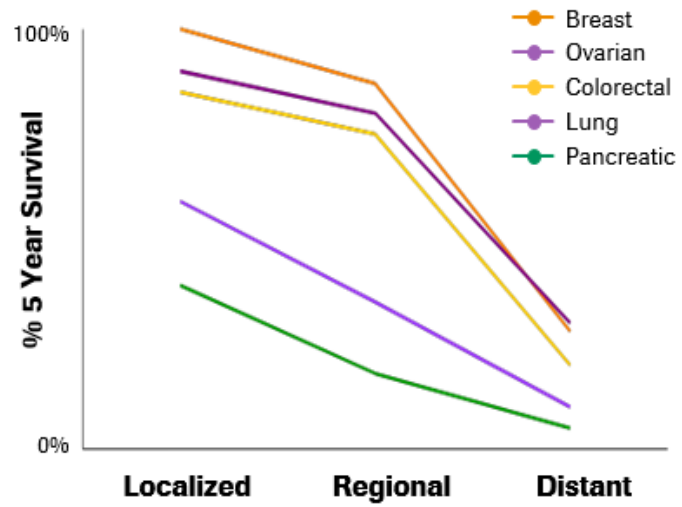
- Strong efficacy in ongoing Ph I/Ib as single agent or as combo with ET (letrozole or fulvestrant) +/- palbociclib in patients with locally advanced or metastatic *PIK3CA*-mutant solid tumors
- Favorable safety as single agent or when combined
- Ph III (INAVO120) inavolisib + palbociclib + letrozole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

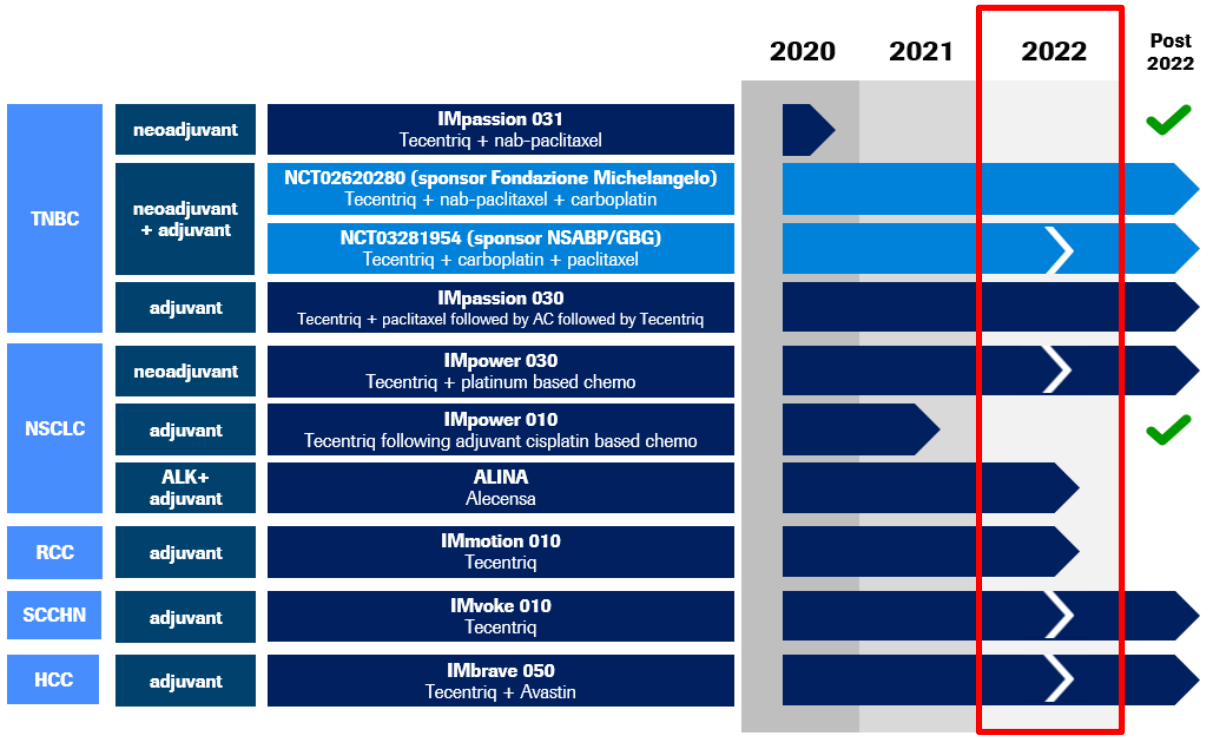
Earlier treatment increases chances for cure

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

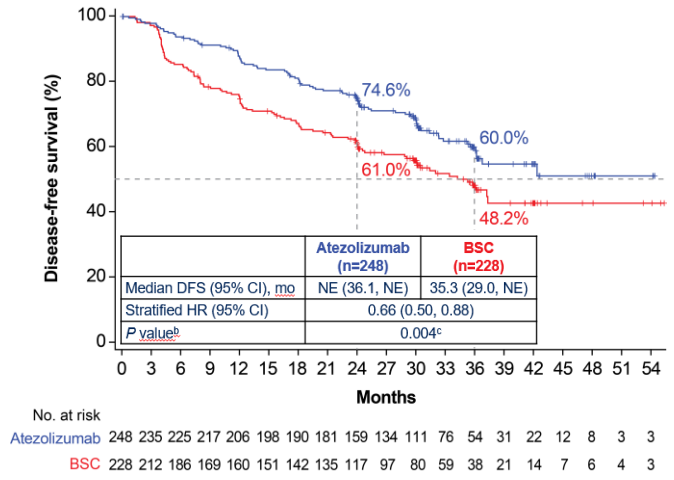
Lung franchise: Tecentriq in adjuvant NSCLC

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

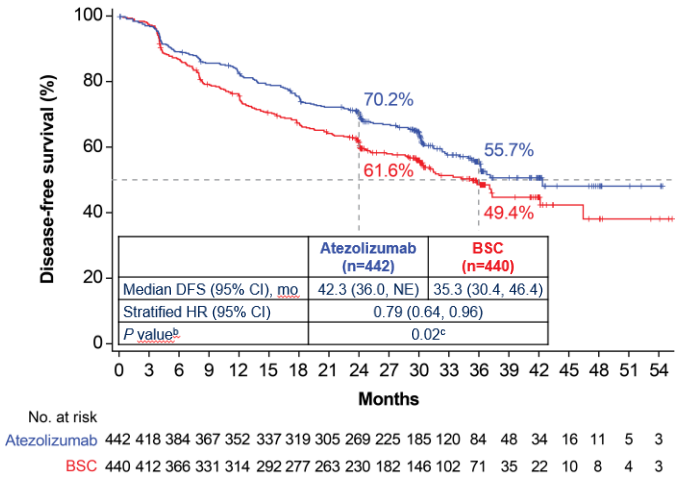
FDA RTOR review

Ph III (IMpower010) interim results in adjuvant NSCLC

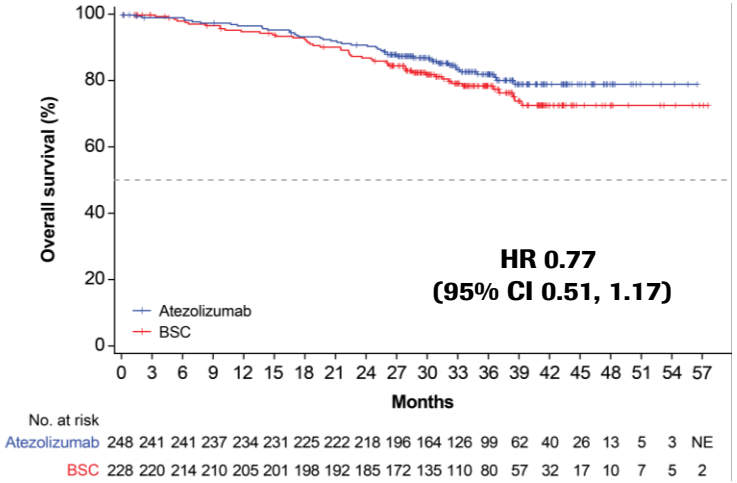
DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population



DFS in the all-randomized stage II-IIIA population



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



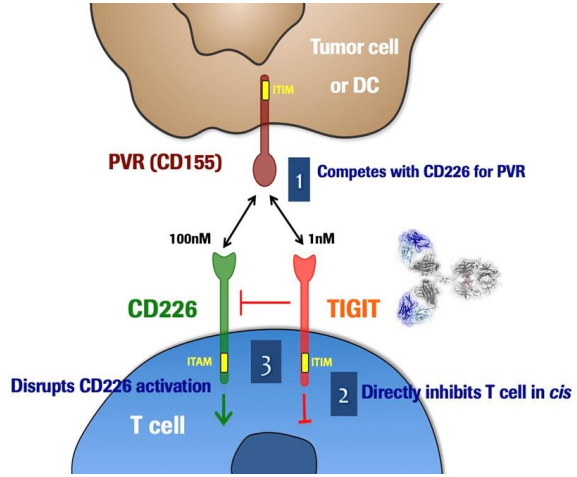
- Improvement in DFS for PD-L1+ Stage II-IIIA (HR=0.66) and all stage II-IIIA patients (HR=0.79); Follow-up will continue for DFS in ITT (Stage IB-IIIA)
- OS data immature at time of DFS interim analysis; next OS interim and DFS final expected in 2022
- Filed with FDA under RTOR and Project Orbis (priority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

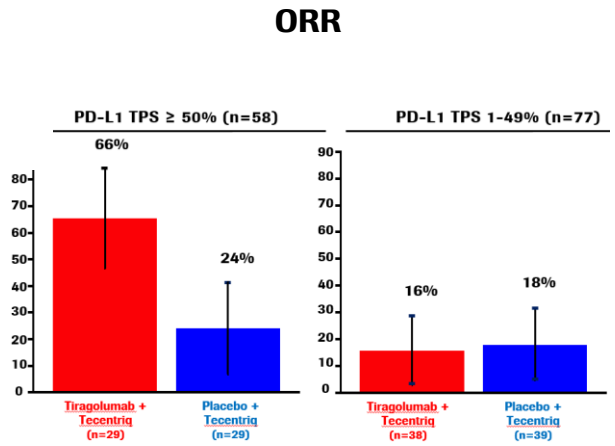
Four Ph II/III tiragolumab studies reading out in 2022

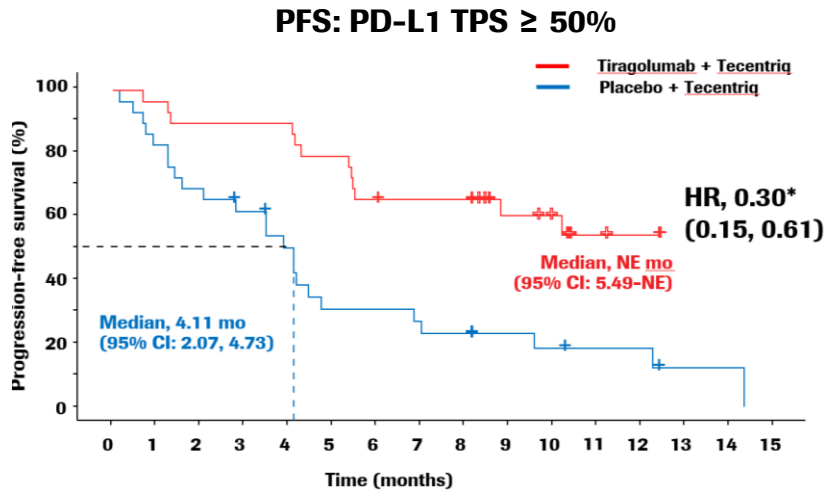
Anti-TIGIT mAb



- 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



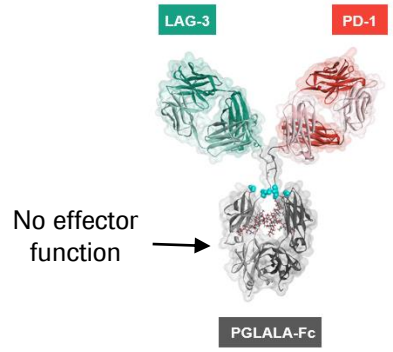


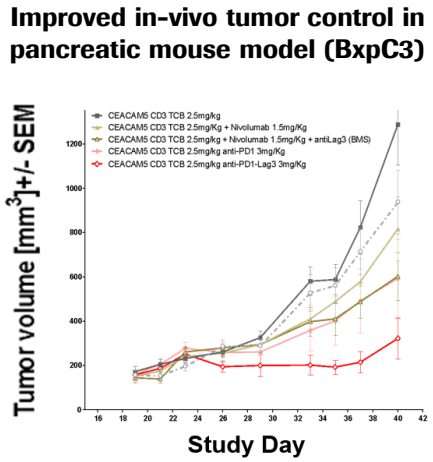
- Tiragolumab + Tecentriq showed clinically meaningful improvement in ORR and PFS in the ITT population with a greater magnitude of improvement in the PD-L1 TPS ≥ 50% subgroup
- Tiragolumab + Tecentriq was well-tolerated with a safety profile similar to the control arm
- Ph III in 1L PDL1+ NSCLC (SKYSCRAPER-01), 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

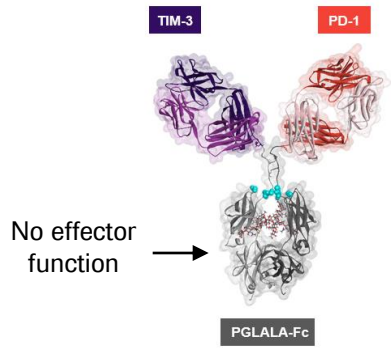


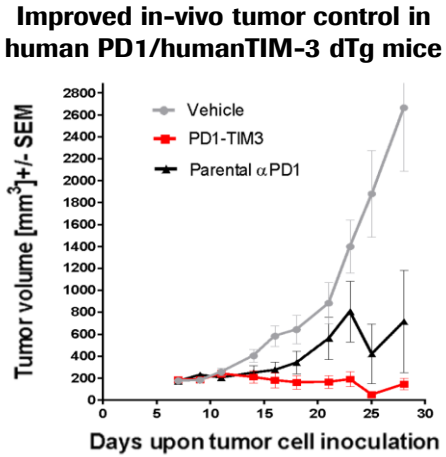


Deak L.C. et al., SITC Meeting 2019

- 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

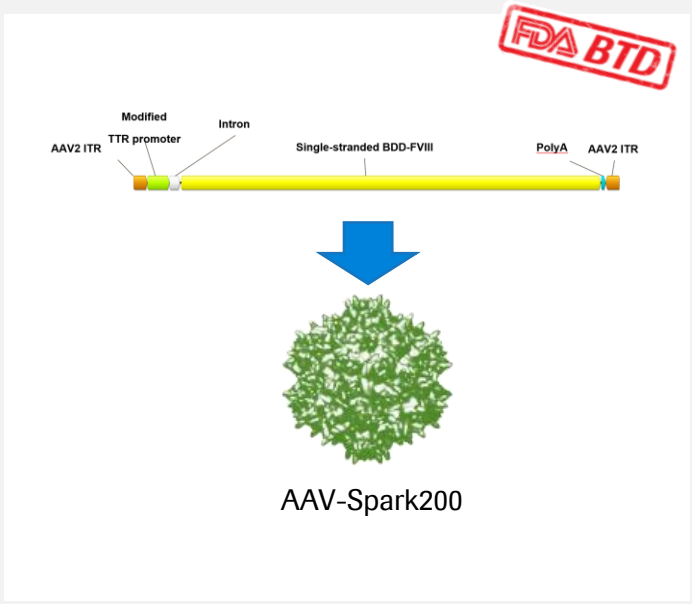
- PD1 x TIM 3 shows improved control of tumor growth and eradication vs. PD1 in animal models
- Bispecific mAb binding to PD-1 (high affinity) and TIM3 (low affinity)
- May reinvigorate exhausted T cells by blocking co-inhibitory checkpoint receptors
- Ph I monotherapy in 2L melanoma, 2/3L NSCLC, 2L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

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

Non-malignant hematology: SPK-8011 in hemophilia A

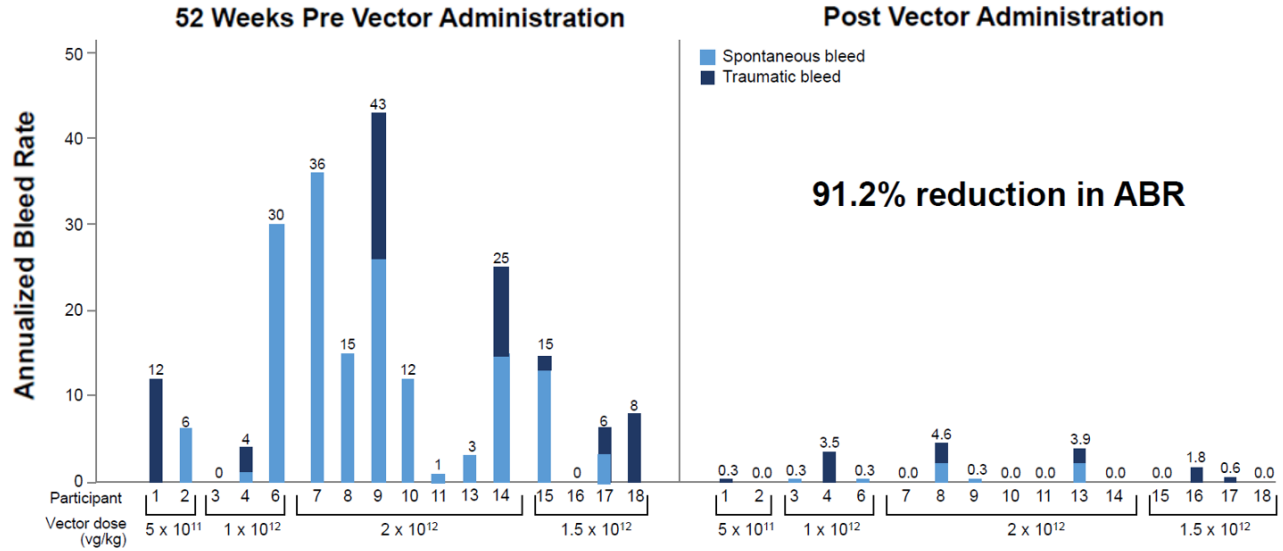
Efficacy and safety data up to 4 years

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)



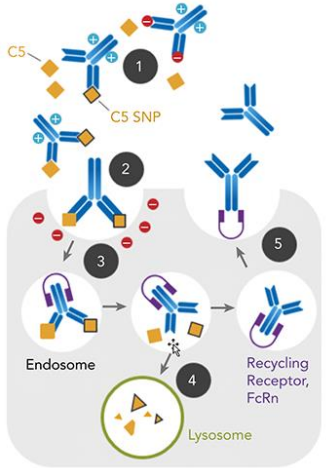
- 15 (out of 17) participants maintained expression with stable, durable Factor VIII activity and a 91% reduction in the ABR and 97% reduction in AIR (median follow up was 2.8 yrs)
- SPK-8011 shows acceptable safety in the ranges of doses studied: $5x10^{11}$–$2x10^{12}$ vg/kg
- Further dose optimization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

