
Roche

Roche Pharma Day 2023

London, 11 September 2023

This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

1 pricing and product initiatives of competitors;
2 legislative and regulatory developments and economic conditions;
3 delay or inability in obtaining regulatory approvals or bringing products to market;
4 fluctuations in currency exchange rates and general financial market conditions;
5 uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6 increased government pricing pressures;
7 interruptions in production;
8 loss of or inability to obtain adequate protection for intellectual property rights;
9 litigation;
10 loss of key executives or other employees; and
11 adverse publicity and news coverage.

Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche’s earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website www.roche.com

Welcome

Bruno Eschli |
Head of Investor Relations

Agenda

Welcome
10:30 – 10:35 BST Bruno Eschli, Head of Investor Relations

Group Update
10:35 – 11:05 BST Thomas Schinecker, CEO Roche Group

Pharma Update and On-Market Portfolio
11:05 – 11:40 BST Teresa Graham, CEO Roche Pharmaceuticals

Late Stage Pipeline Oncology (Solid Tumors)
11:40 – 12:00 BST Levi Garraway, CMO and Head Global of Product Development

12:00 – 12:50 BST **Lunch Break**

Late Stage Pipeline Hematology
12:50 – 13:05 BST Charles Fuchs, SVP Global Head of Oncology and Hematology Product Development

Late Stage Pipeline Neuroscience, Immunology and Cardiovascular-Metabolism
13:05 – 13:30 BST Paulo Fontoura, SVP and Global Head of Neuroscience and Immunology

Late Stage Pipeline Ophthalmology
13:30 – 13:45 BST Christopher Brittain, VP and Global Head of Ophthalmology Product Development

13:45 – 14:30 BST **Q&A**

14:30 – 15:00 BST **Buffet reception**

Roche Pharma Day 2023

Group Update

Thomas Schinecker
CEO Roche Group

New Leadership Team

Performance and Outlook

Pharma R&D Excellence

Upcoming IR Events

Corporate Executive Committee since April 2023

Pharma R&D functions from early to late stage and partnering represented

Dr. Thomas Schinecker
Chief Executive Officer
Roche Group

Teresa Graham
CEO Roche
Pharmaceuticals

Matt Sause
CEO Roche Diagnostics

Dr. Alan Hippe
Chief Financial and
Information Officer

Cristina A. Wilbur
Chief People Officer

Claudia Böckstiegel
General Counsel

Prof. Dr. Hans Clevers
Head of Pharma Research
and Early Development
(pRED)

Dr. Aviv Regev
Head of Genentech
Research and Early
Development (gRED)

Dr. James H. Sabry
Global Head of Pharma
Partnering

Dr. Levi Garraway
Head of Global Product
Development and Chief
Medical Officer

Silke Hörnstein
Head of Corporate Strategy
and Sustainability

Barbara Schädler
Head of Group
Communications

Corporate Executive Committee: New members

Experienced leaders with breadth of scientific, commercial and strategic experience

Dr. Thomas Schinecker
Chief Executive Officer
Roche Group

Teresa Graham
CEO Roche
Pharmaceuticals

- Excellent track record in multiple Pharma functions and across the portfolio
- Accomplished leader with strength in commercial operations combined with scientific depth

Matt Sause
CEO Roche Diagnostics

- 20 years at Roche, experience in Diagnostics and Pharma
- Numerous country general management and global product leadership roles
- Successful leadership of Diagnostics' North America region

Dr. Levi Garraway
Head of Global Product Development and Chief Medical Officer

- Outstanding career at Dana-Farber, Harvard Medical School, and the Broad Institute
- Award-winning cancer researcher with multiple breakthrough discoveries in cancer genomics and precision medicine

Silke Hörnstein
Head of Corporate Strategy
and Sustainability

- 20 years at Roche, experience across general management, global product and strategy leadership roles
- Successfully led Roche Diagnostics' transformation efforts including new strategy and implementation

Claudia Böckstiegel
General Counsel

Prof. Dr. Hans Clevers
Head of Pharma Research
and Early Development
(pRED)

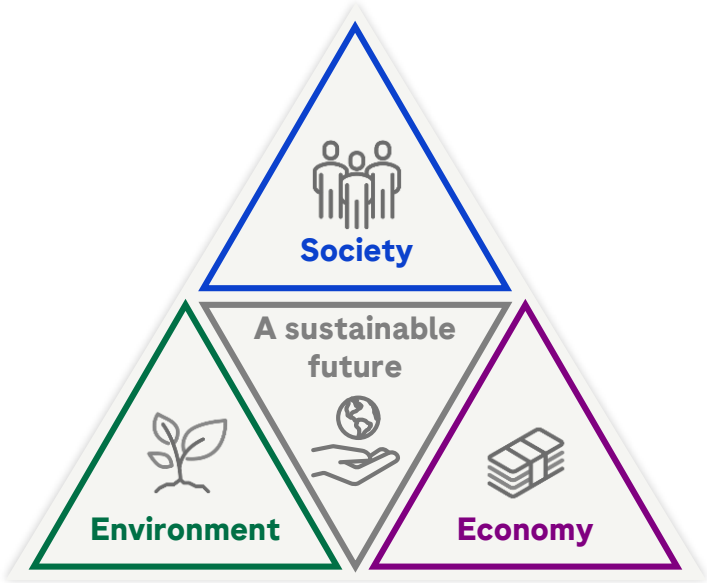
Barbara Schädler
Head of Group
Communications

Sustainability now represented on CEC level

ESG is part of everything we do

- Develop **new medicines, diagnostics** and **integrated health solutions** that address the needs of diverse patient communities
- **Increase access to our innovations** globally with local communities in mind
- **Care for our employees** by prioritizing safety and health, promoting diversity, inclusion and equal opportunities

- **Halve the environmental impact** of our operations and products from 2019-2029
- **Reduce greenhouse gas emissions** to **net zero** no later than 2050
- **Partner with suppliers** to reduce their greenhouse gas emissions



- Invest in **innovation and medical advances**
- Contribute to **economic growth** in over 100 local economies
- **Provide jobs** and **ensure livelihoods**

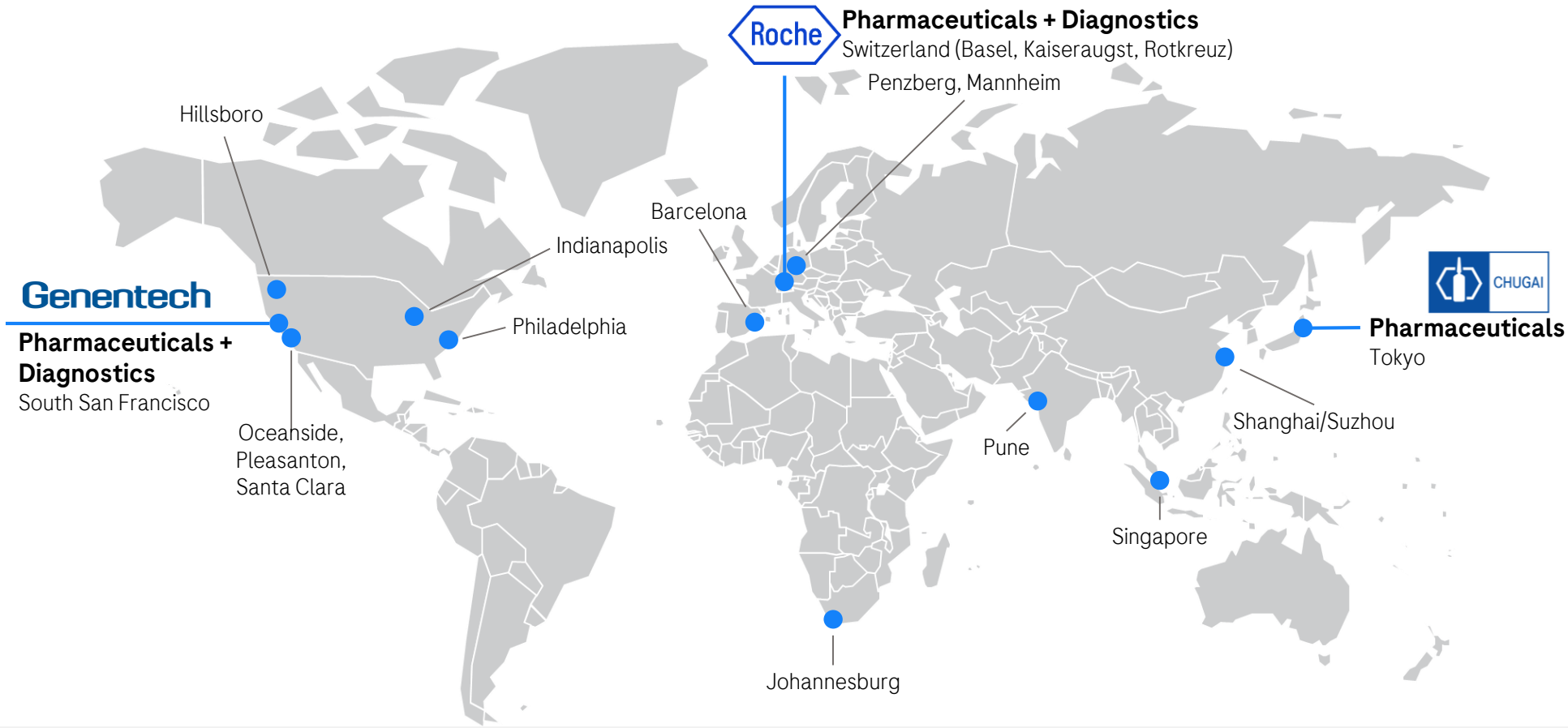
New Leadership Team

Performance and Outlook

Pharma R&D Excellence

Upcoming IR Events

Global Roche network delivering patient benefits worldwide



14mn	Patients treated with Roche medicines in 2022
29bn	Test conducted with Roche systems in 2022
14 yrs	in a row ranked as one of the top 3 most sustainable healthcare companies[1]

[1]Dow Jones Sustainability Indices

Our achievements

Roche is continuously shifting the standard of care

A legacy of patient and business impact...

16	Blockbuster drugs in 2022, up from 7 in 2012
#1	in neurology and hemophilia A[1]
#3	in oncology[1]
#1	in *in vitro* diagnostics[1]
#1	top pharma as ranked by rare disease patient groups[2]
#1	Pharma in AI readiness[3]

...with a track record of establishing standard of care across new therapeutic areas

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

First and only therapy approved for RMS/PPMS

HEMLIBRA emicizumab-kxwh injection for subcutaneous use 150 mg/mL

First and only prophylactic treatment for hemophilia A with/without inhibitors

VABYSMO

First bispecific antibody in AMD and DME

Evrysdi® risdiplam 60 mg powder for oral solution

First-in-class splicing modifier for the treatment of SMA

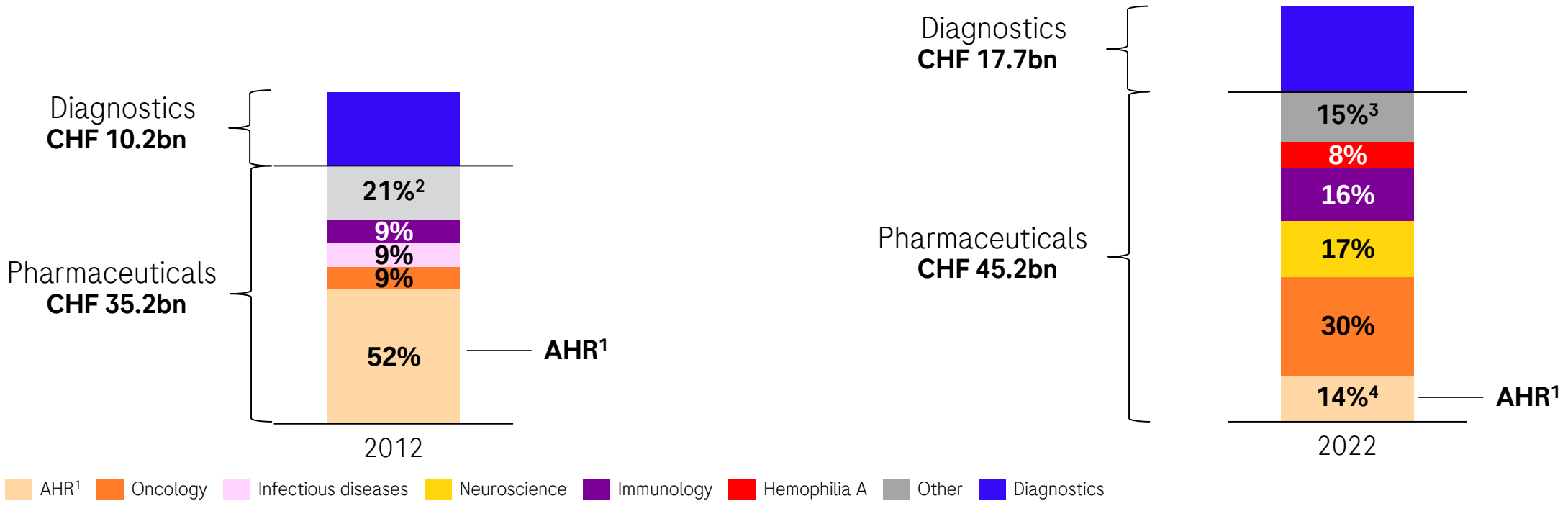
[1]based on FY 2022 sales (Evaluate/Bloomberg); [2]Patient View, 2023; [3]CBInsight, 2023; AI=artificial intelligence; RMS=relapsing; PPMS=primary progressive multiple sclerosis; AMD=age-related macular degeneration; DME=diabetic macular edema; SMA=spinal muscular atrophy

Roche delivered consistent growth through biosimilar erosion

Successful diversification of our portfolio

From three oncology assets driving ~50% of sales in 2012...

