

# **Roche Pharma Day 2020**

# 14 September 2020





# **Roche Pharma Day 2020**

# Welcome

Karl Mahler | Head of Investor Relations and Roche Group Planning

# **Agenda**



#### Welcome

Karl Mahler, Head of Investor Relations and Roche Group Planning

## Pharma Strategy: Sustainable growth, more patient benefits, and less cost to society

Bill Anderson, CEO Roche Pharmaceuticals

### **Commercial Opportunities**

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**

Paulo Fontoura, Global Head Neuroscience and Rare Diseases Clinical Development

### Late Stage Pipeline Immunology & Ophthalmology

Cristin Hubbard, Head I2O (Immunology, Infectious Diseases, Ophthalmology) GPS

## Infectious Diseases: A close look at our HBV pipeline

John Young, Global Head of Infectious Diseases, pRED

### Late Stage Infectious Diseases: Influenza & SARS-CoV-2

Cristin Hubbard, Head I2O (Immunology, Infectious Diseases, Ophthalmology) GPS

### Q&A



# 36 Breakthrough Therapy Designations received since 2013 Reflecting the quality of our research

Year	Molecule	Indication		
2020	mosunetuzumab	3L+ FL		
	Tecentriq	unresectable or metastatic ASPS		
	Esbriet	ulLD		
	Gavreto	RET fusion-positive NSCLC		
	Gavreto	RET mutation-positive MTC		
	Cotellic	Histiocytic neoplasms		
2019	Gazyva	Lupus nephritis		
	rhPentraxin-2 (PRM-151)	IPF		
	Venclexta + Gazyva	1L unfit CLL		
	Kadcyla	Adjuvant HER2+ BC		
	SPK-8011	Hemophilia A		
	Enspryng	NMOSD		
0010	Xolair	Food allergies		
2018	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		



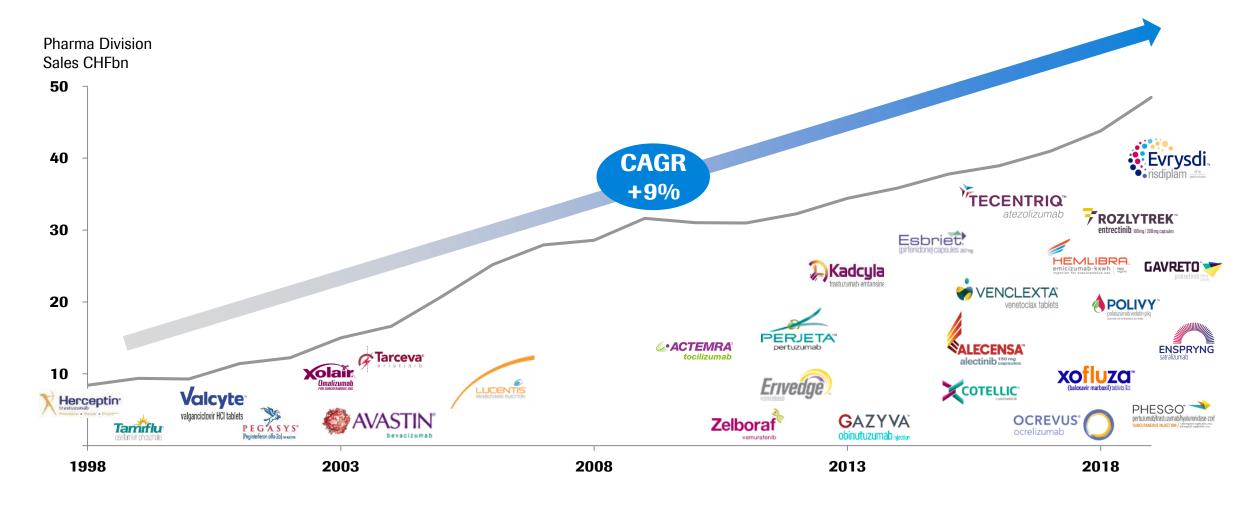
# **Roche Pharma Day 2020**

Pharma Strategy: Sustainable growth, more patient benefits, and less cost to society

**Bill Anderson** CEO Roche Pharmaceuticals

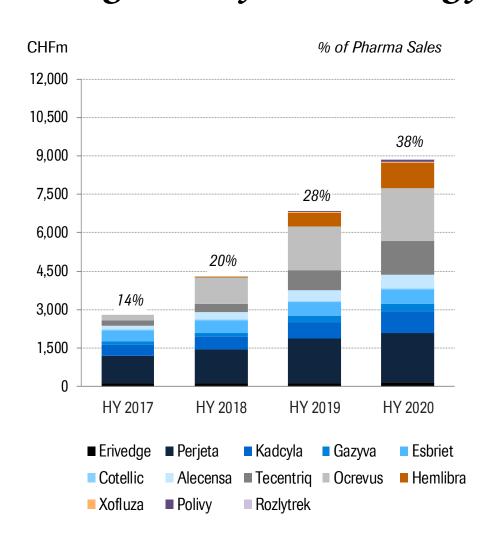


# Roche has a strong track record of innovation Industry leading medicines as basis for our continuous growth

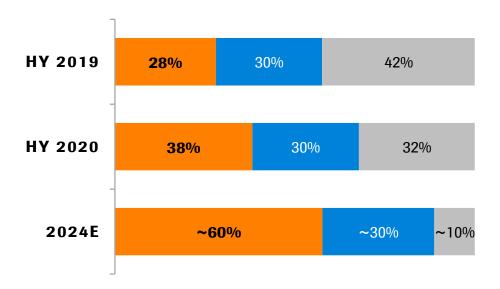


# Innovation driving portfolio rejuvenation Increasing share of sales coming from recent launches





### **Pharma sales mix**



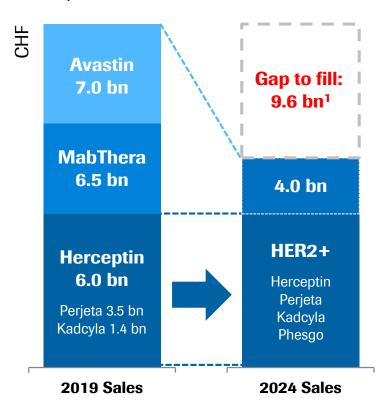
New products launched since 2012Other products ■ Herceptin + Avastin + Rituxan



# New product growth with strong momentum Considerable optionality

## Biosimilar gap (19-24)

**Sensitivity analysis**: Assuming conservative planning assumptions of 60-70% erosion from biosimilars



## **Consensus sales growth (19-24)**

Post-HY 2020	consensus	survey
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Total	17.7 bı
Pipeline value <sup>3</sup>	3.4 br
Other in-market <sup>2</sup>	(0.3) br
Evrysdi	1.4 br
Enspryng	0.4 br
Polivy	1.1 br
Alecensa	0.8 br
Gazyva	0.7 br
Hemlibra	3.0 br
Tecentriq	4.1 br
Ocrevus	3.1 br

### **Up-side potential to consensus above are:**

Oncology (Gavreto, mosunetuzumab, Pl3Kai, SERD),
Ophthalmology (PDS), Neuroscience (gantenerumab,
prasinezumab, SRP-9001), Immunology (Gazyva in lupus,
rhPentraxin-2, crovalimab, etrolizumab in CD), Infectious
diseases (REGN-COV2, chronic HBV)

<sup>&</sup>lt;sup>1</sup> Gap value including the total HER2+ franchise change from 2019 to 2024; <sup>2</sup> Xolair, Pulmozyme, CellCept, Activase/TNKase, Actemra, Lucentis, Erivedge, Esbriet, Cotellic, Xofluza, Rozlytrek;

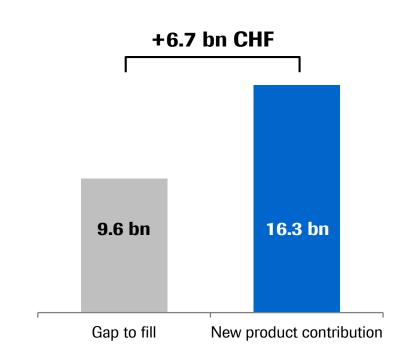
<sup>&</sup>lt;sup>3</sup> glofitamab, tiragolumab, ipatasertib, faricimab, tominersen

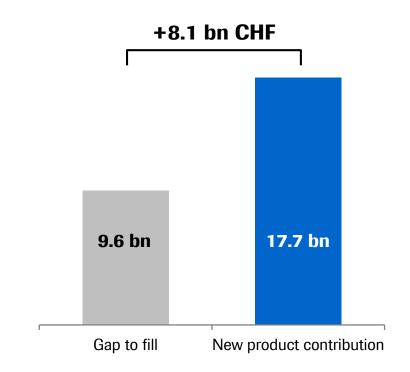


# What has changed since our Pharma day a year ago? Further increased confidence in delivering growth

2018-2023 consensus view<sup>1</sup>

2019-2024 consensus view<sup>2</sup>



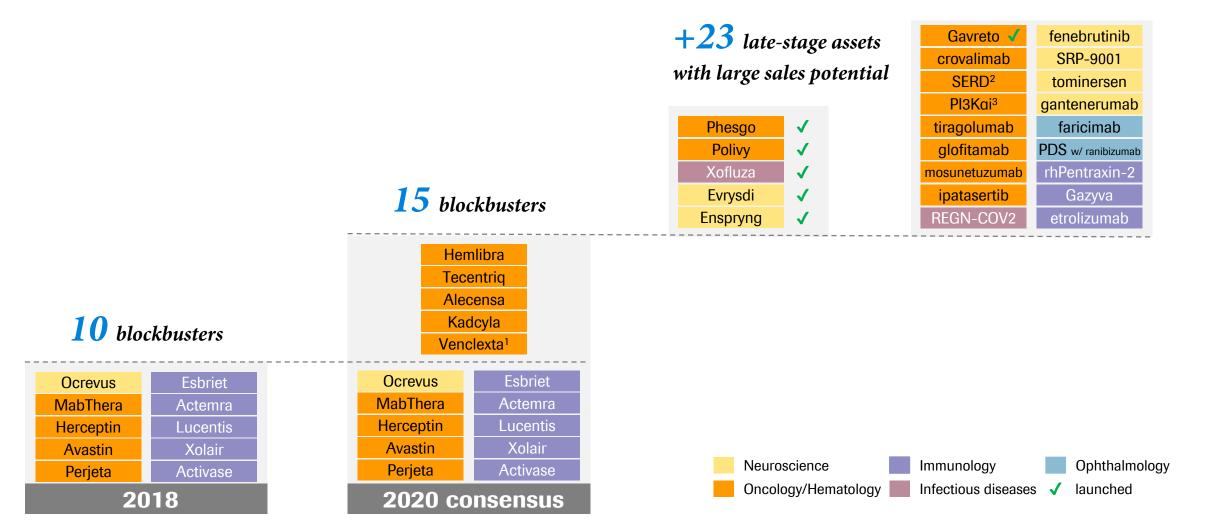


Strong new product contribution and ongoing launches driving growth

<sup>&</sup>lt;sup>1</sup> Roche Post-HY 2019 consensus survey; <sup>2</sup> Roche Post-HY 2020 consensus survey

# Strong commercial potential throughout late stage portfolio



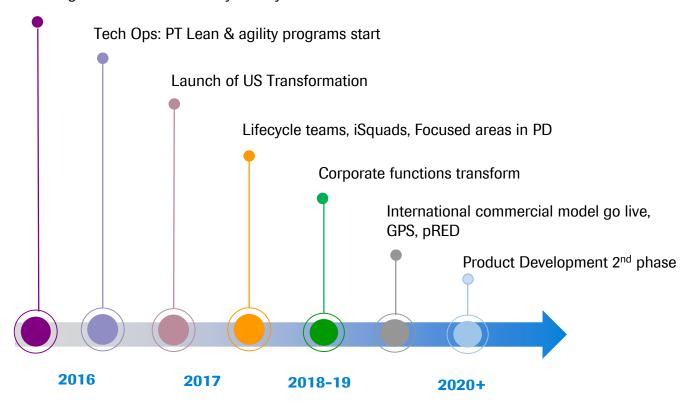


<sup>&</sup>lt;sup>1</sup> Venclexta sales are booked by partner AbbVie; <sup>2</sup> RG6171 (GDC-9545); <sup>3</sup> RG6114 (GDC-0077)



# Transformation is a key enabler of our Pharma Vision Guiding principles & decentralized execution for maximum impact

Executive Committee focus on agile: start of major changes to increase flexibility and dynamism



## **Guiding principles:**

- From silos, functional and top down focus to small empowered accountable teams
- From internal/organization chart orientation to patient and external focus
- From leadership as command & control to setting a vision, architecting the system, coaching, and catalyzing change



# In focus: The VITAL model Dynamic resource allocation

Vision: Align work to our vision and purpose

**Improve Performance:** Lower costs for same output

Talent Flow: Move talents to highest priority work

Accountable to Peers: Share learnings to enhance decision making

Lucid to All: Transparency on results, accountable for continuous improvement

# Increasing our productivity and financial flexibility



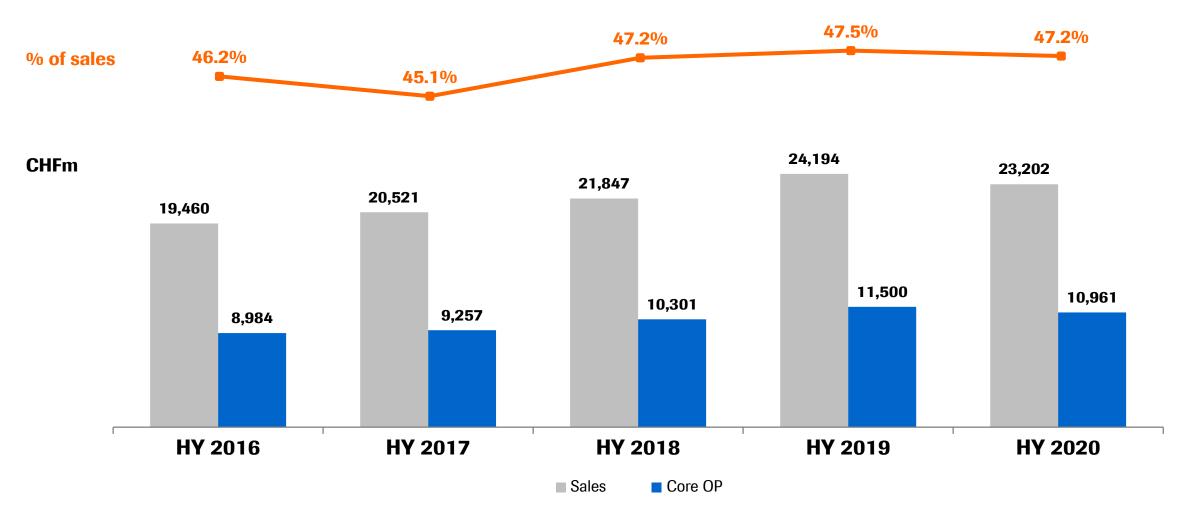
Pharma Technical (HY20 vs. HY16)	Pharma US (HY20 vs. HY16)	Pharma International (HY20 vs. HY16)	Pharma China (HY20 vs. HY16)	Pharma Development (HY20 vs. HY16)
Sales Volume growth +55%	Sales growth +34%	Sales growth +14%	Sales growth +110%	Late stage portfolio* +26%
Direct spend +1% and headcount -19%	OPEX +5% and headcount -19%	OPEX +10% and headcount -3%	OPEX +8% and headcount +25%	PD spend +23% and headcount +14%

Maturity of transformation efforts

<sup>\*</sup> Project count growth







## **Our Pharma Vision 2030**



# Providing more patient benefit at less cost to society

**More patient benefit** 

1



Doubling of medical advances<sup>1</sup>

- Re-allocation of resources into R&D, while working on and protecting profitability
- R&D Mission Support

2



Significantly progress other patient benefits

- Integrated solutions and new engagement models
- Improved outcomes via enhanced disease management

Less cost to society

3



I.e.: Earlier, more targeted, efficacious & shorter interventions

- Breakthrough science and insights to reduce cost of disease
- Reducing societal costs beyond the cost of therapy

Transformation as a key enabler

2030

<sup>&</sup>lt;sup>1</sup> First approval of a new molecule in a new indication

## **Our Pharma Vision 2030**



# Providing more patient benefit at less cost to society

## **More patient benefit**





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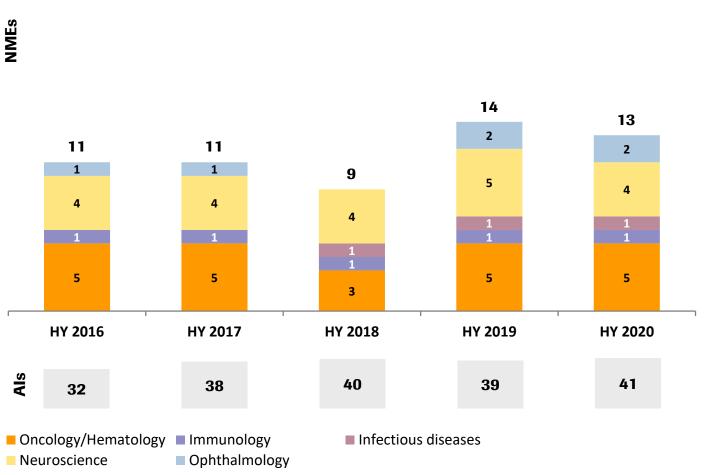
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Transformation as a key enable

<sup>&</sup>lt;sup>1</sup> First approval of a new molecule in a new indication



# Invest in innovation: Assets in Ph III & registration Strong momentum in the second half 2020





Outlook

+10 NMEs to be added until year end

**Gavreto** in RET+ NSCLC & thyroid cancer

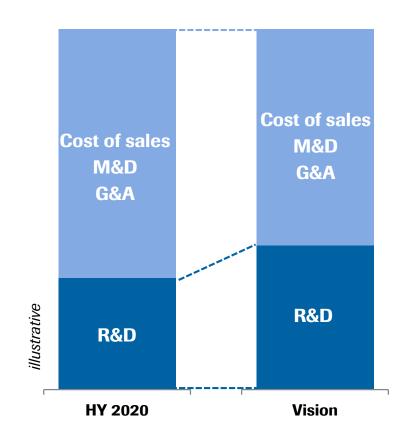
SERD Ph III in 1L HR+ mBC glofitamab Ph III in r/r DLBCL mosunetuzumab Ph III in r/r FL crovalimab Ph III in PNH **REGN-COV2** Ph III in COVID-19 (run by Regeneron)

rhPentraxin-2 Ph III in IPF
Gazyva Ph III in Lupus nephritis
fenebrutinib Ph III in RMS & PPMS
SRP-9001 Ph III in DMD (run by
Sarepta)

# **Strategic re-allocation of resources**



#### Pharma cost structure



## **Principles for resource allocation**

- Re-allocate resources into R&D while working on and protecting profitability
- Optimizing costs and efforts by
  - More targeted and often virtual stakeholder engagement
  - Personalized, digital content & services
- Improve performance by dynamic resource allocation (VITAL model)

# Recent deals and partnerships<sup>1</sup>



# Accelerate drug discovery and driving personalized healthcare

**Early stage assets** 

(HBV) (tominersen)2 **Jecure** 

(NLRP3 inhibitors)



(T-cell therapies)

Dicerna



Late stage assets





**Research technologies** 









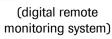
(E3 ligases)



**Digital & PHC** 









78 new agreements in 2019 focused on

**High disease burden / Promising targets / Novel enabling techologies** 

<sup>1</sup> Non-exhaustive overview; <sup>2</sup> at the time of licensing 19

## **Our Pharma Vision 2030**



# Providing more patient benefit at less cost to society

**More patient benefit** 

1)



Doubling of medical advances

- Re-allocation of resources into R&D, while working on and protecting profitability
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Transformation as a key enable

<sup>1</sup> First approval of a new molecule in a new indication

20



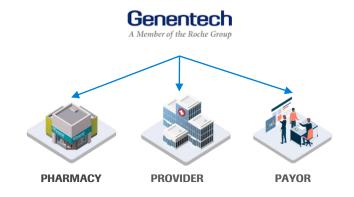
# **Go-to-market Model** *Strategic shifts until 2030*

	From	То		
Engagement	"Mass field" largely in-person	More targeted and often virtual		
Content	Static information	Personalized, digital content and services		
Content release	Synchronized with field force cycles	Continuous and real-time		
Customer targeting	Decided by sales representatives	Supported by advanced analytics		
Conference	Physical attendance	Virtual and real-time exchange		

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# Evolving customer engagement models: US Early progress in "Pioneer" go-first areas

Old structure New structure







- Empower local decision making
- Providing integrated solutions

First large pharmaceutical company in US market to develop Eco-system approach

# Delivering Integrated Solutions Using data & insights to improve patient outcomes



## **Capturing clinical outcomes**

 Leveraging RWD for regulatory filings, publications, policy change, innovative access models



# Access to comprehensive genomic profiling (CGP)

- early, personalized diagnosis

# Molecular tumor board (MTB) / clinical decision support (CDS)

personalized care plan

# Access to molecularly guided treatment options

rapid therapy access and innovative access models

More patients on optimal therapy and creation of 'learning healthcare system'

PHC=personalized healthcare; RWD=real world data

## **Our Pharma Vision 2030**



# Providing more patient benefit at less cost to society

Doubling of medical advances¹

Re-allocation of resources into R&D, while working on and protecting profitability

R&D Mission Support

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Transformation as a key enable



# Responsible pricing strategy: Impact of medicines is at the core, while considering WHO's fair pricing dimensions

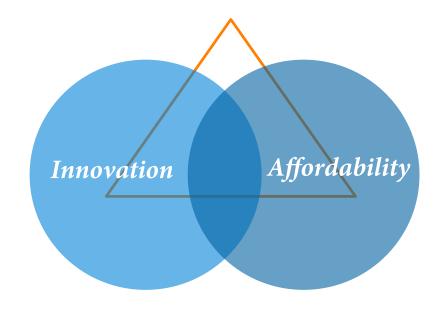
#### **HEALTH IMPACT**

Positive **impact** of medicine for **patients**, **healthcare systems** and **society**.