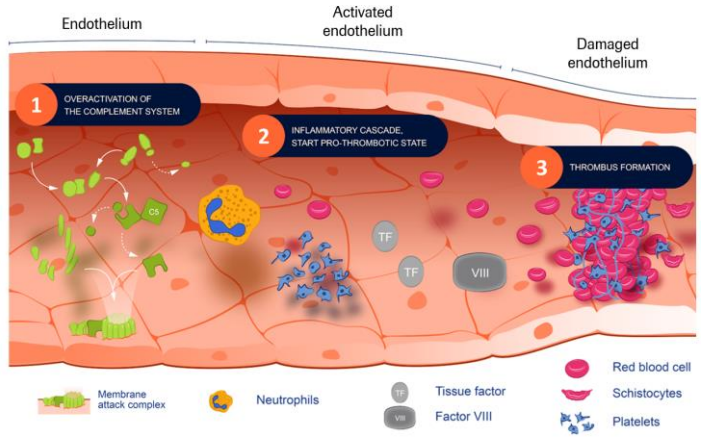
Anti-C5 mAb



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

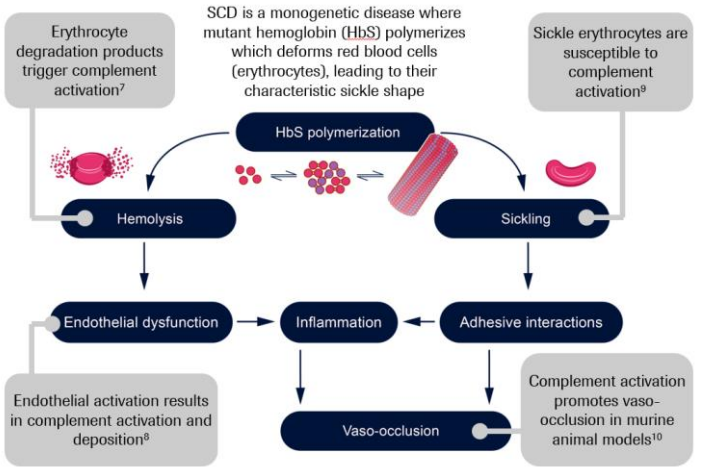
- Chugai engineered, anti complement component 5 (C5) recycling mAb[1–6]
- Engineered to enable maximal, long-lasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

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

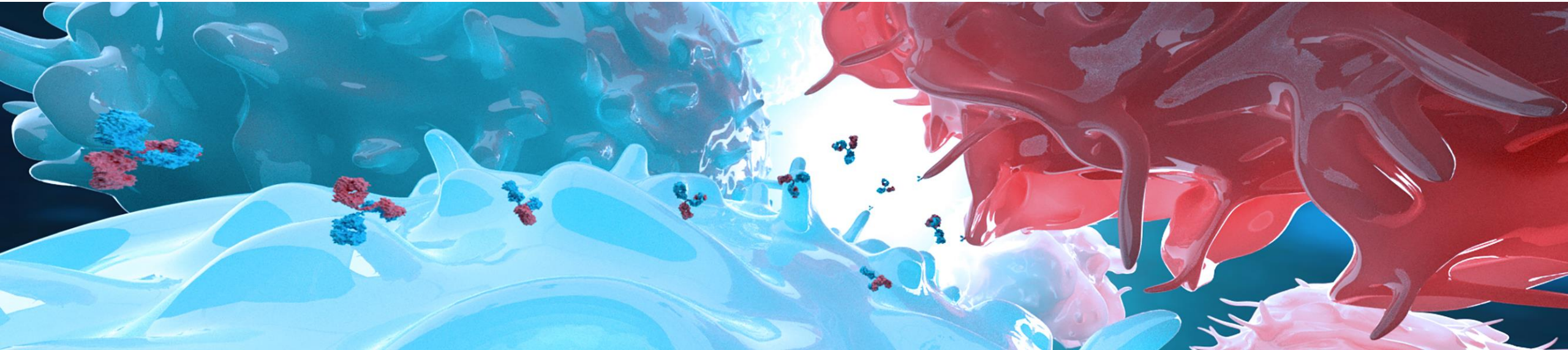
[1] Röth A et al. Blood 2020;135:912–20; [2] Fukuzawa T et al. Sci Rep 2017;7:1080; [3] Sampei Z et al. PLoS One 2018;13:e0209509; [4] Röth A, Nishimura J. Centro Congressi Federico II 2019; [5] Röth A et al. ASH 2018; [6] Sostelly A et al. ASH 2019; [7] Röth A et al. EHA 2019; [8] Peffault de la Tour, 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.

Roche

Roche Late Stage Pipeline Event 2021

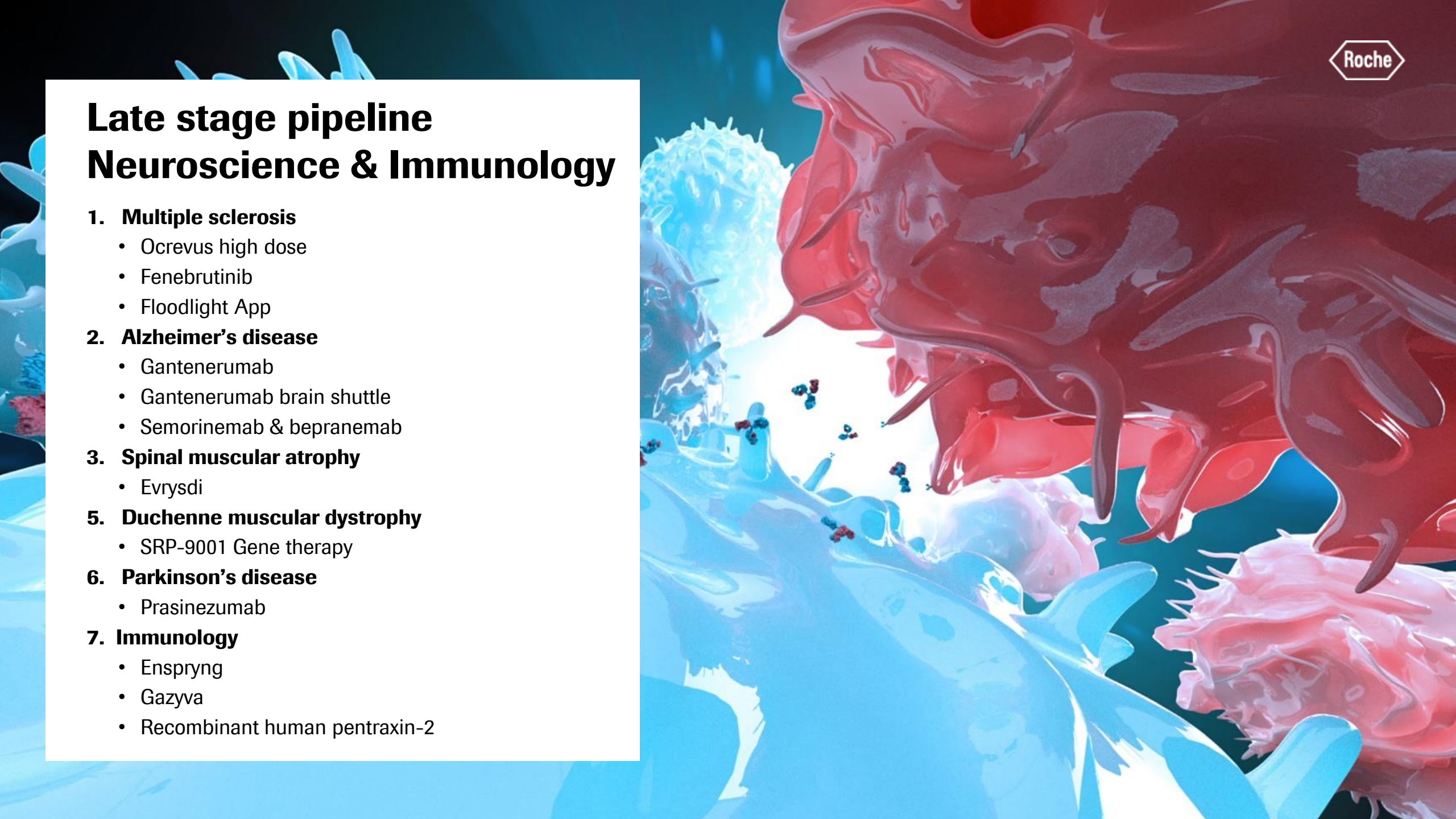
Late Stage Pipeline Neuroscience

Paulo Fontoura M.D. Ph.D. | Global Head Neuroscience, Immunology, Ophthalmology, Infectious and Rare Diseases, Clinical Development



Late stage pipeline
Neuroscience & Immunology

1. **Multiple sclerosis**
   - Ocrevus high dose
   - Fenebrutinib
   - Floodlight App
2. **Alzheimer's disease**
   - Gantenerumab
   - Gantenerumab brain shuttle
   - Semorinemab & bepranemab
3. **Spinal muscular atrophy**
   - Evrysdi
5. **Duchenne muscular dystrophy**
   - SRP-9001 Gene therapy
6. **Parkinson's disease**
   - Prasinezumab
7. **Immunology**
   - Enspryng
   - Gazyva
   - Recombinant human pentraxin-2



Neuroscience and rare diseases portfolio

Strongly differentiated pipeline

Ph I (4 NMEs)	
RG6091	**UBE3A LNA** Angelman syndrome
RG7637	undisclosed
RG6237	undisclosed
RG6182	undisclosed

Ph II (7 NMEs)	
RG7935	**prasinezumab** Parkinson's
RG6100	**semorinemab** Alzheimer's
UCB 0107	**bepranemab** Alzheimer's
RG6102	**brain shuttle gantenerumab** Alzheimer's
RG7412	**crenezumab** Alzheimer's
RG7906	**ralmitaront** Schizophrenia
RG7816	**$GABA_A$ α5 PAM** Autism spectrum disorder

Ph III (3 NMEs, 1LE)	
RG1450	**gantenerumab** Alzheimer's
SRP 9001	**microdystrophin gene therapy** DMD RD
RG7916	**Enspryng** gMG RD
RG7845	**fenebrutinib** MS

Launched (3)		
RG1594	**Ocrevus** MS	✓
RG7916	**Enspryng** NMOSD RD	✓
RG7916	**Evrysdi** SMA type 1/2/3 RD	✓

✓ FDA approval

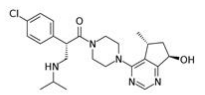
RD RD = Rare disease

Neuro-immunologic disorders | Neuro-degenerative disorders | Neuro-developmental disorders | Neuro-muscular disorders | Psychiatric disorders

NME=new molecular entity; LE=line extension; NMOSD=neuromyelitis optica spectrum disorders; DMD=Duchenne muscular dystrophy; gMG=generalised myasthenia gravis; MS=Multiple sclerosis; SMA=spinal muscular atrophy; Risdiplam is developed in collaboration with PTC therapeutics and the SMA Foundation

New technology platforms applied in Neuroscience and I2O*

Small molecules

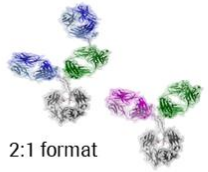


- ipatasertib
- inavolisib
- giredestrant
- KRAS G12C
- TLR7 agonist
- belvarafenib
- SHP2i

Target oncogenes, induce apoptosis, supress tumor growth

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

Bi-specifics

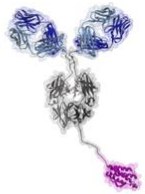


- mosunetuzumab
- glofitamab
- cibisatamab
- Her2 x CD3
- glypican-3 x CD3
- cevostamab
- PD1 x TIM3
- PD1 x LAG3
- TYRP1-CD3

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

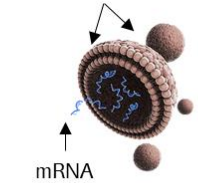
- crovalimab
- gantenerumab
- prasinezumab
- semorinemab
- etrolizumab
- TLR4 mAb
- HtrA1 mAb
- anti-tryptase

Antibody drug conjugate

- preclinic

Targeted toxic payload

Neoantigen vaccines

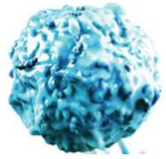


- autogene cevumeran

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

Neuroscience and I2O pipeline

Personalized T cells

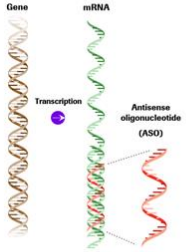


- programmed T cells

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

✓ = Products approved

Antisense RNA

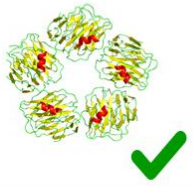


- Factor B ASO
- HBV siRNA
- PDL1 LNA
- UBE3A LNA

Gene therapy

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

Recombinant proteins



- rh pentraxin-2

Oncolytic adenovirus

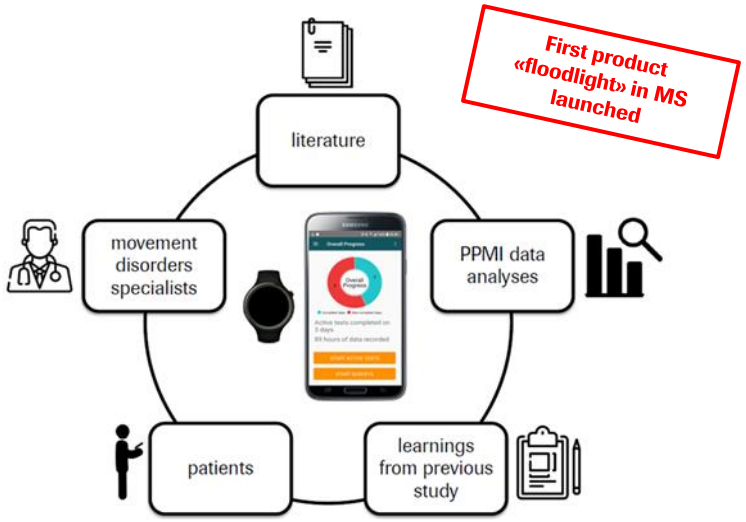
- Type 5 adenovirus

* List of pipeline molecules shown below is not complete; Molecules in the blue box are developed in Neuroscience and I2O (Immunology, Infectious diseases, Ophthalmology)

Digital endpoints to drive scientific progress

Delivering new patient insights and building holistic solutions for patients

Continuous product improvement



Broad development program in neuroscience

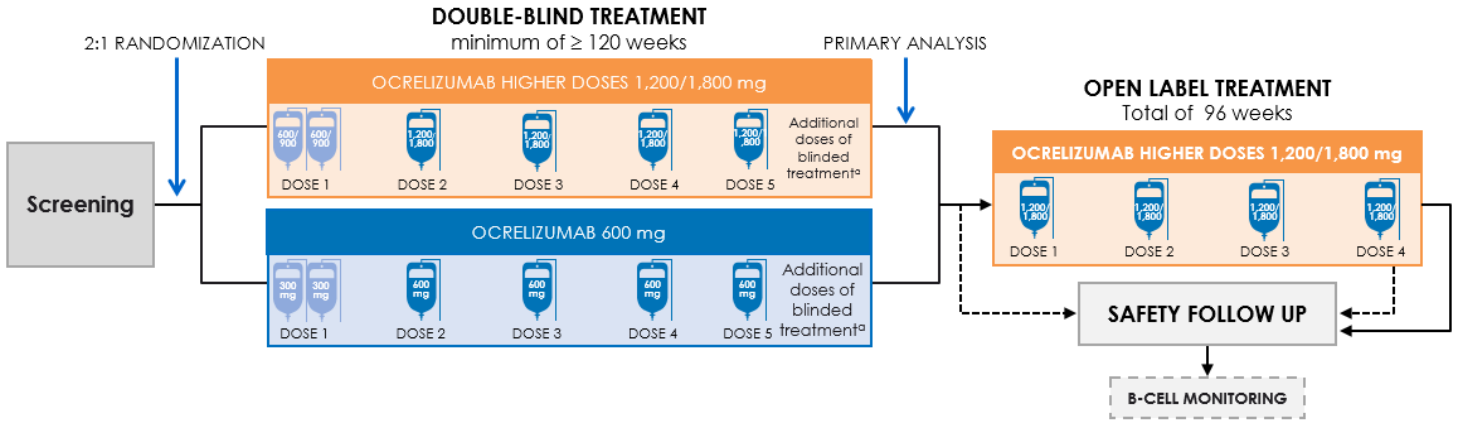
Disease Area	Cognition	Hand Motor Function	Gait & balance	Vocalization	Activity & sociability
Parkinson	●	●	●	●	●
Huntington	●	●	●	●	●
SMA		●	●	●	
Multiple Sclerosis	●	●	●		●
Alzheimer	●			●	●
Autism	●			●	●
Schizophrenia					●

- Clinical trials utilizing mobiles, wearables and gaming devices
- More sensitive, precise and objective data collection and monitoring of disease progression
- Continuous and longitudinal measurement captures episodic and rare events
- Reduced assessment burden and greater real-world relevance benefiting physicians and patients

Multiple sclerosis: Higher dose Ocrevus

New Ph III program in RMS and PPMS started in 2020

Ph III study design for Ocrevus Higher Dose versus 600 mg in RMS and PPMS



Study in patients with RMS (MUSETTE)

- Patient sample size, N=786
- Age: 18–55 years; EDSS score: 0–5.5
- Stratification for region, age, EDSS, weight

Study in patients with PPMS (GAVOTTE)

- Patient sample size, N=699
- Age: 18-55 years; EDSS score: 3–6.5
- Stratification for region, age, sex, weight

- Ocrevus showed a significant benefit on 12/24W-CDP, ARR, MRI measures in Ph III studies in RMS and PPMS and 7 year OLE
- Exposure/response analysis of Ph III data suggests a higher dose could lower the risk of disability progression without compromising safety
- Two double-blind, randomized Ph III studies were designed to test higher dose Ocrevus; the selected higher dose, given every 24 weeks, is 1,200 mg for patients <75 kg or 1,800 mg for patients ≥75 kg
- Ph III (MUSETTE) in RMS and Ph III (GAVOTTE) in PPMS started in 2020

Hauser S.L. et al, ACTRIMS-ECTRIMS 2020; 24W-CDP=24 week confirmed disability progression; AAR=annual relapse rate; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; OLE=open label extension

Multiple sclerosis: Floodlight launched in US and EU

Building ecosystems to serve patients, society and scientific progress

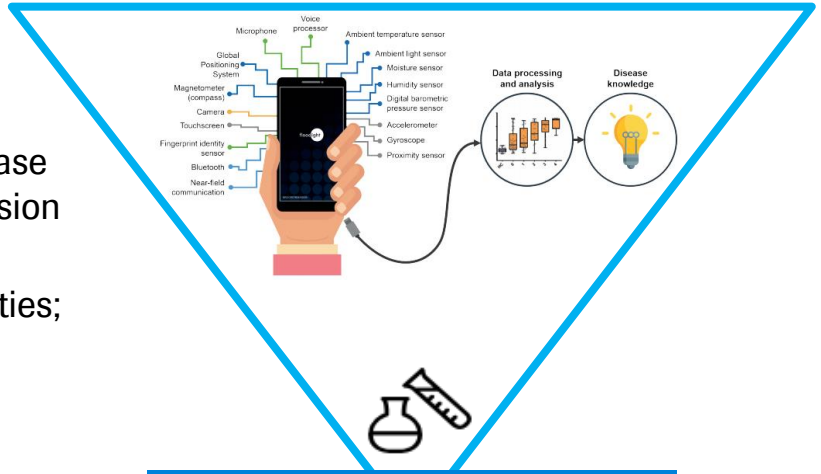
Roche's 1rst approved sensor-based SaMD

Value creation for patients

- MS progression, often undetected by current clinical scales
- Provides an objective assessment of disease status; empowers patients in shared decision making, enhancing earlier access to care
- Closely co-created with patient communities; studies show high retention rates

"The tasks were all straightforward, and some almost fun."
Our 1st patient

Concept is spot on.
US Neurologist



Value creation for science

- Rigor of measurements & robust development define new standards
- Generate disease insights and support future drug development
- Collaborations create consensus on new digital measurements

Value creation for society

- Earlier intervention has the potential to improve health outcomes and reduce long term health care costs
- Floodlight MS is launched in close collaboration with healthcare providers, enabling RWD opportunities that improve health care utilization

"I'm 100% behind the initiative and am very enthusiastic about it. It's cool that this was clearly under development before the pandemic and it fits well with my challenges: 90% of patients are virtual and there are lots of time constraints between clinical visits."
Dr. Shin

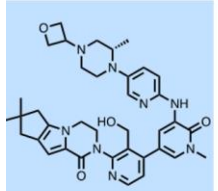
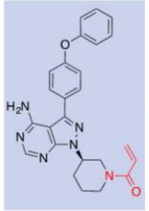
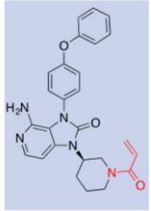
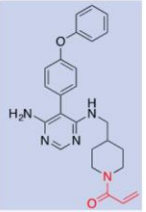
Pharma vision 2030: Providing more patient benefit at less cost to society