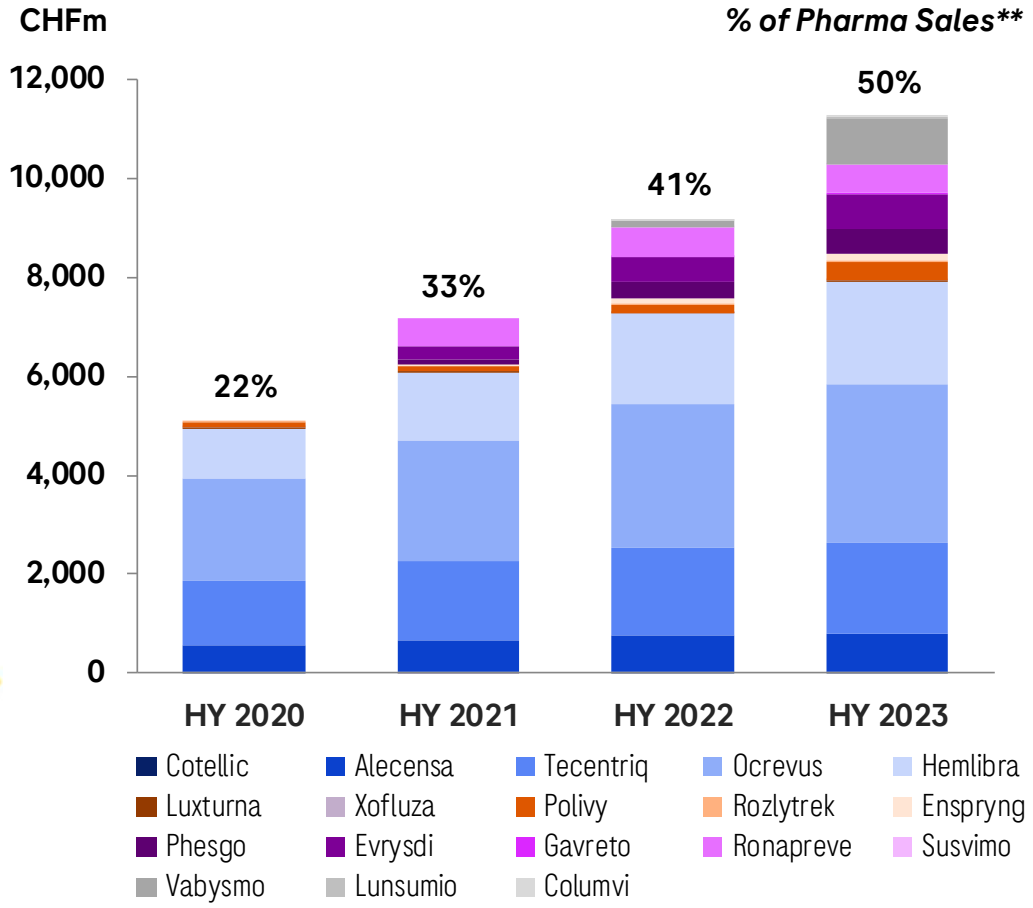
... to a diversified portfolio with assets that span multiple therapeutic areas today



1 AHR: Avastin, Herceptin, Rituxan; 2 Includes Metabolism (5%), Ophthalmology (4%), Respiratory (3%), Cardiovascular (3%) and others (6%); 3 Includes Infectious Diseases (5%), Ophthalmology (4%) and others (7%); 4 Reduction in AHR sales due to Loss of Exclusivity and biosimilar competition. Source: Roche Annual Report 2012, Roche Annual Report 2022, Roche Finance Report 2022

Young portfolio: 20 NMEs launched since 2015 driving growth

Keeping launch momentum with two NMEs approved in 2023

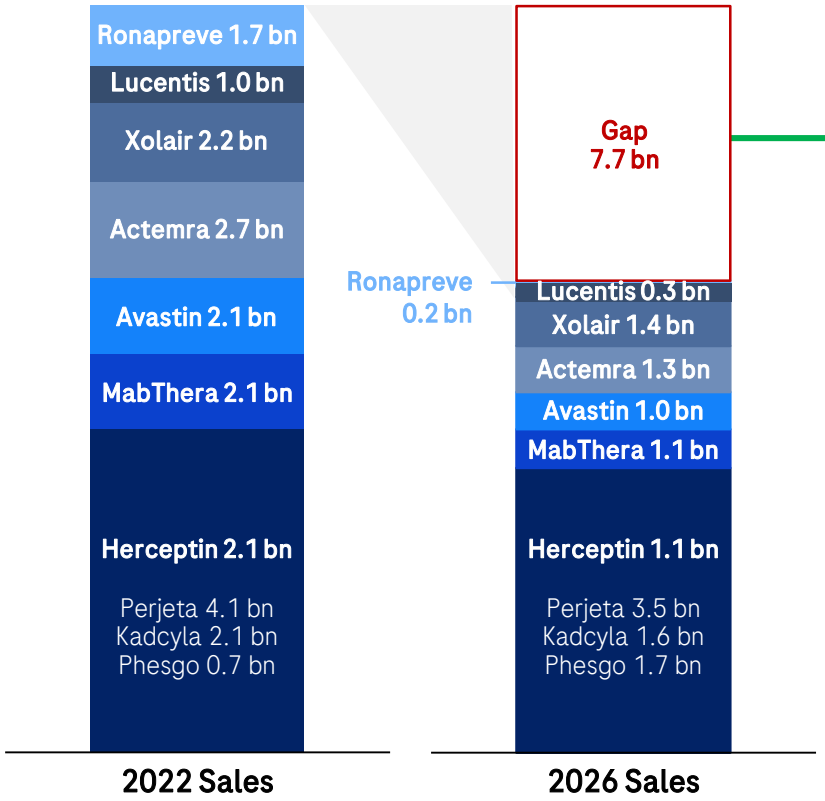


Young portfolio defined as all launches since end of 2015; * Elevidys: Accelerated US approval by partner company Sarepta; ** Venclexta sales booked by AbbVie and therefore not included

Consensus outlook 2022-26*

Growth driven by our young on-market portfolio; potential pipeline up-side

Biosimilar gap (22-26)



Consensus sales growth (22-26)

Post-HY 2023 consensus survey

Vabysmo	4.3 bn
Tecentriq	1.7 bn
Hemlibra	1.6 bn
Ocrevus	1.5 bn
Polivy	1.4 bn
Evrysdi	1.2 bn
Lunsumio	0.7 bn
Columvi	0.5 bn
Gazyva	0.4 bn
Alecensa	0.3 bn
Enspryng	0.3 bn
Susvimo	0.2 bn
Other in-market[1]	(0.5) bn
Pipeline Ph III[2]	**2.4 bn**
thereof Elevidys	*0.8 bn*
thereof tiragolumab	*0.7 bn*
thereof giredestrant	*0.3 bn*
thereof crovalimab	*0.3 bn*
thereof fenebrutinib	*0.2 bn*
Total	**16.1 bn**

Potential up-side[3]

Additional up-side by late-stage NMEs / LEs poorly or not yet covered:

Oncology (inavolisib, divarasib, tobemstomig, autogene cevumeran), **Hematology** (SPK-8011), **Ophthalmology** (ASO factor B in GA, anti-IL-6 mAb, Enspryng in TED), **Neuroscience** (Enspryng in gMG, anti-latent myostatin mAb, trontinemab, prasinezumab), **Immunology** (Gazyva in LN, astegolimab, ASO Factor B in IgAN), **Cardiovascular & Metabolism** (zilebesiran)

*All estimates are based on Post HY 2023 consensus collected by FTI Consulting on behalf of Roche (n=18); [1] Activase/TnKase, Esbriet, Pulmozyme, CellCept, Erivedge, Cotellic, Gavreto, Xofluza, Rozlytrek; Luxturna
[2] included in >50% of the sell-side models; [3]Assets covered on average by only 17% of the sell side models; NME=new molecular entity; LE=line extensions

Important launches ahead in Diagnostics

Diagnostics to deliver mid to high single digit growth in coming years

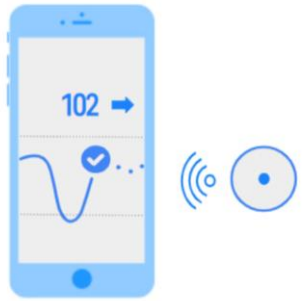
Core & Molecular Lab

- Menu expansion driving growth, averaging >25 assay launches/approvals per year[1]
- >240 assays running on >100k installed cobas® serum work area instruments
- >2.5k installed cobas® 6800/8800/ 5800 instruments

Mass spectrometry

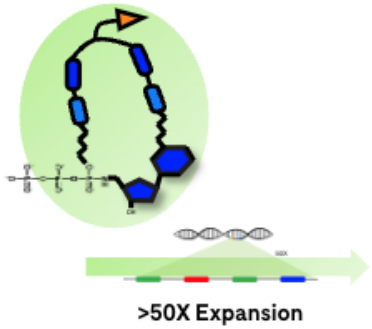
- First fully integrated and automated mass spectrometry
- Launch menu complimentary to immunoassay offering, including >40 key parameters at launch
- CE launch planned for end of 2024 (FDA approval expected in 2025)

Continuous glucose monitoring (CGM)



- Subcutaneously inserted sensor to measure glucose values in interstitial fluid
- Personalized management of diabetes
- Digital tools to support disease management for users and healthcare professionals

Next generation sequencing (NGS)



- Unique sequencing by expansion technology, significantly improving nanopore performance
- Nanopore system delivers flexible run size at competitive cost

1. average 2018 – 2022; excludes claim extensions for new instruments, excludes Biotin updated assays, COVID-19, Custom Biotech, TiB Molbiol & Genmark, RUOs, IVDR transitions; CGM=continuous glucose monitoring; NGS=next generation sequencing

FY guidance confirmed - strong half year performance

Base business with continued strong momentum; COVID sales washed-out by Q1 24

Guidance[1]

Pharma: Key products with strong growth and momentum from ongoing launches

Diagnostics: Base business with solid growth

COVID-19 sales for Diagnostics and Pharma expected to decline by roughly CHF 5bn

AHR[2] sales expected to erode by roughly CHF 1.6bn

HY Results

Pharma: +8% in CER; +32% from products launched since 2015 ✓

Diagnostics: +6% in CER ✓

COVID-19 sales: CHF -2.7bn ✓

AHR[2] sales: CHF -0.6bn ✓

1 At Constant Exchange Rates (CER); 2 AHR: Avastin, Herceptin, Rituxan/MabThera

New Leadership Team

Performance and Outlook

Pharma R&D Excellence

Upcoming IR Events

Roche R&D has multiple proven strengths

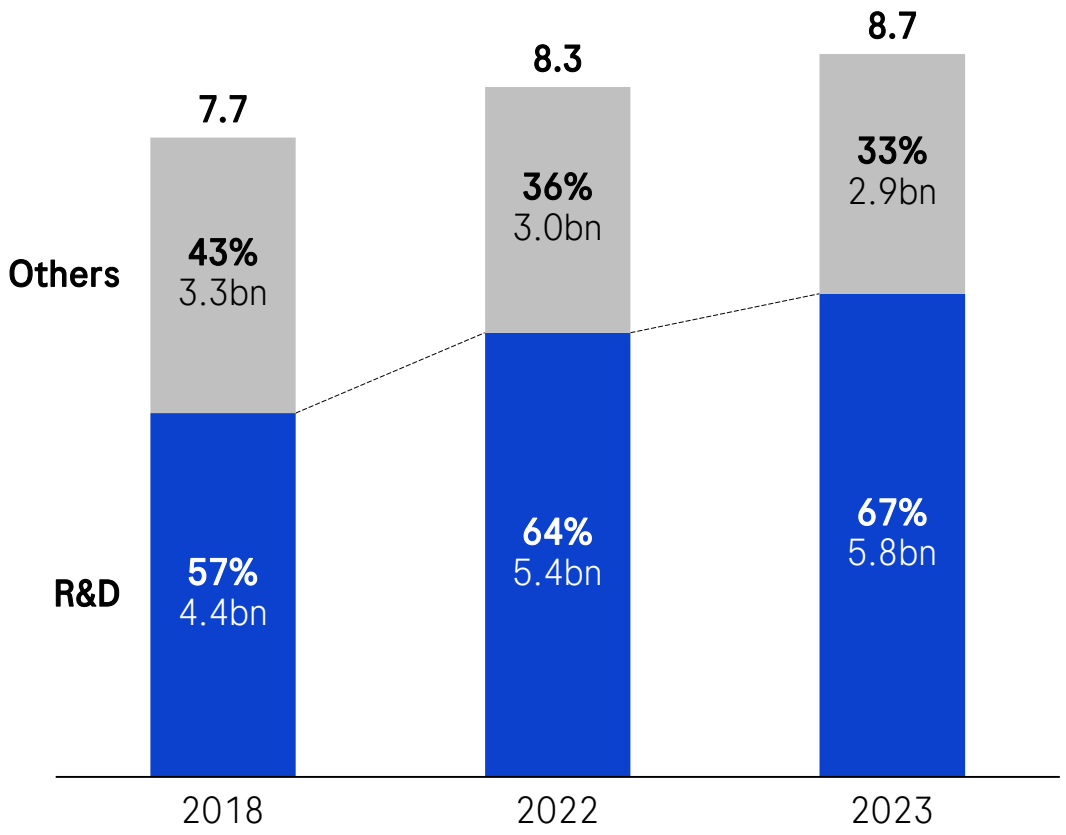
Strategy and portfolio	• Commitment to scientific excellence and discovery of novel modalities (e.g. ADCs, bispecifics) • Ability to expand successfully into new therapeutic areas
Operating model and structure	• Autonomous early stage R&D units gRED, pRED and Chugai, specialized in their respective domains • Successfully launched 20 NMEs in the last 8 years
Talent, culture and mindset	• Breadth and depth of expertise across a range of disease areas • Leaders in emerging areas such as computational biology, new disease models, and protein engineering
Capabilities, tech, and AI	• Strong organizational loyalty, external reputation and ability to attract top scientific talent • Leveraging thought leadership in generative AI and deep learning approaches