#### **FUTURE INNOVATION**

Pricing strategy allows to **invest** into **high risk** and complex disease areas.

Meeting the needs of patients of tomorrow.



Innovation available for patients today and tomorrow

#### **SYSTEM CONTEXT**

Pricing reflects different **healthcare** systems & regulatory environments.

Make medicines as affordable as possible.

# Responsible and innovative pricing solutions



## **Recent examples of responsible pricing**



~25%

discount<sup>3</sup> to Rebif list price in the US





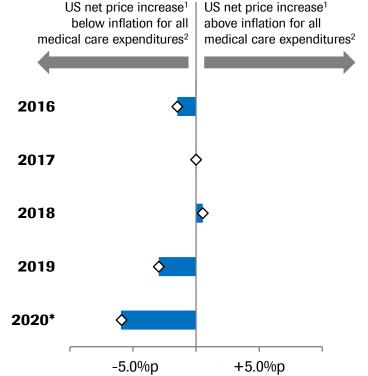
discount<sup>3</sup> to BPA prophylaxis in the US



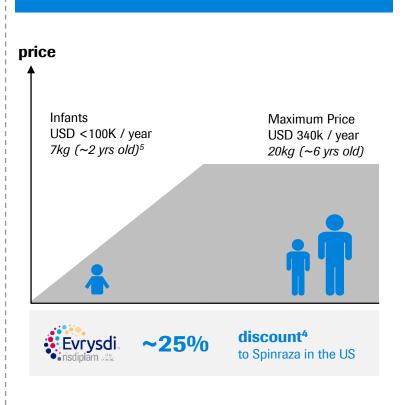


discount<sup>3</sup> to Vitrakvi list price in the US

## **Net price increases in line with medical** inflation in the US US net price increase1 US net price increase<sup>1</sup>



## **Price ceiling for Evrysdi**



<sup>1</sup> Genentech's annual average net price increase in the U.S., weighted by sales; 2 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); 3 discount at launch; 4 discount over 5-yrs (at max Evrysdi price); 5 average infant weight from the FIREFISH trial: \* TTM for CPI-U Medical Care in 2020

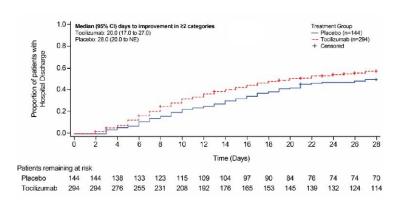
# Roche

# **Costs to society**

# Reducing societal costs of disease beyond the cost of therapy

# Actemra in COVID-19: Positive trend in time to hospital discharge

# Time to hospital discharge/ready for discharge to day 28<sup>‡</sup>

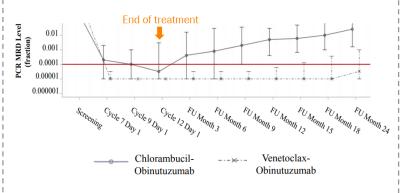


Median Time to Response: TCZ=20.0 [17.0 to 27.0]; PBO=28.0 [20.0 to NE]

Potential for freeing up hospital capacity if confirmed in additional studies

# Venclexta + Gazyva in CLL: Potential for shorter/curative treatment

#### Ph III (CLL14) results\*

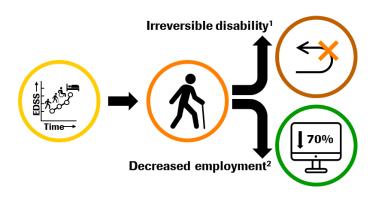


90% of MRD-negative patients remained in remission 2 years after treatment

Fixed treatment duration avoids long term side effects of chronic therapy & generates savings to HC system

# Ocrevus in MS: Delaying the need for walking aid

### **Disability progression in patients with RMS**



Consequences of reaching EDSS score ≥6.0 walking aid required

**Expanding the time patients can live independently & continue working** 

<sup>&</sup>lt;sup>‡</sup> Rosas, et al., 2020, doi: https://doi.org/10.1101/2020.08.27.20183442; \* Fischer, et al., ASH 2019; <sup>1</sup> Tomassini V, et al., MSJ 2019;25:1306–1315; <sup>2</sup> Kobelt G, et al., MSJ 2017;23:1123–1136; ICU=intensive care unit; CLL=Chronic lymphoid leukemia; MRD=minimal residual disease; HC=healthcare; RMS=relapsing multiple sclerosis; EDSS=Expanded Disability Status Scale; Venclexta in collaboration with AbbVie



# Strong short- and mid-term news flow Diversifying the late stage pipeline and setting new standards of care

Product	Indication	Filing	Population	Product	Indication	Filing	Population
tominersen	Huntington's	latest 2022	~83k	Courata	RET+ NSCLC	filed	~2k (Dx+)
gantenerumab	Alzheimer's	2022	~9,300k (prodromal)	Gavreto	thyroid cancer	filed	~6k (Dx+)
			~3,600k (mild)		NeoAdj TNBC	2020	~23k
SRP-9001	DMD	latest 2023	~21k		Adj SCCHN	2021	~8k
etrolizumab	Crohn's	2022	~570k (moderate/severe) Tecentriq	Tecentriq	Adj RCC	2021	~20k
					(Neo)Adj NSCLC	2021/22	~100k
PDS	nAMD DME	2020	nAMD ~3,600k DME ~4,700k		Adj HCC	2022	tbd
		2022		Tecentriq + P+H	NeoAdj HER2+ BC	2021	~40k
faricimab	DME nAMD	2021		inotoportih	1L/2L TNBC	2020	~11k (Dx+)
Actemra +				ipatasertib	1L mCRPC	2020	~100 (Dx+)
remdesivir	COVID-19	2021	n/a	Polivy	1L DLBCL	2021	~51k
REGN-COV2	COVID-19	2021	n/a	tiragolumab + T	1L SCLC	2022	~57k
crovalimab	PNH	2022	~14k	mosunetuzumab	R/R FL	2021	~3k
				glofitamab	R/R DLBCL	2022	~24k
Neuroscience Ophthalmology Infectious diseases			Venclexta	R/R MM t(11;14)	2022	<b>~6k</b> (Dx+)	
Immunology Oncology/Hematology				SERD (RG6171)	2L/3L mBC	2022	~74k



# Replace and extend the business: Improve on the standard of care *Most significant pipeline advances in a year ever*

# Replace/extend existing businesses

Gazyva, Venclexta. MabThera/Rituxan Polivy. mosunetuzumab. alofitamab Perieta. Kadcyla, Herceptin Phesgo Tecentria. Alecensa. Avastin Rozlytrek, tiragolumab Port delivery system (PDS) Lucentis faricimab Tamiflu Xofluza

# **Entering new franchises**

# Oncology: Tecentriq (mUC, TNBC, SCLC, HCC, mM).

SCLC, HCC, mM), ipatasertib (mCRPC), SERD (HR+ BC)

## Hemophilia A:

Hemlibra

#### **Neuroscience:**

Ocrevus (RMS, PPMS)
Enspryng (NMOSD),
Evrysdi (SMA),
tominersen (Huntington),
gantenerumab (AD),
SRP-9001 (DMD)

### Immunology:

etrolizumab (CD), Gazyva (Lupus nephritis)

## Infectious diseases:

REGN-COV2 (COVID-19)

## **New pivotal trial starts in 2020**

PDS	Neuroscience	Diabetic retinopathy without CI-DME (PAVILION)  ■ Immunology ■ Ophthalmology		
 	higher dose	RMS (MUSETTE), PPMS (GAVOTTE)		
fenebrut	_	RMS (FENhance 1/2), PPMS (FENtrepid)		
SRP-900	_	Duchenne muscular dystrophy		
 rhPentra	axin-2	Idiopathic pulmonary fibrosis		
Gazyva		Lupus nephritis (REGENCY)		
REGN-C	0V2	COVID-19 treatment/prophylaxis		
crovalim	nab	PNH (COMMODORE 1/2)		
Venclex	ta	1L fit AML, 1L fit CLL		
mosune	tuzumab	2L+ FL		
glofitam	ab	2L+ DLBCL		
SERD (R	RG6171)	1L HR+ mBC, 2/3L mBC		
Pl3Kai (	RG6114)	HR+ mBC (INAVO120)		
tiragolur	mab	ES-SCLC (SKYSCRAPER-01) stage III unresectable NSCLC (SKYSCRAPER-03) locally adv. esophageal cancer (SKYSCRAPER-07/08)		
		mNSCLC (SKYSCRAPER-01)		

Infectious diseases

Oncology/Hematology

mUC=metastatic urothelial carcinoma; TNBC=triple negative breast cancer; RCC=small cell lung cancer; HCC=hepatocellular carcinoma; mM=metastatic melanoma; mCRPC=metastatic castration resistant prostate cancer; BC=breast cancer; 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; NSCLC=non-small cell lung cancer; ES-SCLC=extensive-stage small cell lung cancer; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; AML=acute myeloid leukemia, CLL=chronic lymphocytic leukemia; MDS=myelodysplastic syndromes; PNH=paroxysmal nocturnal hemoglobinuria; Cl-DME=center-involved diabetic macular edema

# Late stage pipeline update



#### 1. Hematology franchise

- DLBCL: Polivy, glofitamab, mosunetuzumab
- FL: mosunetuzumab, glofitamab, Polivy
- · AML: Venclexta
- MM: Venclexta
- · MDS: Venclexta

#### 2. Breast Cancer franchise

- TNBC: Tecentriq, ipatasertib
- HR+: SERD (RG6171), Pl3Kai (RG6114)
- HER2+: Tecentriq

#### 3. Lung Cancer franchise

- NSCLC: Tecentriq, tiragolumab
- SCLC: Tecentriq, tiragolumab
- ALK+: Alecensa
- ROS1+/NTRK+: Rozlytrek
- RET+: Gavreto
- KRAS G12C+: GDC-6063

#### 4. Other oncology

- · CRPC: ipatasertib
- · Thyroid cancer: Gavreto
- · Esophageal cancer: tiragolumab
- · Melanoma: Tecentriq, Cotellic, Zelboraf

#### 7. Immunology

- IPF: rhPentraxin-2, Esbriet
  - Myelofibrosis: rhPentraxin-2
  - Lupus nephritis: Gazyva
  - · Crohn's disease: etrolizumab

### 5. Non-malignant hematology

- Hemophilia A: Hemlibra
  - Hemophilia A: Factor VIII Gene Therapy
  - PNH: crovalimab

## 8. Ophthalmology

- nAMD, DME, DR: Port Delivery System
- nAMD, DME, RVO: faricimab

#### 6. Neuroscience

5

- MS: Ocrevus; fenebrutinib
- SMA: Evrysdi
- NMOSD: Enspryng
- AD: gantenerumab, anti-Tau, brain shuttle
- Huntington's disease: tominersen
- DMD: Micro-dystrophin Gene Therapy
- Parkinson's disease: prasinezumab

#### 9. Infectious diseases

- HBV: TLR7 agonist, CpAM, RG6346, RG6084
- Influenza A/B: Xofluza
- SARS-CoV2: Actemra
- SARS-CoV2: REGN-COV2

Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

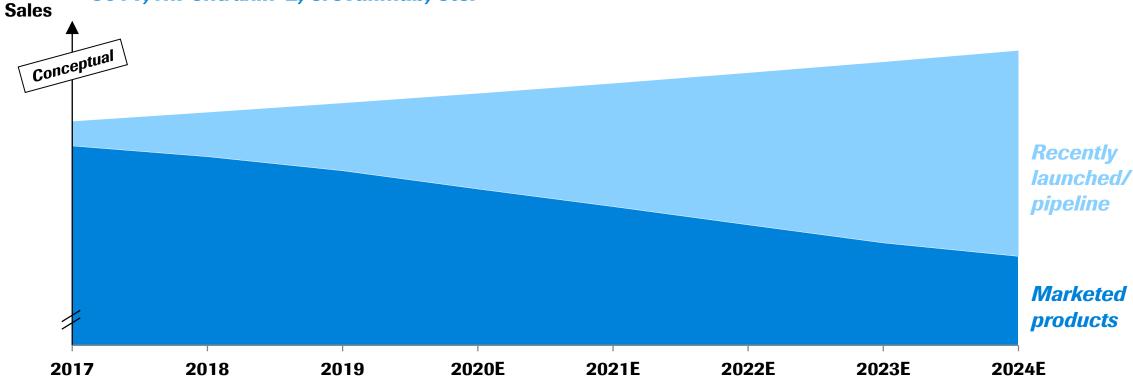
<sup>\*</sup> For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage





## **NME** launches

Ocrevus, Perjeta, Hemlibra, Tecentriq, Venclexta, Gazyva, Alecensa, Xofluza, Polivy, Rozlytrek, Phesgo, Evrysdi, Enspryng, Gavreto, mosunetuzumab, glofitamab, ipatasertib, Pl3Kai, SERD, tiragolumab, faricimab, PDS, tominersen, gantenerumab, prasinezumab, SRP-9001, SPK-8011, rhPentraxin-2, crovalimab, etc.





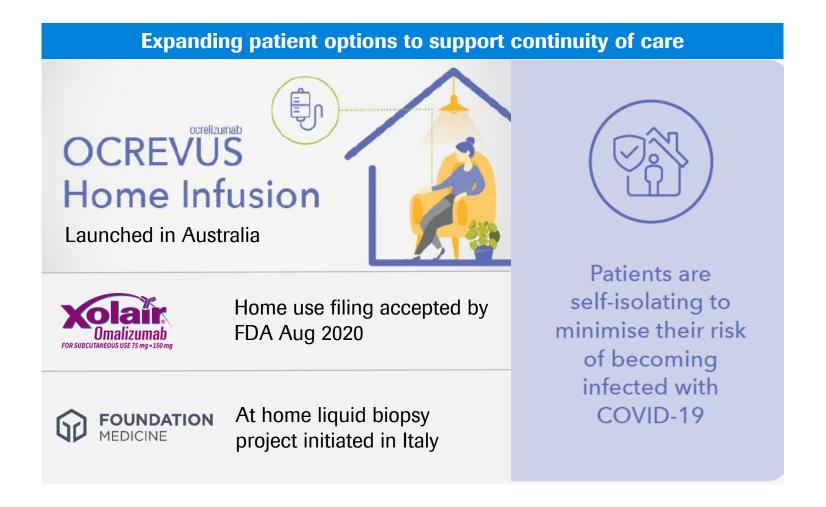
# **Roche Pharma Day 2020**

# Commercial Opportunities

**Teresa Graham** | Head of Global Product Strategy

# **Supporting patient access during COVID-19**





# **Oncology & non-malignant hematology**



#### 1. Hematology franchise

- DLBCL: Polivy, glofitamab, mosunetuzumab
- FL: mosunetuzumab, glofitamab, Polivy
- · AML: Venclexta
- MM: Venclexta
- · MDS: Venclexta

#### 2. Breast Cancer franchise

- TNBC: Tecentriq, ipatasertib
- HR+: SERD (RG6171), Pl3Kai (RG6114)
- HER2+: Tecentriq

#### 3. Lung Cancer franchise

- NSCLC: Tecentriq, tiragolumab
- SCLC: Tecentriq, tiragolumab
- ALK+: Alecensa
- ROS1+/NTRK+: Rozlytrek
- RET+: Gavreto
- KRAS G12C+: GDC-6063

#### 4. Other oncology

- · CRPC: ipatasertib
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  - · Crohn's disease: etrolizumab

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- Hemophilia A: Hemlibra
  - Hemophilia A: Factor VIII Gene Therapy
  - PNH: crovalimab

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- nAMD, DME, DR: Port Delivery System
- nAMD, DME, RVO: faricimab

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- · AD: gantenerumab, anti-Tau, brain shuttle
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- DMD: Micro-dystrophin Gene Therapy
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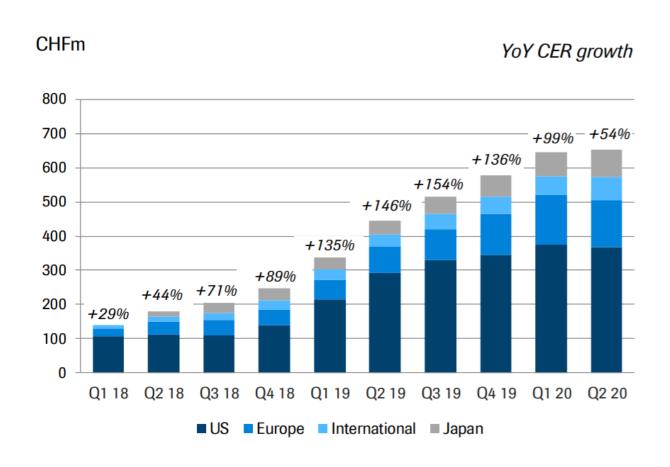
Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
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# **Tecentriq**



# Annualized sales >2b with significant growth opportunities ahead



#### 1L combinations

1L SCLC, 1L TNBC, and 1L NSCLC continuing to drive growth ex-US; Launch of HCC next major growth driver with contributions from 1L mUC and BRAF+ Melanoma

## Neoadjuvant / adjuvant

Continued readouts in early disease: TNBC, NSCLC, SCCHN, RCC, HCC, HER2+ BC

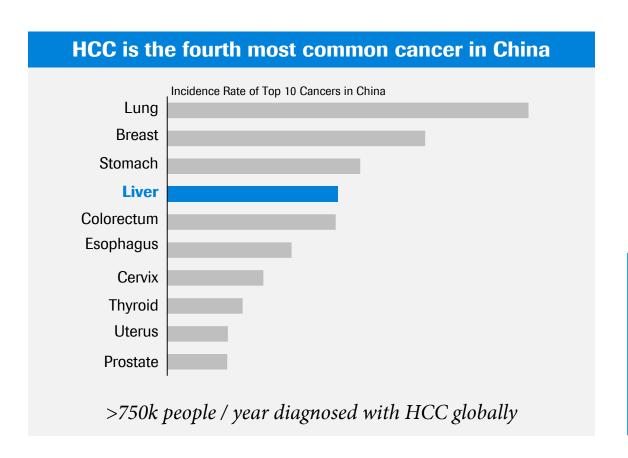
#### **CIT** combinations

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

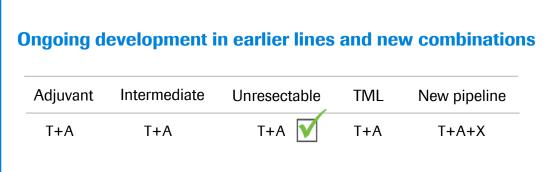


# Tecentriq + Avastin: A new standard in HCC treatment First new therapy with survival benefit in HCC in over a decade









T+A as a new SOC in HCC

# **Tecentriq in early disease**



# Curative potential for the largest number of patients



Breast <u>(</u>	<ul> <li>✓ Positive data in neoadjuvant TNBC will be shared with health authorities</li> <li>• &gt;50% of TNBC pts treated in neoadjuvant setting</li> <li>• Ongoing trials for Tecentriq in adjuvant TNBC and neoadjuvant HER2+ BC</li> </ul>
Lung	Interim Ph III results for neoadjuvant and adjuvant NSCLC expected 2020/2021  • 25-35% of NSCLC patients have resectable disease
GI/GU	Trials initiated in NMIBC, adjuvant RCC, and adjuvant HCC  • >2.5x more patients with early UC than metastatic UC



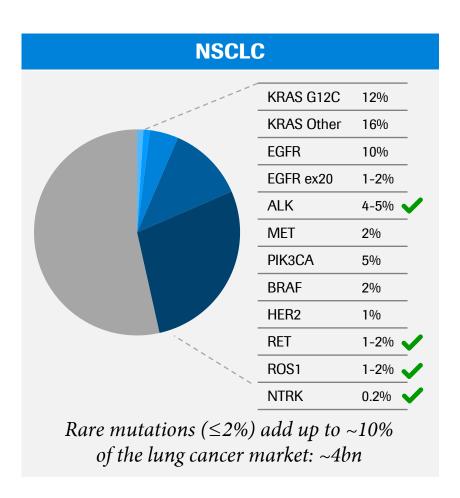
# Tiragolumab (anti-TIGIT) development program First program with randomized data showing benefit on top of PD-L1