SaMD=software as medical device

Multiple sclerosis: Fenebrutinib in MS

Highly differentiated and potentially best-in-class BTKi

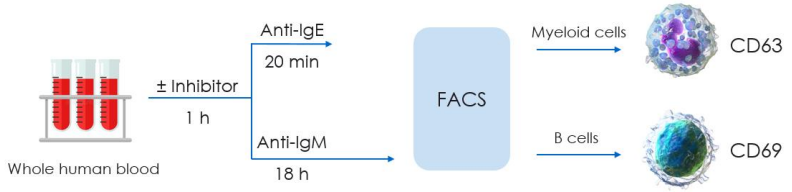
BTK inhibitor

Fenebrutinib (GDC-0853)	Ibrutinib	Tolebrutinib	Evobrutinib
Phase 3	Launched	Phase 3	Phase 3
MS	Oncology	MS	MS
			
Noncovalent, reversible	Covalent, irreversible	Covalent, irreversible	Covalent, irreversible
BTK IC_{50} 2 nM	1 nM	1 nM	32 nM
High selectivity	Low selectivity	Low selectivity	Low selectivity

- Oral, highly selective and only reversible noncovalent BTK inhibitor in Ph III
- Long residence time bound to BTK mimics durable inhibition of a covalent inhibitor, but without the potential safety risks of covalent BTK inhibition

Dual MOA

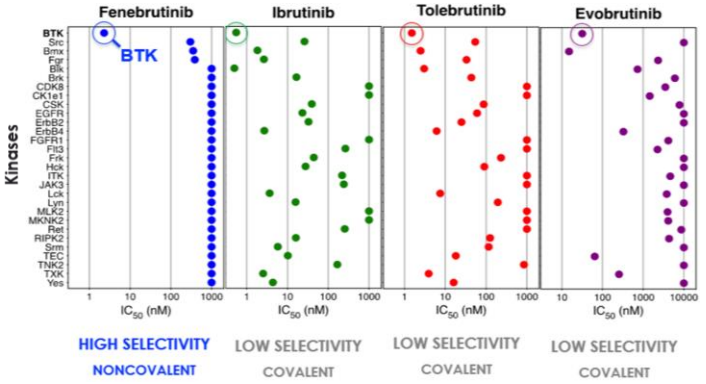
Inhibition of myeloid and B cell activation in whole human blood



Whole human blood assay	Fenebrutinib[1]	Ibrutinib[1]	Tolebrutinib[2]	Evobrutinib[3]
Myeloid cell CD63 IC_{50}, nM	31	171	166	1660
B cell CD69 IC_{50}, nM	8	12	10	84

Outstanding selectivity profile

Kinase selectivity assay



- Dual MOA: Fenebrutinib potently inhibits myeloid (basophil) and B cell activation in human blood; this may reduce both acute and chronic inflammation in MS
- In a kinase selectivity assay fenebrutinib was found to be 130x more selective for BTK which may reduce off target effects and thus improve safety

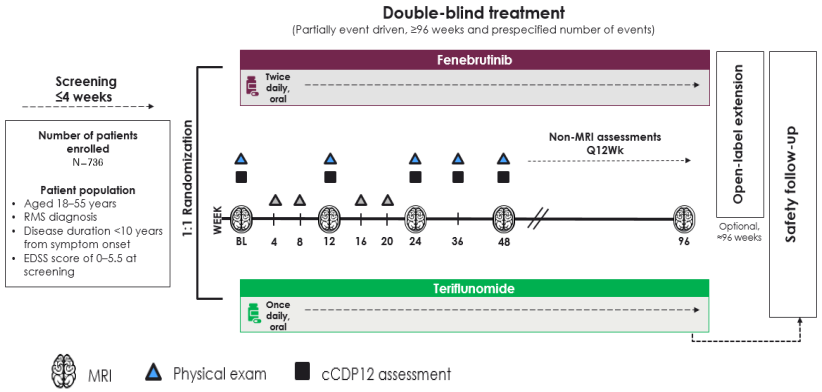
Johnson A. et al, ACTRIMS-ECTRIMS 2020; MOA=mechanism of action; MS=multiple sclerosis; BTK=Bruton's tyrosine kinase; nM=nano molar; FACS=fluorescent activated cell sorting

Multiple sclerosis: Fenebrutinib trials in RMS and PPMS started

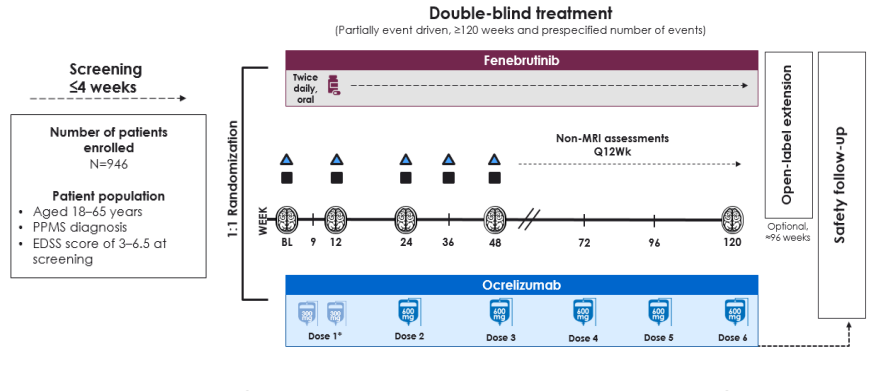
Well established clinical safety profile in autoimmune diseases

Ph III trials in RMS and PPMS run against active comparators

Ph III RMS (FENhance)



Ph III PPMS (FENtrepid)*



***First PPMS study against an active comparator (Ocrevus)**

Key endpoint on progression

cCDP12

≥12 weeks after the initial disability progression, confirmation of ≥1 of the following:

confirmed disability progression on **Expanded Disability Status Scale (EDSS)**[a]

or

≥20% increase from baseline in **9-Hole Peg Test**

or

≥20% increase from baseline in **Timed 25-Foot Walk Test**

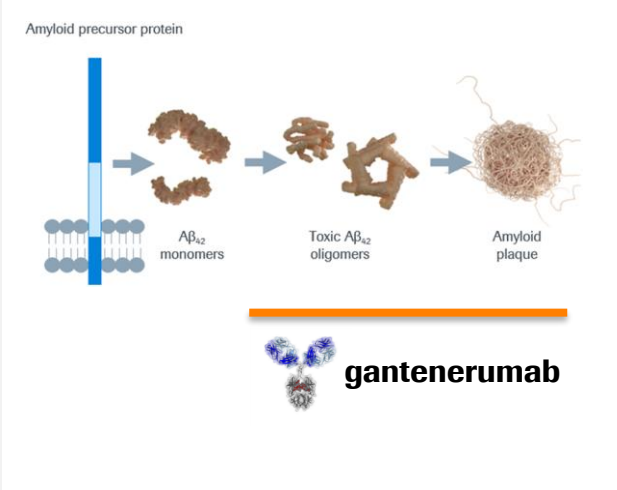
- Innovative Ph III trial design with cCDP12 providing a more thorough approach to “disease progression” by assessing upper limb function, which might lead to earlier detection of disease progression
- Well established safety profile due to 14 clinical studies (across 3 autoimmune diseases) with overall 1360 study participants:
  - Generally well tolerated, mostly non-serious, mild and self-limiting adverse events
  - Other potential BTKi class effects (infection, severe bleeding, tachyarrhythmias) appear less relevant due to the high BTK selectivity seen
- Ph III program in RMS and PPMS started in 2020

Oh. J. et al., AAN 2021; Hauser S. L. et al, ACTRIMS-ECTRIMS 2020; MS=multiple sclerosis; RMS=relapsing MS; PPMS=primary progressive MS; BL=base line; Q12W=every 12 weeks; [a] Defined as an increase of ≥1 point from a baseline score of ≤5.5, or an increase of ≥0.5 points from a baseline score of >5.5; EDSS=Expanded Disability Status Scale; 9HPT=9-Hole Peg Test; T25FWT=Timed 25-Foot Walk Test

Alzheimer's disease: Gantenerumab SC targeting Amyloid β (Aβ)

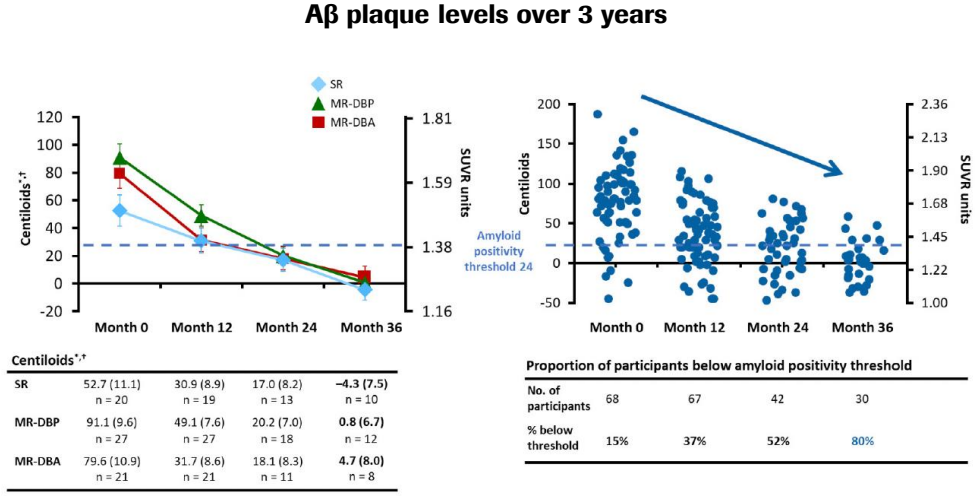
Strong target engagement and downstream biological impact

Anti-Aβ mAb



- Fully human, anti-Aβ mAb (IgG1) with high affinity to aggregated forms of Aβ
- Highest affinity for neurotoxic oligomers and plaques [1,2]
- SC administration enables flexibility of home administration

OLE studies shows robust Aβ plaque removal*



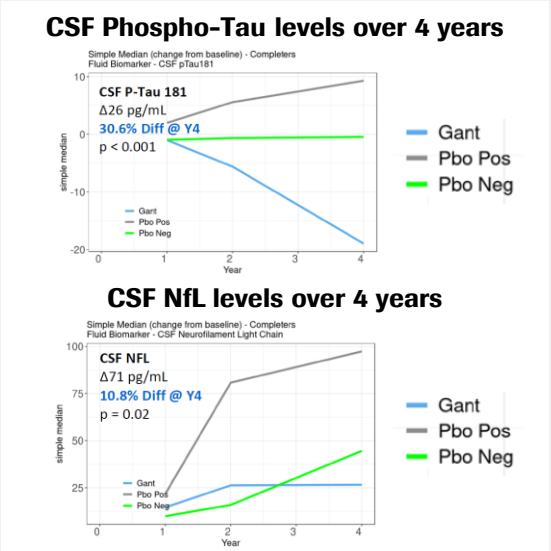
Centiloids*,†

	Month 0	Month 12	Month 24	Month 36
SR	52.7 (11.1) n = 20	30.9 (8.9) n = 19	17.0 (8.2) n = 13	−4.3 (7.5) n = 10
MR-DBP	91.1 (9.6) n = 27	49.1 (7.6) n = 27	20.2 (7.0) n = 18	0.8 (6.7) n = 12
MR-DBA	79.6 (10.9) n = 21	31.7 (8.6) n = 21	18.1 (8.3) n = 11	4.7 (8.0) n = 8

Proportion of participants below amyloid positivity threshold

	Month 0	Month 12	Month 24	Month 36
No. of participants	68	67	42	30
% below threshold	15%	37%	52%	80%

DIAN-TU study shows downstream impact



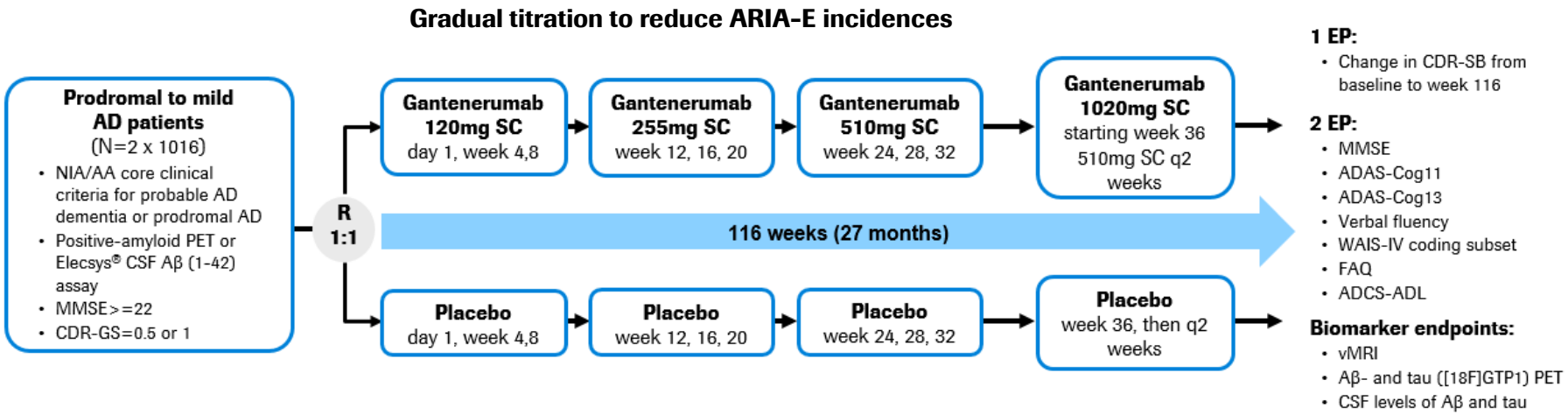
- OLE studies: Gantenerumab lowers Aβ plaques below positivity threshold towards floor levels without plateau
- 80% of patients Aβ-negative after 3 years
- Gantenerumab reduces levels of downstream biomarkers (p-Tau, t-TAU) and blocks increases of markers of neurodegeneration (NfL) in patients with familial AD (DIAN-TU study)

[1] Bohrmann B, et al. J Alzheimer's Dis 2012; 2. Ostrowitzki S, et al. Arch Neurol 2012; Bateman R. J. et al, AAT-AD/PD 2020; Klein G et al, CTAD 2020; Klein G. et al., J Prev Alzheimers Dis 2021;8(1); OLE=open label extension; NfL=neurofilament light chain; * OLE studies for the former Ph III studies SCarlet RoAD and Marguerite RoAD; SC=subcutaneous; CSF=cerebrospinal fluid

Alzheimer's disease: Gantenerumab SC in early AD patients

Ph III program with optimized design to maximize exposure

Global, randomized, double-blind, placebo-controlled Ph III trial design (GRADUATE I/II)



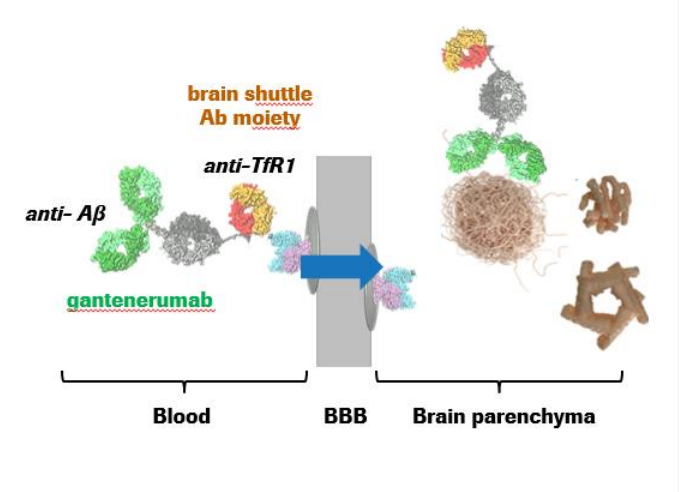
- Two parallel studies with large sample size of ~1,000 participants patients each expected to deliver a clear and robust data set in 2022
- Optimized titration scheme to reduce incidence of ARIA-E and maximize exposure for all patients regardless of ApoE4 genotype
- Well powered PET substudies to detect-biomarker changes including Aβ and tau
- Treatment duration of 27 months to optimize detection of clinical benefit
- First and only late-stage AD program to offer SC formulation enabling flexibility and convenience of home administration

AD=Alzheimer's Disease; SC=subcutaneous; Aβ=amyloid-beta; NIA/AA=National Institute on Aging/Alzheimer's Association; PET=positron emission tomography; CSF=cerebrospinal flu; CDR-SOB=Clinical DementiaRating ScaleSumofBoxes; ADAS-Cog13=Alzheimer's Disease Assessment Scale-Cognitive subscale; MMSE=Mini-Mental State Examination; FAQ=Functional Activities Question; ADCS-ADL=Alzheimer's Disease Cooperative Study-Activities of daily living; vMRI=volumetric magnetic resonance imaging; ARIA-E= amyloid-related imaging abnormalities edema; In collaboration with MorphoSys AG

Alzheimer's disease: Gantenerumab brain shuttle

Vision: Superior target access leading to slowing of AD progression

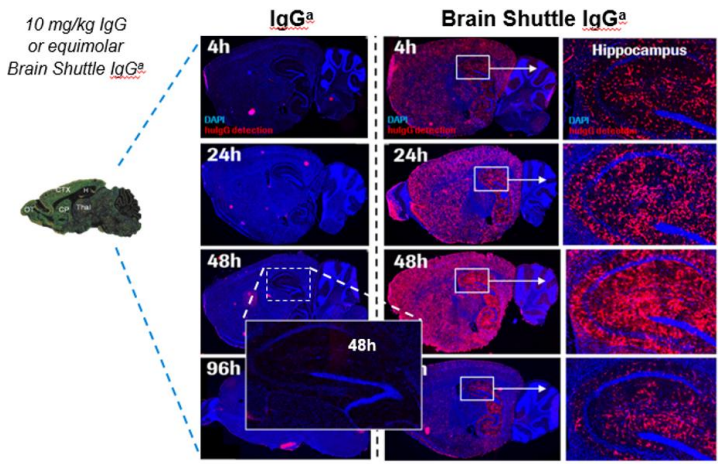
Gantenerumab brain shuttle



- Gantenerumab brain shuttle is a fusion protein combining gantenerumab with a transferrin receptor (TfR1) binding Ab moiety to achieve efficient transport over the BBB and target Aβ plaque engagement in the brain
- Technology could also be applied to other CNS disorders

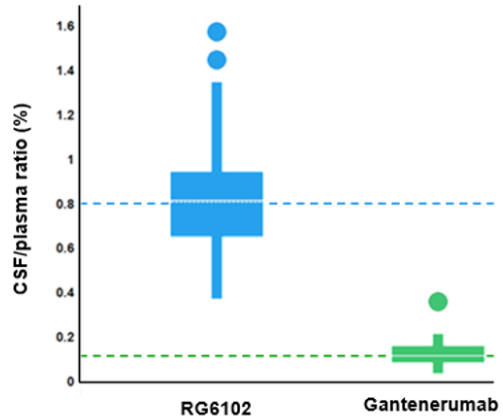
Preclinical data

Immunofluorescence staining[1]



Ph I PK/PD data in healthy volunteers

CSF/plasma ratio[2]



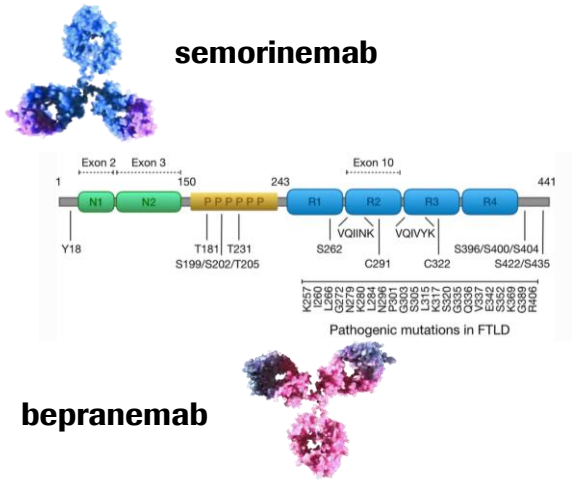
- Preclinical work in mouse and monkey models provides in vitro and in vivo evidence that TfR1 receptor binding facilitates transcellular transport across the Blood Brain Barrier (BBB)
- Initial Ph I PK data show encouraging 6 to 8-fold increase in the CSF/plasma concentration ratio when comparing the gantenerumab brain shuttle to historical gantenerumab data
- Phase I/II study is underway to test safety, tolerability, PK, and PD (amyloid PET) in people with prodromal or mild-to-moderate AD

Kulic L. et al., ADPD 2021; AD=Alzheimer's disease; BBB=blood brain barrier; IgG=immunoglobulin G; mAb=monoclonal antibody; TfR1=transferrin receptor 1; Aβ=Amyloid β; CNS=central nervous system; CSF=cerebrospinal fluid; PD=pharmacodynamics; PK=pharmacokinetics; [1] Unpublished data from Dr E. Urich and Dr T. Poeschinger: Immunofluorescence staining highlights the distribution of classical IgG vs Brain Shuttle IgG targeting a neuronal target in mouse brain at 4, 24, 48, and 96 hours after a single IV dose (10 mg/kg each); [2] Gantenerumab brain shuttle results were compared with historical data obtained from a previous gantenerumab SAD trial (BN18726).