NME=new molecular entity; AI=artifical intelligence; ADC=antibody drug conjugate

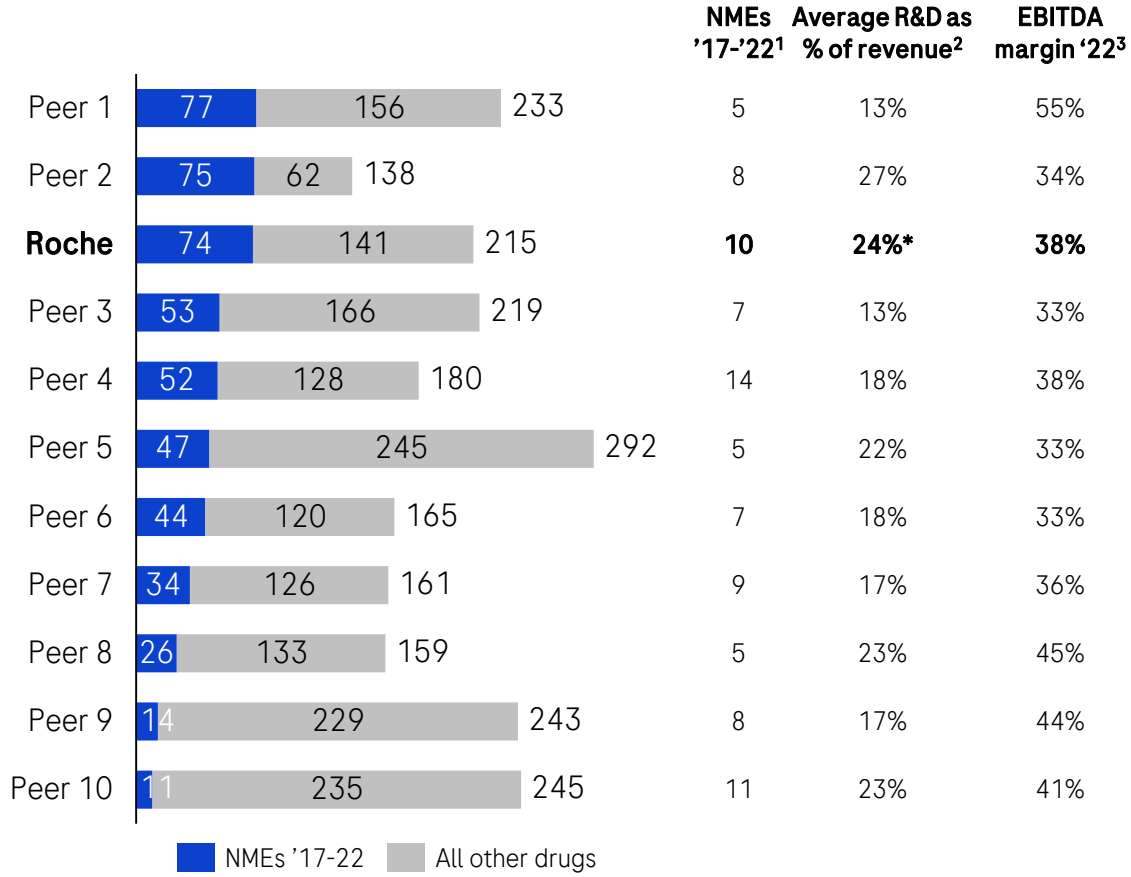
Commitment to innovation

After reallocating resources to R&D, focus is now on 'R&D Excellence'

HY Roche Pharma R&D investment allocation (2018-2023, % of OPEX, CHF bn)



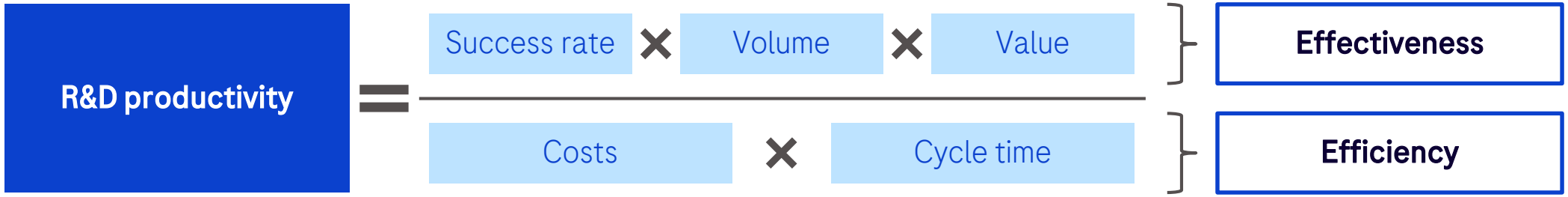
R&D investment and profitability[1] Recently approved NME share of NPV (2022, USD bn)



1 Evaluate Pharma, 2017-H1 2022 data; 2 Company financial reports 2018-2022; 3 Bloomberg; *Roche Pharma only

Holistic, end-to-end analysis of our R&D productivity

Commitment to delivering the worlds most impactful medicines



Holistic and end-to-end

- Teams from early to late stage development, and commercial involved
- *'Leave no stone unturned'* analysis

Strong base

- Ability to capitalize on significant past investments, for example:
  - Breadth of disease area talent
  - Computational biology expertise
  - Platform technologies

New opportunities

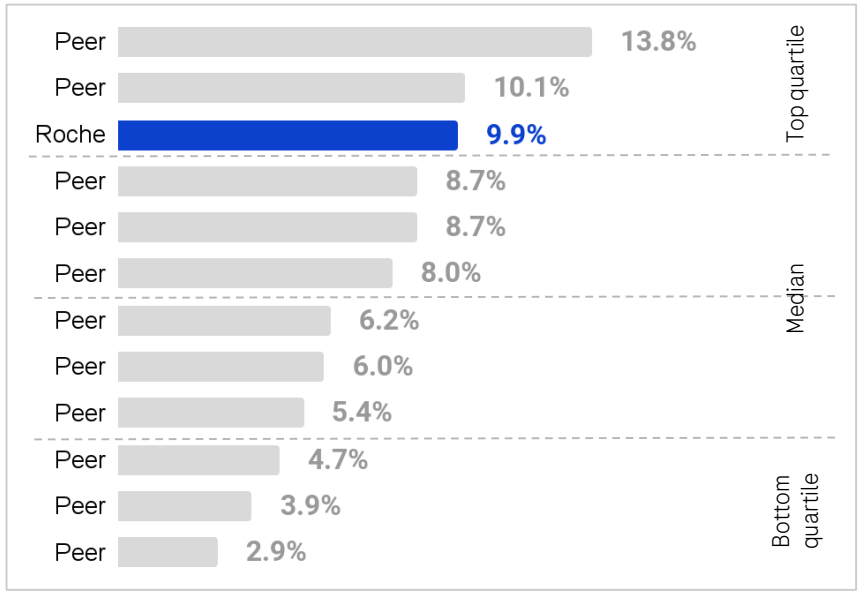
- RWD and AI/ML, computational biology and advanced analytics
- Application of new technologies in R&D
- Institute of Human Biology (IHB)

RWD=real-world data; AI/ML=artificial intelligence/machine learning

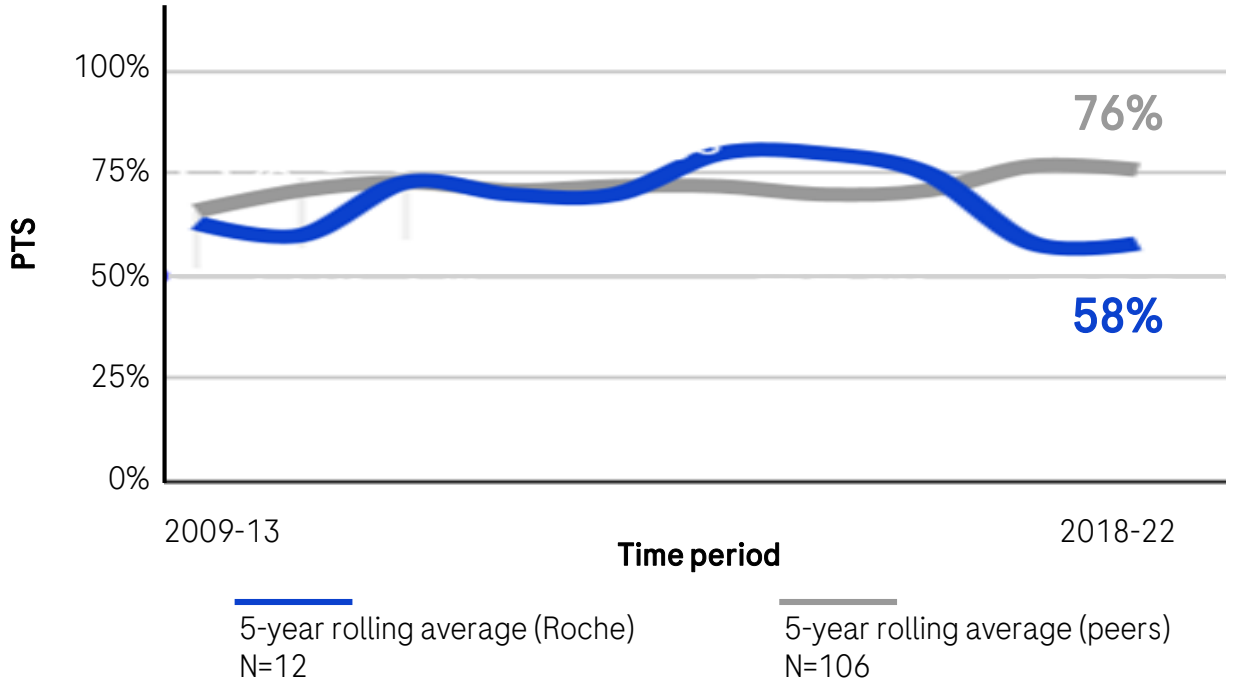
Roche with leading success rate by molecule...

...but higher Phase III failure rate recently

Molecule success (PoL Preclinical - Approval)
2018-22 Industry Distribution



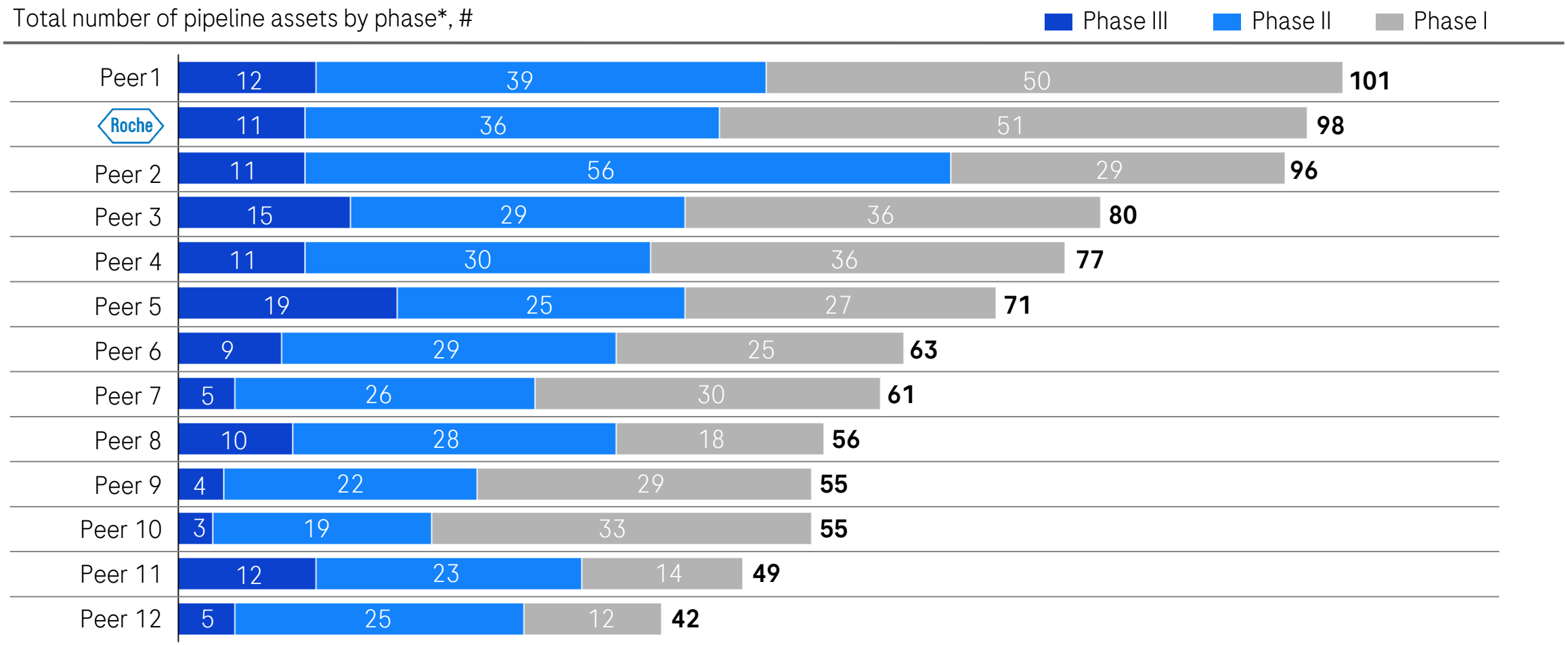
Molecule Success Rate in Phase III*
2009-13 to 2018-22