	Trial	Indication	Market size
	SKYSCRAPER-01	1L NSCLC: PD-L1 high	•00
	SKYSCRAPER-02	ES-SCLC	•••
<b>→</b>	SKYSCRAPER-03	Stage III unresectable NSCLC	•••
	SKYSCRAPER-04	PD-L1+ Cervical Cancer	•00
<b>&gt;</b>	SKYSCRAPER-07	Locally advanced ESCC	•••
<b>&gt;</b>	SKYSCRAPER-08	China 1L ESCC	•00
	Market Size: <	500m Market Size: 500m-1b	Market Size: >1b



## Solid business case for oncogenic driver mutations









**NAVIFY**®

## High ORR and durable benefit drives long duration of therapy

Alecensa PFS ~35m in 1L NSCLC vs. ~8m for PD-1/PD-L1; opportunity in early disease

## NGS testing rate increasing with new technologies and therapeutics

• FMI liquid biopsy approved (30% of NSCLC patients with insufficient tissue for testing)

### **Lean and innovative trial design supported by Real World Data**

- Comparative RWD for Rozlytrek submitted in US, Europe, Japan, and Canada
- B-FAST study with multiple driver mutation cohorts

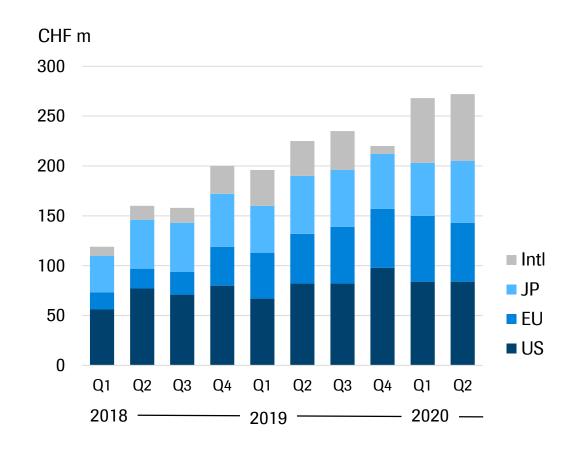
### Pan-tumor potential across multiple programs

TAPISTRY: tumor agnostic basket trial across multiple driver mutations and CIT



# Alecensa annualized sales > 1b with further growth catalysts Market leader with > 70% market share in US, EU, Japan





## **China driving further growth in international markets**

• Significant volume uptake in 2020, following NRDL reimbursement

### **Expanding into early disease**

 ALINA trial in ALK+ adjuvant NSCLC has potential to address 25-35% of ALK+ NSCLC patients

## **Expanding testing to more patients**

 B-FAST trial: Alecensa data in ALK+ patients tested by FMI liquid biopsy presented at ESMO

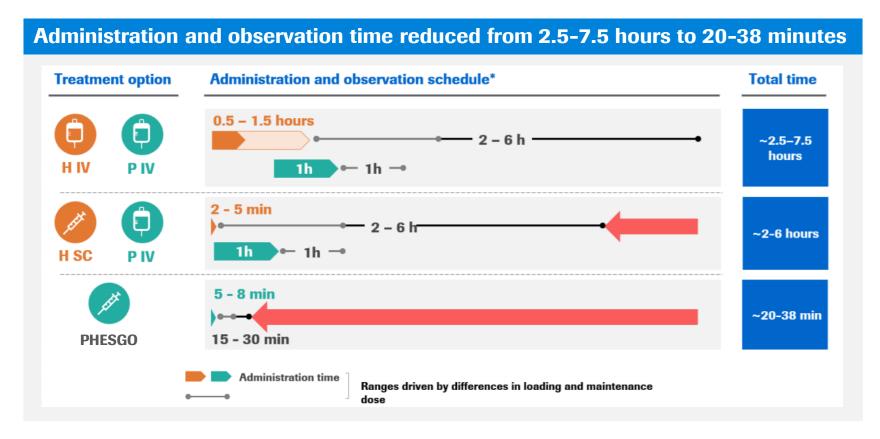
### **Tumor agnostic development**

 Alecensa arm added to TAPISTRY basket trial: ALK fusion prevalence <1% (excluding NSCLC)</li>

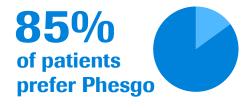
## Phesgo US approval



# Approved by FDA in June, filed in EU



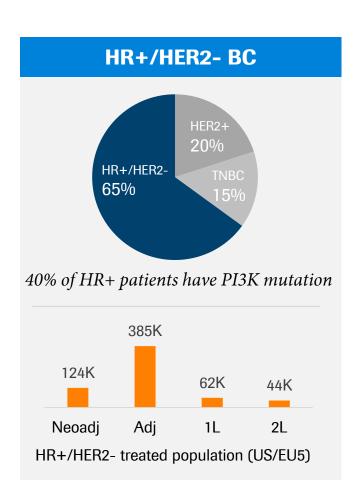


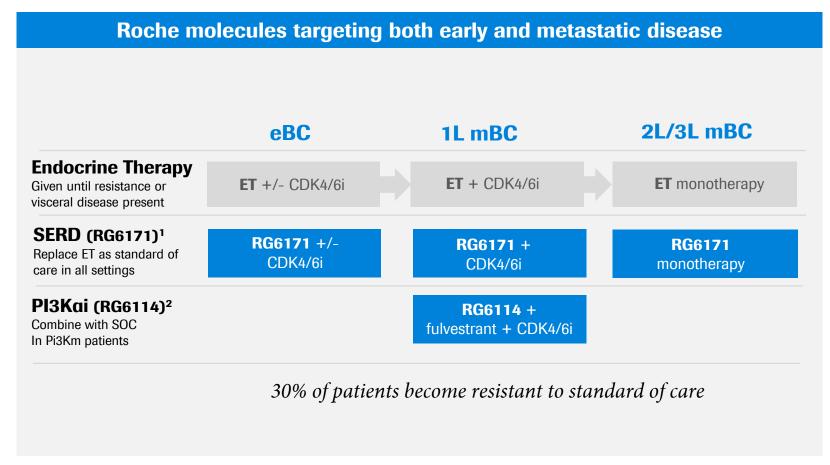


vs. standard IV administration



# High unmet need remains across HR+/HER2- BC Large addressable population for SERD and PI3K programs





## Polivy readout in 1L DLBCL in 2021

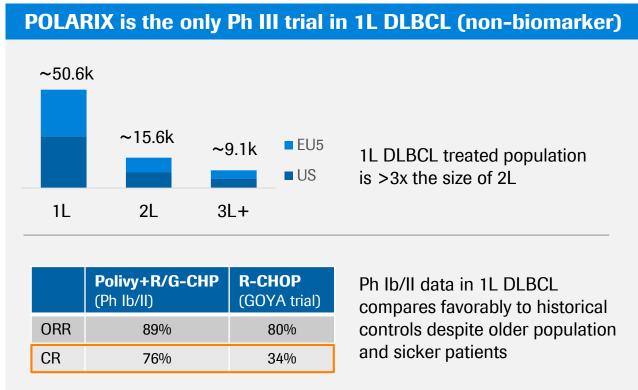


# Opportunity to establish Polivy as standard of care in curative setting



## Rapid uptake in R/R DLBCL

- Strong efficacy: only agent in R/R DLBCL with OS benefit
- Well tolerated: combines with standard of care (BR); no unique safety monitoring requirements
- Off the shelf: readily available; administered in any oncology facility, with no hospitalization required





# Mosunetuzumab and glofitamab (CD20xCD3) Potential first in class bispecifics in DLBCL and FL

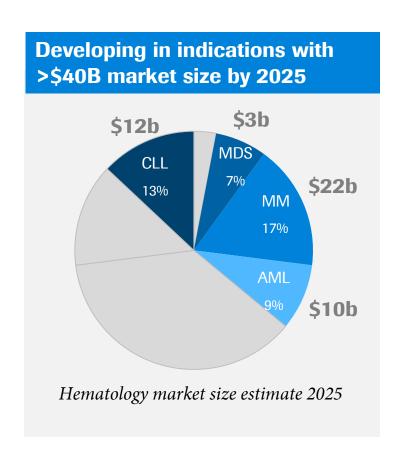
Indication	Unmet Need	Lead Program		
R/R FL	Reduction of chemo and quality of life are important for patients	Mosunetuzumab  BTD in 3L+ FL; Ph III safety run-in initiated in 2L+ FL		
R/R DLBCL	Highly aggressive disease: patient need for durable efficacy	Glofitamab Glofitamab Ph III safety run-in initiated in combination with GemOx		
1L DLBCL	High efficacy bar established; need therapy which is combinable	Chemo free regimens being explored in Ph Ib for both glofitamab and mosunetuzumab including combinations with Polivy, Gazyva, Tecentriq		

Furthest advanced bispecific portfolio with >1000 patients dosed and randomized trials being initiated

## Venclexta



# Annualized sales >1bn driven by CLL and AML





## **✓**1L CLL

Fixed duration, chemo free regimen, with high MRD-negative responses

## **✓** 1L AML

First new medicine in AML in 20 years; >40% US market share in 1L unfit patients

### **Multiple Myeloma**

Ph III CANOVA trial underway in ~20% of patients with t11:14 translocation

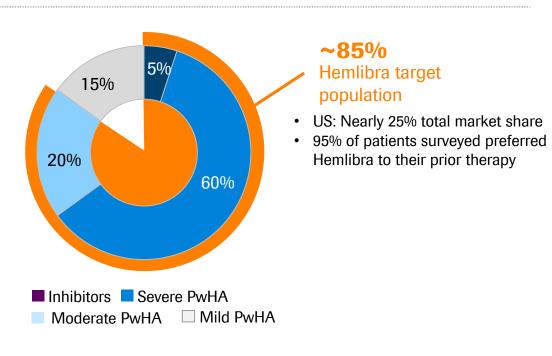
#### **MDS**

Encouraging early data in high unmet need population

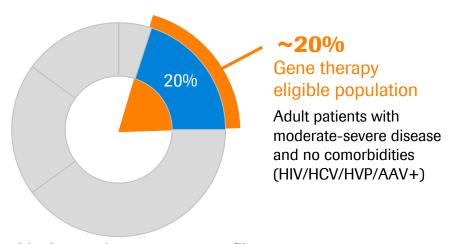


# Hemlibra is a transformational advance for Hemophilia A patients Continued increase in patients with zero bleeds to >85% after 72 weeks





## Gene therapy



#### Ideal gene therapy target profile

- · Works in all eligible patients
- Reliable and predictable expression of FVIII across all patients
- Long-term durability
- Manageable immune-modulatory regimen

# **Ophthalmology**



#### 1. Hematology franchise

- · DLBCL: Polivy, glofitamab, mosunetuzumab
- · FL: mosunetuzumab, glofitamab, Polivy
- · AML: Venclexta
- MM: Venclexta
- MDS: Venclexta

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- HR+: SERD (RG6171), Pl3Kai (RG6114)
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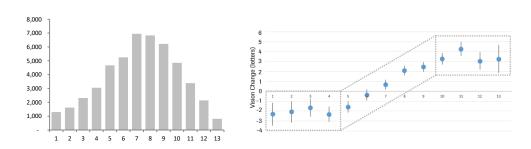


# Roche

# **Port Delivery System (PDS)**

# Potential to improve real world outcomes with twice yearly dosing

# 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

# 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. Patients from Ph I study have had PDS implanted for >10 years.



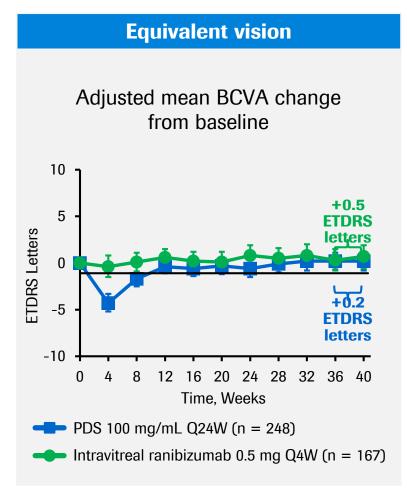
 Refill exchange: twice yearly in-office refill of the device using proprietary needle assembly. Can only be refilled with proprietary formulation (not other molecules or biosimilars)

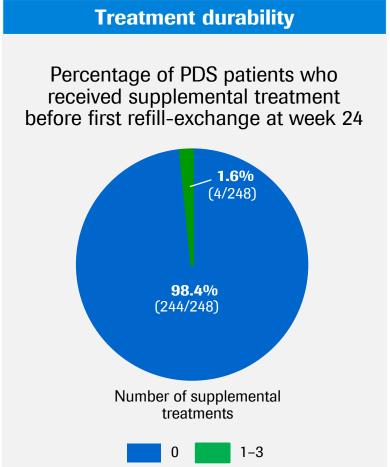
PDS, Port Delivery System with ranibizumab; IVT = intravitreal

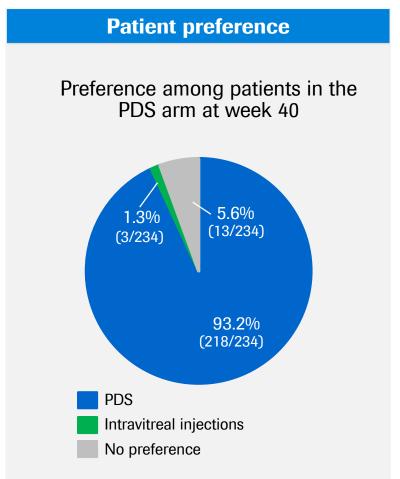
48



# PDS efficacy equivalent to monthly Lucentis for nearly all patients Strong patient preference for PDS







# Preparing for a purposeful global launch in nAMD US launch planned for 2021, ex-US for 2022



## Virtual reality training





- 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

## Field-based support



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

## Remote vision monitoring





- App-based designed test to detect changes in vision in-between office visits
- Vision alerts sent to doctor
- Pilot programs underway

Global retina market growing to ~\$14b by 2024

nAMD = neovascular age related macular degeneration 50

## **Neuroscience and Rare Diseases**



#### 1. Hematology franchise

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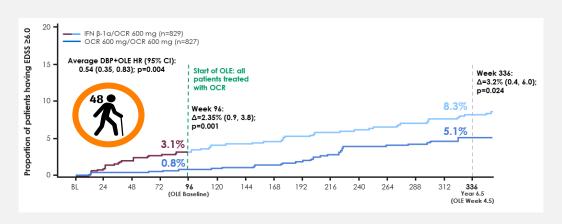




# Ocrevus: Best in disease efficacy with robust, consistent, and sustained delay in disability progression

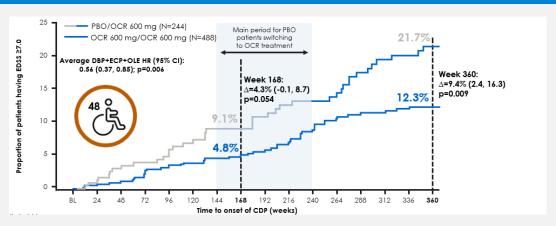


## **Sustained effect on disease progression >6 yrs in RMS**



• 46% lower risk of requiring a walking-aid in those patients who initiated OCR earlier vs delayed treatment (those switching from IFN  $\beta$ -1a)

## Ocrevus is the only therapy approved in PPMS



- 44% lower risk of requiring a wheelchair in those patients who initiated OCR earlier vs delayed treatment (those switching from PBO)
- ~35% of US sales in PPMS

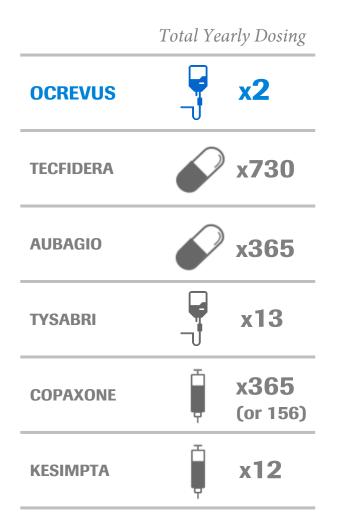
## >170K patients treated with consistent and favorable benefit risk profile

## Ocrevus twice yearly dosing drives better compliance

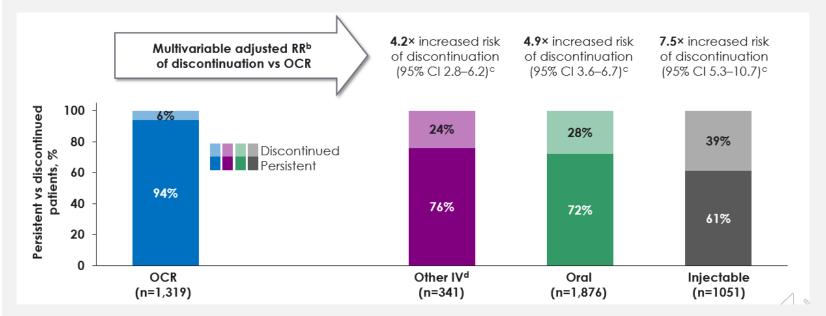




MS<sup>VIRTUAL</sup>



## >90% persistence/adherence after 1 yr; superior to oral and injectable medicines

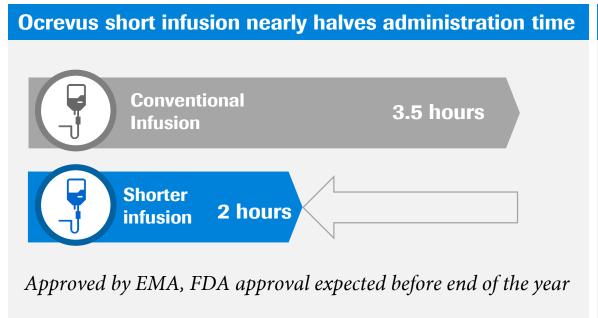


- Superior persistence and adherence and the lowest discontinuation rate at both 12 and 18 months of follow-up compared with patients initiating other classes of MS DMTs
- Persistence and adherence to treatment are critical for achieving therapeutic goals in MS



# Continuing to improve patient convenience with shorter infusion Favorable access with no price increases since launch





## Ocrevus pricing in US results in broad access



## \$65k per year

- Priced ~32% below US market average WAC of \$94k
- >80% RMS and 98% PPMS covered without step edits



## **Expansion in infusion options for patients**

- Ocrevus has been infused in >46K locations in the US
- ~50% of infusions occur outside of the hospital

# **Enspryng: First and only subcutaneous treatment for NMOSD**





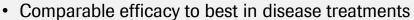
## Significant unmet need still exists with NMOSD



- 200K patients worldwide
- 70-80% of patients are AQP4+
- Half of patients are blind or require a wheelchair within 5 yrs
- 40% of patients with NMOSD are first misdiagnosed as having MS
- 50% of patients treated with steroids/immunosuppressants

**Approved in US, Canada, Japan, Switzerland** *Additional applications are under review including the EU and China* 





### Flexible and convenient

- Q4w SC dosing at home
- Studied as monotherapy and in combination with immunosuppressants

## **✓** Well tolerated safety profile

 No black box warning; lower rate of infections incl. serious infections than placebo group

## Competitively priced

 Priced 72% below eculizumab and 27% below inebilizumab after first year



## **Evrysdi**





# Proven efficacy in infants, children and adults with SMA



## **Best-in-class efficacy and safety potential**

Durably increases SMN protein in CNS and periphery
Out of 450+ patients studied, none withdrew from treatment due to treatment-related AEs



## **Broad population studied**

Newborn to 60 years old, Type 1/2/3, naïve and pre-treated Real world population that exhibits a broad range of disease severity & functional ability



## **Advantages of oral administration**

Oral liquid solution, administered at home Delivered directly to patient, with contactless delivery

56

<sup>\*</sup> Based on the average infant weight from the FIREFISH trial

# Evrysdi: Evidence being generated across all SMA patients



# Representative range of ages, type, prior treatment, disease severity

Presymptomatic Newborns	Symptomatic Infants	Younger Children	Older Children	Teenagers	Adults
RAINBOWFISH	FIREFISH	1	JEWELFISH	FISH	
≤ 5 years old			> 5 years old		
~15% prevalence*			~85% prevalence*		
Focus of I	many recent trial	s in SMA	Large prevalent population that remains underserved lacking treatment options and supporting evidence		
The majority of patients are not receiving disease modifying therapy					