Alzheimer's disease: Two anti-TAU mAbs in development

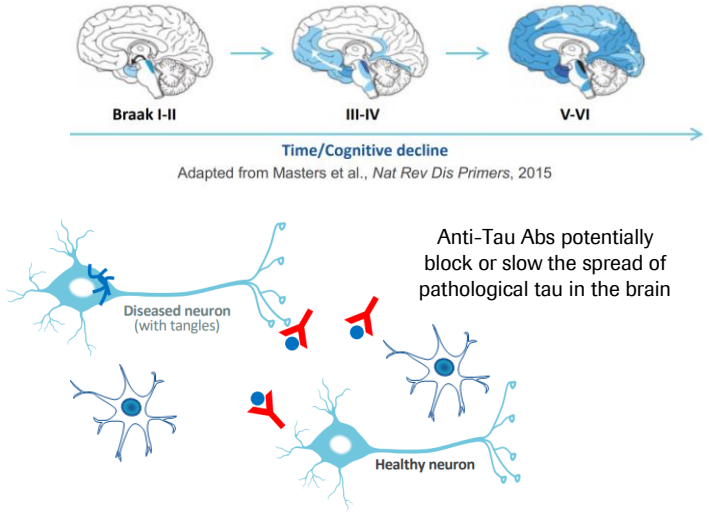
Ph II (LAURIET) semorinemab results show first hint of clinical activity

Anti-Tau mAbs



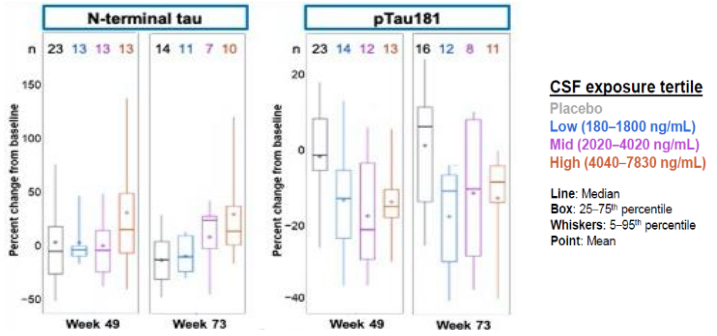
- Semorinemab: N-terminal anti-tau mAb binding to all isoforms independent of their phosphorylation status; optimized for high dosing
- Bepranemab: Mid-domain anti-tau mAb binding to a different epitope

Proposed MOA



Ph II (TAURIEL) PD results

Semorinemab had pharmacodynamic activity suggestive of target engagement



- Ph II (LAURIET) study with semorinemab in mild-to moderate AD showed statistically significant and potentially clinically meaningful effect on cognition as measured by ADAS-Cog11; no treatment effect observed on ADCS-ADL, MMSE or CDR-SB
- LAURIET OLE is continuing, with additional analyses in progress; data to be presented at CTAD
- Ph II study in early AD (TAURIEL) did not meet its primary (CDR-SB) or secondary endpoints

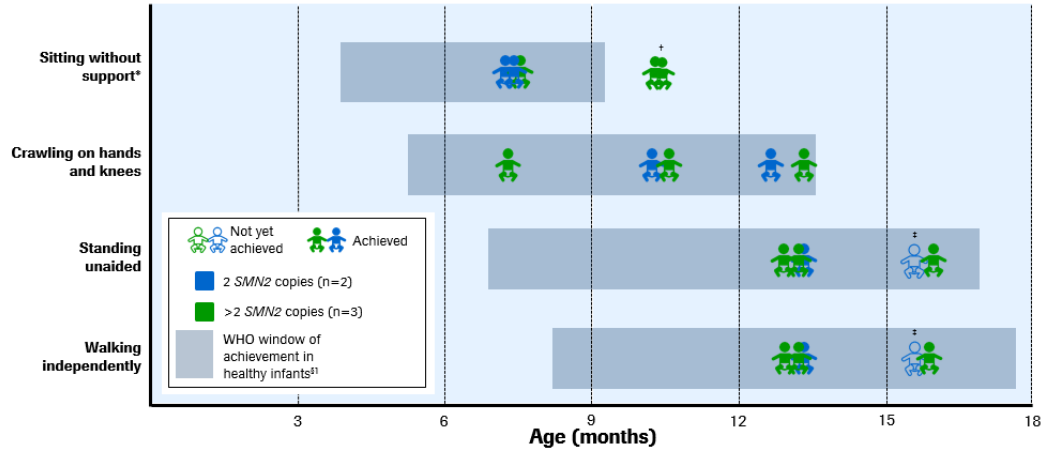
Wildsmith et al, AAT-AD/PD 2021; Teng E. et al. CTAD 2019; PD=pharmacodynamics; AD=Alzheimer's disease; ADAS-Cog=Alzheimer's Disease Assessment Scale–Cognitive subscale; ADCS-ADL=Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory; MMSE=Mini-Mental State Examination; CDR-SB=Clinical Dementia Rating–Sum of Boxes; Semorinemab partnered with AC Immune; Bepranemab (UCB0107) partnered with UCB.

Spinal muscular atrophy: Evrysdi in type 1/2/3 SMA

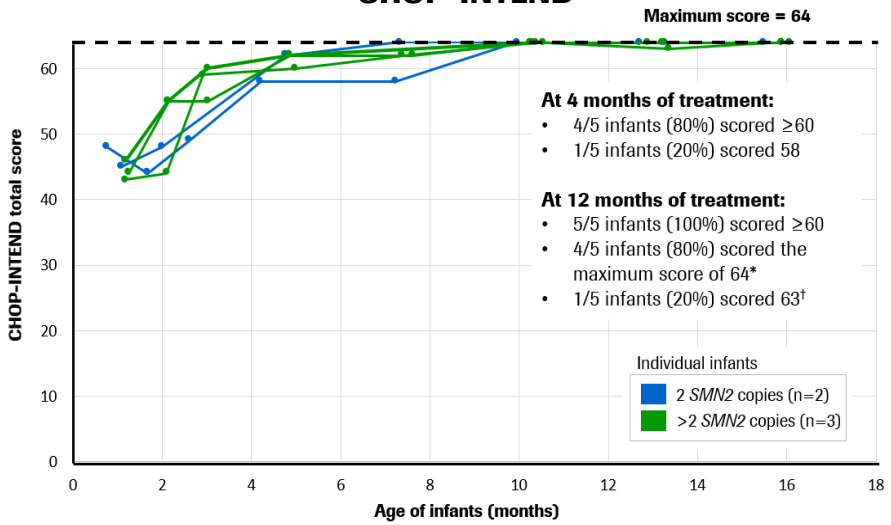
Excellent preliminary data in presymptomatic babies

Ph III (RAINBOWFISH) interim results in presymptomatic babies with SMA

Motor milestones within the WHO windows for healthy children



CHOP-INTEND



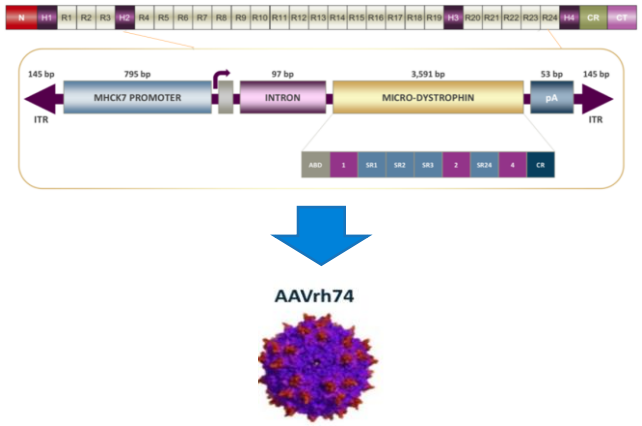
- Presymptomatic babies treated with Evrysdi for at least 12 months were able to sit, stand and walk and achieved motor milestones within the WHO windows for healthy children
- They reached near maximum CHOP-INTEND scores by 4–5 months of age
- Evrysdi expected to become the most prescribed SMA treatment in the US in 2021

Finkel R. S. et al. CureSMA 2021; Third edition; WHO=world health organization; CHOP-INTEND=Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; Risdiplam in collaboration with PTC Therapeutics and the SMA Foundation

Duchenne muscular dystrophy: Gene therapy SRP-9001

Positive expression and safety data for commercial drug material

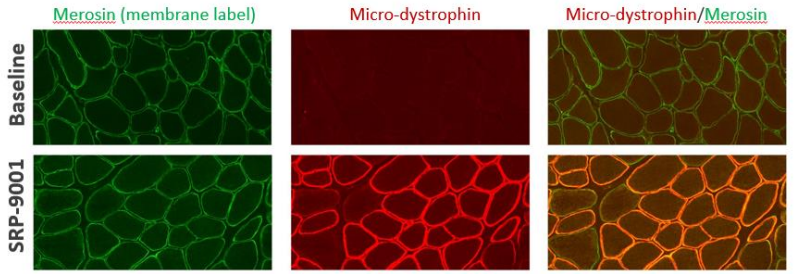
Micro-dystrophin gene therapy



- AAVrh74 vector: low likelihood of pre-existing immunity and high tropism for skeletal & cardiac muscles
- Expression potentiated by the MHCK7 promoter in cardiac & skeletal muscles
- Transgene retains critical elements of dystrophin for a functional protein

Ph Ib (SRP-9001-103, cohort 1) expression results at week 12 in 4-7 y.o. ambulatory patients (n=11)

Immunofluorescence (IF) staining



Expression summary

Vector genome copies per nucleus	3.87
% Normal expression by Western Blot	55.4 ± 43.4*
% Dystrophin positive fibers by IF	57.7 ± 22.2*
% Intensity by IF	75.9 ± 46.4*

* Change from baseline (CBO)

- Micro-dystrophin protein expression increased by +55.4% from baseline and muscle fibers positive for micro-dystrophin increased by +57.7% from baseline
- Safety profile consistent with prior studies, with no new safety signals identified
- Results provide preliminary confirmation of the manufacturing and analytics of commercially grade material, which enables building capacity to supply the DMD population
- Planning for global Ph III trials in ambulatory and non-ambulatory DMD patients are ongoing

Sarepta company presentation, May 18 2020; SRP-9001 partnered with Sarepta; License and collaboration agreement with Sarepta Therapeutics in Duchenne Muscular Dystrophy (DMD), securing exclusive ex-US commercial rights to SRP-9001, their gene therapy for DMD, and the right to opt-in to their broader DMD portfolio outside of the US; DMD=Duchenne's muscular dystrophy

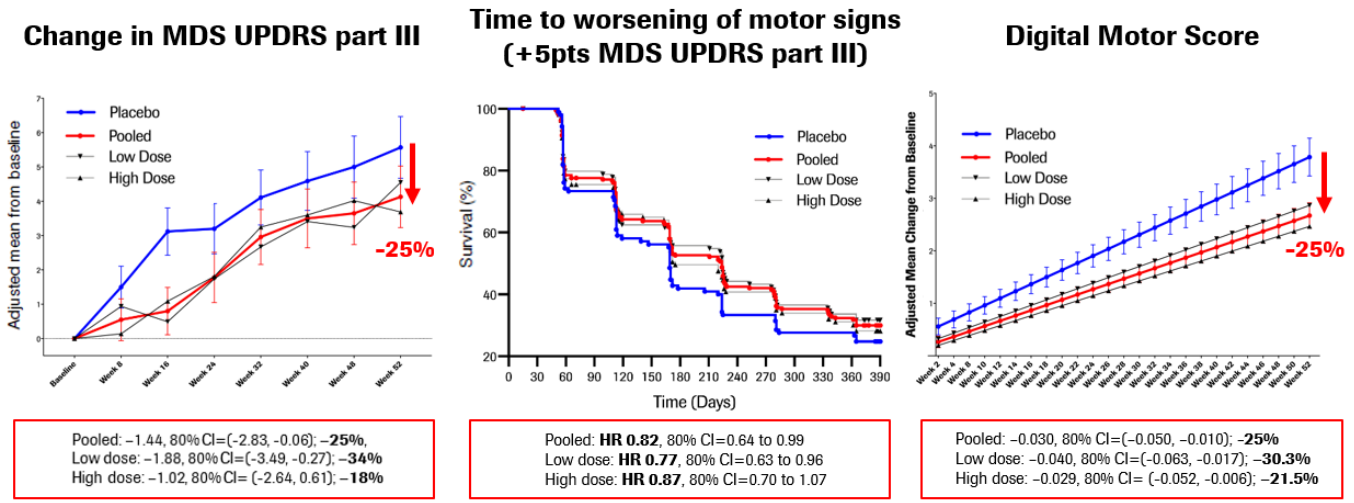
Parkinson's disease: Prasinezumab with signals of efficacy

Ph IIb started to further define patient population and endpoints

Anti-α-synuclein mAb

- Humanized mAb designed to target aggregated forms of α-synuclein
- Inhibiting cell-to-cell spreading of pathogenic forms of α-synuclein, resulting in slowing of Parkinson's disease progression

Ph II (PASADENA part 1) results at 52 weeks



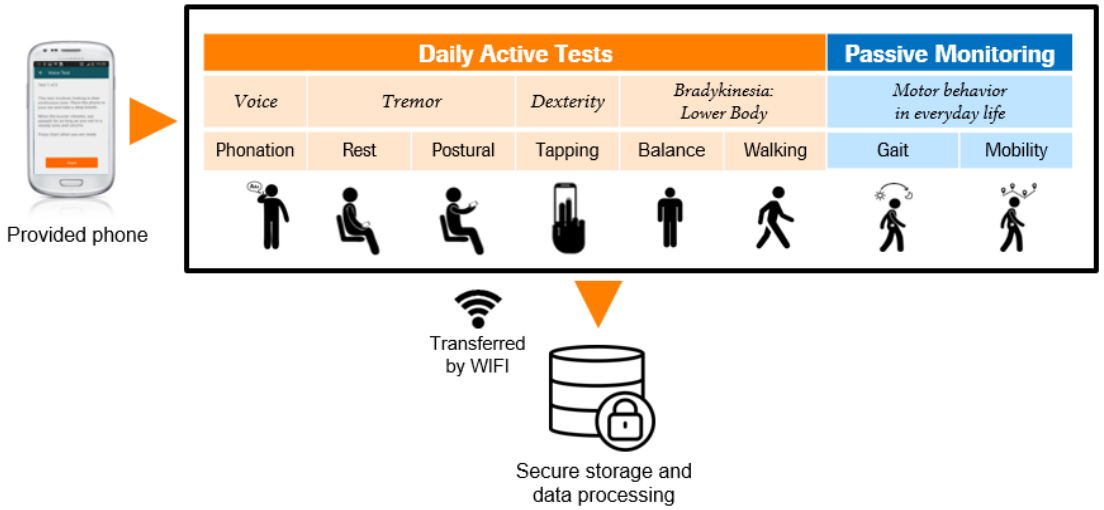
- Ph II (PASADENA) study did not meet its primary endpoint (MDS UPDRS total score)
- Prasinezumab was well tolerated showing efficacy signals in slowing of clinical decline of motor symptoms (MDS UPDRS part IIII, digital motor outcome measures) warranting further follow up; longer term data to be presented at upcoming conferences
- Ph IIb (PADOVA) started in 2021 in patients with early PD that are on symtomatics incl L-DOPA

Pagano, G et al, MDS poster 2020; MDS-UPDRS=Movement Disorder Society-Unified Parkinson's Disease Rating Scale (Sum of Parts I, II and III which assess non-motor [I and II] and motor [III] experiences in daily living); Prasinezumab partnered with Prothena Biosciences; HR=hazard ratio; CI=confidence interval; PD=Parkinson's disease

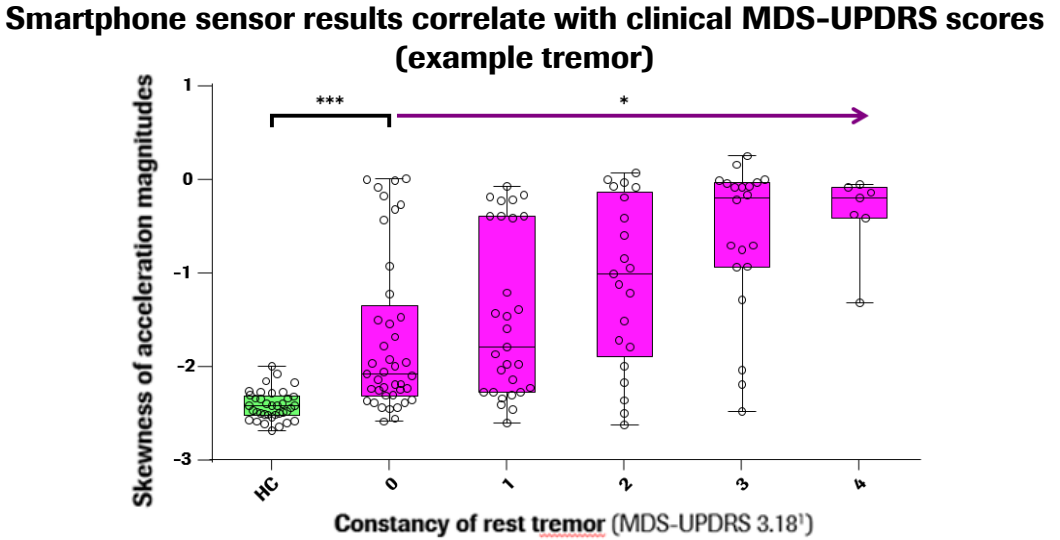
Parkinson's disease: First Ph II digital biomarker results

Digital biomarkers support clinical drug development

Daily assessment for 6 months



Ph II (PASADENA) digital biomarker results



- The PASADENA digital biomarker test suite on the smart phone enables daily quantification of fluctuating symptoms in Parkinson's disease
- Preliminary data show clinical validity, strong patient adherence and high test-retest reliability
- Digital endpoints provide already today decision-making support for drug development
- Potential future use in patient & treatment monitoring, identifying subclinical signs in prodromal patients, or as primary outcomes measures

http://www.roche.com/media/store/roche_stories/roche-stories-2015-08-10.htm

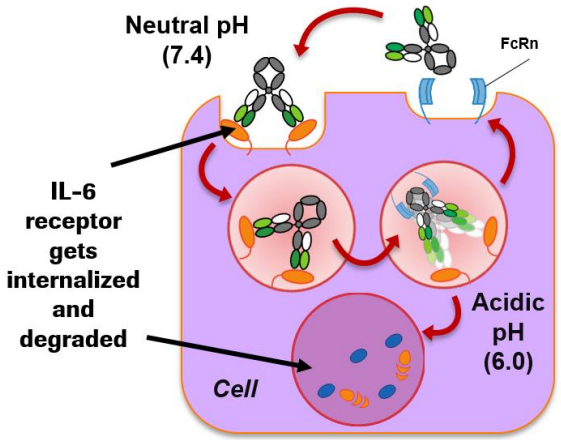
Enspryng in myasthenia gravis (MG)