*Values on the Molecule Success Rate trend in phase III graph represent outcomes in the 2018-22 horizon. Graphs start with 2009-13 data and then show 5-year average trend through 2018-22 horizon; PTS=probability of technical success; Source: KMR Benchmarking analysis

Number of pipeline assets in Phase I to III

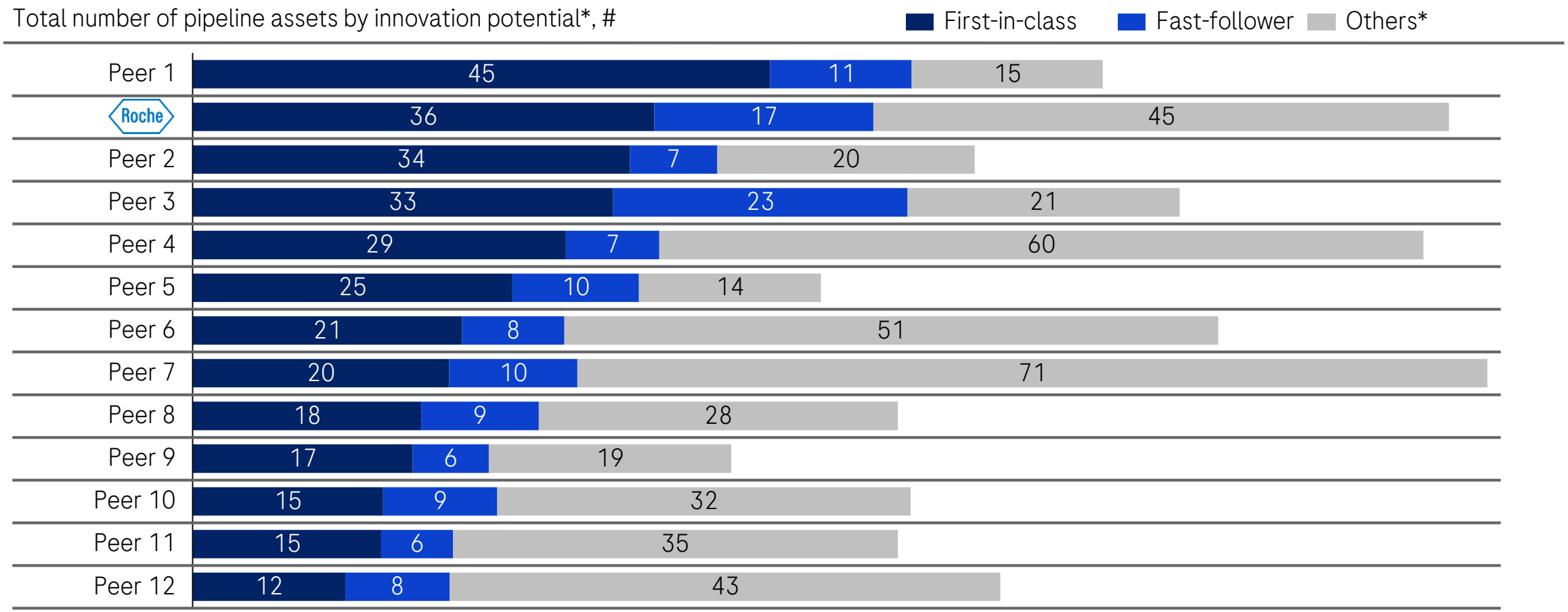
Roche ranks #2 in total pipeline volume



*Excludes pipeline products in pre-registration, registration and filed; Peer 1-12 are other large-cap Pharma
Source: Pharmaprojects (February 2023), McKinsey attrition analytics

Pipeline assets segmented by innovation potential

Roche ranks #2 in number of NMEs with first-in-class potential

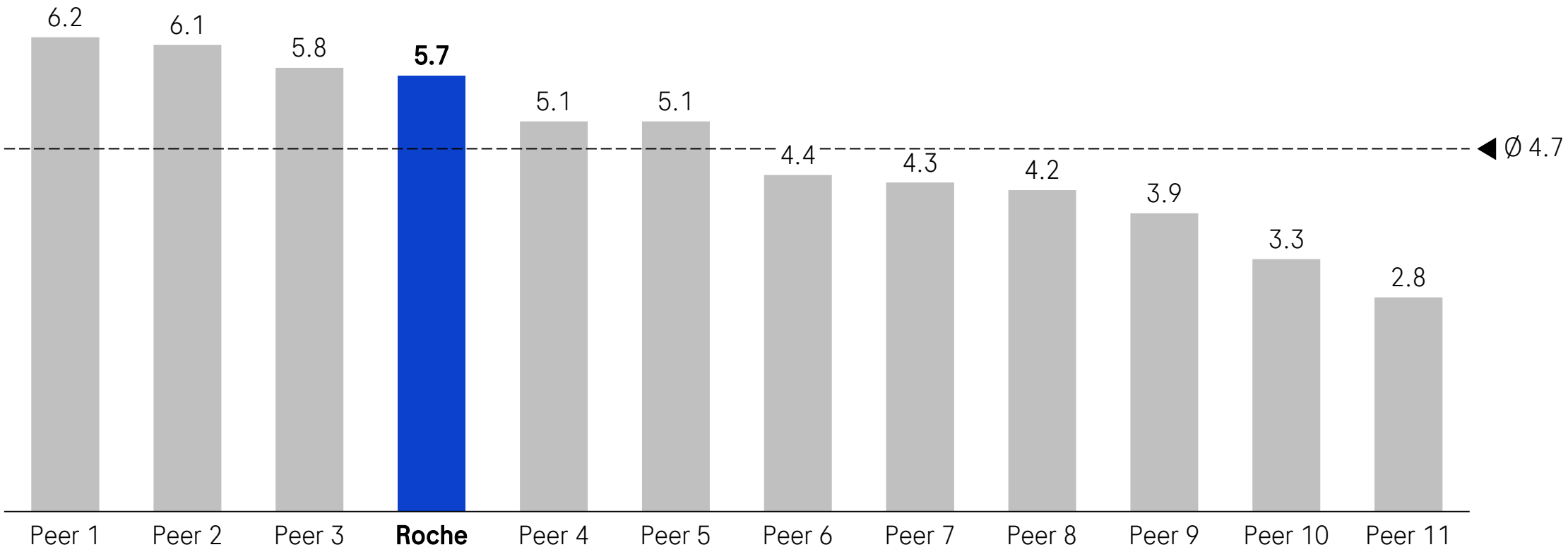


*NMEs that are neither first-in-class or best-in-disease, or without disclosed MoA, are grouped as 'Others'; Peer 1-12 are other large-cap Pharma
Source: Pharmaprojects (March 2023)

R&D spend per NME launch

Roche spend is above industry average

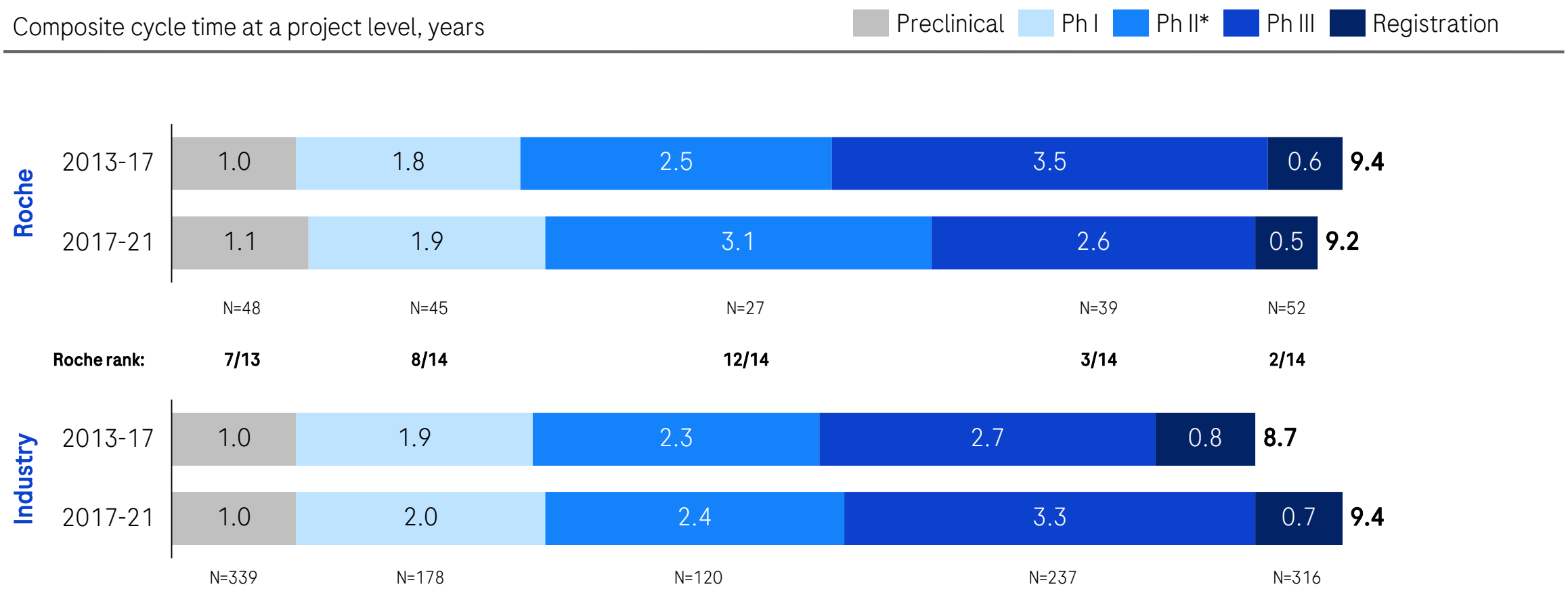
R&D spend per NME launch[2], bn USD, 2018-2022[1]



1. Average annual pharmaceutical R&D Spend from 2018-2022 (device and generics R&D spend excluded whenever reported separately). Pre-acquisition R&D spend for mega-merged entities (M&A >$10Bn) is included to account for NME pipeline continuity; Only asset products sales included; 2. Restricted to NMEs launched 2018-23 with visible revenues for that company (any year in visible forecast data). NME = New Molecular Entity (including novel biologics). Partnered launches can be assigned to multiple companies if there are revenues associated with several players; Source: EvaluatePharma March 2023

Development timelines compared to industry

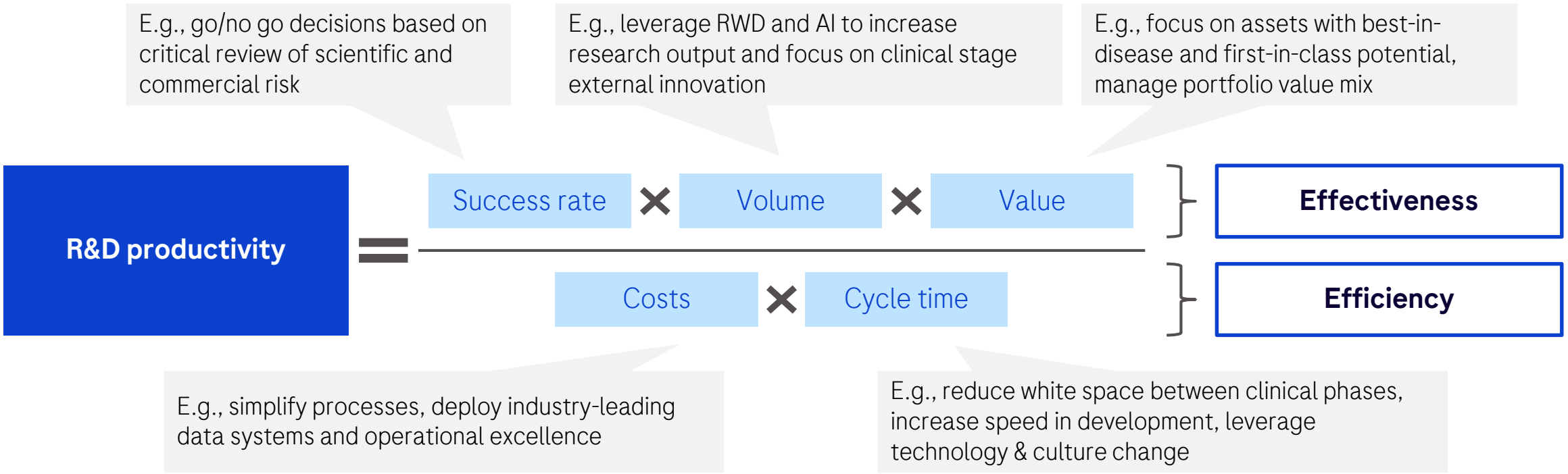
Roche with faster than average Phase III cycle time, but lagging in Phase II



* Phase II cycle time encompasses Phase Ib expansions (in Oncology), single arm Phase IIs and randomized Phase IIs. A great portion of projects in Phase II are Oncology Phase Ib expansions, where a higher SoC bar in most indications (requiring assessment of time-to-event endpoints in order to ungate a larger Phase III study) might be one of the factors contributing to longer duration over time