\* Estimated 2020 prevalence in US and EU5

# Successful virtual launch of Evrysdi in the US SMA patients being treated across all segments





## Broad uptake across segments in first month of approval



**Patients treated with all SMA types** 

~25% of patients with Type I SMA



**Treatment naïve and switch patients** 

Have treated pts switching from both Spinraza / Zolgensma



**Broad range of ages** 

5m old infants to 70+ year old adults



Commercial and state Medicaid plans moving fast to

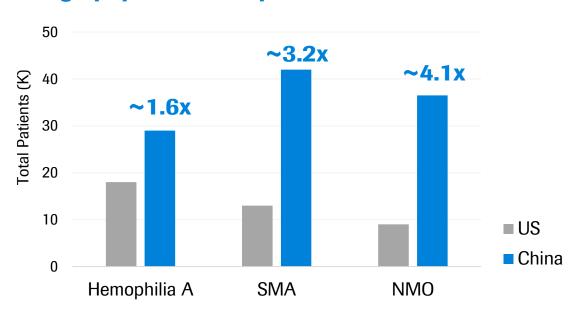
establish coverage policies

\* Based on the average infant weight from the FIREFISH trial

## Rare diseases present significant opportunity in China



## **Large populations of patients with rare diseases**



China Rare Disease List established to enable faster filing and approval timelines



- China was the #1 enrolling country in FIREFISH Part II trial
- Regulatory submission completed in China with approval expected H1 2021



- Enspryng China filing dossier accepted with priority review
- NMOSD included on China Rare Disease List

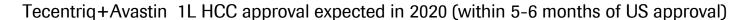


- NRDL negotiations for Inhibitor expected in 2020
- Regulatory submission completed for Non-Inhibitor label expansion with approval expected in H1 2021

Source: McKinsey Report 59

# Closing the approval gap in China Bringing innovative medicines to Chinese patients faster

## **Time from US approval to China approval** 2005 2010 2015 2020 2000 Herceptin<sup>®</sup> Prior to 2015: 48-198m HEMLIBRA 2015 to 2020: 9-12m ★ NRDL¹ listing





# NRDL negotiations expected in 2020 for Kadycla, Tecentriq, Hemlibra

3-5x volume growth seen with other Roche medicines within 2 years of addition to NRDL



# Strong short- and mid-term news flow Diversifying the late stage pipeline and setting new standards of care

Product	Indication	Filing	Market potential	Product	Indication	Filing	Market potential
tominersen	Huntington's	latest 2022	•••	Gavreto	RET+ NSCLC	filed	•••
gantenerumab	Alzheimer's	2022	•••	Gavreto	thyroid cancer	filed	000
SRP-9001	DMD	latest 2023	•••		NeoAdj TNBC	2020	000
etrolizumab	Crohn's	2022	000		Adj SCCHN	2021	000
				Tecentriq	Adj RCC	2021	000
PDS	nAMD DME	2020 2022			(Neo)Adj NSCLC	2021/22	000
	DME				Adj HCC	2022	000
faricimab	nAMD	2021	Tecentriq + P+H	NeoAdj HER2+ BC	2021	000	
Actemra +	000//10 10	2001		inotocortib	1L/2L TNBC	2020	000
remdesivir	COVID-19	2021		ipatasertib	1L mCRPC	2020	000
REGN-COV2	COVID-19	2021	000	Polivy	1L DLBCL	2021	000
crovalimab	PNH	2022	000	tiragolumab + T	1L SCLC	2022	000
				mosunetuzumab	R/R FL	2021	000
Neuroscience	Ophthalmology	000	Small: up to CHF 0.5 bn	glofitamab	R/R DLBCL	2022	000
Immunology	Oncology/Hematol		medium= CHF 0.5 to CHF 1bn	Venclexta	R/R MM t(11;14)	2022	•••
Infectious diseases		•••	large > CHF1bn	SERD (RG6171)	2L/3L mBC	2022	000

Source: Roche/Genentech, incidence/prevalence in the major markets (US, FR, DE, IT, ES, GB); DMD=duchenne muscular dystrophy; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; NSCLC=non-small cell lung cancer; TNBC=triple-negative breast cancer; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma; mCRPC=metastatic castration resistant prostate cancer; DLBCL=diffuse large B-cell lymphoma; SCLC=small cell lung cancer; FL=follicular lymphoma; PNH=paroxysmal nocturnal hemoglobinuria



# short break



## **Roche Late Stage Pipeline Event 2020**

Late Stage Pipeline Oncology & Non-malignant Hematology

Levi Garraway, M.D., Ph.D. | Executive Vice President, Head of Global Product Development and Chief Medical Officer

## Late stage pipeline update



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#### Infectious diseases

- HBV: TLR7 agonist, CpAM, RG6346, RG6084
- Influenza A/B: Xofluza
- SARS-CoV2: Actemra
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Oncology / Hematology Neuroscience Ophthalmology Infectious diseases **Immunology** 

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## Late stage pipeline update



#### 1. Hematology franchise

- DLBCL: Polivy, glofitamab, mosunetuzumab
- FL: mosunetuzumab, glofitamab, Polivy
- · AML: Venclexta
- MM: Venclexta
- · MDS: Venclexta

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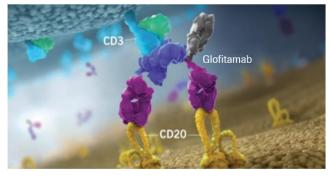
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# **Hematology: Glofitamab in NHL** Potential for early filing in R/R DLBCL



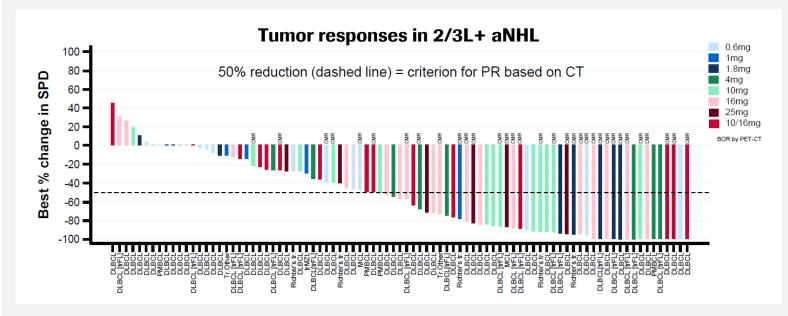
# CD20 x CD3 program



Combination	Indication	Ph1 Ph2 Ph3
glofi+GemOx	2L+ DLBCL	
glofi	R/R DLBCL/FL	
glofi+G/R+CHOP	1L DLBCL	
glofi+T	R/R DLBCL/FL	
glofi+G	R/R FL	
glofi+P	R/R DLBCL	

- ~1000 Patients have been treated in the CD20xCD3 program (glofit and mosun)
- Initial registration potential for glofitamab in R/R DLBCL and for mosunetuzumab in R/R FL

## Ph I (NP30179) dosing in R/R aNHL\*



- The ≥10mg cohorts in R/R aNHL showed an ORR of 49.4% and a CR rate of 34.1%; CRs appeared durable with the mDOR not reached after a median follow up of 10.2m
- Good safety profile with manageable CRS confined to cycle 1
- Combination development with R-CHOP and Polivy in DLBCL on-going
- Ph III safety run-in for glofitamab + GemOx in 2L+ DLBCL initiated

66

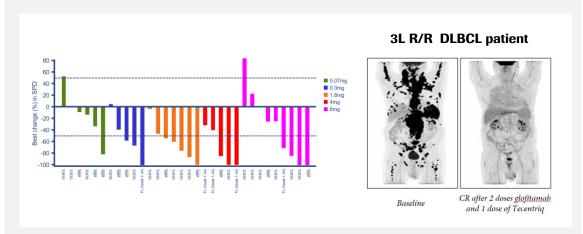
# **Hematology: Exploring feasible combinations**





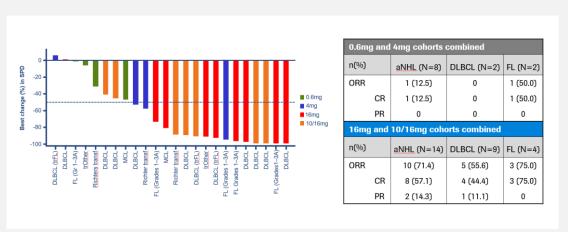


## Ph I results of glofitamab + Tecentriq in R/R NHL



- T-cell activation observed consistent with the hypothesized MOA of the combination
- Trend towards increased response rate was observed starting at glofitamab doses ≥1.8mg
- Manageable safety in R/R NHL

## Ph I results of glofitamab + Gazyva in R/R NHL



- Highly promising activity in heavily pre-treated patients
- ORR and CR rates by investigator assessment were 54% (15/28 pts) and 46% (13/28); CR appear durable
- Safety profile consistent with known safety profiles of the individual drugs

Further development work needed to identify most promising paths forward for chemo-free combinations

# Hematology: Mosunetuzumab in NHL

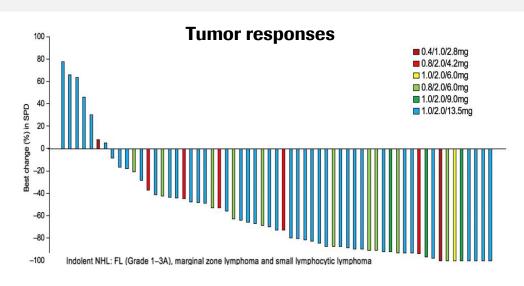






### CD20 x CD3 program Mosunetuzumab CD20 Combination Indication mosun+len R/R FL mosun+CHOP \* 1L DLBCL mosun+CHP+P 1L DLBCL R/R DLBCL/FL/MCL mosun 1L/2L (unfit) DLBCL mosun 3L+ DLBCL/FL/ mosun ibrutinib R/R MCL R/R DLBCL mosun+P R/R DLBCL/FL mosun+T mosun SC \* R/R DLBCL/FL \* Data submitted to ASH 2020

### Mosunetuzumab in 3L+ FL



- Pooled data from 2.8mg to 13.5mg cohorts showed an ORR of 62.7% and CR of 43.3%; 82.8% patients remain in complete remission for up to 26m off initial treatment
- Overall CRS rate of 28.9% (predominantly fever Gr1) with only 1.1% CRS events of Gr≥3
- Ph III safety run-in for mosunetuzumab + lenalidomide in R/R FL initiated
- First Ph I data on mosunetuzumab SC to be presented at ASH 2020

# Hematology: Venclexta in CLL, AML, MM, MDS Ph III studies to be initiated in various indications

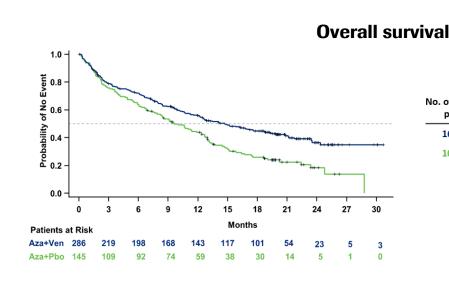






#### Venclexta progam **Bcl-2** inhibitor Indication R/R DLBCL/FL V+G 1L unfit CLL V+RR/R CLL CLL R/R CLL 17p R/R CLL after ibru/idel V+G 1L fit CLL V+dex t(11;14) R/R MM V+carfilzomib+ t(11;14) R/R MM V+aza 1L AML V+LDAC 1L AML AML V+AMG176 R/R AML R/R AML 1L MDS V+aza MDS V+/-aza R/R MDS V+fulvestrant 2L+ HR+

### Ph III (VIALE-A) results in 1L unfit AML



No. of events/No. of patients (%)	Median duration of study treatment, months (range)	Median overall survival, months (95% CI)
161/286 (56)	7.6 (<0.1 – 30.7)	14.7 (11.9 – 18.7)
109/145 (75)	4.3 (0.1 – 24.0)	9.6 (7.4 – 12.7)

Hazard ratio: 0.66 (95% CI: 0.52 - 0.85), p<0.001

- Ph III (Viale-A) results in 1L unfit AML filed in US (RTOR) and EU
- Ph III (Viale-M) in 1L fit AML initiated
- Ph III (CristaLLo) in 1L fit CLL with MRD as primary endpoint started in Q2 2020
- Additional Ph III studies in AML and MDS planned

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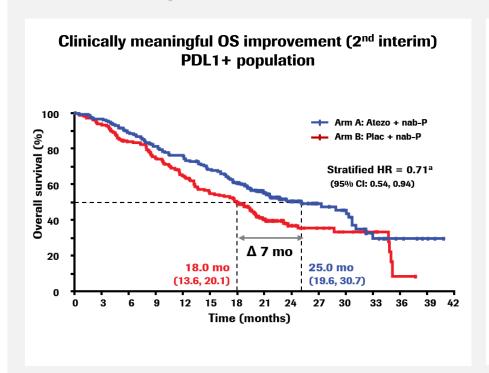
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# TNBC franchise: Tecentriq + nab-pac new SOC in 1L Positive Ph III results in neoadjuvant

### Ph III (IMpassion130) results in 1L



## **TNBC** program covering all lines of treatment\*



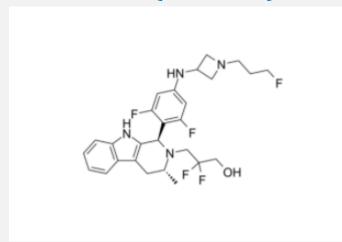
• Positive Ph III (IMpassion031) results for Tecentriq+nab-pac in neoadjuvant TNBC announced; data to be presented



# HR+/HER2- franchise: Potentially best in class 3<sup>rd</sup> gen SERD Strong efficacy as a single agent and in combination

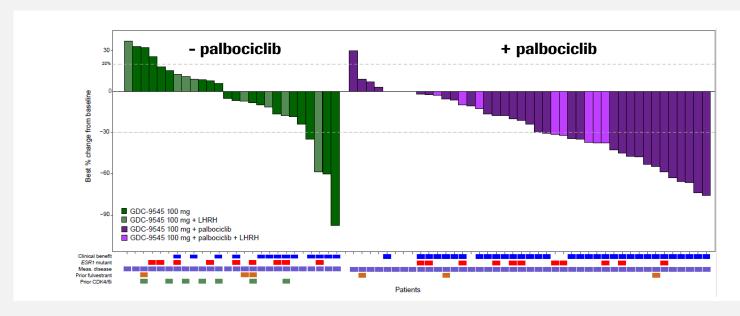


## Selective ER degrader (SERD) RG6171 (GDC-9545)



- · 3rd generation oral SERD
- Highly potent in vitro and improved efficacy in vivo versus previous SERDs
- High potency + minimal safety findings lead to wide nonclinical safety margins
- First SERD with positive combination data with a CDK4/6 inhibitor

## Ph Ib results: Tumor responses RG6171 +/- palbociclib

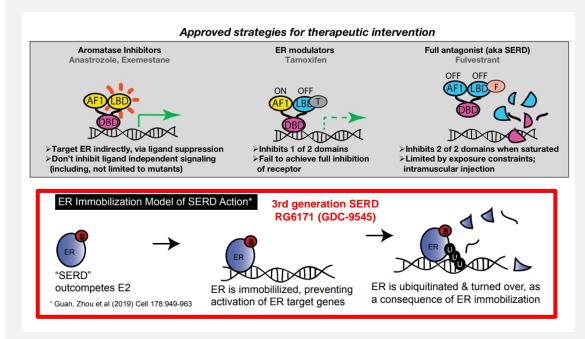


- Strong potentially best-in-class efficacy as single agent or in combination with a CDK4/6 inhibitor in pre-treated ER+ patients, regardless of ESR1 resistance mutations
- · Well-tolerated up to doses of 100 mg daily
- Expansion cohort at 30 mg daily on-going given the promising efficacy with a clinical benefit rate of 50%\*



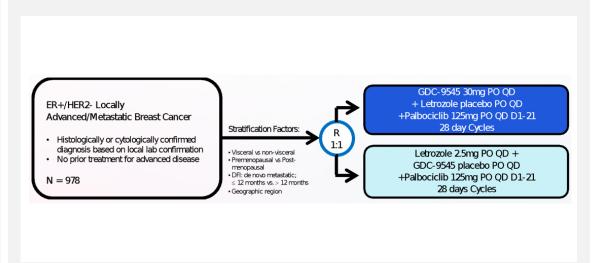
# HR+/HER2- franchise: Potentially best in class $3^{rd}$ gen SERD *Ph III program in* 1L+ *and* eBC *initiated*

## **3rd gen SERD: Overcoming fulvestrant limitations Improved MOA for a well established target**



 RG6171 is a 3<sup>rd</sup> generation SERD with improved bioavailability and a novel MOA: Increased efficacy is due to "ER immobilization" which supressess transcriptional activity prior to ER degradation

#### Ph III trial design in 1L mBC

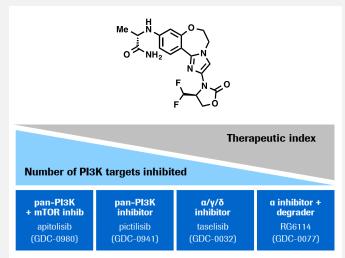


- Ph III RG6171 + palbociclib in 1L mBC to start in 2H 2020
- Ph II RG6171 + palbociclib in neoadjuvant started in Q3 2020; Ph III adjuvant study planned
- Pivotal Ph II RG6171 in 2/3L to start in Q4 2020; results expected in 2022

# HR+/HER2- franchise: Pl3Kai in *PlK3CA*-mutant tumors *Ph III for potentially best in class Pl3Kα inhibitor started*

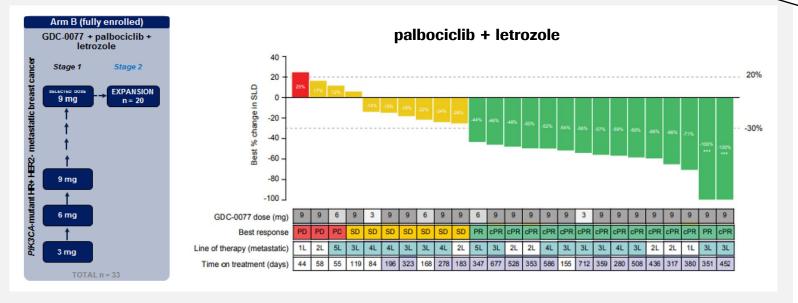


## Pl3Ka selective inhibitor + mutant Pl3Ka degrader



- Dual MOA: More potent and selective for Pl3Ka + degrades mutant Pl3Ka
- Greater safety margins
- Better in vivo efficacy
- Greater, more durable target inhibition
- Combinations with other therapies

#### Ph I (dose escalation and expansion cohort)



- Strong efficacy in on-going 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
- Good safety as single agent or combined
- Ph III (INAVO120) RG6114\* + palbociclib + fulvestrant in 1L PIK3CA-mutant HR+/HER2- mBC started in Q1 2020

74

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## **Lung franchise**

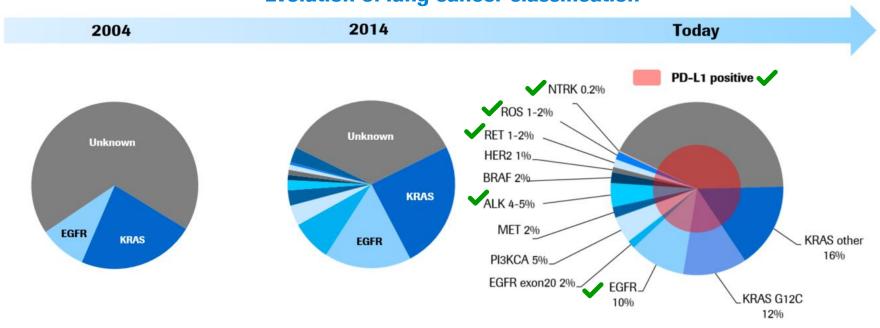
## Roche











- Roche uniquely positioned to establish integrated PHC solutions
- Develop rare mutation agents faster and cheaper leveraging B-FAST, FMI, Flatiron, PHC
- Multiple lung pilots focused on integrated offerings underway (Taiwan, Croatia, Australia)



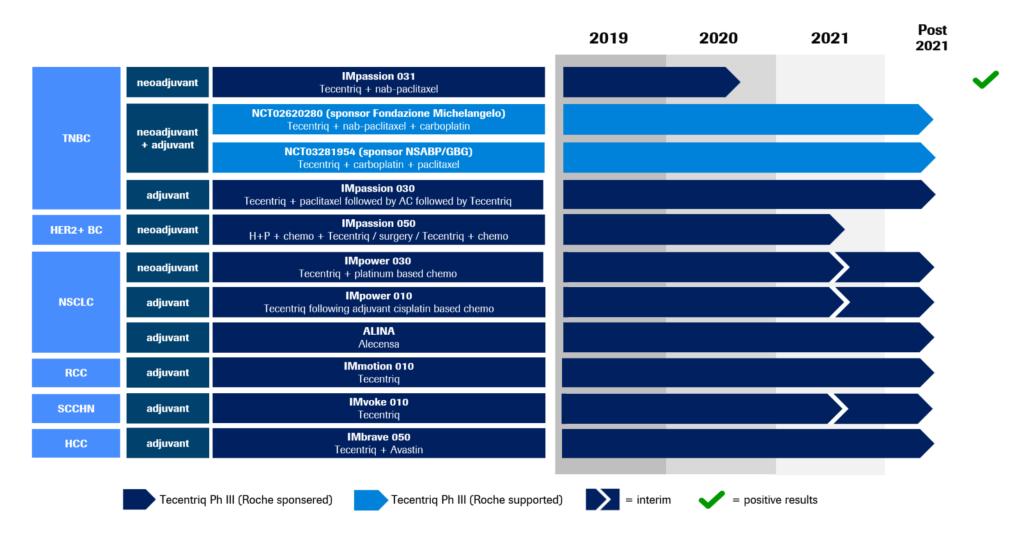
tiragolumab

GDC-6036 (KRAS*G12C*)