Recycling Ab for maximal inhibition of IL-6 signaling

ENSPRYNG™ satralizumab-mwge subcutaneous injection 120 mg/mL

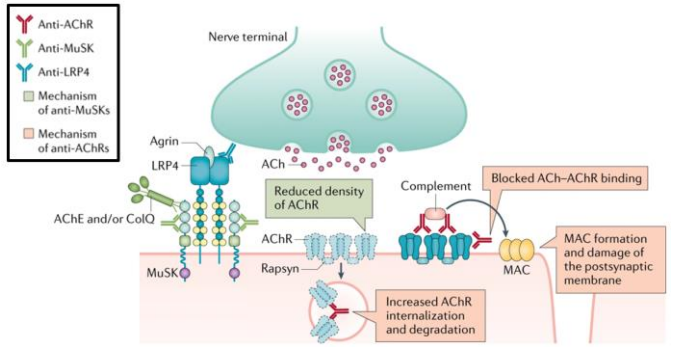
Roche

Anti-IL-6 receptor mAb

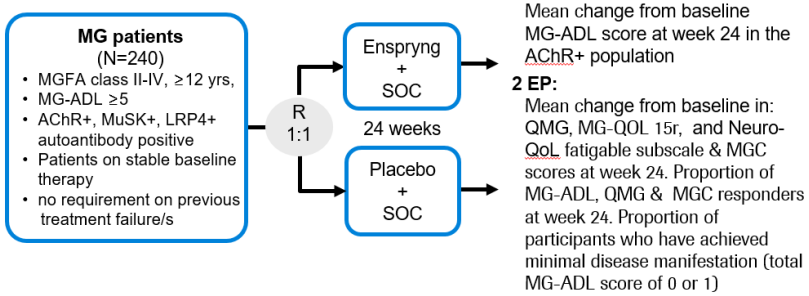


- Recycling mAb with high-affinity to soluble and membrane-bound IL-6R
- Engineered to enable maximal inhibition of IL-6 signalling
- Convenient SC Q4W home dosing

MG: Autoantibodies at the neuromuscular junction



Ph III (LUMINESCE) trial design



- MG is a chronic, autoimmune disease of the neuromuscular junction, causing fatigable muscle weakness; pathophysiology involves autoantibodies (~80% have anti-AChR Abs; 10% anti-MuSK Abs; <5% anti-LRP4 Abs) at the neuromuscular junction disrupting neuromuscular transmission
- IL6 blockade has the potential to lower pathogenic autoantibody production
- High unmet need: 10% of patients failing therapies; ~80% with no complete stable remission
- Ph III (LUMINESCE) in MG initiated; actively exploring other potential indications

Gilhus N.E. et al., Nat Rev Dis Primers. 2019 May 2;5(1):30.; MG=myasthenia gravis; SC=subcutaneous; Q4W=every 4 weeks; MOA=mechanism of action; AChR=acetylcholine receptor; MuSK= muscle-specific tyrosine kinase; LRP4=lipoprotein receptor-related protein 4; MG-ADL=Myasthenia Gravis Activities of Daily Living; QMG=Quantitative Myasthenia Gravis; MG-QOL 15r=Myasthenia Gravis Quality of Life 15 Scale; Neuro-QoL=Quality of Life in Neurological Disorders; MGC=Myasthenia Gravis Composite

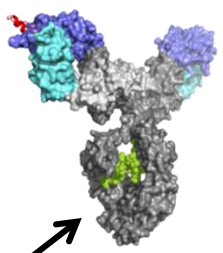
Immunology: Gazyva in LN, MN, SLE

Potential benefit in autoimmune diseases through sustained B cell depletion

Glycoengineered anti-CD20 mAb to increases B-cell depletion

Type II anti-CD20 region

- Increased direct cell death
- Decreased CDC
- Reduced internalization



Glycoengineered Fc region

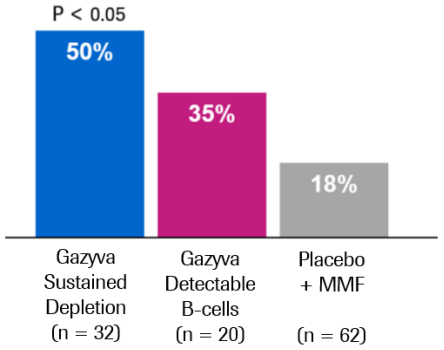
- Higher FcγR affinity
- Increased ADCC/ADCP

- Greater potency than Rituxan in depleting peripheral and tissue B-cells
- Studies suggest that tissue based B-cells play a major role in lupus nephritis

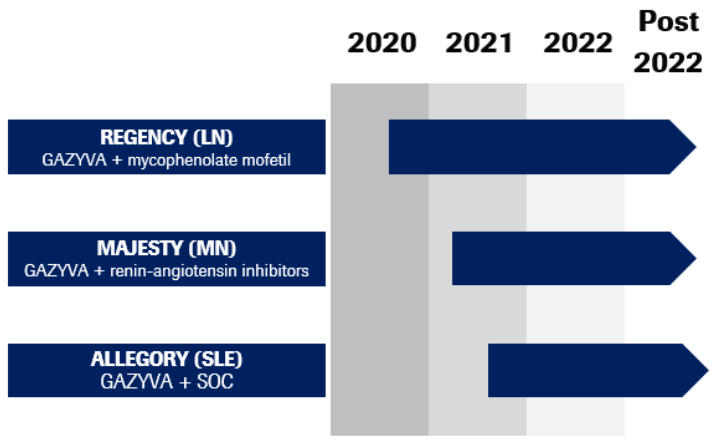
Ph II (NOBILITY) results in LN

FDA BTD

Sustained depletion leads to increased complete renal responses (CRR) at week 76



Ph III trial program



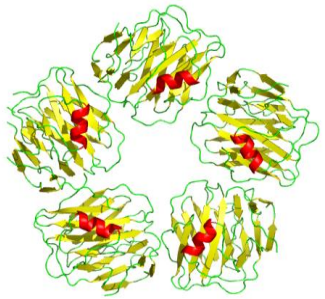
- Ph II (NOBILITY) met both primary and key secondary endpoints with no new safety signals; Ph III (REGENCY) in lupus nephritis (LN) started in Q3 2020
- Ph III (MAJESTY) in membranous nephropathy (MN) started in Q2 2021
- Ph III (ALLEGORY) in systemic lupus erythematosus (SLE) to start in Q4 2021
- Additional indications and combination studies with pipeline assets under evaluation

Furie R et al. Lupus Science & Medicine 2020;7 (Suppl 1):A27; Furie R. et al; ACR 2019; LN=lupus nephritis; MN=membranous nephropathy; SLE=systemic lupus erythematosus; CDC=complement-dependent cytotoxicity; ADCC=antibody-dependent cell-mediated cytotoxicity; ADCP=antibody-dependant cellular phagocytosis; MMF=mycophenolate mofetil

Immunology: Recombinant human pentraxin-2 in fibrotic diseases

Ph III in IPF started in 2021

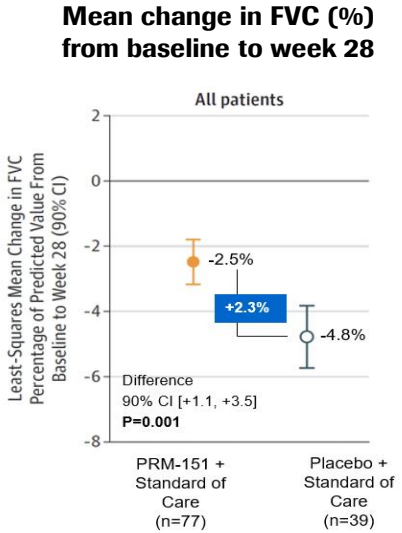
Recombinant human pentraxin-2 (rhPTX-2)



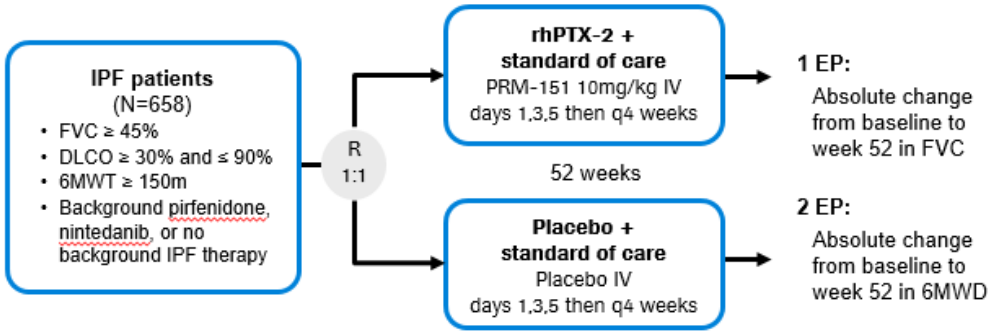
- PTX-2 is an immune regulatory protein that binds DAMPs (cell signals released from dying cells) with specificity for fibrotic tissue
- It plays a critical benefitial role during fibrosis shifting macrophages from a pro-inflammatory and pro-fibrotic to a pro-resolutive state

Ph II results

FDA BTD



Ph III (STARSCAPE) trial design in IPF



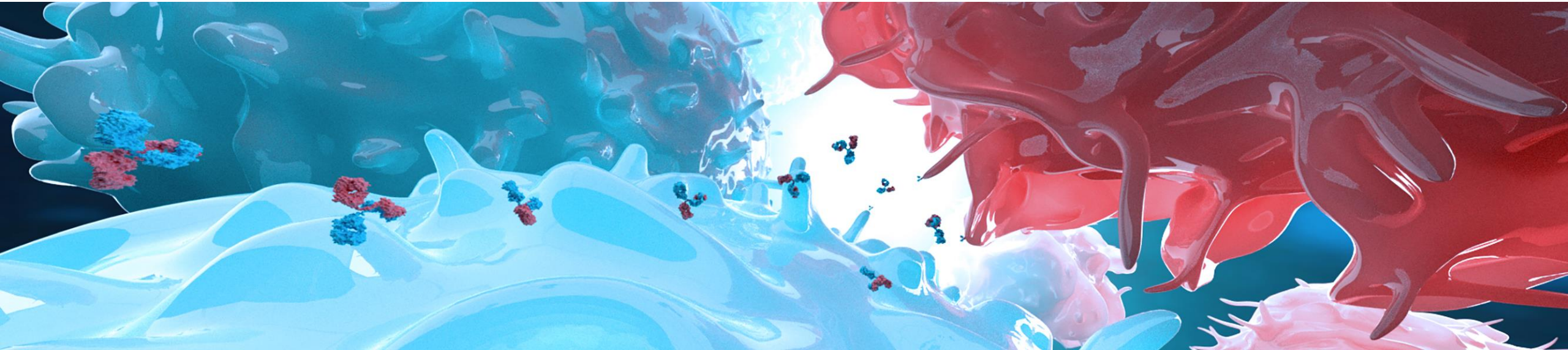
- Ph II results: rhPTX-2 slowed decline in lung function (FVC) and exercise capacity (6MWD) over 28 weeks compared with placebo, and a persistent treatment effect was observed in the open label extension study [1,2]
- Ph III (STARSCAPE) of rhPTX-2 + SOC (Esbriet or Ofev) in IPF started in Q1 2021

[1] Raghu et al; JAMA 2018;319(22):2299-2307; [2] Raghu G et al. Lancet Respir Med 2019;7:657-664; IPF=interstitial pulmonary fibrosis; FVC=forced vital capacity; 6MWD= Six minute walk distance; SOC=standard of care; PTX-2=pentraxin-2; DAMPs=damage-associated molecular patterns

Roche Late Stage Pipeline Event 2021

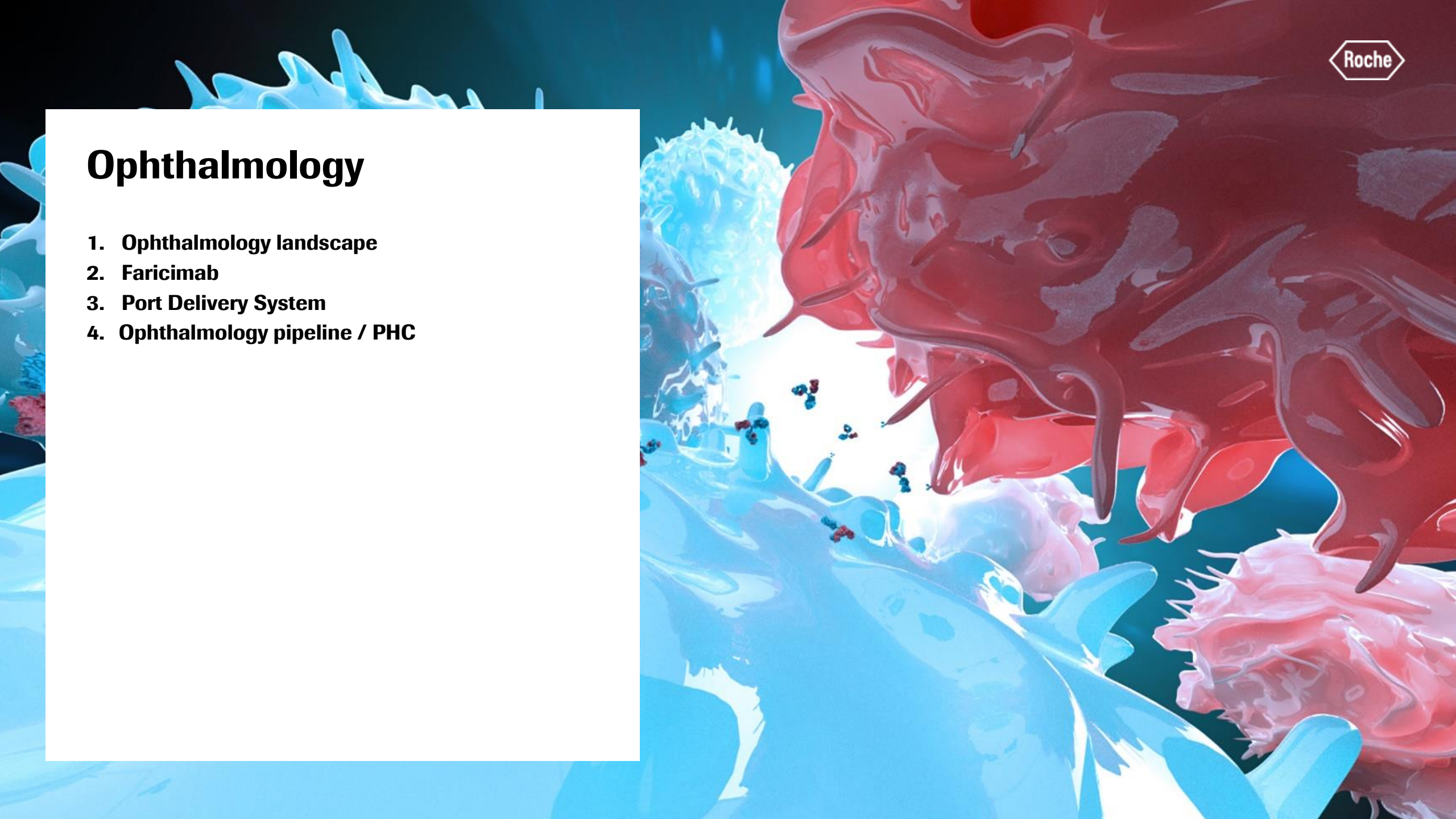
Ophthalmology portfolio

Nilesh Mehta | Lifecycle Leader, faricimab



Ophthalmology

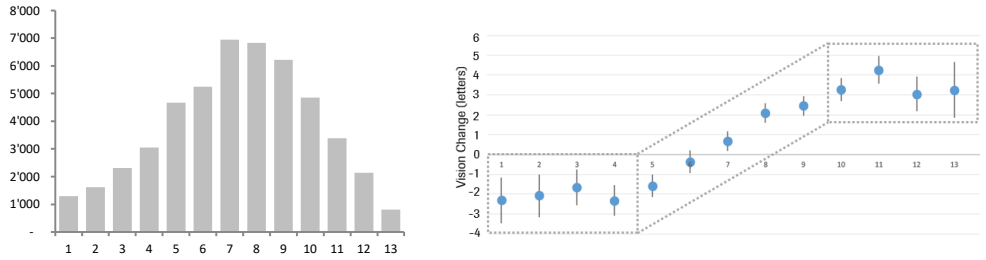
1. Ophthalmology landscape
2. Faricimab
3. Port Delivery System
4. Ophthalmology pipeline / PHC



Reduction in treatment burden is a key unmet medical need

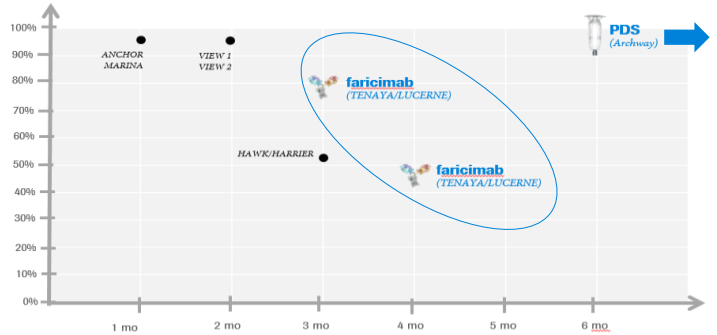
Real world vision outcomes are suboptimal

Adherence to IVT therapies is low and infrequent dosing in the real world correlates with vision loss



Only 50% of patients can be extended to Q3M dosing with current IVT therapies

Improved durability will help improve real world outcomes



faricimab and PDS are potential new standards of care

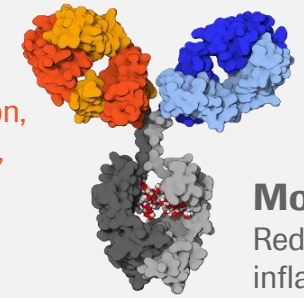
IVT=intravitreal; PDS = Port Delivery System

Faricimab

Filed in US and EU with approvals expected in 2022

Faricimab improves vascular stability via neutralization of both Ang-2 and VEGF-A

Anti–Ang-2 Fab
Ang-2 binding leads to pericyte loss, inflammation, cell membrane instability, and increased VEGF sensitivity



Anti–VEGF-A Fab
VEGF-A promotes leakage, abnormal vessel sprouting

Modified Fc
Reduces systemic exposure and inflammatory potential

Positive results over four studies in nAMD/DME

Indication	Ph1	Ph2	Ph3	
DME	*YOSEMITE/RHINE*			✓
nAMD	*TENAYA/LUCERNE*			✓
RVO	*BALATON/COMINO*			

- Joint filing in nAMD/DME in US, EU, and Japan
- Two Ph 3 studies initiated in RVO
- Long-term extension studies initiated in DME and nAMD

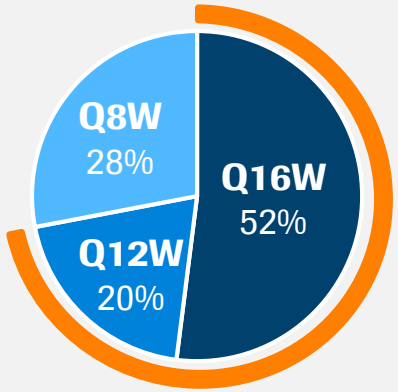
CrossMAb molecule representative of faricimab; Regula JT et al. *EMBO Mol Med*. 2016;8(11):1265-1288, with correction in Regula JT et al. *EMBO Mol Med*. 2019;11(5):e10666; Ang-2=angiopoietin-2; Fab=fragment antigen binding; Fc=fragment crystallizable; VEGF-A=vascular endothelial growth factor-A; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO = retinal vein occlusion

Faricimab: positive data in DME and nAMD

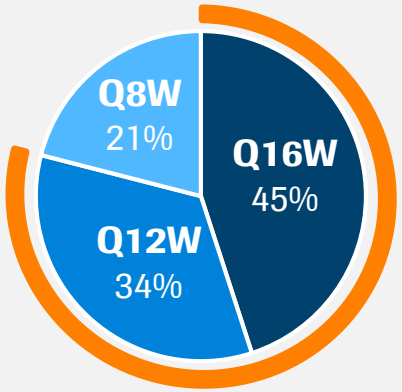
Demonstrating advantages in durability (up to Q16W) and anatomy

75–80% of patients maintained on ≥Q12W dosing, ~50% of patients maintained on ≥Q16W dosing

YOSEMITE/RHINE (DME)



TENAYA/LUCERNE (nAMD)



BCVA	• BCVA gains with faricimab Q8W or up to Q16W non-inferior to aflibercept Q8W

Disease control	• DME: better anatomic outcomes vs. aflibercept:
	  • Change in CST favoring faricimab
	  • More patients showing absence of DME
	  • More patients showing absence of IRF
	• nAMD: Meaningful reductions in CST

Safety	• Faricimab was well tolerated • IOI event rates were low • No cases of vasculitis or occlusive retinitis reported
Long-term data	• Year 2 data and long-term studies (RHONE-X, AVONELLE-X) are ongoing in DME, nAMD

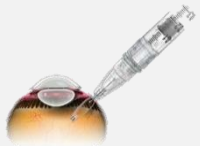
DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; CST = central subfield thickness; IRF=intraretinal fluid; IOI=intraocular inflammation

Port Delivery System (PDS)

Filed in US and EU in Q2 2021, with FDA approval expected this year

With PDS, nearly all patients can be maintained on 6m dosing, improving patient compliance and real world outcomes

- **PDS implant:** permanent, refillable intraocular implant. One-time ~30 min outpatient surgical procedure.