Composite cycle time only includes projects which successfully completed a certain phase in the time window of interest and is calculated by the sum of each phase cycle time (sum of median CT for all projects which completed Preclinical, Ph1, Ph2, Ph3, Registration in the time window of interest, e.g., 2017-21). This method allows for a more current view of phase completion, as each phase is calculated using the most current CT window. Projects originated externally are included in the calculation (if in-licensed and/or acquired mid-stream, CT calculated from the start of the following phase); Source: KMR

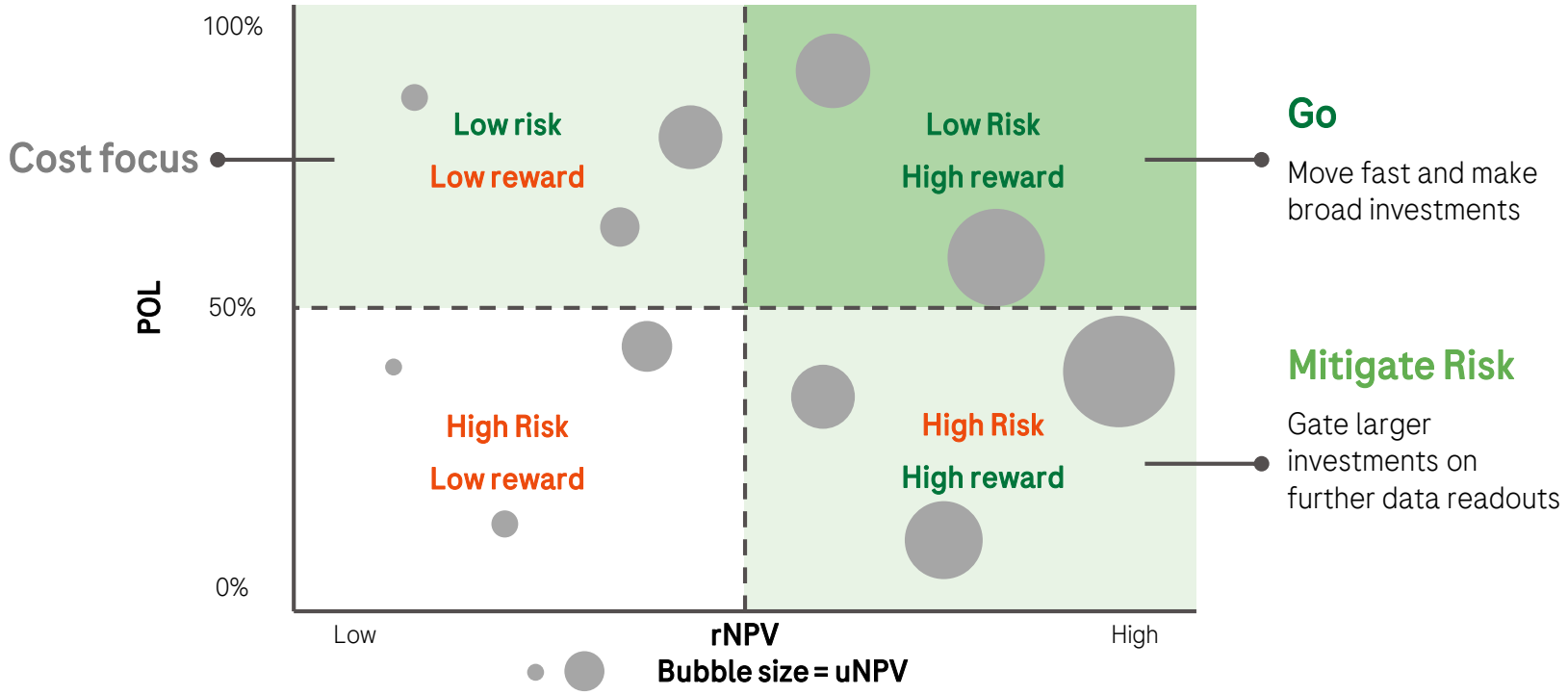
Levers to drive R&D excellence were identified



RWD=real-world data; AI=artificial intelligence

Prioritization of our R&D investments

Pharma portfolio management with an end-to-end perspective



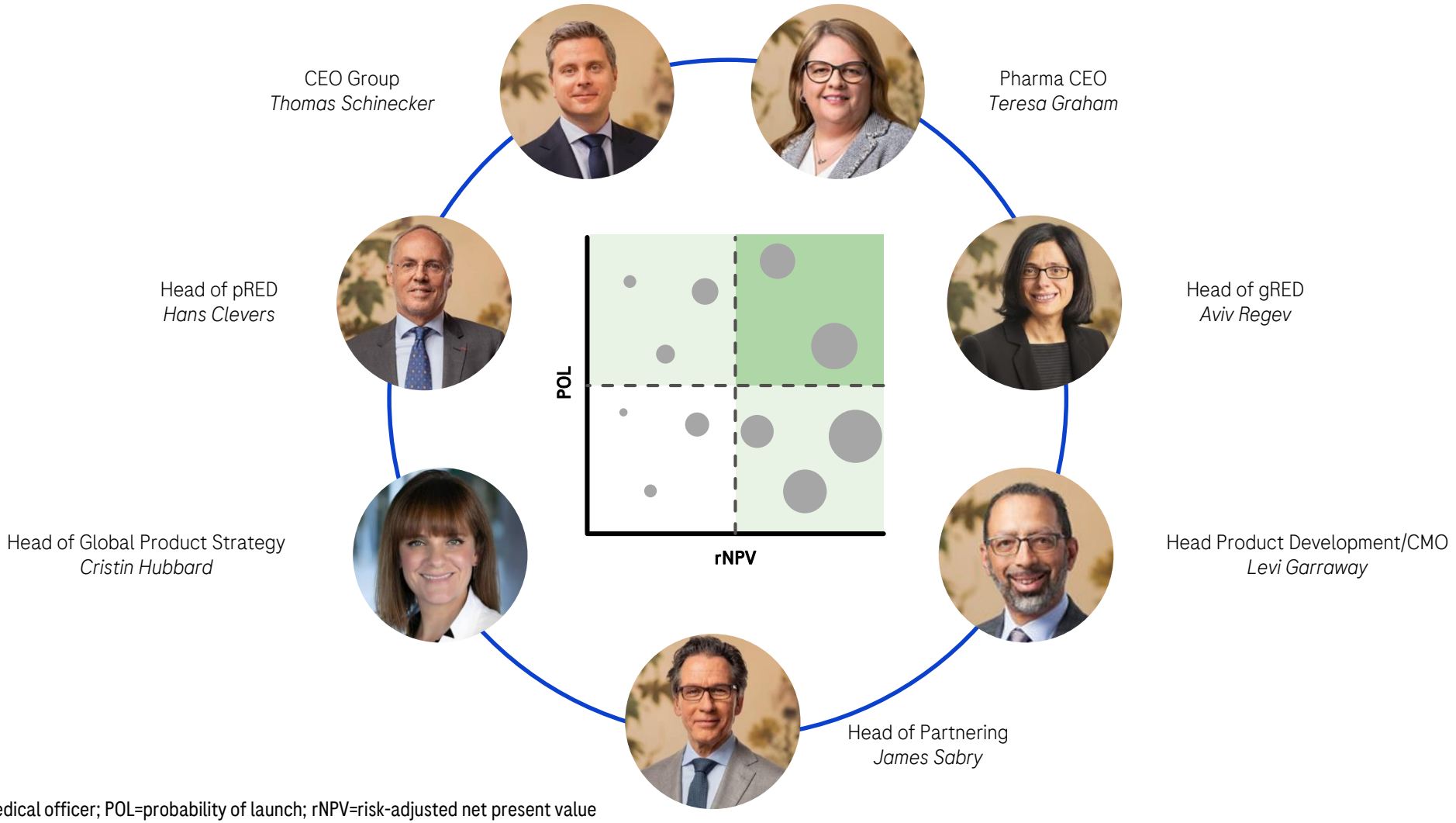
Additional dimensions

- Disease area strategy
- First-in-class / best-in-disease
- Platform technologies

POL=probability of launch; rNPV=risk-adjusted net present value; uNPV=unadjusted net present value

Portfolio committee established

Taking a holistic view and managing R&D productivity end-to-end



CMO=chief medical officer; POL=probability of launch; rNPV=risk-adjusted net present value

Pipeline acceleration via partnering

*Deals of the past two years increasingly focused on clinical stage NMEs**

TA	NME	Indication	Partner	Development stage
Oncology / Hematology	P-CD19CD20-ALLO1	B-cell malignancies	POSEIDA THERAPEUTICS	Pre-clin. → Ph I
Oncology / Hematology	P-BCMA-ALLO1	Multiple myeloma	POSEIDA THERAPEUTICS	Ph I
Oncology / Hematology	AR degrader	mCRPC	Jemincare	Ph I
Oncology / Hematology	camonsertib	Solid tumors	REPARE THERAPEUTICS	Ph I
Oncology / Hematology	KSQ-4279	Solid tumors	KSQ	Ph I
Ophthalmology	OpRegen	Geographic atrophy	LINEAGE CELL THERAPEUTICS	Ph II
Immunology	ASO factor B	IgAN	IONIS	Ph II → Ph III ✓
Immunology	vixarelimab	IPF & SSc-ILD	KINIKSA	Ph II
Cardiovascular & Metabolism	zilebesiran	Hypertension	Alnylam PHARMACEUTICALS	Ph II ✓

Oncology / Hematology; Ophthalmology; Immunology; Cardiovascular & Metabolism

Development stage at time of deal; Current development stage; ✓ Positive proof of concept data

*Table shows clinical stage NME deals completed 2021-2023 YTD; TA=therapeutic area; mCRPC=metastatic castrations-resistant prostate cancer; AR=androgen receptor; IgAN=immunuglobululin A nephropathy; ASO=antisense oligonucleotide; IPF=idiopathic pulmonary fibrosis; SSC-ILD=systemic sclerosis-interstitial lung disease

Evolution of our R&D engines, with impact on the full value chain

Leveraging the newest technologies to bring unprecedented changes

Computational Biology, AI/ML and advanced computation

- Acceleration of biological insights
- Systematic discovery of targets and biomarkers
- More efficient target prioritization and development (efficacy, safety, tractability)
- Digital endpoints delivering new patient insights and building holistic solutions for patients

Organoids: Creating reliable predictive models emulating the human body

- Roche launched the Institute of Human Biology (IHB)
- Engineering the most advanced organoids to explore physiology, understand diseases and develop new therapies
- Accelerate discovery and development of new medicines
- Core areas: exploratory research, bioengineering, translation & technologies

Roche Leader

Head of gRED

Aviv Regev

Head of gRED Computation

John Marioni

Head of pRED

Hans Clevers

Head of IHB

Matthias Lütolf

New technologies enabling unprecedented changes along the full value chains of Pharma and Diagnostics

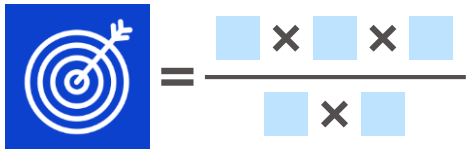
Our Operating Principles: How we shape our culture

Putting patients first is at our core; additional key areas to focus on going forward

Put patients first	I always act as if patients I know are in the room and do what's best for them.
Follow the science	I seek answers through experiments, data and debate, and act on facts.
Act as one team	I care, collaborate and commit without boundaries, and trust others to do their part.
Embrace differences	I seek diverse perspectives, invite opposing views, and challenge myself and others.
Accelerate learning	I push to learn new things even if difficult, and openly share my successes and failures.
Simplify radically	I eliminate complexity, reuse with pride, and accomplish more with less.
Make impact now	I take accountability to do what's right, deliver value fast, and don't wait for certainty.
Think long term	I choose actions today that benefit future generations.