Pl3Kai (RG6114)



# Lung franchise: Overview adjuvant program NSCLC, HER2+ BC, SCCHN reading out in 2021



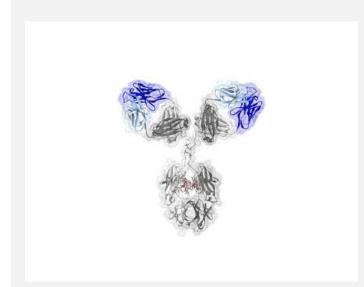


# Lung franchise: Tiragolumab + Tecentriq in NSCLC & SCLC Pivotal Ph III study in stage III NSCLC initiated



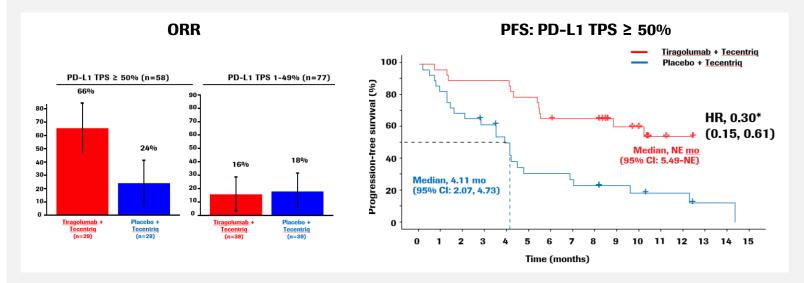
ASCO 20 Virtual

#### **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) 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 stage III NSCLC (SKYSCRAPER-03) on-going
- Ph II (CITYSCAPE) update including OS in 2021



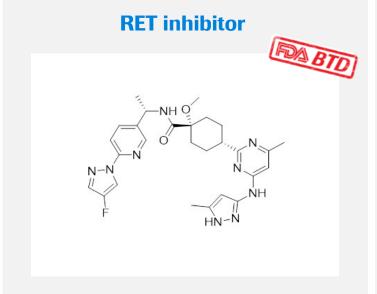


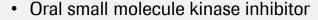




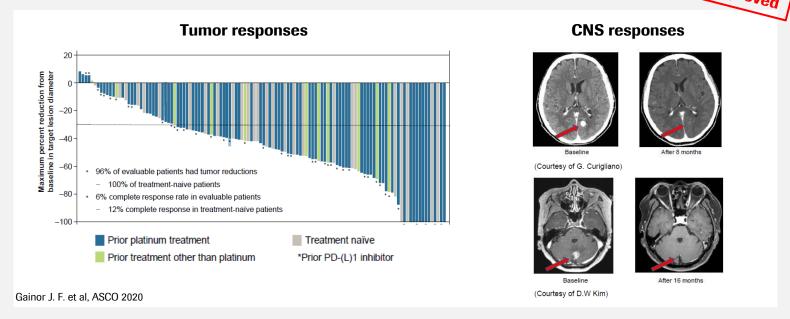


## Ph I/II (ARROW) results in RET fusion+ mNSCLC





- Highly selective for RET fusions and mutations, including predicted resistence mutations
- Brain penetrant and CNS active
- ~1-2% of NSCLC patients with RET fusions, thereof ~40% with brain metastases

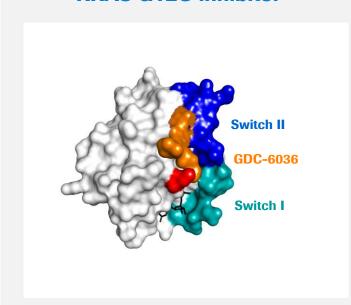


- 70% ORR in naive including 11% CR and 57% ORR in post-platinum patients including 6% CR\*
- CNS ORR at 56% (n=9) including 33% CR; rapid and durable responses; mDOR not reached
- Well-tolerated across tumor types with most AEs of grade 1–2
- Ph III (AcceleRET Lung) in 1L advanced or metastatic RET+ NSCLC on-going
- US accelerated approval in RET+ mNSCLC achieved in Q3 2020; filed in the EU



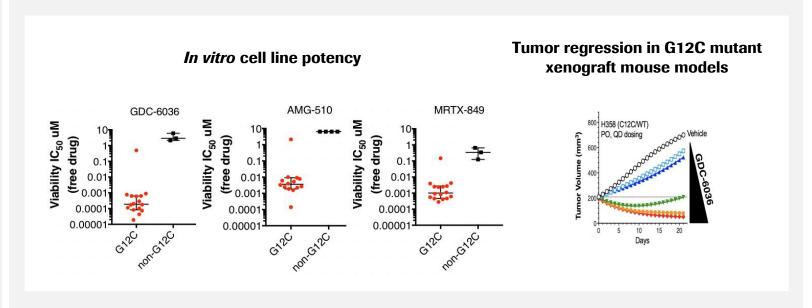
# Lung franchise: GDC-6036 (KRAS G12C inhibitor) in solid tumors G12C driver mutations found in 12% of all NSCLC patients

#### **KRAS G12C** inhibitor



- Highly potent irreversible covalent inhibitor of the KRAS G12C mutant protein, which becomes locked in an inactive state
- Minimal safety findings leading to wide nonclinical safety margins

#### In vitro and in vivo tumor growth inhibition



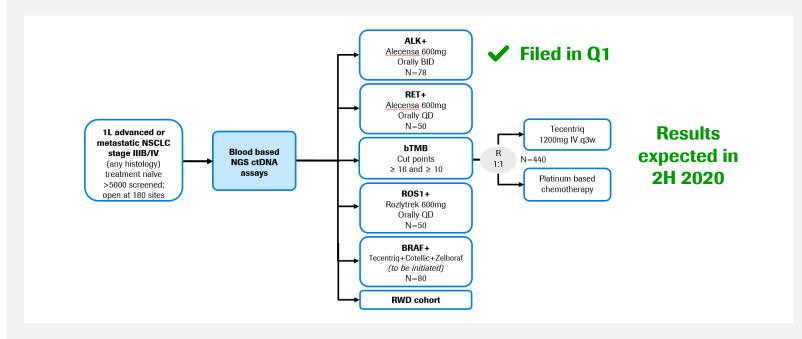
- GDC-6036 causes tumor growth inhibition in multiple patient derived KRAS G12C+ cell lines and in xenograft mouse models
- GDC-6036 synergizes with multiple targeted therapies; strong scientific rationale for combining with medicines that act on other parts of RAS pathway to deepen responses, extend duration of disease control, and limit treatment resistance.
- Ph I dose escalation and expansion in KRAS G12C+ solid tumors started in Q2 2020

Genentech unpublished results

# Lung franchise: Blood-based NGS ctDNA assays 30% of lung cancer patients with insufficient biopsy material



#### Ph III trial design (B-FAST) for 1L treatment naive NSCLC



- Allows for serial liquid biopsy testing to follow tumor evolution and resistance
- RWD cohort paired with NGS testing provides additional natural history & epidemiological data
- Primary endpoint in the ALK+ cohort met; filed in Q1 2020

#### **Blood based biomarkers**



- Liquid biopsy test that detects the 4 main classes of genomic alterations (324 genes), bTMB, MSI
- Comprehensive genomic profiling including resistance mutations or fusions in NSCLC
- Guides therapy selection and clinical trials

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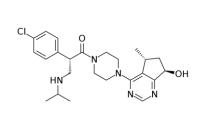
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# **GU** franchise: Ipatasertib in 1L mCRPC Positive Ph III results for patients with PTEN loss



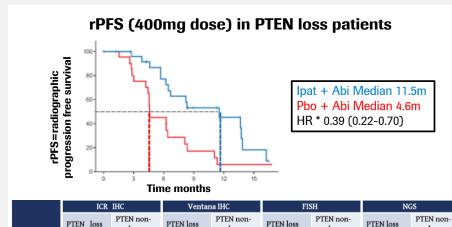
### OUNDATION MEDICINE

#### **Highly selective AKT inhibitor**



- Oral, highly specific inhibitor of all three activated isoforms of AKT and potentially preventing cancer cell growth and survival
- Clinical development in tumors with high frequency of PI3K/AKT pathway activation (CRPC, TNBC, HR+ mBC)

#### Ph II (A.MARTIN) results



	ICR IHC		Ventana IHC		FISH		NGS	
	PTEN loss	TEN non- loss	PTEN loss	PTEN non- loss	PTEN loss	PTEN non- loss	PTEN loss	PTEN non- loss
rPFS, mo								
Ipat	11.5	7.5	11,0	7.5	13.7	6,5	13,8	7.4
Pbo	4,6	5,6	4.6	5.7	6,5	5,6	6,2	4.5
rPFS HR *	0.39	0.84	0.50	0.74	0.67	0.77	0.24	0.52
90% CI	0.22-0.70	0.51-1.37	0,29-0.87	0.41-1.32	0,36- 1.24	0.50-1.20	0.10-0.60	0.25-1.13
rPFS HR <sup>a</sup> 90% CI								

#### **Biomarker assay**

#### **Roche VENTANA PTEN (SP218)**



 IHC detection of PTEN protein loss in formalin-fixed, paraffinembedded tissue



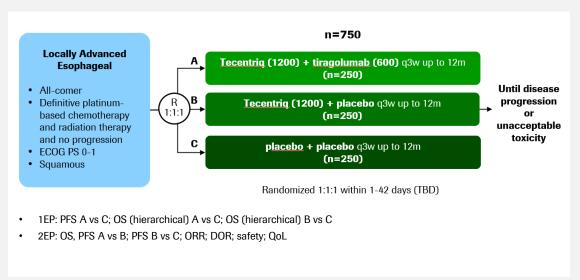
 Strong concordance to DNA technologies (NGS and FISH)

- Ph II: rPFS was prolonged in the ipatasertib 400 mg arm (8.2m vs 6.4m; HR=0.75); Dose-dependent improvement was observed in OS
- PTEN loss was associated with an improved rPFS outcome (HR of 0.39 at 400mg dose) as measured by NGS, FISH and IHC
- Ph III (IPATential150) met co-primary endpoint of rPFS in patients with PTEN loss

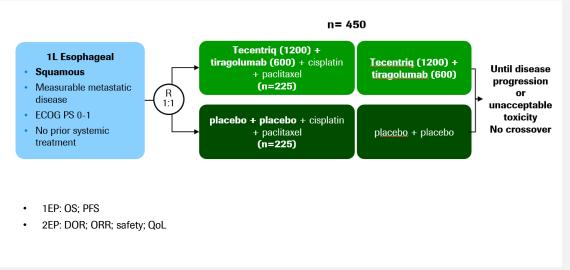
# GI franchise: Tiragolumab in esophageal cancer (EC) Pivotal Ph III studies initiated



## Ph III trial design (SKYSCRAPER-07) in locally advanced EC



## Ph III trial design (SKYSCRAPER-08) in 1L esophageal squamous cancers (ESCC)



- Preliminary Ph Ib safety and efficacy data in EC to be presented at upcoming conference
- Global development program with focus on Asia, especially China
- Ph III starts expected in 2020

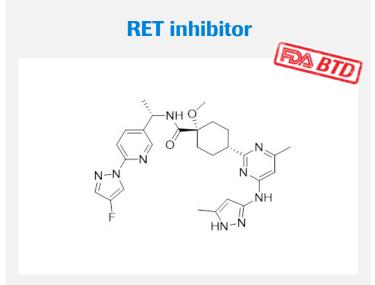
## Thyroid cancer franchise: Gavreto in RET+ TC



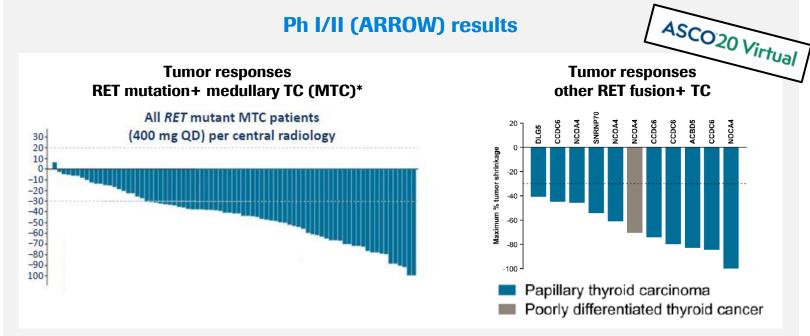




# Excellent efficacy and durability across thyroid cancer types



- Oral small molecule kinase inhibitor
- Highly selective for RET fusions and mutations, including predicted resistance mutations
- Brain penetrant and CNS active
- 90% of advanced MTC patients with RET activating mutations and ~10-20% of PTC patients with RET fusions



- RET+ MTC: ORR 74% in naive patients and 60% ORR in pretreated patients; mDOR not reached \*
- RFT+ TC: 91% ORR and 6-month DOR stands at 100%
- Registrational data on Ph I/II (ARROW) MTC results to be presented at ESMO
- Ph III (AcceleRET MTC) in MTC to start in H2 2020
- US priority review and RTOR for advanced or metastatic RET+ thyroid cancer on-going

<sup>\*</sup> MTC data released by Blueprint Medicines on April 1, 2020; Subbiah V. et al, ASCO 2020; SOC=standard of care; TC=thyroid cancer; MTC=medullary thyroid cancer PTC=papillary thyroid cáncer; CNS=central nervous system; BTD=breakthrough therapy designation; RTOR=real time oncology review; ORR=overall response rate; mDOR=median duration of response; Gavreto (pralsetinib) in collaboration with Blueprint Medicines; Gavreto, Blueprint Medicines and associated logos are trademarks of Blueprint Medicines Corporation; Gavreto was discovered by Blueprint Medicines

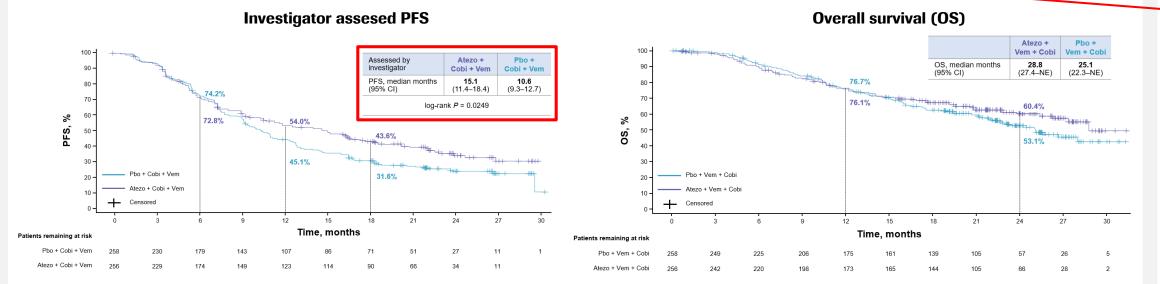


# Melanoma franchise: Tecentriq + Cotellic + Zelboraf First CIT+targeted therapy in BRAF V600+ melanoma



#### Ph III (IMspire150/TRILOGY) results in BRAF+ melanoma

FDA approved



- Statistically significant and clinically meaningful improvement in investigator-assessed PFS (HR=0.78; 15.1m vs 10.6m) and clinically meaningful improvement in mDOR (21.0m vs 12.6m); no new safety signals were identified
- OS data not mature but favored triplet; next interim expected H1 2021
- FDA approval granted in Q2 2020 under priority review and being part of FDA's project Orbis

## Late stage pipeline update



#### 1. Hematology franchise

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- FL: mosunetuzumab, glofitamab, Polivy
- · AML: Venclexta
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Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

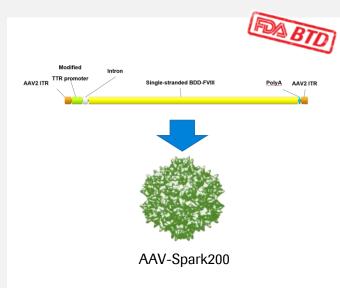
<sup>\*</sup> For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage

# Non-malignant hematology: RG6357 (SPK-8011) in hem A Early efficacy and safety data after 2 to 3.3 years of follow-up





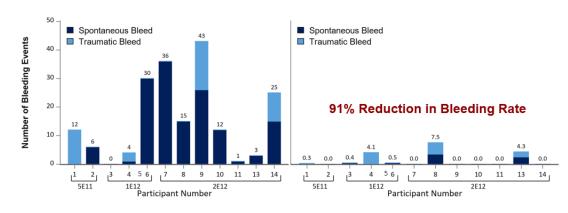
#### **Hemophilia A gene therapy**



- 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 (SPK-8011) results





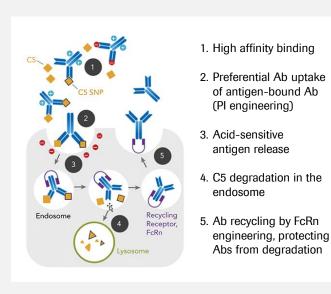
- Data from 5 participants in the 5x10<sup>11</sup> and 1×10<sup>12</sup> vg/kg dose cohorts and 7 participants in the 2x10<sup>12</sup> vg/kg dose cohort showed a 91% ABR reduction and a 96 % reduction in FVIII infusions
- The 5 participants in the 5x10<sup>11</sup> and 1x10<sup>12</sup> vg/kg cohorts demonstrated durable and stable FVIII expression, had a clinically significant reduction in bleeding and factor use and showed an acceptable safety profile for 2 to 3.3 years of follow up
- Further dose optimization and selection of immunomodulatory regimen on-going
- Ph III to be initiated in 2021

# Non-malignant hematology: Crovalimab in PNH Recycling Ab for maximal inhibition of C5



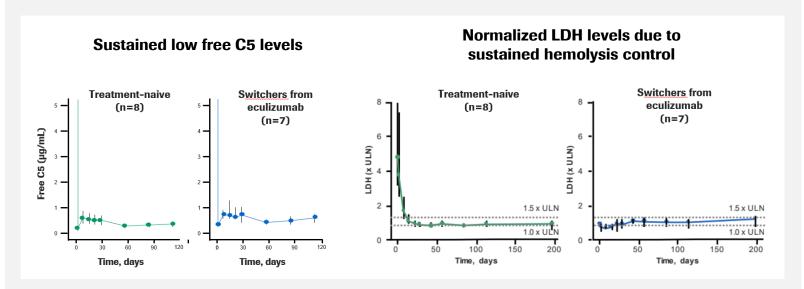


#### Anti-C5 mAb



- Chugai engineered, anti complement component 5 (C5) recycling mAb<sup>1-6</sup>
- Engineered to enable maximal, longlasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

#### Ph I/II (COMPOSER) results



- Ph I/II (COMPOSER) results show complete complement inhibition and a well-tolerated safety profile in C5i-naive patients and eculizumab pre-treated patients<sup>1</sup>
- Efficacy was maintained over long-term treatment (44 patients treated for a median of 71 weeks) and breakthrough hemolysis events were infrequent<sup>7</sup>
- Ph III switch and naive studies (COMMODORE 1/2) in PNH to start in 2020
- Development in additional complement-mediated diseases is being explored

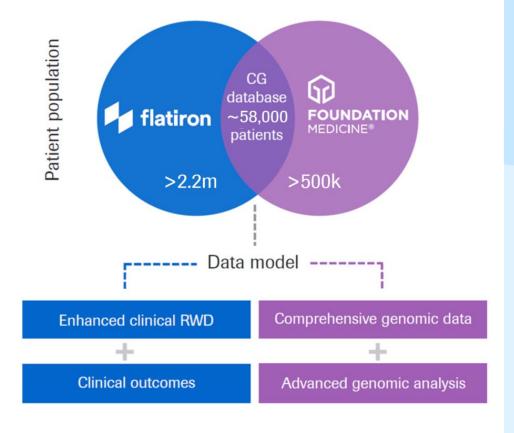
## **Clinico-Genomic Database**







## Combining RWD and genomics drives R&D



#### **Database R&D applications:**

- Understanding genomics of rapidly progressive disease
- Natural history cohorts for defined populations (ALK, NTRK, EGFR, ROS-1, RET, KRAS, etc.), including patterns of metastatic spread
- Mechanisms of resistance
- Improved prognostic classifiers

#### **Recent R&D examples:**

- Analysis found cumulative incidence of brain metastases in patients with a certain mutation is significantly higher than in patients with wild-type allele or other mutations; decision to develop brain-penetrant molecule as part of the broader development strategy
- Analysis of CGDB used to decipher a molecular mechanism for checkpoint inhibitor resistance and ultimately helped address a fundamental question that can potentially benefit many cancer immunotherapy projects

Linking advanced tumor genetics with clinical outcomes drives scientific hypothesis generation