- **Refill exchange:** twice yearly in-office refill of the device using proprietary needle assembly. Can only be refilled with proprietary formulation (not other molecules or biosimilars)

Positive Ph 3 results in nAMD with additional trials ongoing in DME, DR

Indication	Ph1	Ph2	Ph3
nAMD	*Archway*		✓
DME	*Pagoda*		
DR	*Pavilion*		

- Ph 3b Velodrome study investigating 9m dosing initiated
- Ph 2/3 long-term extension study (Portal) in nAMD initiated
- Ph 3 Pagoda fully recruited; data expected in 2022

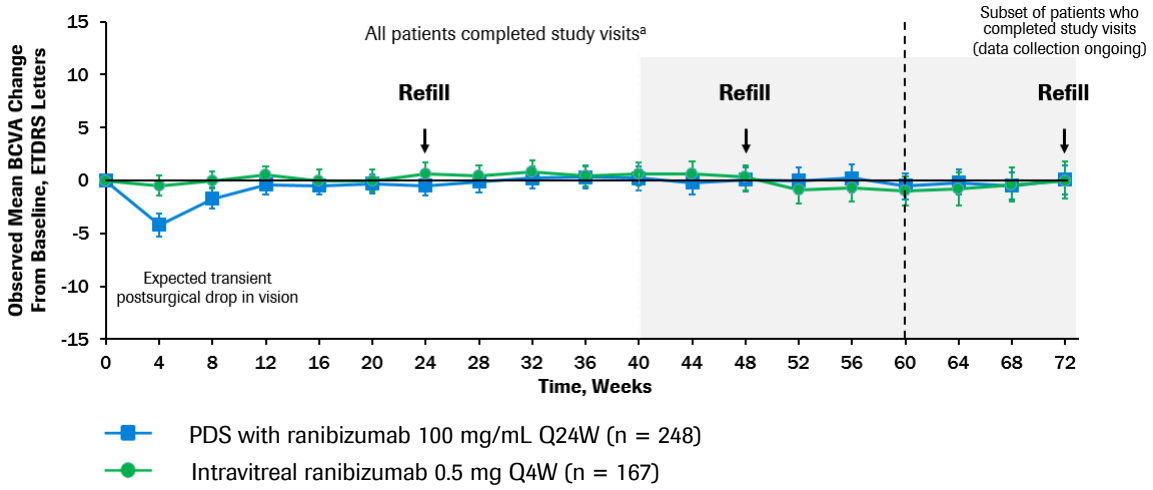
PDS=Port Delivery System with ranibizumab; IVT=intravitreal; DME=diabetic macular edema; DR=diabetic retinopathy; nAMD=neovascular age-related macular degeneration; RVO=retinal vein occlusion

PDS: nearly all patients able to be maintained on 6m dosing

Strong patient preference for PDS

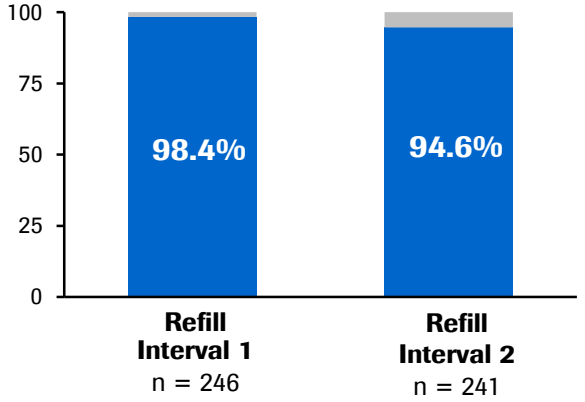
Equivalent Vision

PDS maintained vision through week 72



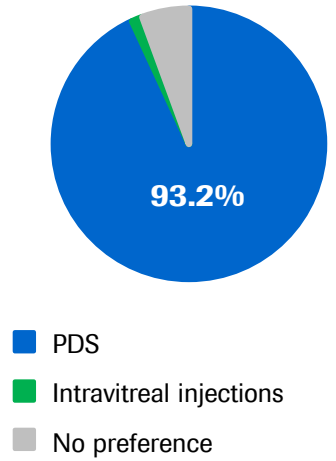
Treatment Durability

> 90% of patients did not receive supplemental treatment before each refill-exchange procedure



Patient preference

93% of patients preferred PDS over intravitreal injections



BCVA=best-corrected visual acuity; PDS=Port Delivery System with ranibizumab

Preparing for a global launch in nAMD

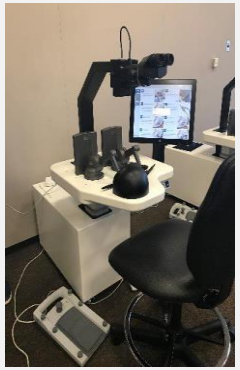
US launch planned for 2021, ex-US for 2022

Virtual reality training


THE WALL STREET JOURNAL.

Genentech Uses Virtual Reality to Train Eye Surgeons

Adopts technology in clinical trial for eye-implant procedure

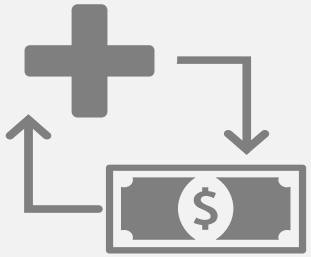


- Virtual reality (VR) technology enables preoperative training of surgeons on PDS procedures (implant insertion and refill)
- >200 US surgeons trained in Ph III across ~100 sites; ex-US VELODROME trial ongoing in 15+ countries

Field-based support

- Surgical Device Specialists (SDS) support training on site, and facilitate peer to peer discussion and education
- Focus on ensuring consistency in outcomes and enhancing the patient experience

Payer discussions ongoing

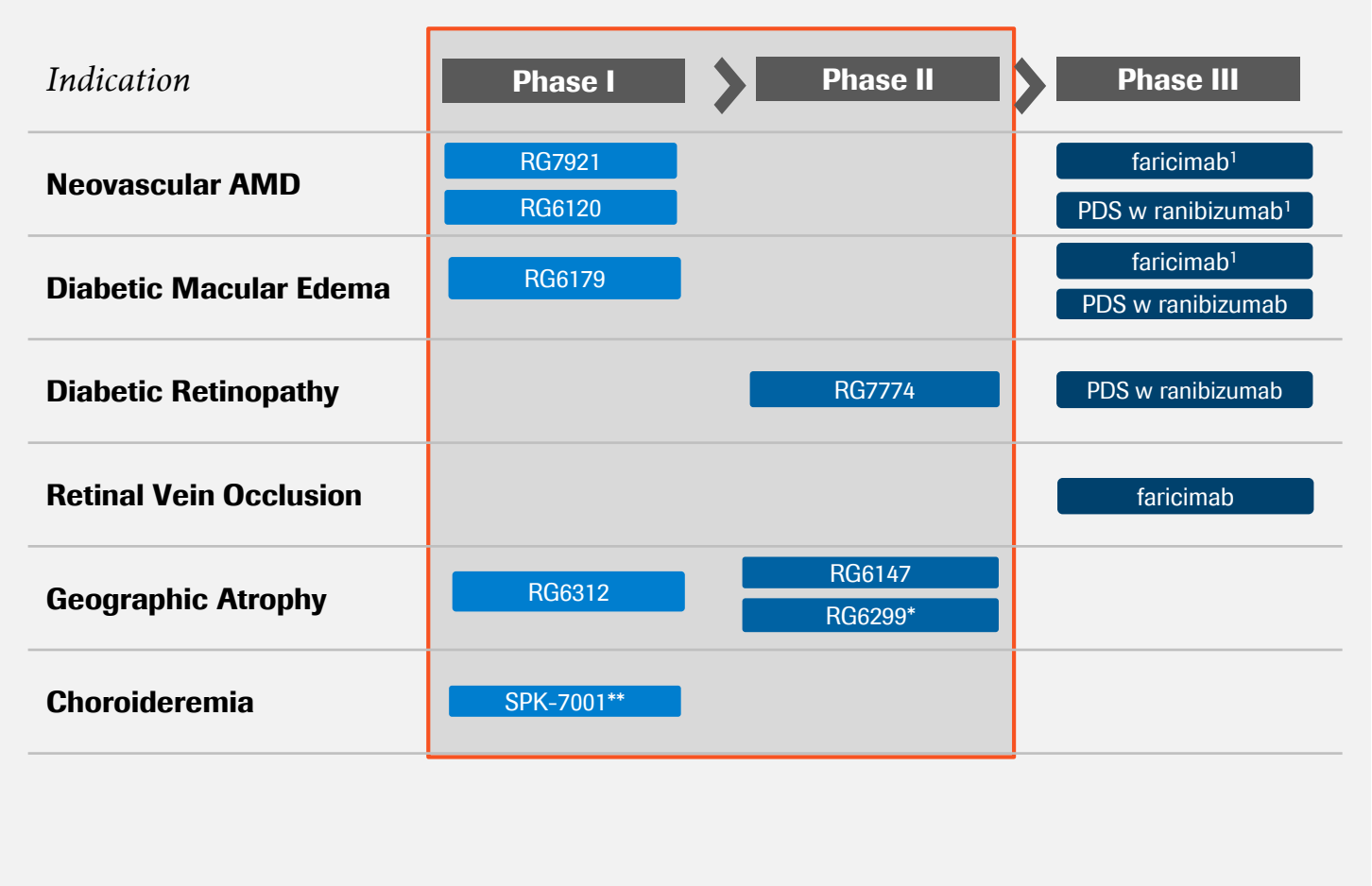


- Currently engaging with payers
- Considerations for reimbursement: PDS device, implant procedure, drug, refill procedure

nAMD=neovascular age related macular degeneration; PDS = Port Delivery System

Industry leading ophthalmology pipeline

Eight NMEs in early stage development (Ph 1/2)



Approved:

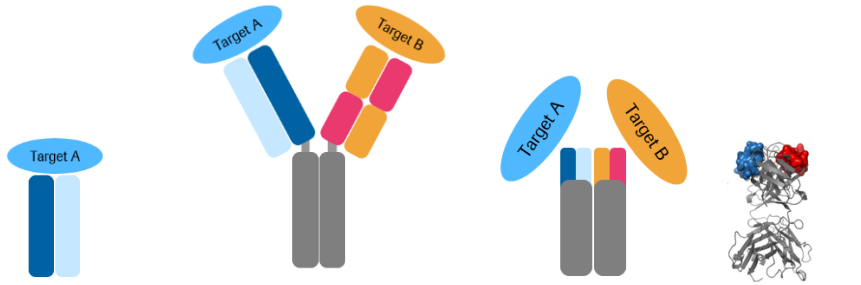
LUCENTIS® RANIBIZUMAB INJECTION

LUXTURNA™ voretigene neparvovec-rzyl for subretinal injection

PDS=Port Delivery System; NME=new molecular entity; Lucentis PFS is marketed by Novartis outside the U.S.; * Study conducted by Ionis, Roche option to in-license; Roche option to in-license; **with Spark Therapeutics, approved for patients with biallelic *RPE65* mutation-associated retinal dystrophy; [1] regulatory submissions initiated

Port Delivery System is a platform technology

DutaFabs are next generation bispecifics designed for increased efficacy & durability*



Monospecific Fab fragment

e.g. *Lucentis*

Bispecific mAb (Crossmab)

e.g. faricimab

Bispecific Fab fragment (DutaFab)

Positive PDS Ph3 has enabled acceleration of DutaFabs in PDS platform

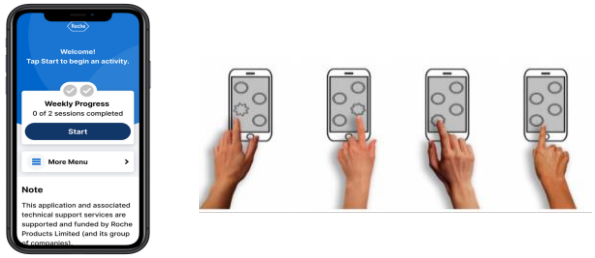
- DutaFabs are a novel bispecific Fab format significantly smaller than bispecific antibodies
- DutaFabs are compatible with the Port Delivery System enabling increased durability beyond Q6M
- Two DutaFabs are in clinical development with distinct targets, including Ang2/VEGF

* Nature Communications, volume 12, Article number: 708 (2021); PDS = Port Delivery System

Ophthalmology Personalized Healthcare

Remote monitoring & advanced analytics to help treat vision loss early

Remote vision monitoring

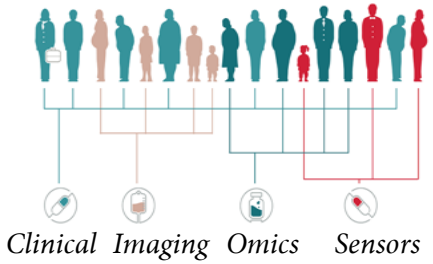


- App-based designed test to detect changes in vision in-between office visits
- Vision alerts sent to doctor
- Ongoing Home Vision Monitoring pilot to support patients during COVID-19

Retinal imaging and algorithms

- Demonstrated PoC utilizing internal algorithms in disease detection, prediction of progression and response to treatment

Data portfolio



- RWD and data sharing partnerships:

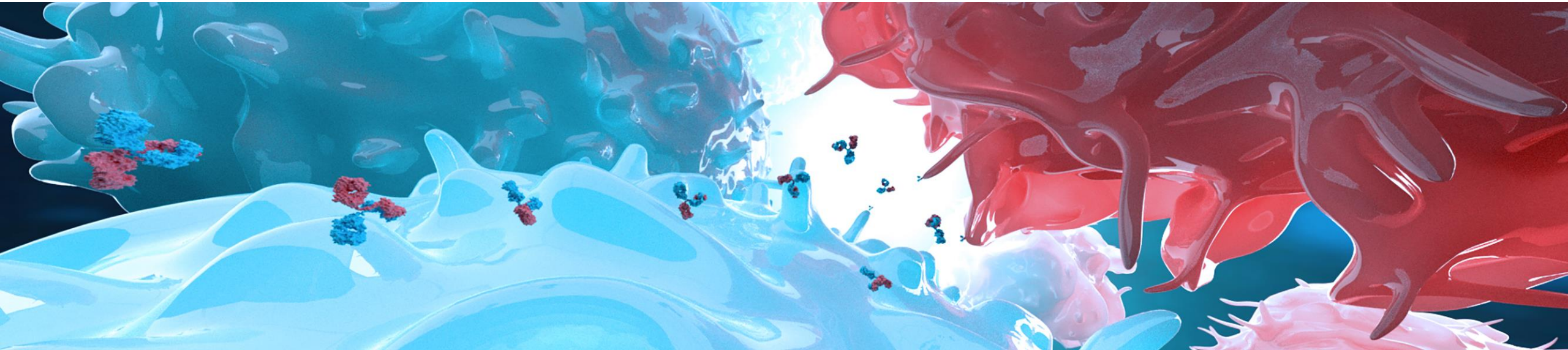
INSIGHT Health Data Research Hub · Verana Health · CATT · inoveon

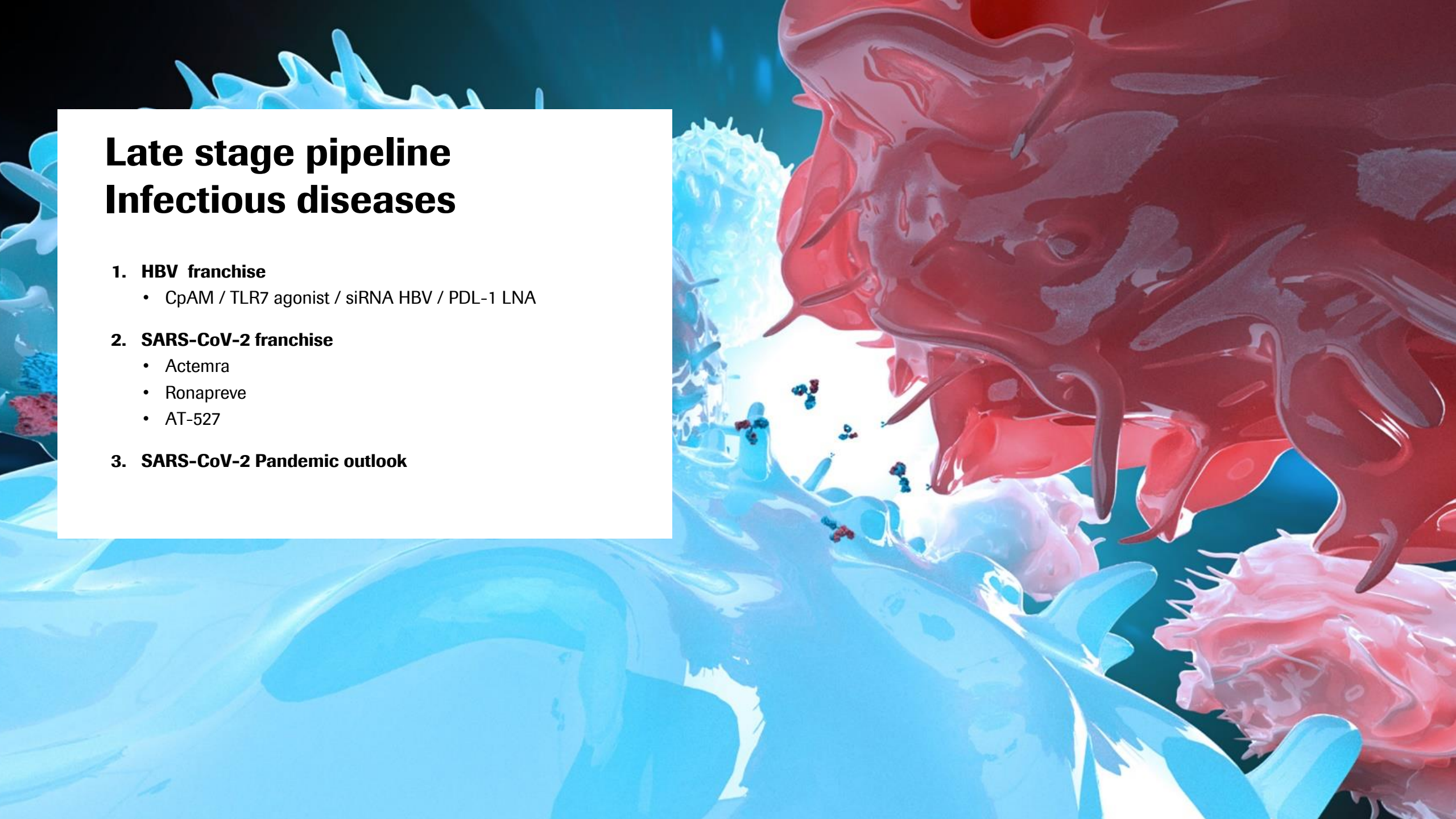
nAMD=neovascular age related macular degeneration; PoC=proof of concept