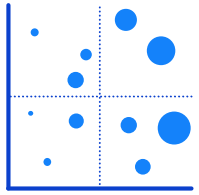
R&D focus areas to speed up delivery of our medicines

1



Set ambitious R&D objectives

2



Strengthen portfolio framework

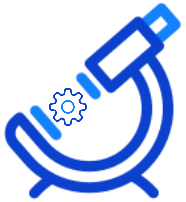
3

Transform portfolio management & governance

4

Access the best external innovation

5



Optimize R&D engines and invest in emerging technologies

6

Evolve talent, culture and mindset to achieve objectives

New Leadership Team

Performance and Outlook

Pharma R&D Excellence

Upcoming IR Events

Upcoming IR events on Neuroscience, Digitalization and Diagnostics

Neuroscience Update on Oct 30
Virtual event

- Neuroscience pipeline and strategy
- Latest data on:
  - Ocrevus Ph III (OCARINA II) in MS
  - fenebrutinib Ph II (FENopta) in MS
  - trontinemab Ph I dose escalation in AD
  - GSM (Gamma secretase modulator) Ph I in AD

Roche Digitalization Day on Nov 29
Virtual event

- Roche experts to present how digitalization (incl. RWD and AI/ML) transforms our Pharmaceuticals and Diagnostics businesses in an unprecedented way
- Use cases covering early R&D, clinical development, regulatory, manufacturing, supply chain and commercialization to be presented
- Discussion of novel product opportunities at the interface between Diagnostics and Pharmaceuticals

Roche Diagnostics Day in H1 2024
Hybrid event (virtual / on-site)

- Management to update on Diagnostics mid-term outlook
- Deep-dives into the current product portfolio
- Updates on key development projects, including mass spectrometry (launch scheduled for 2024), continuous glucose monitoring (CGM) and next-generation sequencing (NGS)

Angiogenesis 2023 ✓	**Roche ESG Day** ✓	**EHA 2023** ✓	**Roche Pharma Day**	**Neuroscience Update**	**Roche Digitalization Day**	**ASH 2023**	**Roche Diagnostics Day**
Virtual	Virtual	Virtual	London	Virtual	Virtual	Virtual	Virtual / hybrid
Monday, 13 February	Tuesday, 23 May	Monday, 12 June	Monday, 11 September	Monday, 30 October	Wednesday, 29 November	December	H1 2024
16:30 to 18:00 CET	15:30 to 17:00 CEST	16:30 to 17:30 CEST	10:30 to 14:30 BST	TBA	TBA	TBA	TBA

MS=multiple sclerosis; AD=Alzheimer's disease; RWD=real-world data; AI/ML=artificial intelligence and machine learning

Pharma Update & On-Market Portfolio

Teresa Graham **|**
CEO Roche Pharmaceuticals

Pharma Update

On-Market Portfolio With Further Growth Potential

Significant Growth Opportunities Ahead

HY 2023: Pharmaceuticals Division sales

All regions delivering strong growth, intensifying currency headwinds in Q2

	2023 CHFm	2022 CHFm	Change in % CHF	Change in % CER
Pharmaceuticals Division	**22,681**	**22,347**	**1**	**8**
United States	11,743	11,363	3	7
Europe	4,105	4,104	0	5
Japan	2,210	2,202	0	14
International	4,623	4,678	-1	9

CER=Constant Exchange Rates

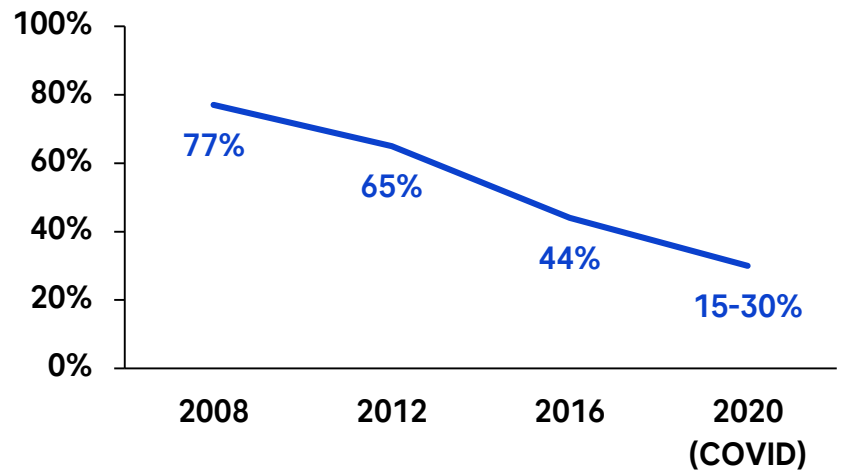
Why we changed our customer engagement model

Why we changed

- Roche's changing portfolio
- Shifting customer expectations for industry engagement
- Data and technology as disrupters
- Price pressures
- Patient influence in healthcare decision making

In-person, product-specific field approach not meeting customer needs

Industry representative's access to physicians (US)

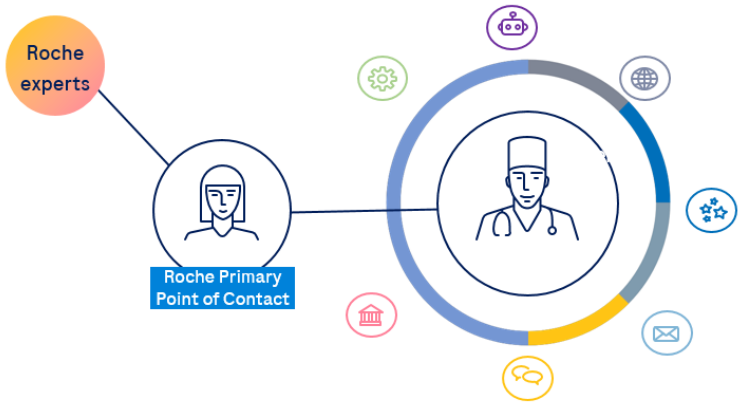


- Providers increasingly refused to meet industry; customers confused by multiple touchpoints
- Desire for more scientific exchange and patient/ account support

New customer engagement model driving future growth

Integrated customer experience and greater agility

How we are changing



- Empowered teams organized around local healthcare markets, with accountability for the whole portfolio
- Improved customer experiences and partnerships with a reduced number of broader and more impactful roles
- Delivering coordinated, personalized experiences through all channels

Impact we see today

1. Successful uptake of new products (e.g. Vabysmo)
2. Increased P&L flexibility
3. Flexibility in resource deployment to higher impact channels (e.g. digital patient support)
4. Positive customer feedback

P&L=Profit and loss

Pharma Corporate Access Goal

Opportunities to remove barriers and substantially increase access

Access levers	Inclusive clinical trials	Regulatory filing & reimbursement	Affordability	Capacity enablement	Partnerships
Mid-term outcomes	Support health equity and diversity in our clinical research and trials	Substantial acceleration of regulatory filling & reimbursement approval	Support development of new, integrated and tailored affordability solutions for different population health/group needs	Support infrastructure development through external partnerships	Mobilize partnerships with global/regional organizations to solve a gap in local care

Our mission

Accelerate & adapt internal processes → Expand local capabilities → Design & deploy fit-for-purpose integrated solutions

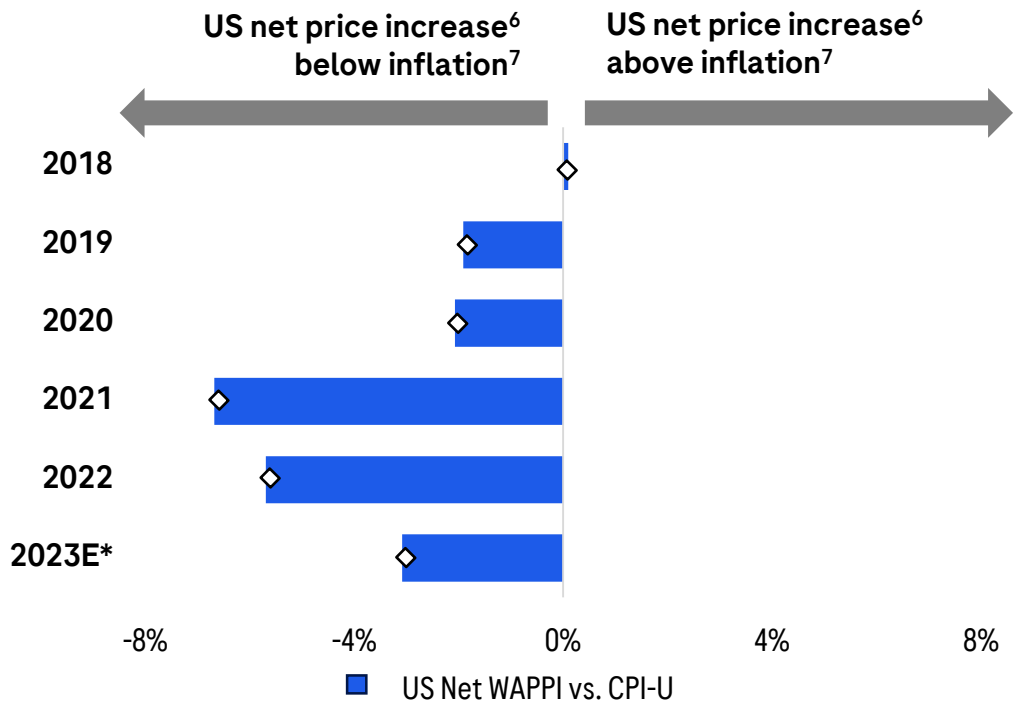
Responsible pricing as we advance the standard of care

Savings for healthcare systems and lower out-of-pocket costs for patients

Key products priced below competitors in the US

COLUMVI glofitamab	~12%	lower price[1] vs. Epkinly
VABYSMO	~20%	lower price[2] vs. Eylea High Dose
Evrysdi risdiplam	~22%	lower price[3] vs. Spinraza
HEMLIBRA emicizumab-kxwh	~36%	lower price[4] vs. Altuviiio
OCREVUS ocrelizumab	~25%	lower price[5] vs. Rebif

Historical net price increases below CPI in the US



No impact expected from IRA inflationary penalties

[1] Annual cost of Epkinly; [2] discount based on WAC per vial; [3] discount over 5-yrs (at max Evrysdi price); [4] discount at launch based on WAC, annualized average for prophylaxis in a patient weighing 63.4kg. Based on US label dosing, including 50 IU/kg for Altuviiio. Cost of drug can be highly variable depending on several factors including dosing schedule and disease severity.; [5] discount at launch, based on list price; [6] Genentech's annual average net price increase in the U.S., weighted by sales; [7] source: U.S. Bureau of Labor Statistics; *2023 Net WAPPI of 1.28%; CPI-U forecast of 4.36% (S&P Global Market Intelligence); WAPPI = weighted average portfolio price increase; CPI=Consumer Price Index