RWD=real world data; CGDB=Clinico-Genomic Database

## Our technology platforms keep expanding\*



Small molecules	Bi-specifics	Fusion protein	mAb	Antibody drug conjugate	Personalized mRNA vaccine	Personalized T cells	RNA technologies	Gene therapy
CL O N N N OH	2:1 format 1:1 format			***	iNeST platform: mRNA- LPX Liposome	Activated T cell with neoantigen specificity	Transcription Araisanse oligenucieotide (ASC)	AVV Adeno associated virus
<ul> <li>Gavreto</li> <li>Alecensa</li> <li>ipatasertib</li> <li>RG6114</li> <li>RG6171</li> <li>KRAS G12C</li> </ul>	<ul> <li>mosunetuzumab</li> <li>glofitamab</li> <li>cibisatamab</li> <li>Her2 x CD3</li> <li>glypican-3 x CD3</li> <li>FcRH5 x CD3</li> <li>PD1 x TIM3</li> </ul>	<ul> <li>FAP x IL2v</li> <li>PD1-IL2v</li> <li>CD19-4-1BBL</li> <li>FAP-4-1BBL</li> <li>MAGE-A4</li> <li>ImmTAC</li> <li>IL15/IL15Ra-Fc</li> </ul>	<ul><li>tiragolumab</li><li>CD25 mAb</li><li>CD47 mAb</li><li>selicrelumab</li><li>codrituzumab</li></ul>	Polivy     Kadcyla	• iNeST	programmed     T cells	<ul><li>tominersen</li><li>UBE3A-LNA</li><li>Factor B ASO</li><li>HBV siRNA</li></ul>	<ul> <li>Luxturma</li> <li>SPK-8011</li> <li>SPK-8016</li> <li>SPK-7001</li> <li>SRP-9001</li> <li>4D-R110</li> </ul>
Target oncogenes, induce apoptosis, supress tumor growth	<ul> <li>PD1 x LAG3</li> <li>BCMA x CD16a Engage and activate T cells to kill tumour cells</li> </ul>	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	Recombinant proteins	= Oncology
<ul> <li>Evrysdi</li> <li>fenebrutinib</li> <li>ralmitaront</li> <li>TLR7 agonist</li> <li>GABA Aa5 PAM</li> <li>PTH1R agonist</li> </ul>	<ul><li>Hemlibra</li><li>faricimab</li><li>FIXa x FX</li><li>FGFR1 x KLB</li></ul>	<ul> <li>brain shuttle gantenerumab</li> <li>IL22-Fc</li> <li>IgG-IL2</li> </ul>	<ul> <li>Enspryng</li> <li>crovalimab</li> <li>gantenerumab</li> <li>prasinezumab</li> <li>semorinemab</li> <li>TLR4 mAb</li> </ul>	Anti-S.aureus TAC			Activase     Pulmozyme	Products approved

<sup>\*</sup> List of pipeline and launched molecules shown is not complete; iNeST=Individualized Neoantigen-Specific Therapy



## **Roche Late Stage Pipeline Event 2020**

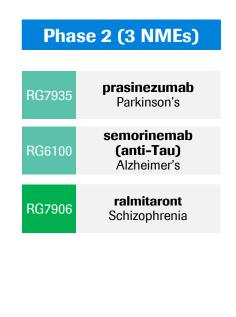
## Late Stage Pipeline Neuroscience

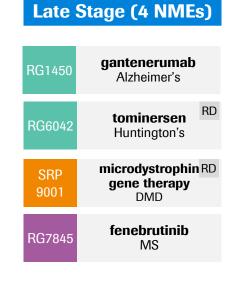
Paulo Fontoura, M.D. Ph.D. | Senior Vice President, Global Head Neuroscience and Rare Diseases Clinical Development

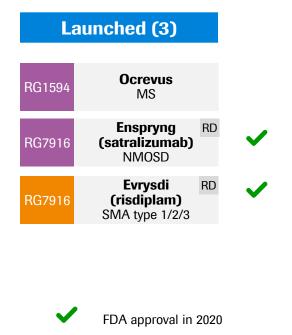
## Neuroscience and rare diseases portfolio Strongly differentiated pipeline



#### Phase 1 (5 NMEs) brain shuttle RG6102 gantenerumab Alzheimer's GABA<sub>A</sub> α5 PAM Autism spectrum **RG7816** disorder **RG7637** undisclosed **UBE3A-LNA** RG609 Angelman syndrome RG6237 undisclosed







RD=Rare Diseases



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

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## MS franchise: Ocrevus shifting the standard of care

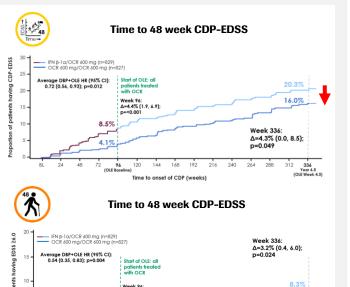
## Robust, consistent, sustained impact on slowing disability progression

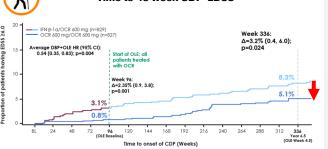


#### RMS: Ph III (OPERA) 6.5-year follow-up

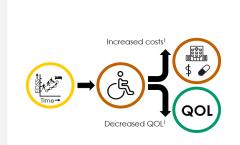


Reaching EDSS score ≥6.0, a key clinical disability milestone representing the requirement of a walking aid, which is associated with increased patient and societal burden

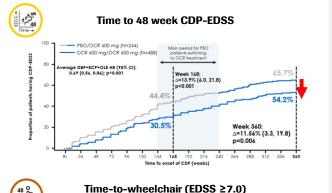




#### PPMS: Ph III (ORATORIO) 7-year follow-up



Reaching EDSS score ≥7.0, a key clinical disability milestone representing wheelchair confinement, has a major impact on patients' quality of life and associated treatment costs1





RMS patients on Ocrevus over 6.5 yrs had a 46% reduction in the risk of needing a walking aid vs those who switched over from IFN β-1α treatment at the end of the double-blind period (p=0.004)

PPMS patients on Ocrevus over 7 yrs had a 44% reduction in the risk of needing a wheelchair (EDSS) vs those who switched over from IFN β-1α treatment at the end of the double-blind period (p=0.006)



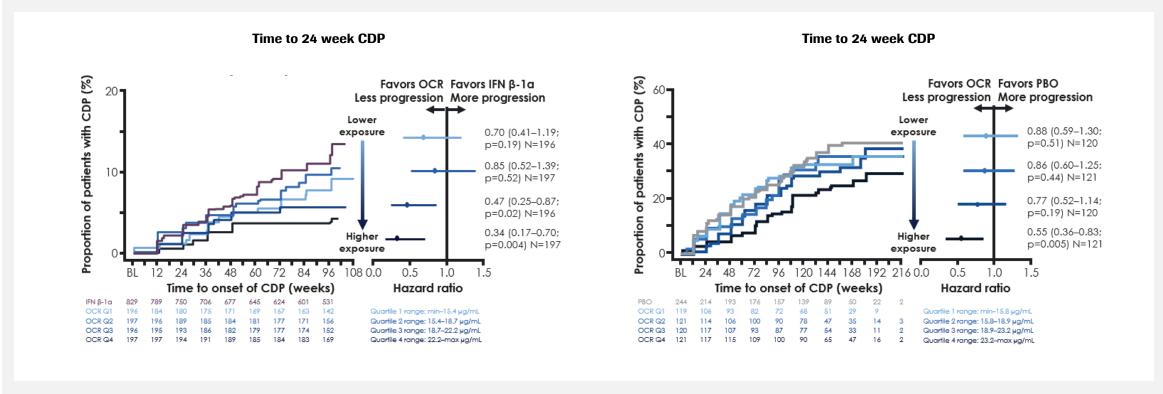


# MS franchise: Scientific rationale for higher dose Ocrevus Higher Ocrevus exposure reduces risk of disability progression





#### **Exposure-response analysis in PPMS**



Higher Ocrevus exposure was associated with lower B-cell levels and with greater control of disability progression without impacting safety



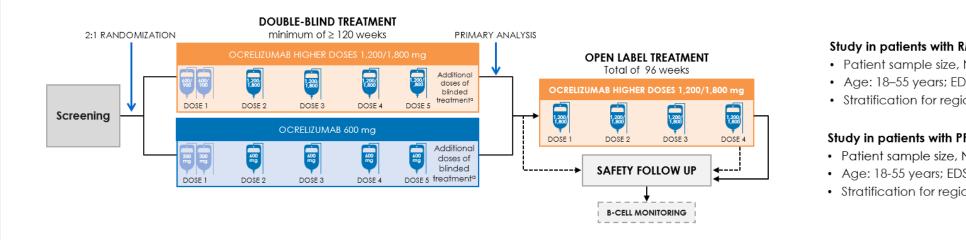


## **MS** franchise: Higher dose Ocrevus

## New Ph III program in RMS and PPMS planned to start 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 suggests a higher dose could further lower the risk of disability progression without compromising safety
- Two double-blind, randomized Ph III studies designed to test higher dose Ocrevus; 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 to start in 2020

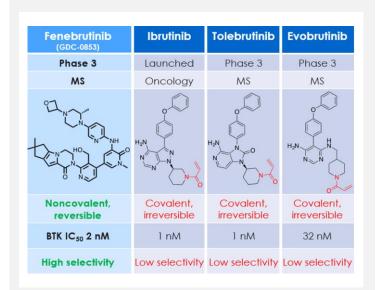




## Highly differentiated and potentially best-in-class BTKi in MS

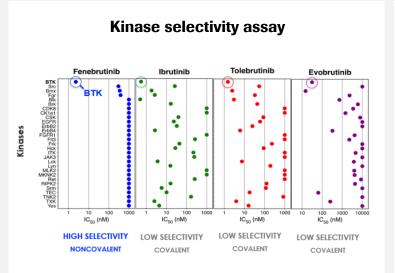


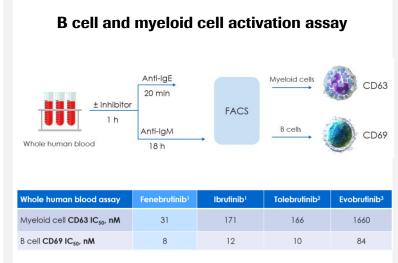
#### **BTK** inhibitor



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

#### Molecular and biological characterization





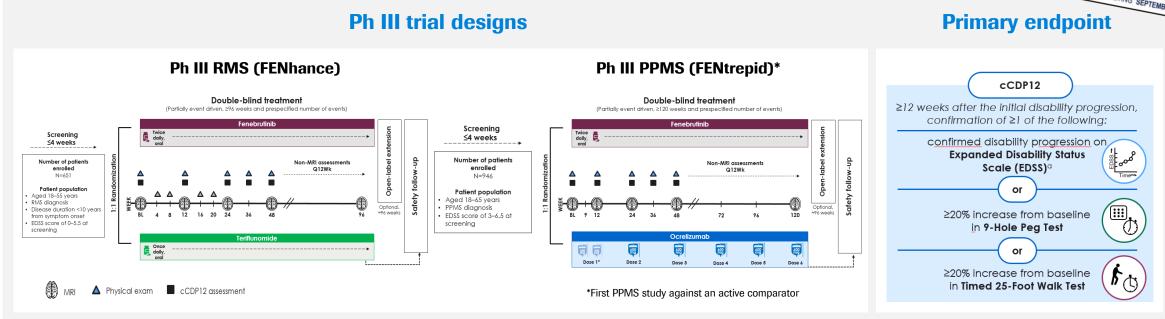
- Fenebrutinib's BTK inhibition potential and kinase selectivity were assessed in a panel of 219 human kinases. fenebrutinib was found to be highly BTK selective over other kinases which may reduce off target effects and improve safety
- Dual MOA: Fenebrutinib was shown to potently inhibit B cell and myeloid cell (macrophages, microglia) activation in whole human blood and thus may reduce both acute and chronic inflammation in MS, simultaneously





## Ph III program to assess disease progression in RMS and PPMS





- Fenebrutinib has a well established safety profile due to 13 clinical studies with >1200 patients, thereof 535 patients exposed for >1year; generally well tolerated, mostly non-serious, mild and self-limiting AEs
- Primary endpoint is composite Confirmed Disability Progression 12 (cCDP12); co-primary endpoint in RMS is ARR
- cCDP12 provides a more thorough approach to disability progression, including EDSS (global assessment scale), 9HPT (hand function) and
   T25FWT (ambulation ability). cCDP12 assesses upper limb function and may detect disease progression earlier
- Ph III program in RMS and PPMS to start enrollment in 2020

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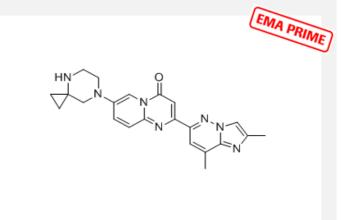
## SMA franchise: Evrysdi in type 1/2/3 SMA





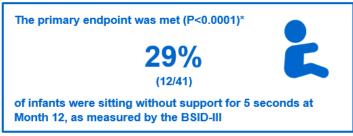


#### **SMN2** splicing modifier



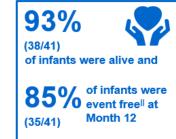
- · Efficacy in infants, children, adults
- Durably increases SMN protein throughout the CNS and in peripheral tissues
- Consistent safety profile in over 450 risdiplam-treated patients in trials
- First and only at-home treatment

#### FIREFISH part 2 results in type 1 SMA confirm highly competitive profile















- Positive Ph III (FIREFISH part 2) in older, symptomatic type 1 infants
- Positive Ph III (SUNFISH part 2) the only placebo controlled study in a broad spectrum of type 2/3 patients (age 2-25)
- US approval achieved in Q3 2020; filed in EU, Brazil, Canada, China and 14 further countries

## SMA franchise: Evrysdi in type 1/2/3 SMA





## Additional data for switching patients and newborns

#### **Broadest Ph III program in SMA on-going**



Presymptomatic Newborns	Symptomatic Infants	Younger Children	Older Children	Teenagers	Adults		
	<u> — —</u> —			<u> </u>			
			_ 🧽 –				
			<b>V</b>				
	≤ 5 years old		> 5 years old				
~	15% prevalence	*	~85% prevalence*				
Focus of I	many recent trial	s in SMA	Large prevalent population that remains underserved lacking treatment options and supporting evidence				

- Ph III (JEWELFISH) switching study fully recruited (n=174); Prior treatments were olesoxime (n=74), Spinraza (n=73), Zolgensa (n=14); RG7800 (n=13); JEWELFISH exploratory efficacy to be reported after 1 year of follow-up in 2021
- Ph III (RAINBOWFISH) presymptomatic study enrollment on-going
- Evrysdi has the potential to become the treatment of choice for the majority of SMA patients as our broad clinical trial program covers the broad, real-world spectrum of people living with SMA including under-served and under-represented patient populations

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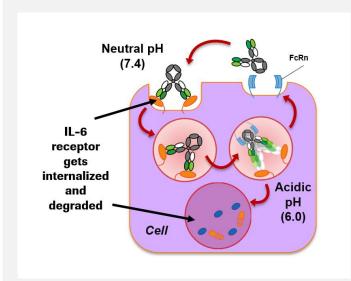
## **Enspryng in NMOSD**





## Significantly reduced frequency and severity of relapses

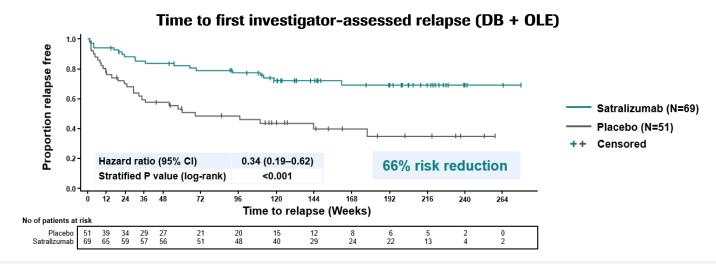
#### **Anti-IL-6 receptor mAb**



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

#### Ph III (SAkura) up to 5 year follow-up (AQP4+ patients)





- Continued risk reduction of relapse for up to 5 years; AQP4+ patients experiencing a 66% risk reduction, and all patients experiencing a 51% risk reduction vs those originally randomized to placebo; treatment associated with a significant reduction in severe relapses vs placebo
- Pooled longer-term data from the SAkura studies show a continued favorable safety profile
- Roche is actively exploring Enspryng in other rare indications where IL-6 is implicated

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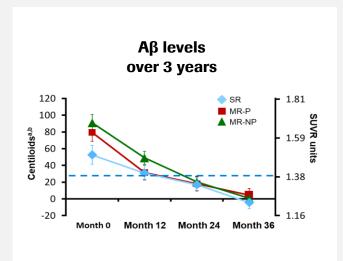


# **AD:** Gantenerumab targeting Amyloid β (Aβ) Strong target engagement and downstream biological impact

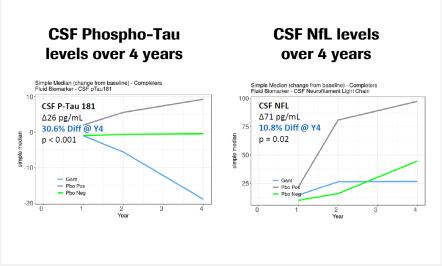
# Amyloid precursor protein Aβ<sub>42</sub> Toxic Aβ<sub>42</sub> oligomers Amyloid plaque gantenerumab

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

#### **OLE shows robust Aβ removal\***



#### **DIAN-TU** shows downstream impact



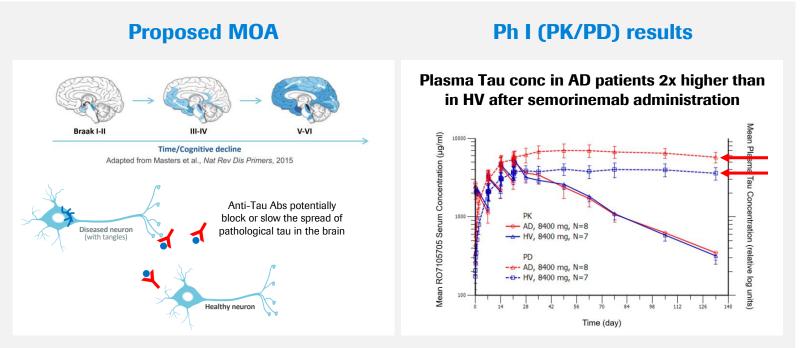
- Gantenerumab lowers  $A\beta$  below positivity threshold towards floor levels without plateau; at 3 years 80% of patients were  $A\beta$ -negative in OLE studies
- Gantenerumab reduces levels of downstream biomarkers (phosphorylated Tau) and blocks increases of markers of neurodegeneration (NfL) in patients with familial AD (DIAN-TU study)
- Ph III (GRADUATE 1/2) program with optimized exposure by dose (single dosing scheme) and duration (27 months of treatment) on-going; results expected in 2022



# AD: Semorinemab targeting anti-Tau Ph II (TAURIEL) results for semorinemab expected in H2 2020

# 

- First-in-class humanized Ab
- Recognizes N-terminal epitope
- Targets all known isoforms of full length Tau independent of their phosphorylation status



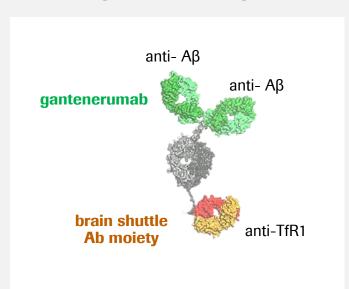
- No AEs associated with semorinemab in pre-clinical studies; safe and well tolerated in Ph I
- Robust biomarker development with two tau PET tracers in development
- Results from blinded portion of Ph II (TAURIEL) in prodromal-to-mild AD expected in H2 2020; primary endpoint includes CDR-SB; secondary endpoints include cognitive tests (ADAS-Cog13, RBANS Total Score) and functional tests (ADCS-ADL, Amsterdam iADL)
- Second Ph II (LAURIET) in patients with moderate AD on-going

## **AD:** Gantenerumab brain shuttle (RG 6102)



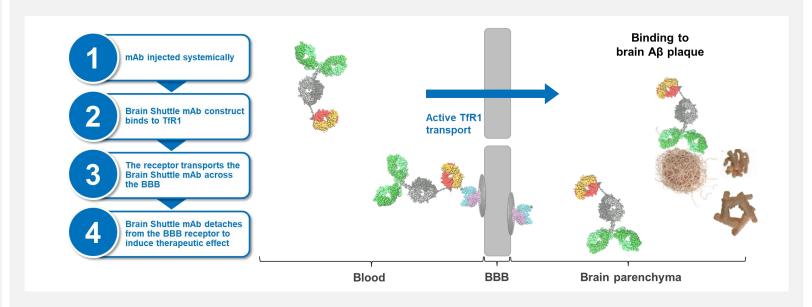
## Vision: Superior target access leading to slowing of AD progression

#### **Anti-Aβ-TfR1** fusion protein



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

#### **MOA:** Superior brain access through brain shuttle technology



- Preclinical work provides in vitro and in vivo evidence that binding to the TfR1 receptor facilitates transcellular transport across the Blood Brain Barrier (BBB)
- The first brain shuttle mAb entered the clinic in 2019
- Preliminary Ph I PK/PD data are currently under evaluation to determine next steps