Roche Pharma Day 2021

Late Stage Pipeline Infectious Diseases

Barry Clinch| Global Head of Infectious Diseases, Clinical development





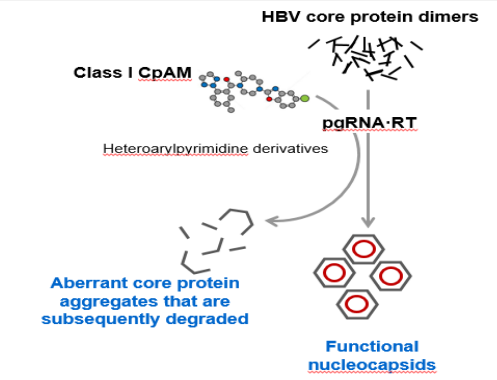
Late stage pipeline
Infectious diseases

1. **HBV franchise**
   - CpAM / TLR7 agonist / siRNA HBV / PDL-1 LNA
2. **SARS-CoV-2 franchise**
   - Actemra
   - Ronapreve
   - AT-527
3. **SARS-CoV-2 Pandemic outlook**

Hepatitis B virus: CpAM / TLR7 agonist / HBV siRNA / PDL-1 LNA

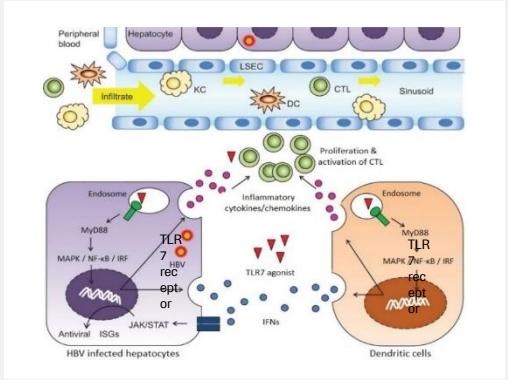
4 new MOAs in clinical development

Core protein allosteric modulator (CpAM)



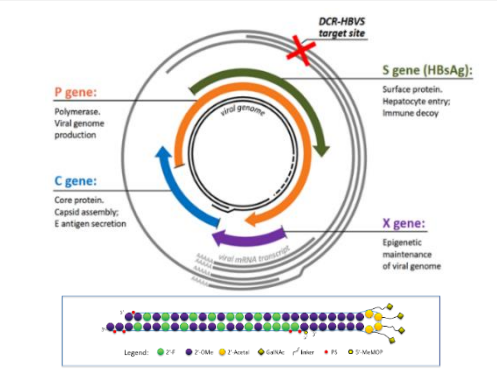
- Effective against all major HBV genotypes
- Showing successful HBsAg reduction in mouse model

Toll like receptor 7 (TLR7) agonist



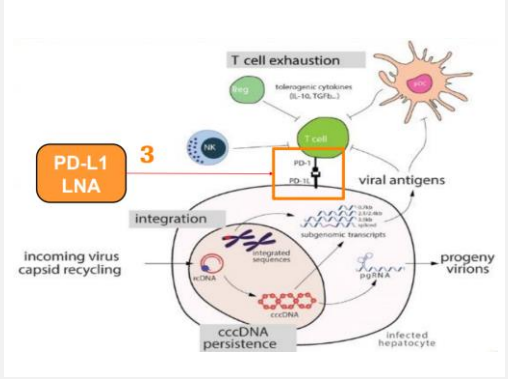
- TLR7 detects single-stranded viral RNA and mediates anti-viral cytokine production and dendritic cell activation
- Unique double pro-drug selectively activated in the liver

siRNA inhibiting multiple HBV genes



- Dicerna proprietary liver-targeted RNAi technology (GalXC™) with unique 'tetraloop' folded design
- Designed to inhibit HBV gene expression by targeting of HBV genome S open reading frame

PDL-1 LNA



- Inhibition of the PD-L1/PD-1 interaction removes a T cell inhibitory signal
- Liver-directed locked nucleic acid oligonucleotide (RNA) targeting PDL-1 expression on hepatocytes to minimize systemic toxicity

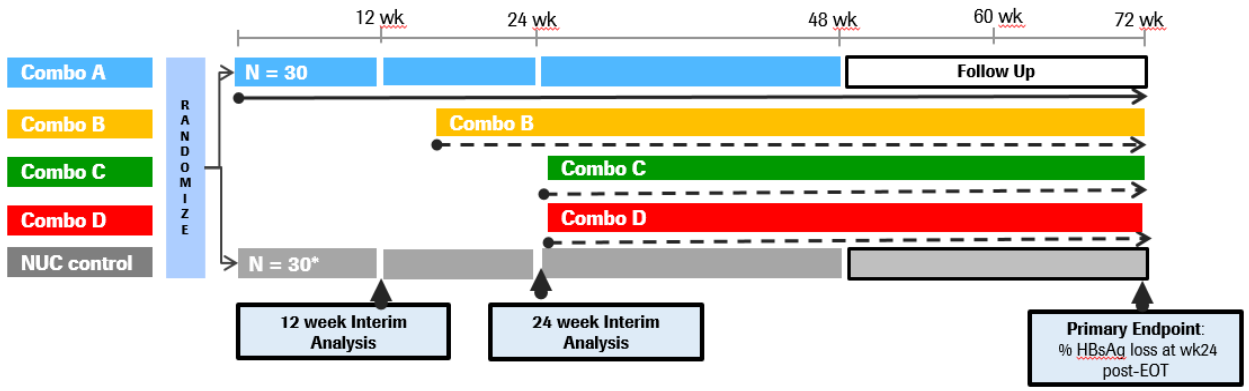
MOA=mechanism of action; HBsAg=Hepatitis B surface-antigen; LNA=locked nucleic acid

Hepatitis B virus: Combination platform initiated

Multiple combinations now in Ph II testing

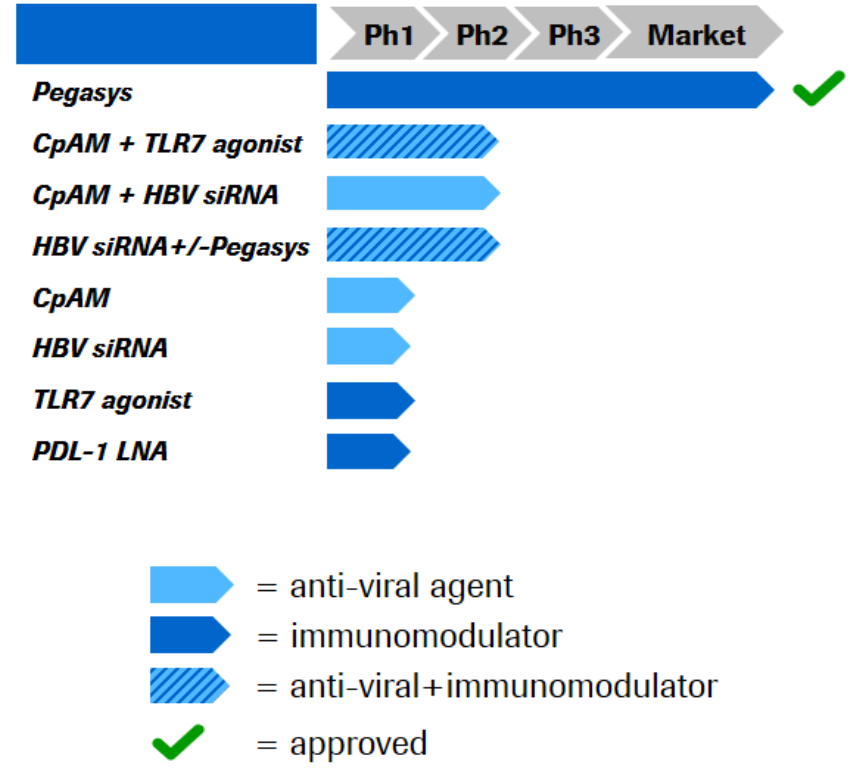
Screening drug combinations efficiently

Highly adaptive HBV combination platform



- Adaptive platform for Ph II study with shared control arm
- Designed to find the best combination therapy for HBV cure
- Opportunity to seamlessly add and terminate drug combinations

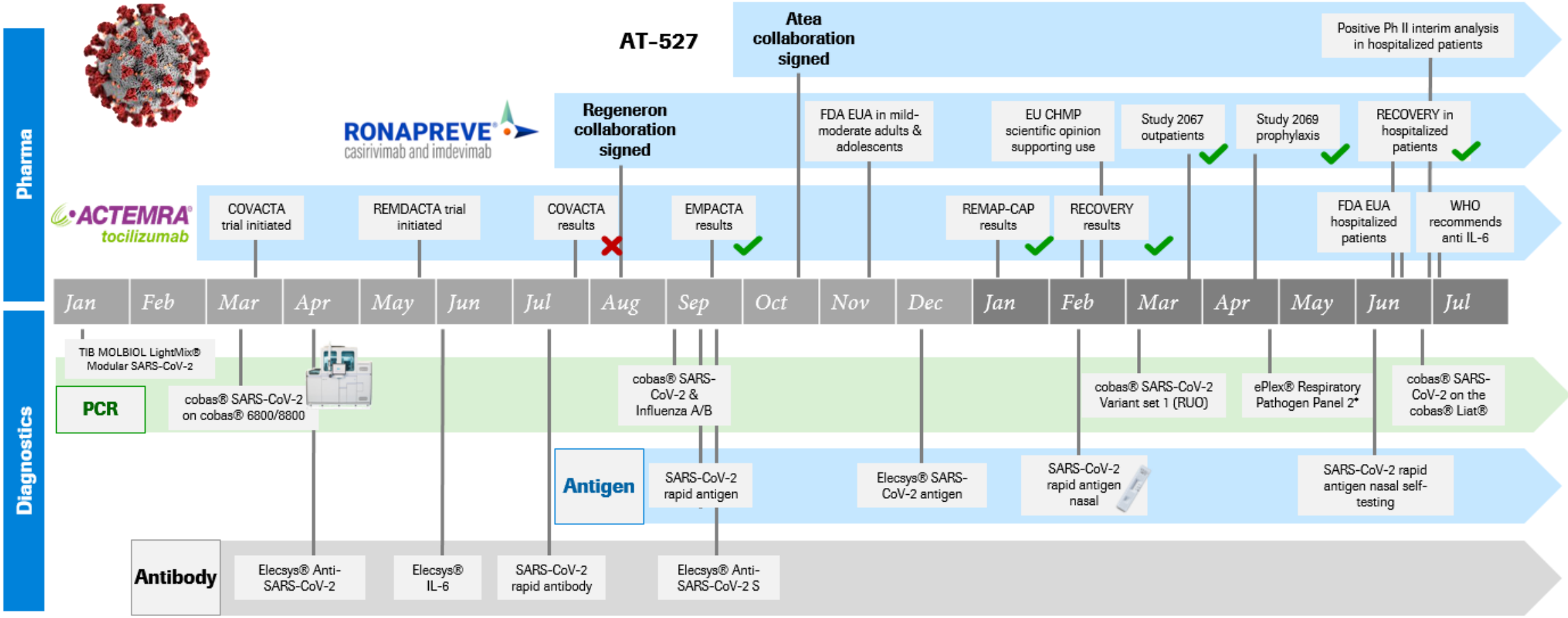
HBV development program progresses



NUC=nucleosides

SARS-CoV-2: Our outstanding contribution battling the pandemic

> 1 million hospitalized patients received Roche's treatments

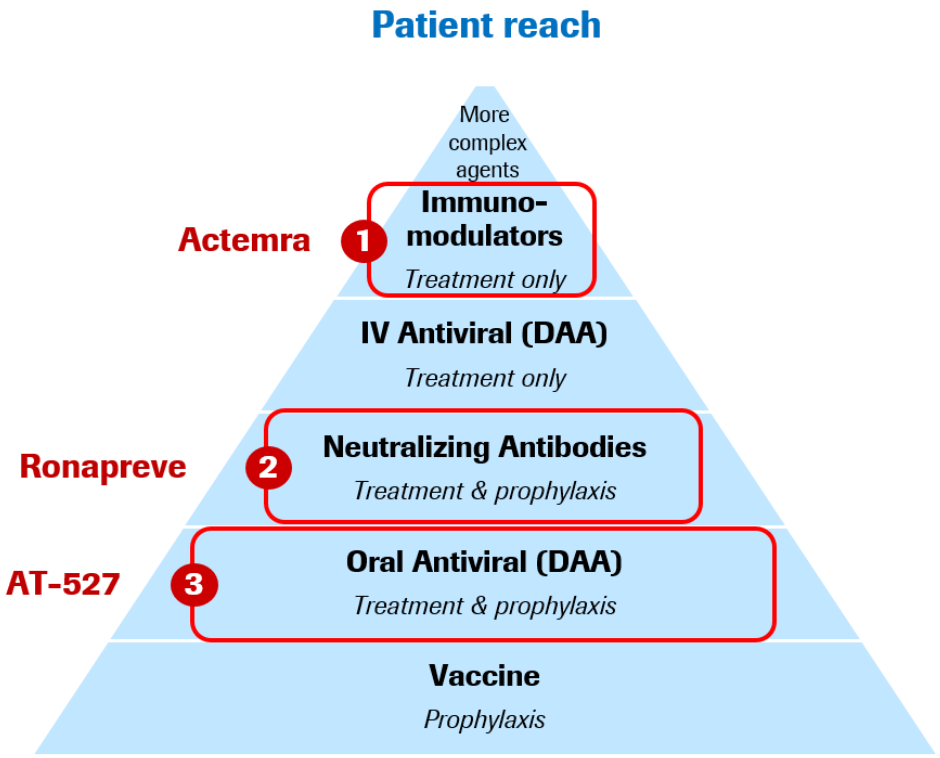


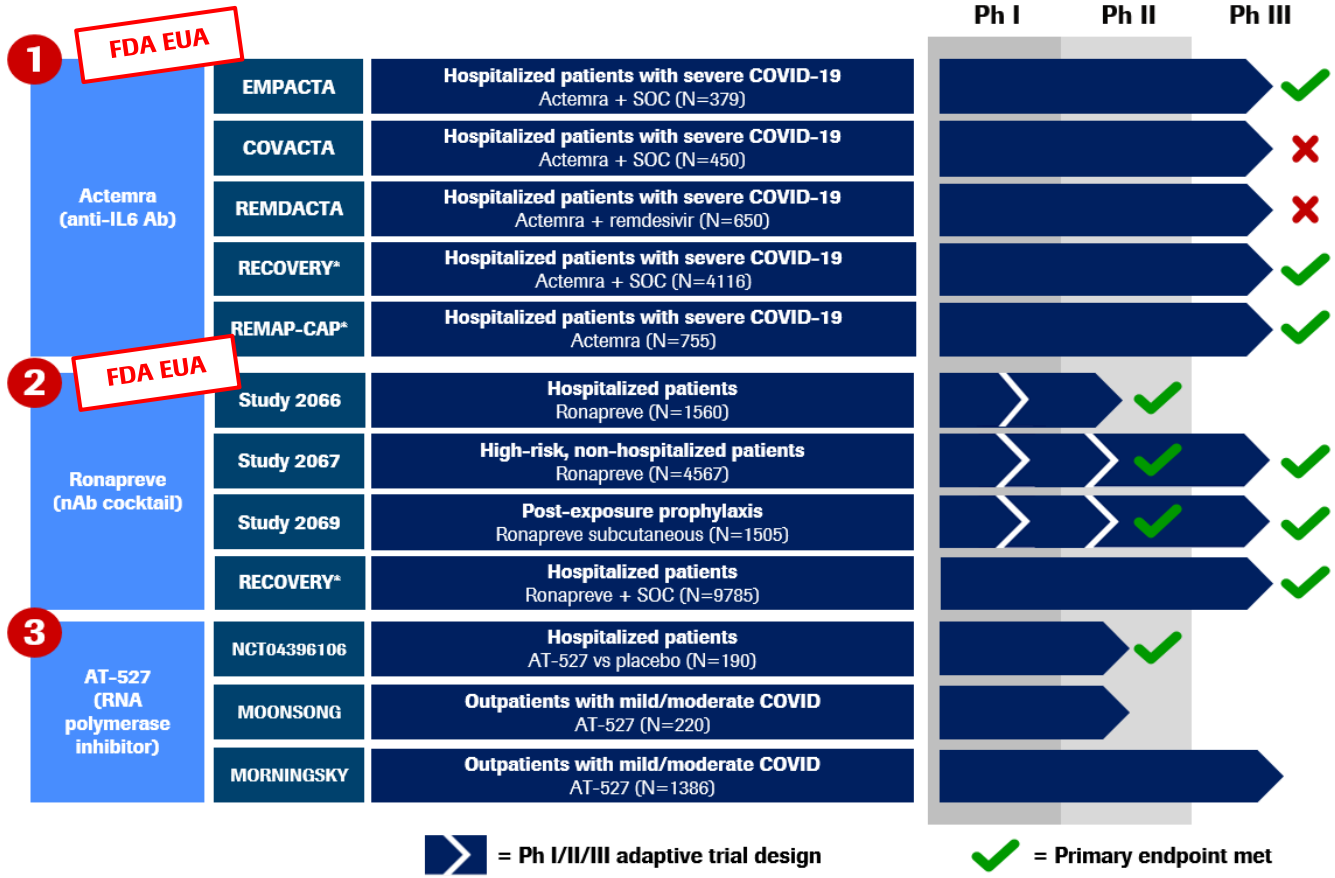
✔ = positive Ph III results

Overview: not all COVID-19 related developments and health solutions captured; EUA=emergency use authorization; RUO=Research use only; * through GenMark acquisition

SARS-CoV-2: Broad development program ongoing

Different scientific approaches serving different pandemic needs





EUA=emergency use authorization; nAb=neutralizing antibodies; DAA=direct acting antiviral; * RECOVERY trial conducted by the University of Oxford; REMAP-CAP trial conducted by the Imperial College London; AT-527 Ph II study in hospitalized patients run by ATEA Pharmaceuticals

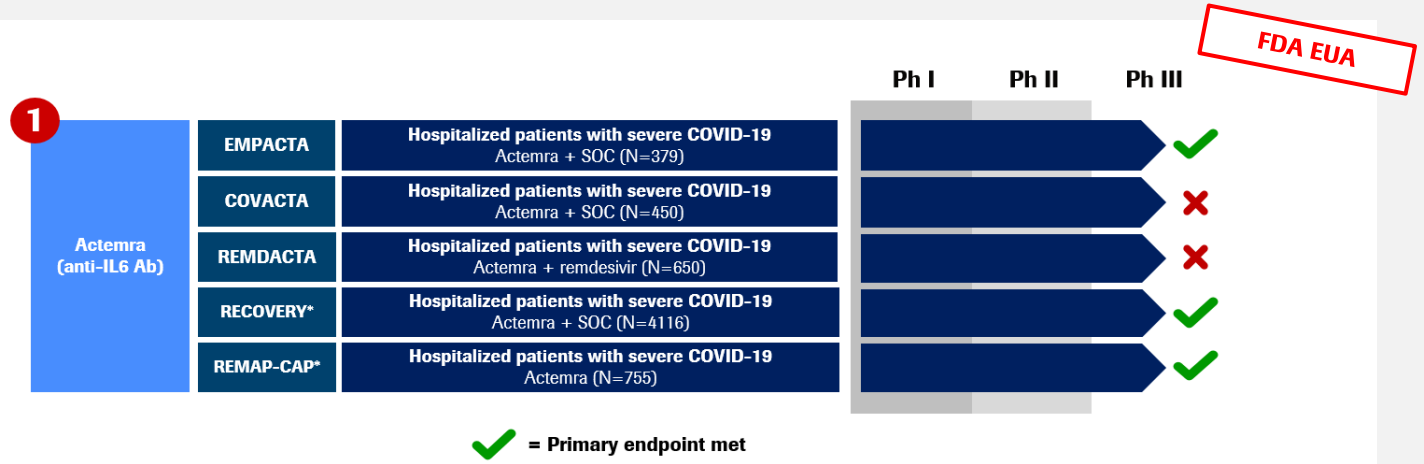
SARS-CoV-2: Actemra for severe COVID-19 associated pneumonia