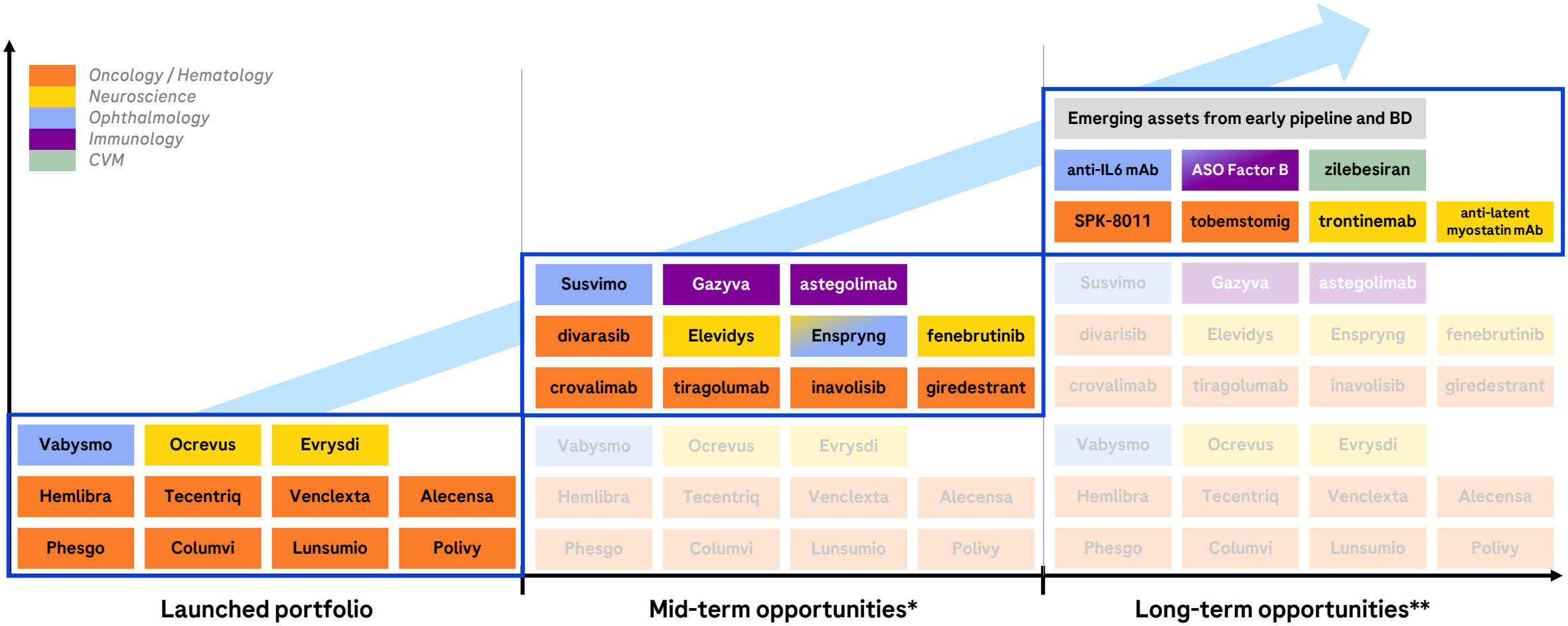
Pharma Update

On-Market Portfolio With Further Growth Potential

Significant Growth Opportunities Ahead

Building blocks for future growth through 2030

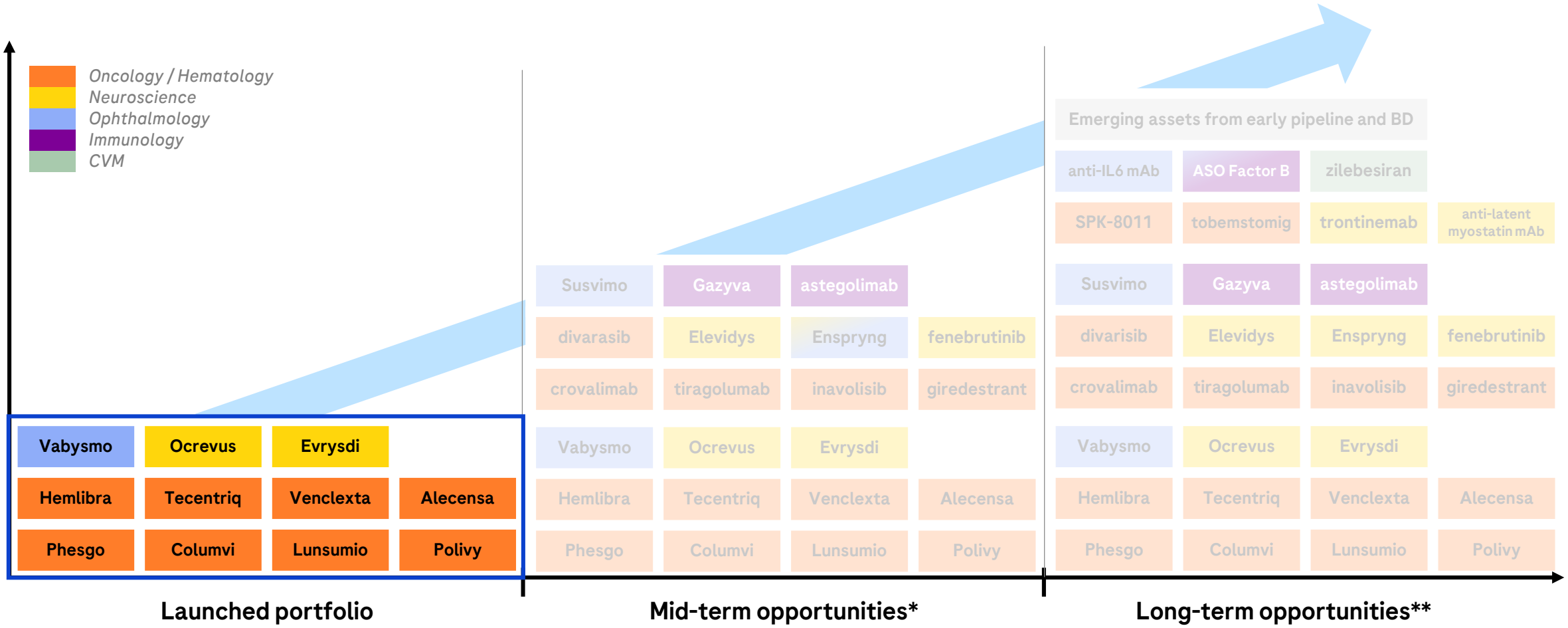
Currently 16 blockbusters on the market



CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

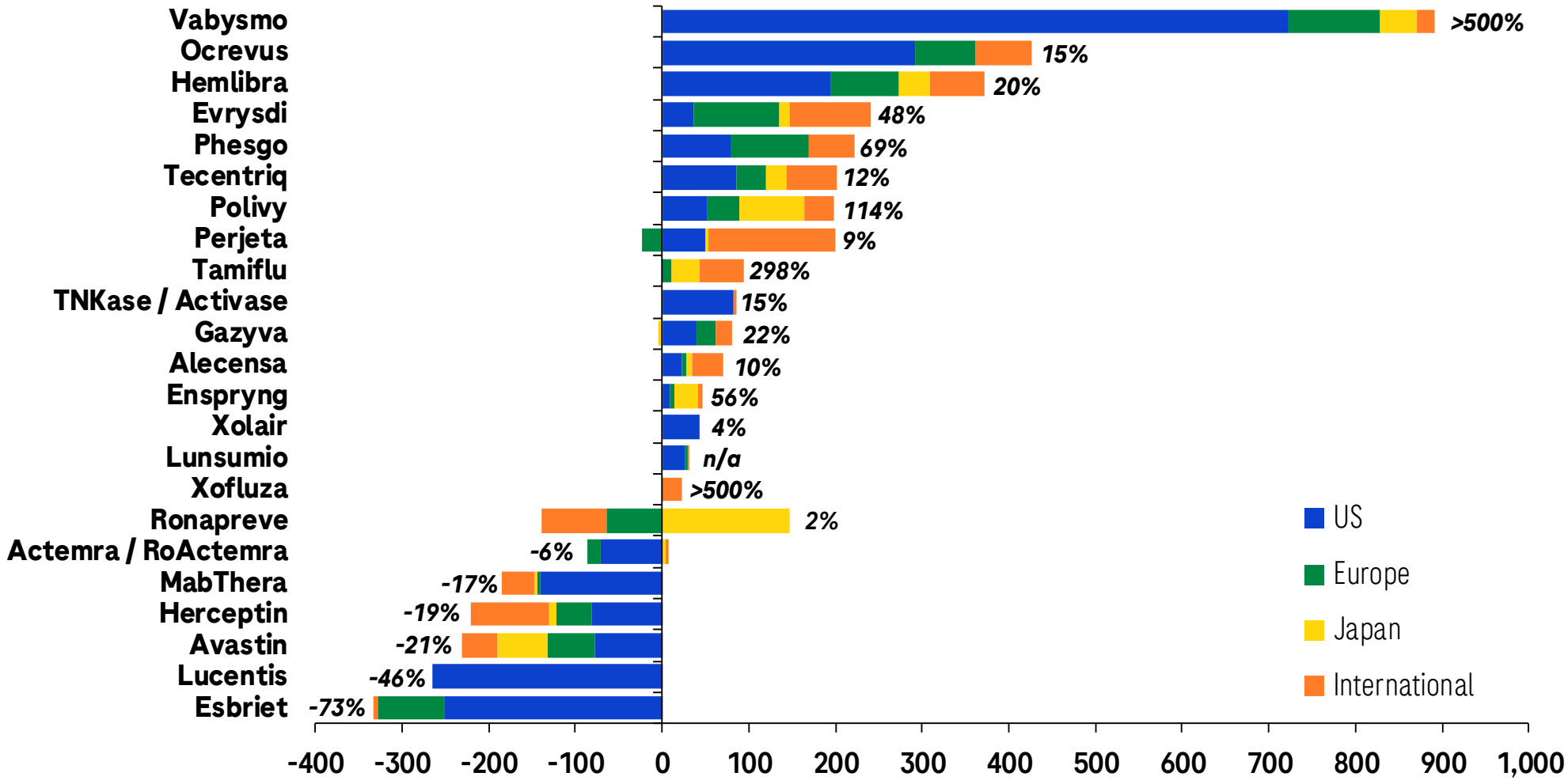
Building blocks for future growth through 2030

Young on-market portfolio with strong momentum and potential for line extensions



CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

HY 2023: Strong momentum for key growth drivers

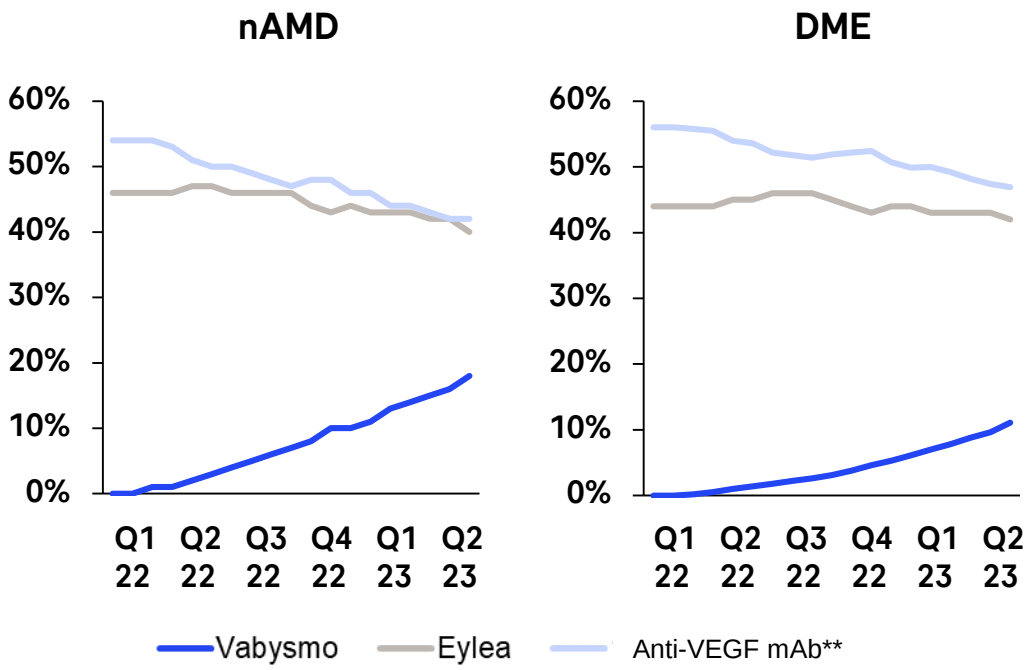


Absolute values and growth rates at Constant Exchange Rates (CER)

Vabysmo: Expecting more than CHF 2bn sales in 2023

Highly successful first launch under new commercial model

US patient share since launch*



Vabysmo performance update

- US market share reaches 18% in nAMD, and 11% in DME in Q2; 1/3 naive patients and 2/3 switches (mostly from aflibercept)
- >20% market-share in UK, Switzerland within 1 year of launch; Double-digit market shares achieved in Japan, Australia
- Anatomic benefits observed in switch patients in the real world drive confidence for earlier line usage (TRUCKEE)[1]

Outlook

- Filed for 3rd indication RVO in US/EU (FDA PDUFA date set for 22 December)
- Expect public reimbursement for all EU-5 by end 2023

Further potential to grow our Ophthalmology franchise:
Relaunch of Susvimo, satralizumab in TED and anti-IL-6 mAb in UME and DME

*Claims data based on Verana shares through July 2023; **Avastin, Lucentis and biosimilars; 1 Khanani et al., Eye 2023; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; RVO=retinal vein occlusion; TED=thyroid eye disease; UME=uveitic macular edema; PDUFA=prescription drug user fee act; Eylea (aflibercept) is a registered trademark/product of Regeneron/Bayer

Vabysmo: Benefits of dual pathway supported by anatomic results

Comprehensive disease control and extended durability

Roche

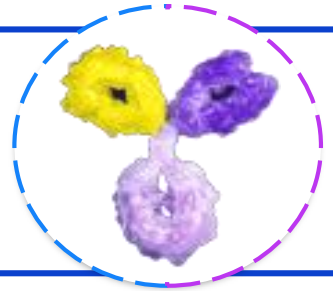
VABYSMO

Effects of elevated VEGF-A and Ang2 on vasculature

Elevated VEGF-A → *Primary Effects* → **Neovascularization**

Elevated Ang-2 leading to Vascular Instability → *Primary Effects* → **Vascular Leakage**, **Inflammation**, **Fibrosis**

Dual pathway inhibition with Vabysmo



Clinical Biomarkers for disease control

- ✓ **Drying**[1,2,*]
- ✓ **Macular Leakage**[3,*]
- ✓ **HRF**[4,*]
- ✓ **ERM**[5,*]

New post hoc analyses on anatomical endpoints presented throughout this year all favor Vabysmo over 2mg Aflibercept*

[1] Dhoot et al. Macula Society 2023 Annual Meeting; [2] Csaky et al. Angiogenesis 2023 Annual Meeting; [3] Goldberg et al. ARVO 2023 Annual Meeting; [4] Maunz et al. ARVO 2023; [5] Jaffe et al. ASRS 2023 Annual Meeting;
*based on post-hoc, exploratory analysis with nominal p-value statistical analysis not adjusted for multiple testing, no formal statistical conclusions can be drawn; Ang-2=angiopoietin-2; VEGF-A=vascular endothelial growth factor A; HRF=hyper-reflective foci; ERM=epiretinal membrane; Eylea (aflibercept) is a registered trademark/product of Regeneron/Bayer

Vabysmo: Disease activity criteria chosen affect durability outcomes

Vabysmo nAMD trials use vision or anatomical disease activity criteria, reflecting clinical practice[1]

Different ≥Q12W disease criteria as applied to Vabysmo or aflibercept 8 mg patients*

Vabysmo

Stringent criteria (as actually applied in our clinical trials)

*Treatment change if **ANY** criteria are met (based on criteria used in pivotal trials)*

A OR B OR C OR D OR E

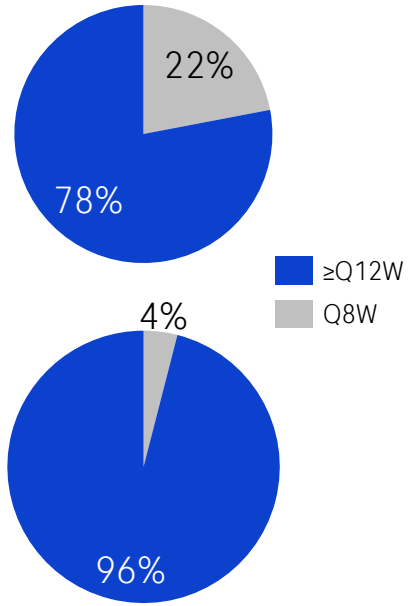
Less stringent criteria (post hoc analysis)**

*Treatment change if **ALL** criteria are met*

F AND G

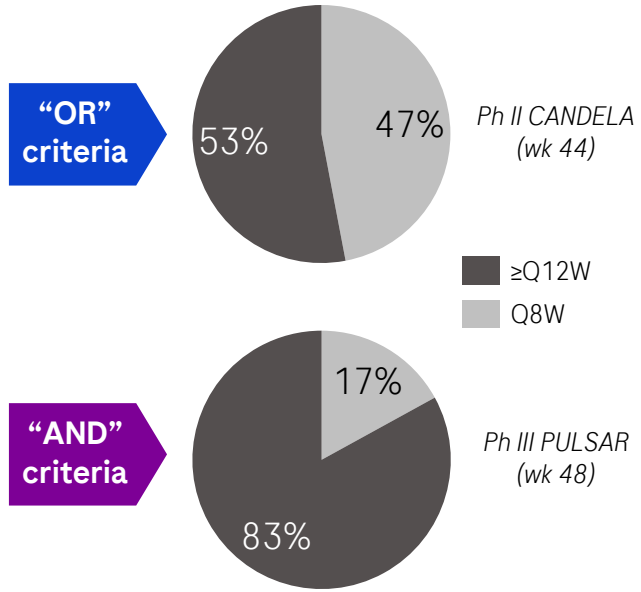
Share of patients assigned to ≥Q12W dosing