<sup>1.</sup> Niewoehner J, et al. Neuron 2014; 81:49–60; BBB=blood brain barrier; IgG=immunoglobulin G; mAb=monoclonal antibody; TfR1=transferrin receptor 1; Aβ=Amyloid β; CNS=central nervous system; PD=pharmacodynamics; 108 PK=pharmacokinetics



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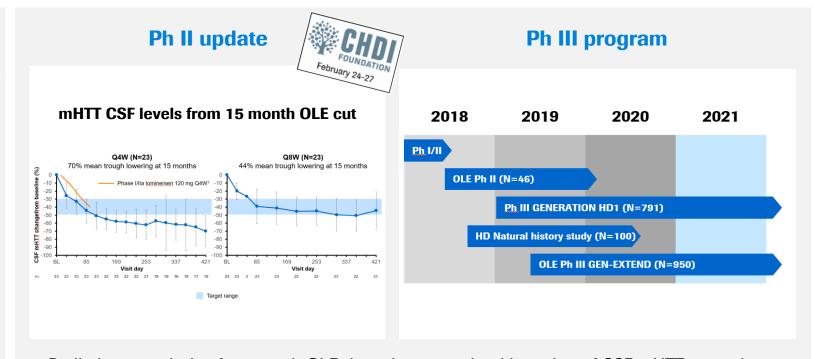
# **Tominersen (HTT-ASO) in Huntington's disease** *First drug to reduce toxic mHTT*





# wtHTT allele CAG tract CAG tract The company of the company of

- Antisense drug binds to wtHTT and mHTT sequence leading to RNase H1 mediated degradation of wild-type and mutant HTT mRNA
- · Addresses all patients



- Preliminary analysis of 15 month OLE data show sustained lowering of CSF mHTT exceeds or achieves target reduction range of 30-50% (Q4W; Q8W)
- Safe and well tolerated with no dose-limiting toxicities identified and no patients discontinuing
- Ph III (GENERATION HD1) enrollment completed in Q2 2020; results expected in 2022
- Data from the Ph I/II and Ph III OLE studies and the HD Natural History study expected in 2021



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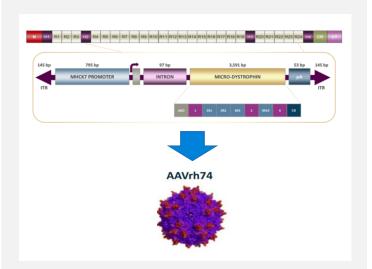
## Micro-dystrophin Gene Therapy (SRP-9001) in DMD



## Positive 1 year safety & efficacy data published in JAMA Neurology

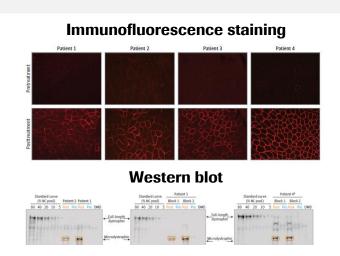


#### Micro-dystrophin gene therapy



- AAVrh74 vector: low likelihood of preexisting 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 I/IIa open-label trial results (n=4)



## North Star Ambulatory Assessment (NSAA)

Patient	Parameter	Baseline -	Change from baseline at day 365
1	NSAA	18	7
	CK level, U/L	20 691	-46.48%
2	NSAA	19	8
	CK level, U/L	23 414	-55.18%
3	NSAA	26	2
	CK level, U/L	34 942	-81.66%
4	NSAA	19	5
	CK level, U/L	29 210	-85.75%

- 81.2% of muscle fibers expressing micro-dystrophin by immunohistochemistry with a mean intensity of 96% at the sarcolemma at 12-wks; adjusted for fat and fibrotic tissue Western blot showed a mean expression of 95.8%
- All patients showed improvements in NSAA score (mean, 5.5 points up to one year); therapy
  was well tolerated with minimal adverse events up to one year after treatment
- Planning for two global Ph III trials in ambulatory and non-ambulatory DMD patients are ongoing



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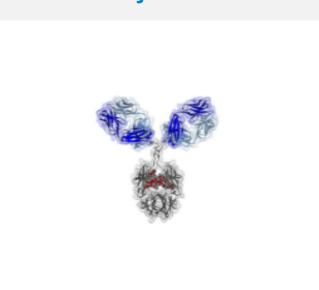
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# Prasinezumab in Parkinson's disease (PD) Primary not met, but encouraging core PD motor signs



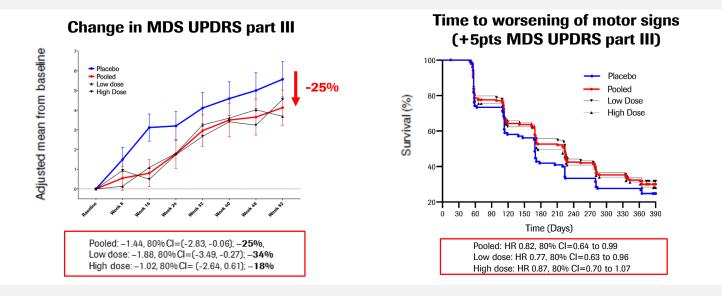


#### Anti-a-synuclein mAb



- 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 PD progression

#### Ph II (PASADENA part 1) 52 weeks results



- First Ph II (PASADENA) results were presented at MDS 2020 (poster session); additional results (including digital biomarker data) to be presented at the MDS presentation on Sep 15
- Study did not meet its primary endpoint (MDS UPDRS total score)
- Positive signals of efficacy on multiple pre-specified secondary assessments of motor function including motor signs (MDS UPDRS part III)
- Totality of data is being evaluated to determine next steps



## Prasinezumab in Parkinson's disease

## Digital biomarker active tests supporting clinical development





## **Novel measurements & digital endpoints**

## Digital biomarkers - providing enhanced patient insights and novel endpoints

#### **Apps, wearables and gaming devices**



#### Digital biomarker program in neuroscience

		3	Ķ		
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
- Continuous and longitudinal measurement captures episodic and rare events
- Reduced assessment burden and greater real-world relevance



## **Roche Pharma Day 2020**

## Late Stage Immunology, Ophthalmology & Infectious Disease

**Cristin Hubbard** | Senior Vice President, Immunology, Infectious Disease & Ophthalmology, Global Product Strategy



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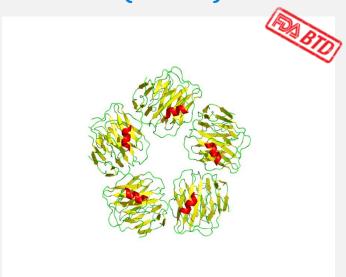
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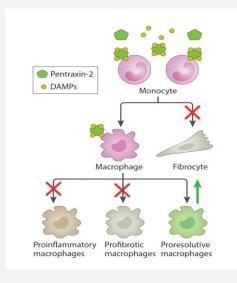
# Recombinant human Pentraxin-2 in fibrotic diseases Evaluating new options to treat fibrosis in multiple diseases

## Recombinant human pentraxin-2 (rhPTX-2)

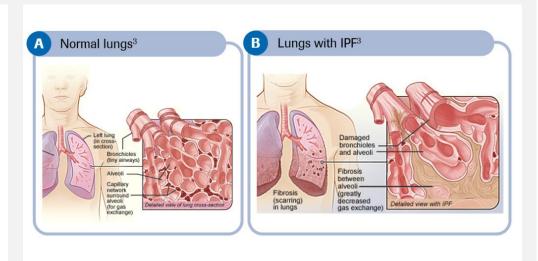


- First-in-class rhPTX-2
- PTX-2 is an immune regulatory protein that binds DAMPs with specificity for fibrotic tissue
- Received BTD for IPF

## **MOA: PTX-2 inhibits fibrosis formation**



#### **Fibrotic tissue in IPF**



- PTX-2 binds monocytes and macrophages via the FcγR and shifts the balance of monocyte differentiation from pro-fibrotic macrophages, fibrocytes to pro-resolutive macrophages
- Serum PTX-2 levels are reduced in patients with IPF, myelofibrosis and other fibrotic diseases;
   low PTX-2 levels correlate with increased disease severity
- High unmet medical need remains for further slowing lung function decline on top of SOC



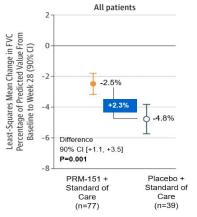


## Efficacy as monotherapy or in combination with standard of care

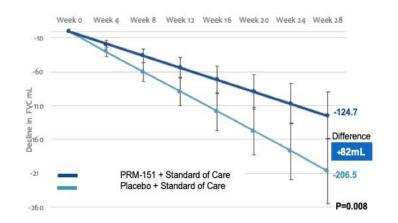
#### Ph II results in IPF



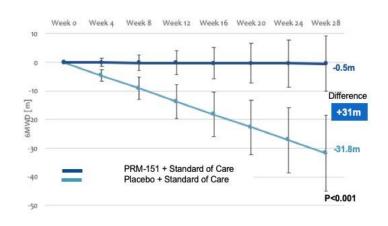




#### Change in FVC (mL) from baseline to week 28



#### Change in 6MWD (m) from baseline to week 28



- rhPTX-2 resulted in a significantly slower decline in lung function over 28 weeks vs placebo (-2.5% vs -4.8%); most patients received parallel treatment with SoC and no unexpected adverse events with combination treatment were noted
- Ph III (STARSCAPE) of rhPTX-2 + SOC (Esbriet or Ofev) in IPF to start in Q4 2020
- Ph II trial in myelofibrosis on-going; first results expected in Q4 2020



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#### **Gazyva increases B-cell depletion**

#### Type II anti-CD20 region

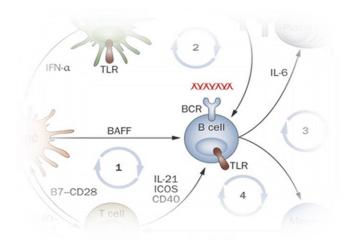
- · Increased direct cell death
- Decreased CDC
- Reducted CD20 internalization

#### **Glycoengineered Fc region**

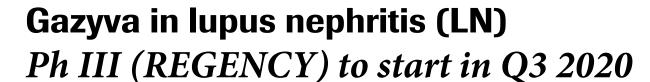
- · Higher FcYR affinity
- Increased ADCC/ADCP
- Greater potency than Rituxan in depleting peripheral and tissue B-cells
- Recent studies suggest that tissue based B-cells play a major role in lupus nephritis and a more complete depletion is needed

## **Evaluating Gazyva in B-cell mediated diseases** with high unmet need

- Autoreactive B cells in LN:
- Secrete pathogenic autoantibodies & proinflammatory cytokines
- Present self-antigens
- Activate T cells

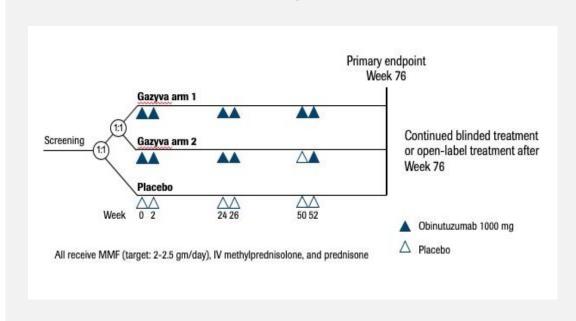


- Lupus nephritis (Ph III (REGENCY) to start in Q3 2020)
  - Membranous nephropathy (Ph III expected to start H1 2021)
  - Potential additional opportunities
    - Non-renal systemic lupus erythematosus
    - · Several other diseases



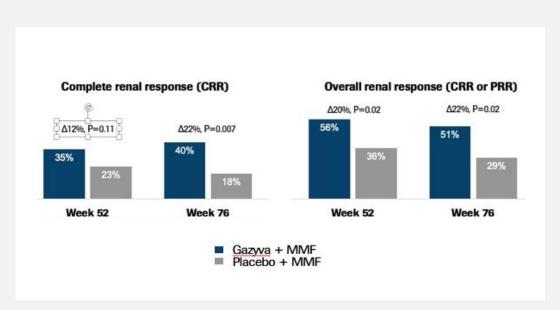


## Ph III trial design (REGENCY)



- Single pivotal Ph III to replicate Ph II (NOBILITY)
- Primary endpoint is complete renal response (CRR); secondary endpoints include partial clinical response (PRR)
- Ph III (REGENCY) to start in Q3 2020

#### Ph II (NOBILITY) results



- Ph II (NOBILITY) met both primary and key secondary endpoints with no new safety signals
- BTD for Gazyva in LN awarded by the FDA
- Ph II update (104 weeks) to be presented

Furie R. et al; ACR 2019; MMF=mycophenolate mofetil

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#### 1. Hematology franchise

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# Inflammatory bowel disease (IBD) program on-going Ph III program of etrolizumab in Crohn's Disease reading out in 2021

## Ph III

#### **Etrolizumab**

- Gut-selective, dual α4β7/αΕβ7 antiintegrin antibody
- Development of novel patient-reported outcome measures for UC and Crohn's disease continues



#### **IL-22-Fc fusion protein**

- Novel non-immunosuppressive MOA
- Restores and protects gut epithelium
- Ph IIb in UC ongoing; N~270

### Ph I

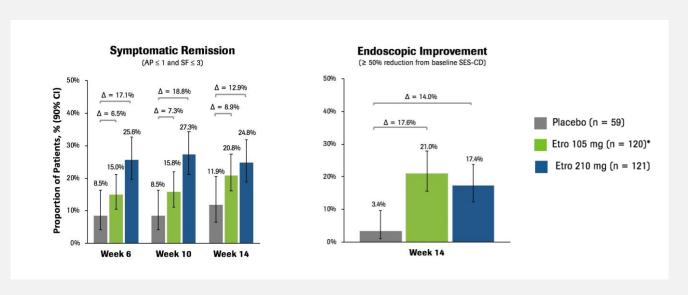
#### **RG6287**

- Preserves epithelial cell survival
- Ph1 on-going

#### **IgG-IL-2** fusion protein

- · Promotes regulatory T-cell proliferation
- · Ph Ib on-going

#### **Etrolizumab in CD: Ph III (BERGAMOT) interim results**



- >70% of patients in cohort 1 were TNF IR, representing a population with high unmet need; symptomatic remission was seen at week 6 and observed through week 14; clinically meaningful endoscopic improvement was demonstrated
- Well tolerated; frequency of adverse events comparable to placebo
- Ph III enrolling with final data expected in 2021



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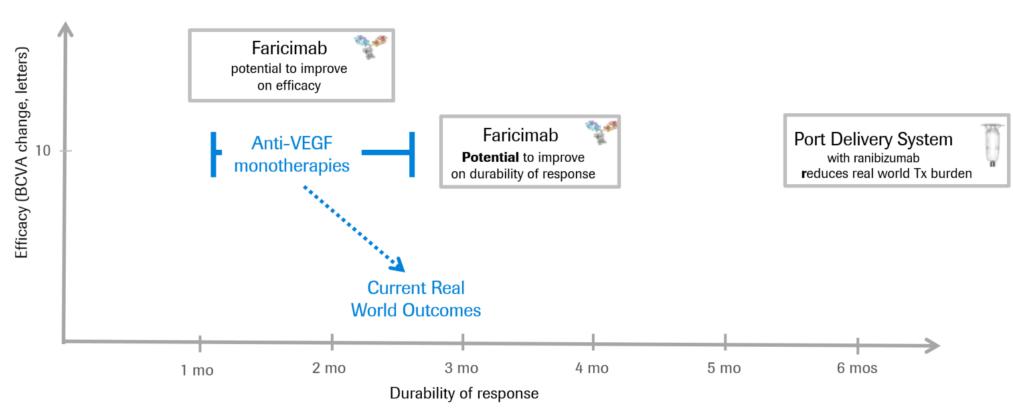
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# Late stage ophthalmology progressing rapidly PDS and faricimab with the potential to address key unmet needs

#### Opportunity to differentiate on durability and improved efficacy



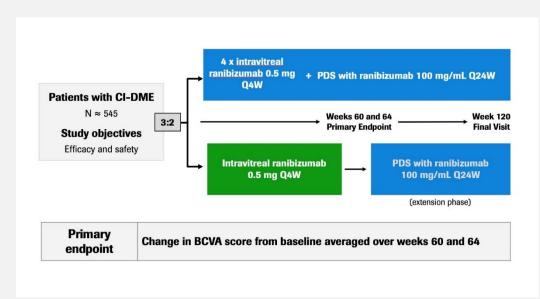
For illustrative purposes only

## **Port Delivery System (PDS) Platform**



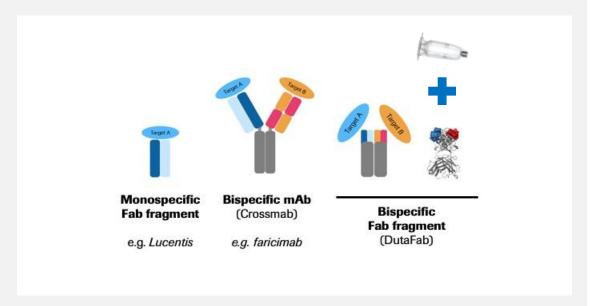
## New indications and next generation bispecifics (DutaFabs)

#### Ph III trial design (PAGODA) in DME



- In the US and EU diabetic eye disease (DME, DR) is the leading cause of vision loss in working age adults
- Ph III (PAGODA) results in DME expected in H1 2022
- Ph III (PAVILION) in DR started in Q3 2020

#### **DutaFabs: A new PDS compatible bispecific format**



- DutaFabs are a novel bispecific Fab format significantly smaller than traditional full seized bispecific antibodies
- DutaFabs are compatible with the PDS technology, potentially enabling increased durability beyond Q6M
- 3 DutaFabs with novel dual MOAs in development



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#### Faricimab in nAMD

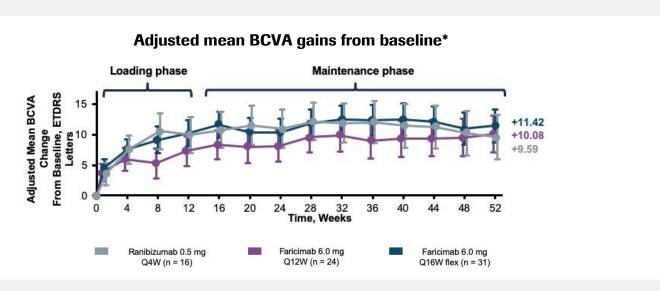


## Potential to stabilize retinal vasculature and improve treatment durability

# Anti-VEGF/Ang2 bispecific mAb Anti-Ang-2 Fab • Enhanced vessel stabilisation through Ang-2 inhibition Anti-VEGF-A Fab • Proven efficacy through VEGF-A inhibition Optimized Fc • Faster systemic clearance • No effector function

- First bispecific Ab in ophthalmology binding simultaneously to VEGF and Angiopoietin2 (Ang2)
- Ang2 inhibition may improve vascular stability and reduce retinal inflammation





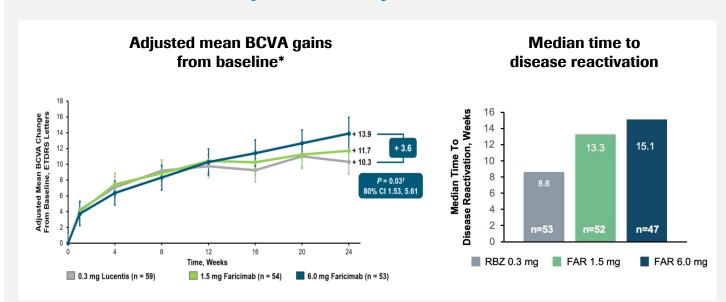
- BCVA gains with faricimab Q16W flexible dose and Q12W comparable with ranibizumab Q4W
- 12 weeks after last loading dose 65% of patients had no disease activity and could potentially benefit from Q16W dosing
- Ph III (TENAYA and LUCERNE) enrollment completed; results expected Q1 2021

### **Faricimab in DME**

## Roche

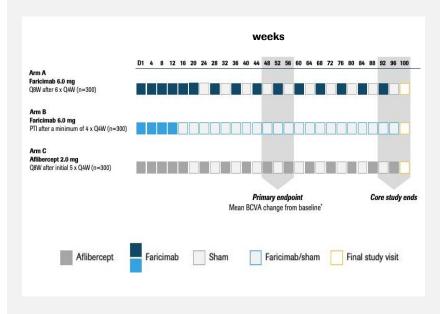
## Potential for improved efficacy and durability

#### Ph II (BOULEVARD) results in DME



- Robust BCVA efficacy gains with a mean of +13.9 letters from baseline
- Statistically significant gain of +3.6 letters over Lucentis
- Durability shown with median time to disease reactivation of 15.1 weeks for faricimab vs 8.6 weeks for Lucentis

#### Ph III trial design (YOSEMITE, RHINE)



- Primary endpoint: Mean BCVA △ from baseline at 1yr; arm B to evaluate personalized treatment interval of Q12W or Q16W
- Ph III data expected in Q4 2020
- Ph III in RVO to start in 2021



## **Roche Pharma Day 2020**

Infectious Diseases: A close look at our HBV pipeline

John Young | Global Head of Infectious Diseases, pRED



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## High burden of disease with life-threatening complications