WHO recommends IL-6 inhibitors for hospitalized patients

Anti-IL6 receptor mAb

- Approved in RA, JIA, GCA and for CAR T-cell induced CRS
- As IL-6 plays an important role in SARS-CoV-2 infections and is considered a prognostic marker for disease severity, Roche initiated a Ph III program in hospitalized patients

Totality of randomized Ph IIIs demonstrates efficacy in hospitalized patients



- Ph III (RECOVERY)* results showed that when Actemra is administered to hospitalized COVID-19 patients who received corticosteroids and require supplemental oxygen or breathing support the risk of death is reduced by 14% and enables faster recovery
- Based on a meta-analysis including Actemra in >8,000 hospitalized patients the WHO issued new treatment guidelines, recommending IL-6 inhibitors for severe COVID-19; the analysis showed Actemra to reduce mortality in hospitalized patients receiving corticosteroids

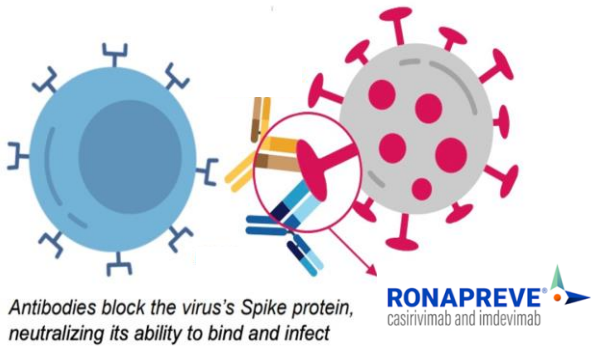
WHO=world health organization; RA=rheumatoid arthritis; JIA=juvenile idiopathic arthritis; GCA=giant cell arteritis; CRS=cytokine release syndrome; * RECOVERY trial conducted by the University of Oxford; REMAP-CAP trial conducted by the Imperial College London

2

SARS-CoV-2: Ronapreve maintains activity against key variants

Positive data in prophylaxis, non-hospitalized & hospitalized patients

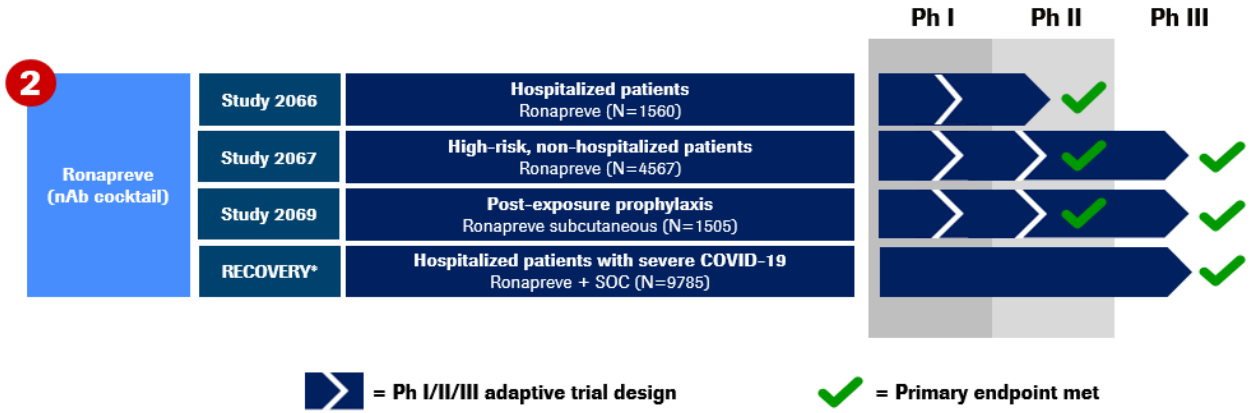
Neutralizing Ab cocktail



- Two potent, virus neutralizing Abs binding non-competitively to the critical receptor binding domain of the virus's spike protein[1]
- Multiple simultaneous virus mutations needed to escape the nAb cocktail, which is an unlikely scenario[2,3]

Extensive trial program with >25.000 patients

FDA EUA Approval Japan



- Ph I-III (Study 2067) results show that Ronapreve reduces the risk of hospitalization or death by 70% for the low dose and by 71% for the high dose
- Ph I-III (Study 2069) results show that a low dose of 1,200 mg SC Ronapreve reduces the risk of symptomatic infections by 81% in those who were not infected when they entered the trial
- Ph III (RECOVERY)* results for Ronapreve show a 20% reduction in the risk of death for patients who do not mount their own antibody response against SARS-CoV-2

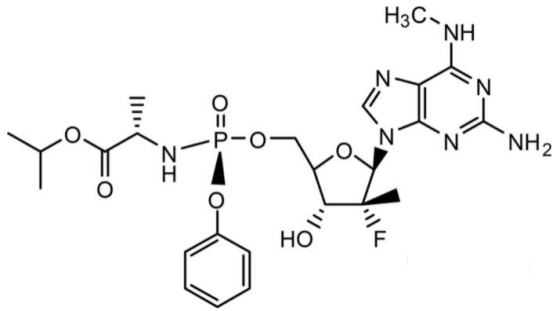
Ronapreve in collaboration with Regeneron; [1] A. Baum et al., Science (2020); [2] Copin R, et al., Cell (2021); [3] Chen R. et al., Nature (2020); Ab=antibody; * RECOVERY trial conducted by the University of Oxford; REMAP-CAP trial conducted by the Imperial College London

3

SARS-CoV-2: AT-527 for the outpatient setting

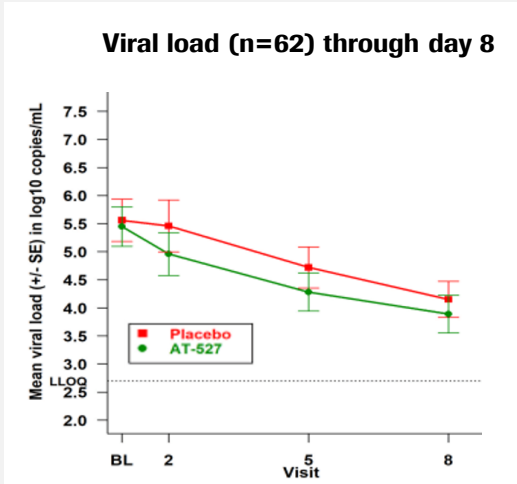
Ph II interim viral load results in hospitalized patients

Purine nucleotide prodrug

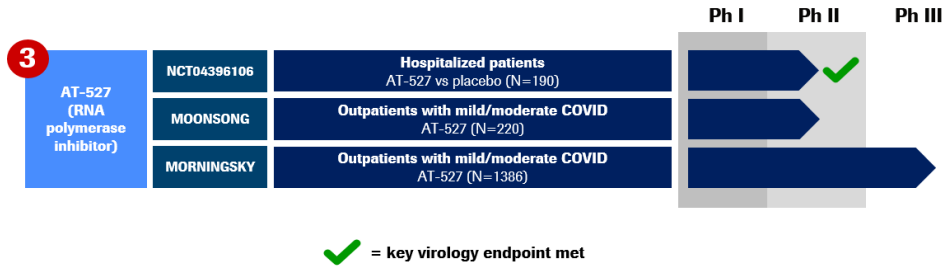


- Oral, direct acting antiviral (DAA)
- Inhibits SARS-CoV-2 viral replication via a unique dual mechanism of action: Inhibits both NiRAN and RdRp, potentially creating a high barrier to resistance
- Generally safe and well tolerated

Ph II interim results*



Ph III results expected end of 2021

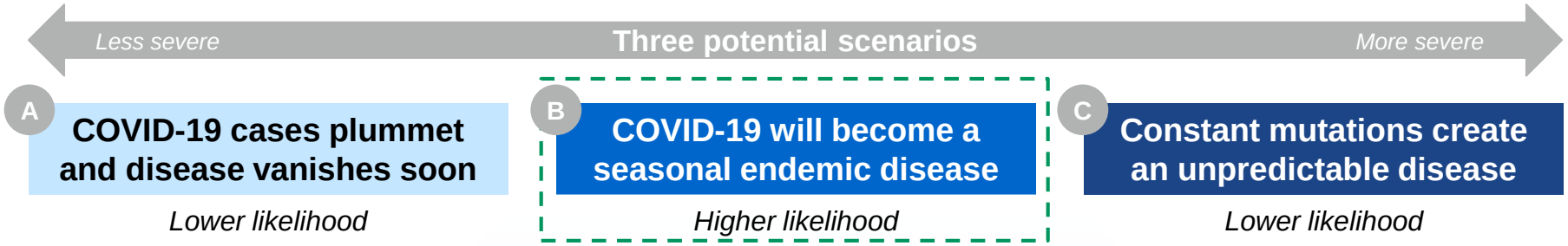


- Ph II in mild/moderate hospitalized patients ongoing; interim results indicate antiviral activity: 0.7$\log_{10}$ reduction in viral titres at day 2; sustained viral reduction through day 8
- Ph II (MOONSONG) in outpatients evaluates alternative doses
- Ph III (MORNINGSKY) in outpatients achieved first-patient-in; results expected later in 2021

NiRAN=Nidovirus RdRp-Associated Nucleotidyltransferase; RdRp=RNA-dependent RNA polymerase; *ATEA Pharmaceuticals presentation from June 30, 2021; AT-527 in collaboration with Atea Pharmaceuticals

SARS-CoV-2: Pandemic outlook

Three scenarios how the pandemic might evolve in coming years



Core beliefs

1. COVID-19 will become **endemic** and **seasonal,** with 200-500m new infections per year
2. **Severity** of disease will **decrease** over time, but **unlikely** to **become** another **"common cold"**
3. **Mutations will continue to arise** as virus further adapts to humans, but **we expect to be able to evolve** Vx/Tx/Dx accordingly

COVID-19 is here to stay, and there will still be a need for new treatments and diagnostics

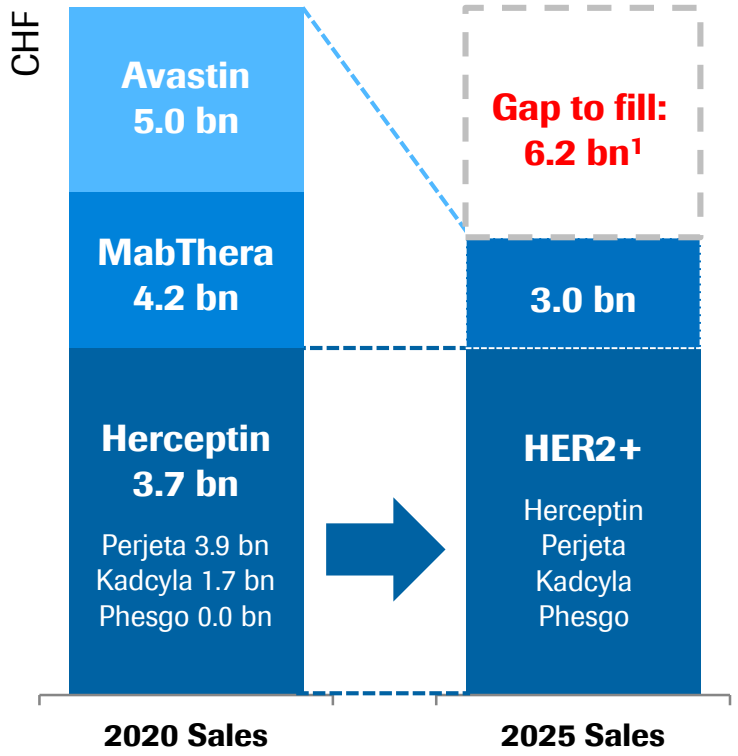
Roche medicines against SARS-CoV-2 expected to be used by millions of patients in coming years

Doing now what patients need next

New product growth with strong momentum
Considerable optionality

Biosimilar gap (20-25)

Sensitivity analysis:
Assuming conservative planning assumptions



Consensus sales growth (20-25)

Post-HY 2021 consensus survey

Ocrevus	2.6 bn
Tecentriq	3.8 bn
Hemlibra	2.7 bn
Gazyva	0.7 bn
Alecensa	0.5 bn
Polivy	1.0 bn
Enspryng	0.5 bn
Evrysdi	2.2 bn
Other in-market[2]	(2.3) bn
Pipeline value[3]	6.4 bn
Total	**18.1 bn**

Up-side potential to consensus above are:

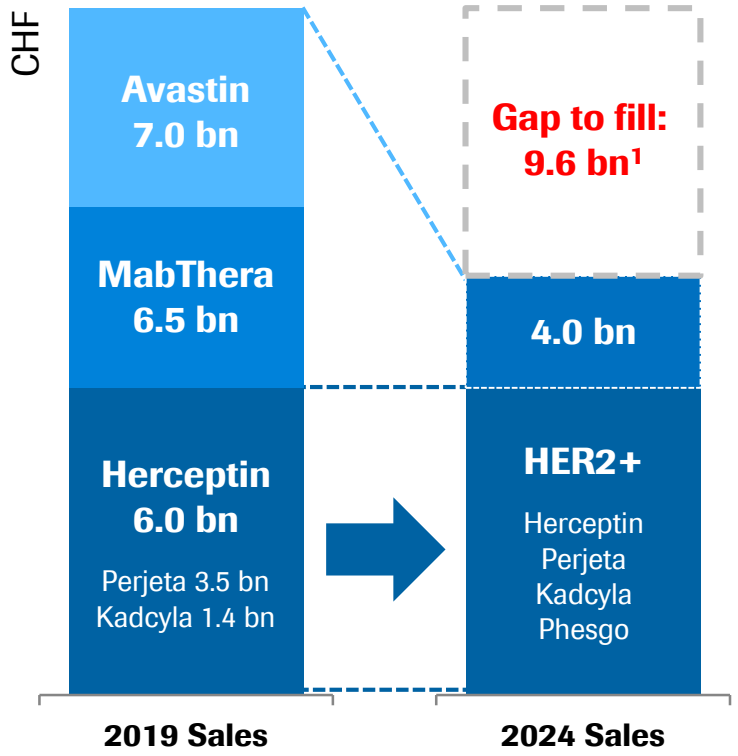
Oncology (Gavreto, inavolisib, KRAS G12C+), **Ophthalmology** (DutaFabs), **Neuroscience** (prasinezumab, fenebrutinib, SRP-9001), **Immunology** (rh-Pentraxin-2, etrolizumab in CD), **Infectious diseases** (Ronapreve, AT-527, chronic HBV)

[1] Gap value including the total HER2+ franchise change from 2020 to 2025; [2] Xolair, Pulmozyme, CellCept, Activase/TNKase, Actemra, Lucentis, Erivedge, Esbriet, Cotellic, Xofluza, Rozlytrek; [3] crovalimab, mosunetuzumab, glofitamab, tiragolumab, gantenerumab, giredestrant, ipatasertib, PDS, faricimab

New product growth with strong momentum
Considerable optionality

Biosimilar gap (19-24)

Sensitivity analysis:
Assuming conservative planning assumptions



Consensus sales growth (19-24)

Post-HY 2020 consensus survey

Ocrevus	3.1 bn
Tecentriq	4.1 bn
Hemlibra	3.0 bn
Gazyva	0.7 bn
Alecensa	0.8 bn
Polivy	1.1 bn
Enspryng	0.4 bn
Evrysdi	1.4 bn
Other in-market[2]	(0.3) bn
Pipeline value[3]	3.4 bn
Total	**17.7 bn**

Up-side potential to consensus above are:

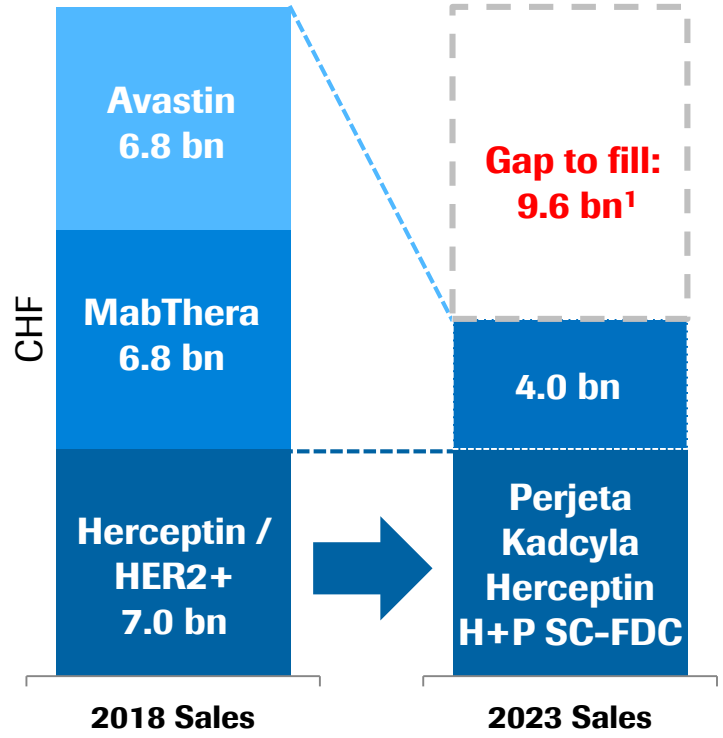
Oncology (Gavreto, mosunetuzumab, PI3Kαi, SERD), **Ophthalmology** (PDS), **Neuroscience** (gantenerumab, prasinezumab, SRP-9001), **Immunology** (Gazyva in lupus, rhPentraxin-2, crovalimab, etrolizumab in CD), **Infectious diseases** (REGN-COV2, chronic HBV)

[1] Gap value including the total HER2+ franchise change from 2019 to 2024; [2] Xolair, Pulmozyme, CellCept, Activase/TNKase, Actemra, Lucentis, Erivedge, Esbriet, Cotellic, Xofluza, Rozlytrek; [3] glofitamab, tiragolumab, ipatasertib, faricimab, tominersen

New product growth with strong momentum
Considerable optionality

Biosimilar gap (18-23)

Sensitivity analysis:
Assuming conservative planning assumptions



Consensus sales growth (18-23)

Post-HY 2019 consensus survey

Ocrevus	3.8 bn
Tecentriq	3.5 bn
Hemlibra	3.5 bn
Gazyva	0.8 bn
Alecensa	0.9 bn
Xofluza	0.5 bn
Polivy	0.9 bn
Rozlytrek	0.4 bn
In-market & mature[2]	(0.9) bn
Pipeline value[3]	2.9 bn
Total	**16.3 bn**

Up-side potential to consensus above are:
Oncology (Venclexta, mosunetuzumab/ CD20xCD3, PI3Kα, SERD) **Autism** (balovaptan), **Alzheimer's** (gantenerumab), **Ophthalmology** (port delivery system), **Immunology** (Gazyva in lupus), **Infectious diseases** (chronic hepatitis B)

[1] Gap value including the total HER2 franchise change from 2017 to 2023, assuming Lucentis will be replaced by faricimab; [2] Esbriet, Tarceva, Xolair, Pulmozyme, Rocephin, CellCept, Mircera, NeoRecormon/Epogin, Activase/TNKase, Xeloda, Valcyte/Cymevene, Actemra/RoActemra, Tamiflu, Madopar, Pegasys; [3] satralizumab, etrolizumab, idasanutlin, ipatasertib, risdiplam, HTT-ASO