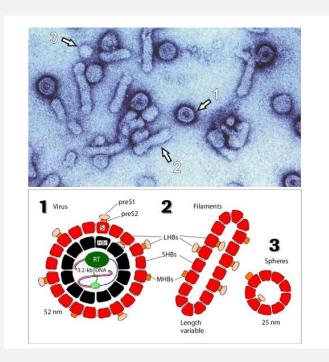
#### **Hepatitis B Virus (HBV)** HCC Infection **Treatment** Death **257**<sup>m</sup> 887<sup>k</sup> **25**% Low cure rates and of untreated HBV patients die yearly patients are infected with life-long therapy patients from complications of Hepatitis B with current SOC will develop **HBV** hepatocellular 86m in China (<0-3% cure rate 7<sup>th</sup> leading cause of carcinoma after 1yr of therapy) death worldwide

Reference: WHO July 2018



# Hepatitis B surface Antigen (HBsAg) loss is the most important endpoint for functional cure with finite treatment duration

#### **HBsAg** detection



 Total HBsAg is quantatively measured by Immunoassay (Elecsys HBsAg II quant II, Roche)

#### **HBsAg** decline associated with signitificantly improved patient outcomes

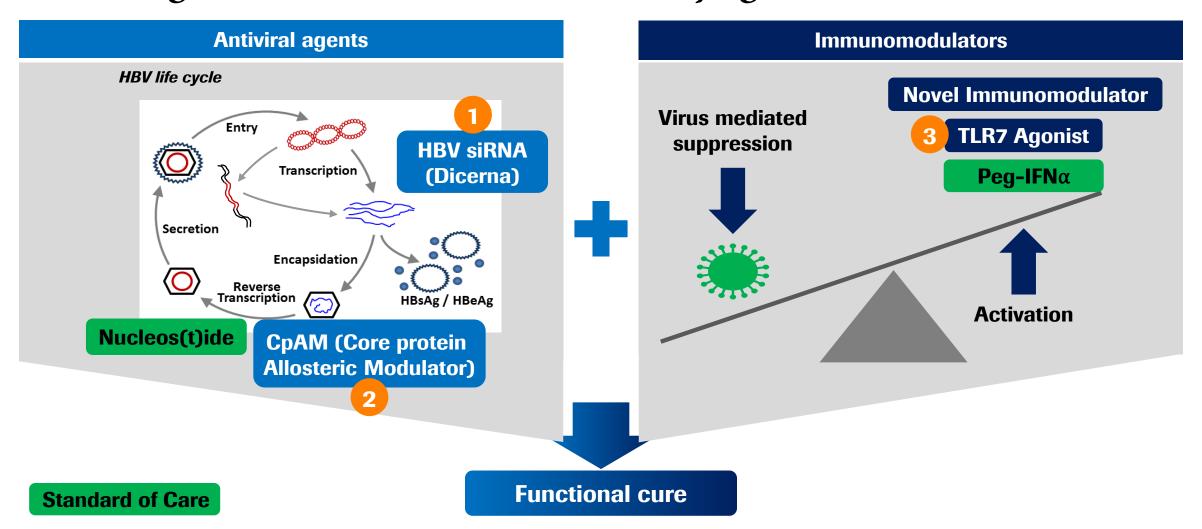
	Relative Risk	Lower limit	Upper limit	P-value
Liver decompensation	0.28	0.13	0.59	0.001
HCC	0.30	0.20	0.44	< 0.001
Transplant/Death	0.22	0.13	0.39	< 0.001
Composite first clinical event	0.31	0.23	0.43	<0.001

- Meta-analysis of 28 studies with nearly 190,000 chronic HBV patients
- Clear association between HBsAg seroclearance and improved outcome
- HBsAg seroclearance as primary endpoint in clinical trials supported



## **Roche HBV strategy**

## Combining antiviral and immunomodulatory agents



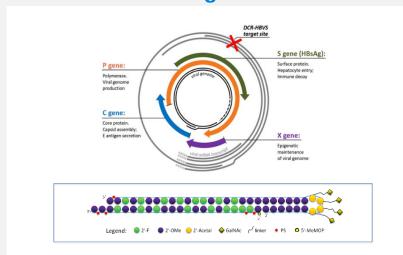


## HBV siRNA (RG6346)

# Roche Dicerna™

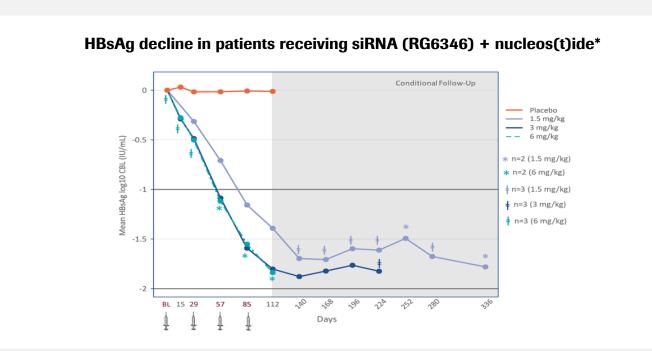
## Inhibiting HBV gene expression by targeting the viral genome

## siRNA simultaneously inhibiting multiple HBV genes



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

#### Ph I (dose finding) interim results



- Durable HBsAg decline up to day 336
- 6 out of 10 patients, who completed day 112, had HBsAg < 100 IU/mL</li>
- Safe and well tolerated

<sup>\*</sup> Interim analysis from 25 June 2020 data cutoff; https://investors.dicerna.com/static-files/0507fc43-4023-4a40-92fb-0c06b9c4a4b7; In collaboration with Dicerna

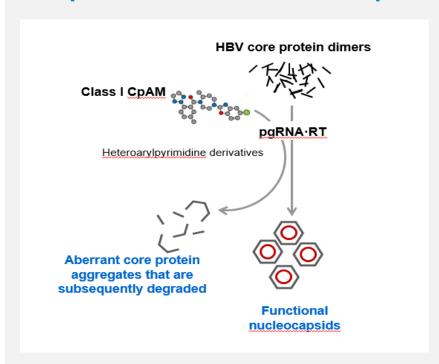


## **CpAM (RG7907)**



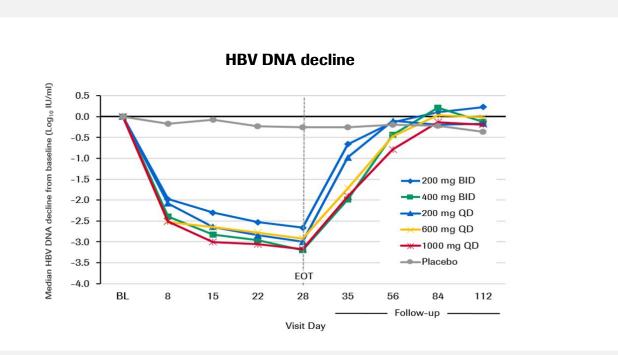
## Leads to incorrect assembly of HBV core protein followed by degradation

#### **Core protein allosteric modulator (CpAM)**



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

#### Ph I (dose finding)



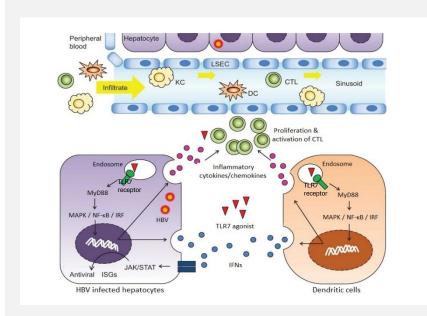
- Strong HBV DNA decline in all patients within first week of treatment
- 81% (13/16) HBeAg-negative patients achieved HBV DNA levels below LLOQ (20 IU/ml)





# TLR7 agonist (RG7854) Stimulating innate and adaptive antiviral response via TLR7 pathway

#### 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

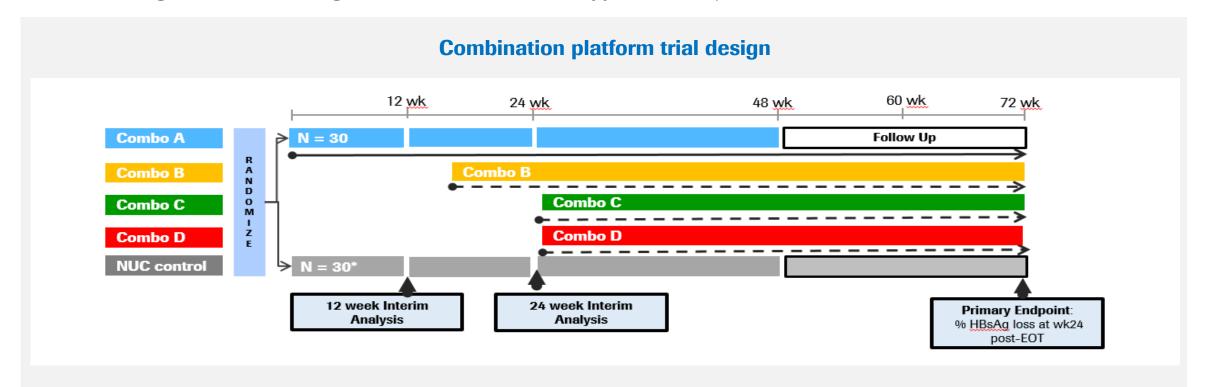
#### Ph I (dose finding) results

	ISG15		OAS1		
Dose (mg)	Fraction responding	Geometric mean fold change (range)	Fraction responding	Geometric mean fold change (range)	
Placebo	0/16	-	0/16	-	
3	1/8	2.4 (2.4–2.4)	0/8	=	
10	0/8	-	0/8	-	
20	1/8	2.6 (2.6–2.6)	0/8	-	
40	1/8	2.9 (2.9–2.9)	0/8	-	
60	1/8	2.6 (2.6–2.6)	2/8	2.4 (2.0-2.9)	
100	6/8	5.9 (2.3-29.3)	5/8	3.8 (1.9-6.9)	
140	8/8	11.6 (2.3–48.0)	8/8	5.5 (2.2–18.1)	
170	8/8	11.2 (2.5–132.2)	8/8	5.5 (2.0–19.0)	

- Dose dependent immunomodulatory activity established
- TLR7 activation induces mRNA expression of interferon-inducible genes (e.g. ISG15, OAS1) first observed at 100 mg dose and plateaued at 170 mg dose



## Highly adaptive HBV combination platform Screening novel drug combinations efficiently



- Nimble and adaptive platform for Ph II screening with shared control arm
- First interim analysis after 12 weeks; second interim analysis after 24 weeks; interim analysis helps inform combos B, C and D
- Opportunity to seamlessly add and terminate different drug combinations

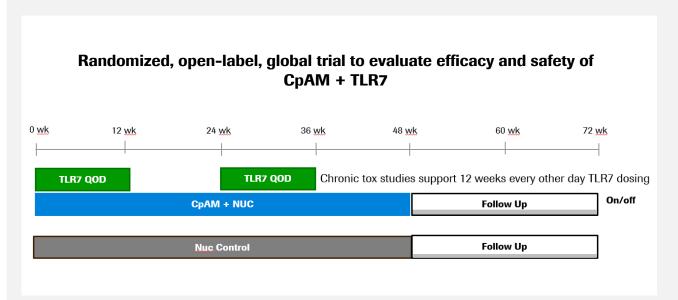






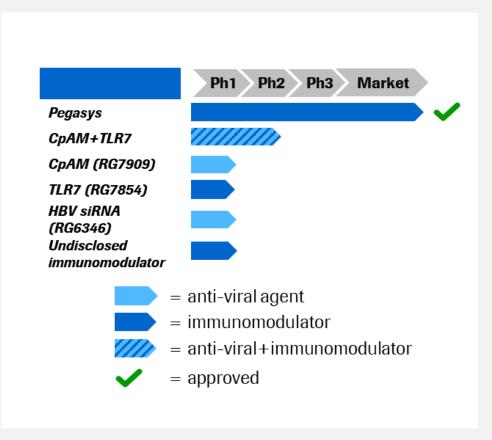
## First combination to move into Ph II testing

#### Ph II combination trial design



- Ph II combination trial (n=60) started in Q3 2020
- First 12-week interim analysis planned for Q2 2021
- A 4<sup>th</sup> HBV program molecule (undisclosed novel immunomodulator) moved into Ph I testing

#### **Overview HBV development program**





## **Roche Pharma Day 2020**

## Late Stage Immunology, Ophthalmology and Infectious Disease

**Cristin Hubbard** | Senior Vice President Immunology, Infectious Disease & Ophthalmology, Global Product Strategy



## Roche's response to the pandemic Commitment every step of the way

## **Diagnostics**

- Research & development for best-in-class solutions
- Deliver high quality diagnostics with flexible throughput
- Strong local support and partnership
- Holistic disease and patient-oriented approach

- SARS-CoV-2 PCR, Ab & rapid antigen test
- SARS-CoV-2/Influenza A/B differentiation test
- Other routine and diagnostic tests







- Innovative therapies with various MOAs
- World-leading biologics manufacturing capacity
- Strong partnerships with healthcare ecosystems across the globe

- Xofluza
- Actemra
- REGN-COV2 nAB cocktail











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## Xofluza in influenza A/B

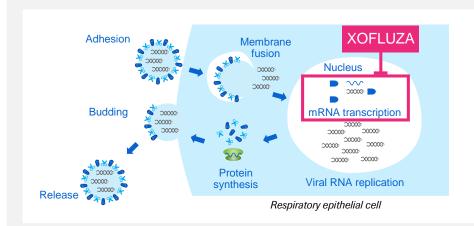




Ph III studies «prevention of transmission» and infants on-going

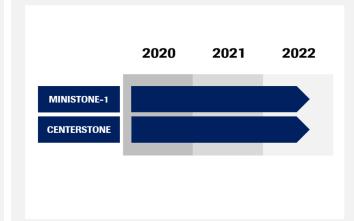
FDA emergency use authorization

#### **CAP** dependent endonuclease inhibitor



- First-in-class small molecule inhibiting viral RNA replication; stops viral shedding + reduces viral load significantly faster than the current SOC
- Oral, single-dosing
- Safety similar to placebo
- Activity against Tamiflu-resistant and avian strains (H7N9, H5N1)

#### Ph III development



## SARS-CoV-2 & Influenza A/B test for cobas 6800/8800

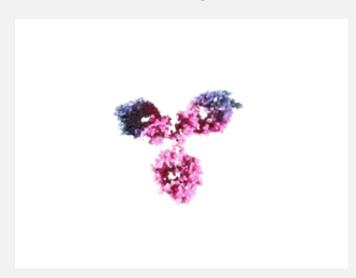


- Ph III (miniSTONE-1) for infants < 1yr; results expected in 2022</li>
- Ph III (CENTERSTONE) for prevention of influenza transmission; results expected 2022
- Xofluza approved for healthy people in 24 countries; Global filings for high-risk patients, pediatrics, post-exposure prophylaxis on-going
- FDA emergency use authorization for the cobas SARS-CoV-2 + Influenza A/B test with a single sample, obtained in Q3 2020



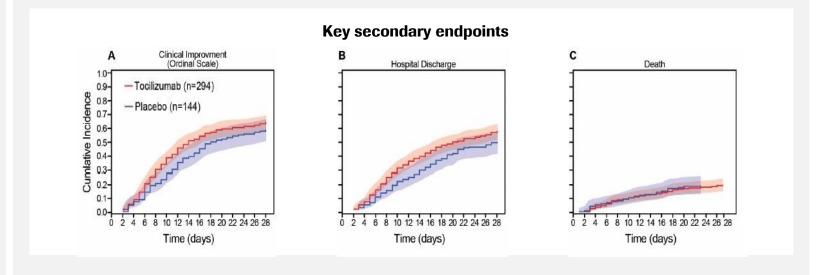
# Actemra in severe COVID-19 associated pneumonia Ph III COVACTA: Primary and key secondary endpoints not met

#### **Anti-IL6 receptor mAb**



- Initially approved in RA and GCA
- Approved for CAR T-cell-induced cytokine release syndrome
- Ph III program (REMDACTA, EMPACTA, MARIPOSA, J-COVACTA) in COVID-19 associated pneumonia on-going\*

#### Ph III (COVACTA) in severe COVID-19 associated pneumonia<sup>1</sup>



- Ph III (COVACTA) did not meet its primary endpoint of improved clinical status of patients or key secondary endpoint of reduced mortality at day 28
- Potentially clinically meaningful benefits in time to hospital discharge and duration of ICU stay
- Ph III (REMDACTA) results for Actemra + remdesivir expected in Q4 2020

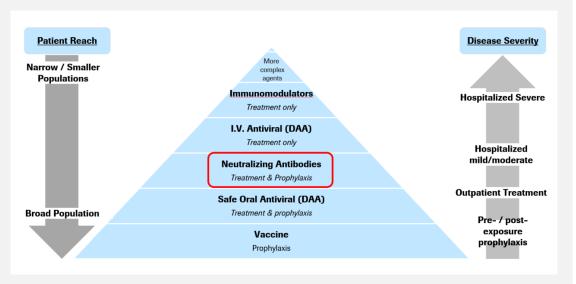
# Neutralizing antibodies (nAbs) against SARS-CoV2 Promising for treatment and prophylaxis



# REGN-COV2 (nAb cocktail) REGN10987 REGN10983 Antibodies block the virus's Spike protein, neutralizing its ability to bind and infect

- Two potent, virus-neutralizing Abs binding non-competitively to the critical receptor-binding domain of the virus's spike protein
- The virus would need to have multiple simultaneous mutations at multiple genetic sites in order to escape the nAb cocktail, which is an unlikely scenario\*

#### nAb cocktails for treatment & prophylaxis



#### Currently enrolling trials:

- Ph II/III study in hospitalized COVID-19 patients
- Ph II/III study in non-hospitalized COVID-19 patients
- Ph I multidose study in adult volunteers (pre-exposure)
- Ph III prophylaxis of housemates of infected individuals \*\*
- First results expected in September 2020

<sup>\*</sup> A. Baum et al., Science 10.1126/science.abd0831 (2020); In collaboration with Regeneron; \*\* In collaboration with NIAID



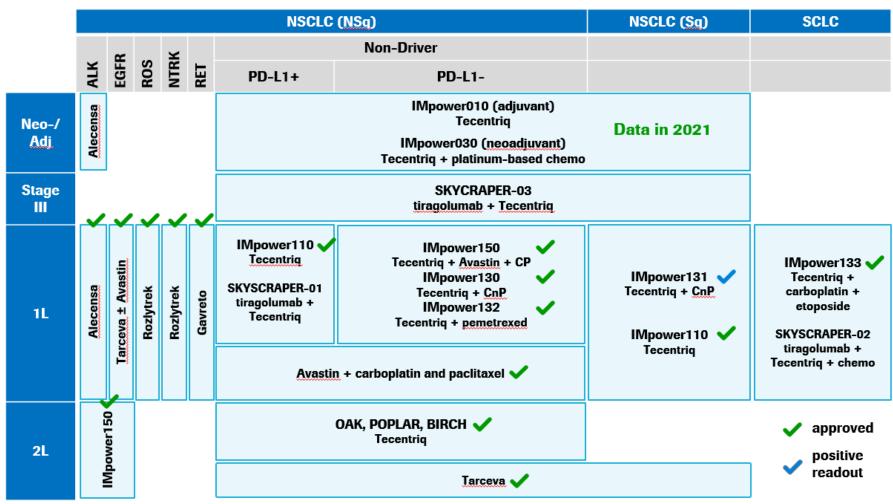
## Doing now what patients need next



## Roche Virtual Late Stage Pipeline Event 2020 Appendix



# Lung cancer franchise overview Expanding coverage throughout lung cancer

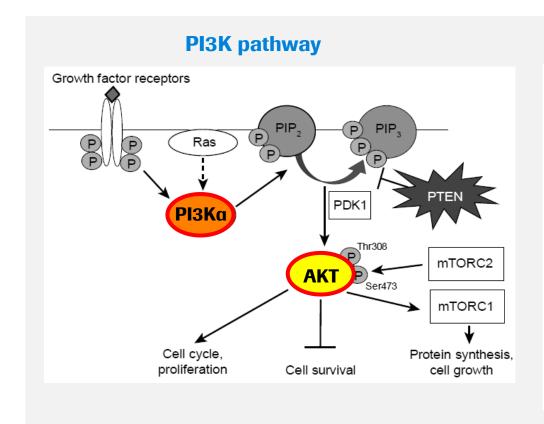


<sup>\*</sup> IMpower132 approved in Japan

NSq=non-squamous; Sq=squamous

## PI3K/AKT is the most frequently altered pathway in cancer





#### **Frequency of PI3K mutations across tumor types**

Tumor type	PIK3CA mutation
HR+ Breast Cancer	~40%
Ovarian	~33%
Endometrial	~25%
HER2+ Breast Cancer	~25%
Colon	~20%
Bladder	~20%
Cervix	~20%
HNSCC	~15%
TNBC	~8%
Gastric	~7%

14 million cancer patients diagnosed annually world wide, ~17% are *PIK3CA* mutant ~2.4M patients



## Doing now what patients need next