Assessment done at week 20



aflibercept 8mg

Share of patients assigned to ≥Q12W dosing



- Ph III TENAYA/LUCERNE trial with stringent patient-centric criteria resulted in 22% of patients being allocated to Q8W dosing
- Using less stringent criteria, only 4% of patients would have been assigned to Q8W dosing (post hoc analysis)

1. Zarbin et al. ASRS, 2023; *Criteria: A=≥ 5 letters BCVA loss vs avg. BCVA over previous 2 scheduled visits, due to nAMD, B=≥ 10 letters BCVA loss vs highest BCVA recorded over previous 2 scheduled visits, due to nAMD; C= > 50 µm CST increase vs avg. CST over previous 2 scheduled visits; D=≥ 75 µm CST increase vs lowest CST recorded at either of previous 2 scheduled visits; E=Presence of new macular hemorrhage*, due to nAMD activity; F=>5 letters BCVA loss vs week 16 BCVA; G= > 25 µm CST increase vs week 16 CST or new macular hemorrhage; **Post-hoc analysis of patients dosing eligibility at week 20, patients not actually assigned based on 'and' criteria in TENAYA/LUCERNE; This analysis is not intended as a cross-trial comparison; This analysis cannot predict whether faricimab-treated patients in TENAYA & LUCERNE would have achieved non-inferiority vs aflibercept 2mg / 8mg if the treatment regimen had been modified; additional patients with a missing Week 20 assessment were considered to have met disease activity criteria and were treated Q8W; Q8W=every 8 weeks

Susvimo: Continuous 6m delivery preferred by 93 % patients vs IVT

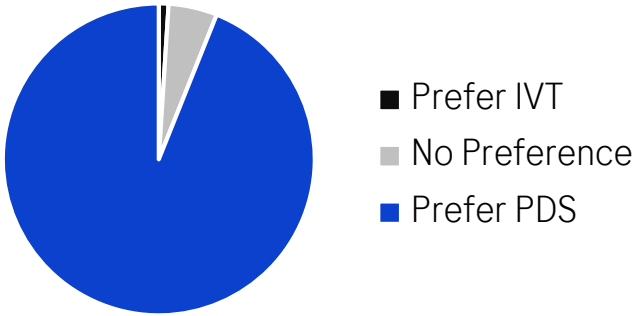
Commercial US relaunch expected in 2024 and ex-US 2025+

Stronger vision outcomes with potential for extended ≥Q6M dosing

Continuous delivery of aVEGF via PD implant

1-2 refill exchanges per year

93% of patients prefer Susvimo to IVT injections[1]



Ongoing development for the Port Delivery Platform

- October 2022: SUSVIMO voluntarily recalled due to manufacturing variability; root cause identified and progress made to implement technical solution
- February 2023: Positive data from pivotal Ph III studies in DME (PAGODA) and DR (PAVILLION) presented at Angiogenesis:
  - DME: Improved vision (Q6M dosing)[2]
  - DR: Superior improvement in ≥ 2-Step ETDRS-DRSS (Q9M dosing)[3]
  - Trend toward improved safety profile with evolved surgical implantation training and technique[2,3]
- Q4 2023: Clinical trials expected to restart
  - Ph IIIb (VELODROME) assessing Q9M dosing in nAMD
  - First trials of next generation bispecifics (DutaFabs)

1. Holekamp N et al. ARCHWAY Ph III Trial of the PDS for nAMD, American Academy of Ophthalmology, 129(3), 2022; 2. Campochiaro P et al. Port Delivery System With Ranibizumab in Diabetic Macular Edema: Primary Analysis Results of the Ph III PAGODA Trial, Presented at the Macula Society 46th Annual Meeting, Miami, FL, February 15–18, 2023. 3. Holekamp N et al. Port Delivery System With Ranibizumab in the Treatment of Diabetic Retinopathy Without Center-Involved Diabetic Macular Edema: Primary Analysis Results of the Ph III PAVILION Trial, Presented at the Macula Society 46th Annual Meeting, Miami, FL, February 15–18, 2023. VEGF = Vascular Endothelial Growth Factor; Q6M=every 6 months; PD = Port Delivery; IVT=intravitreal injection; DME=diabetic macular edema; DR=diabetic retinopathy; EDTRDS-DRSS=early treatment diabetic retinopathy study-diabetic retinopathy severity scale; Q9M=every 9 months; nAMD = neovascular age related macular degeneration;

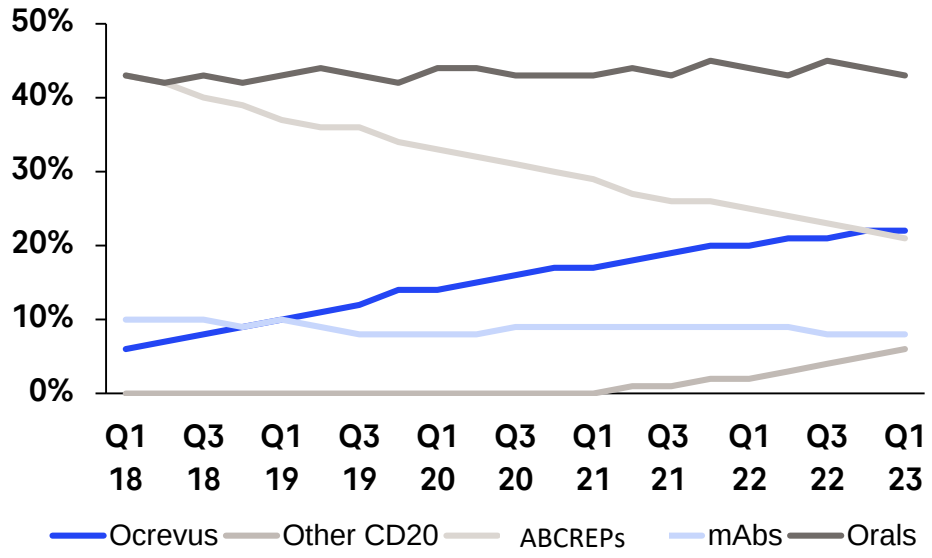
Ocrevus: Continued growth in all markets around the world

Opportunity to expand overall CD20 class and gain class share

OCREVUS® ocrelizumab

IR call on October 30

MS total patient share (global)*



Ocrevus performance update

- Ocrevus with 22% patient share globally (>300k pts treated)
- High proportion of patients free of disease progression after 10 years of treatment highlighting importance of early treatment
- Higher retention rate than other MS medicines
- Only drug in RMS and PPMS

Outlook

- Positive Ph III (OCARINA II) results to be presented at ECTRIMS
- 10 year safety/efficacy data to be presented at ECTRIMS
- Treatment of choice for family planning: Pregnancy/lactation data to be submitted to health authorities in 2024
- Ph III (GAVOTTE/MUSETTE) Ocrevus high dose: Trials fully recruited; potential to further improve control of disability progression

Further potential to grow our MS franchise:
fenebrutinib has opportunity to disrupt oral class, currently comprising >40% of the global market

*Global patient share includes US, I8, JP; ABCREPs includes interferons and Copaxone, Other mAbs includes Tysabri, Lemtrada, and Zinbryta; Other CD20 includes Kesimpta, Briumvi; MS=multiple sclerosis; SC=subcutaneous

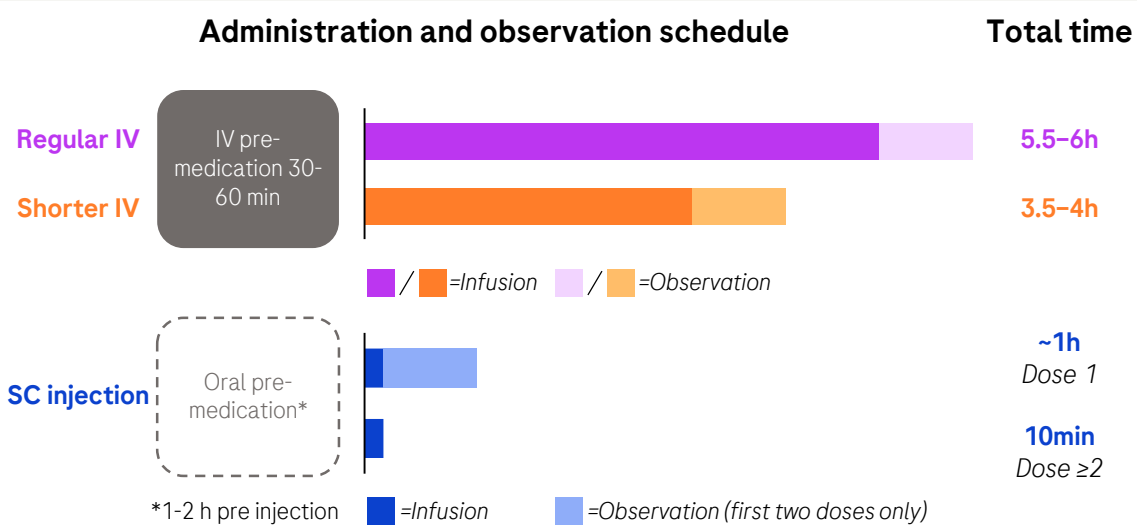
Ocrevus: Positive Ph III (OCARINA II) results for Q6M SC dosing

Further improving treatment experience and expand usage

OCREVUS® ocrelizumab

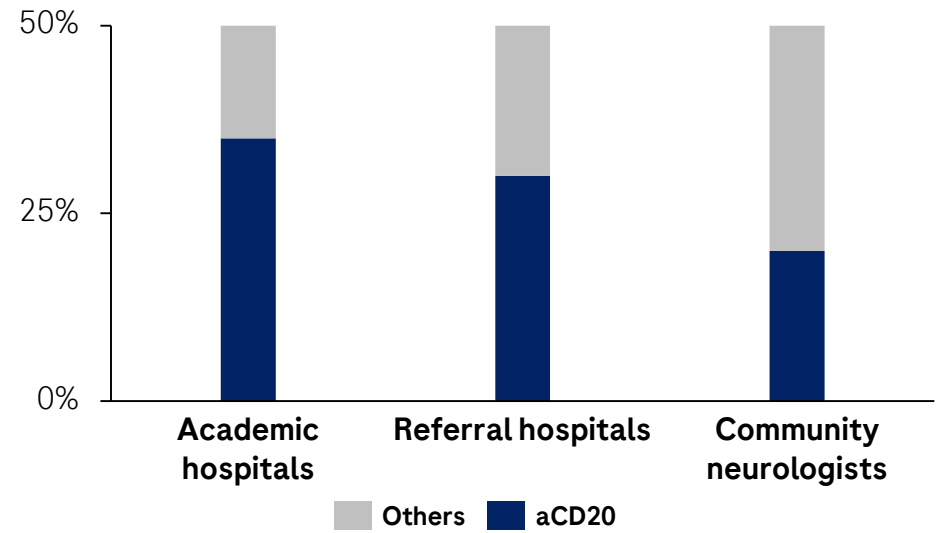
IR call on October 30

Cutting administration time from 3.5-6hrs to 10 min



- Ph III (OCARINA II) evaluating subcutaneous Q6M dosing of Ocrevus for non-inferiority vs Ocrevus IV in RMS and PPMS met primary and secondary endpoints
- Ocrevus SC has the potential to enable at-home administration and increases potential for Ocrevus use in centers with IV capacity constraints
- 6m dosing drives best-in-disease compliance/retention with improved convenience while continuing to deliver equivalent safety/efficacy

US: Estimated aCD20 patient share by Tx setting*



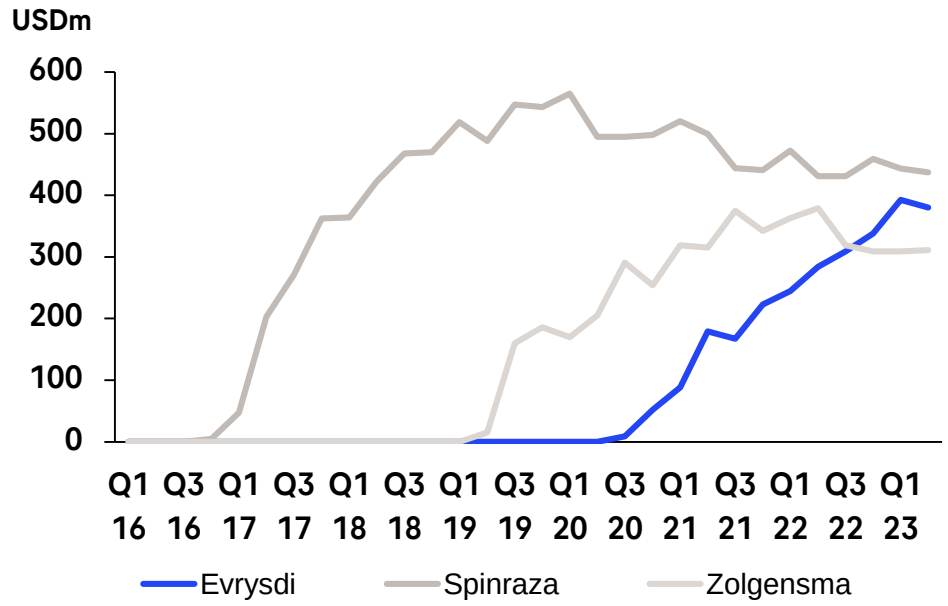
- Academic hospitals: Strong aCD20 use, strong Ocrevus IV presence
- Referral hospitals: Ocrevus SC will enable on-site treatment, complementing already strong aCD20 use
- Community neurologists: Ocrevus SC with the potential to address low aCD20 penetration due to limited infusion capabilities

[1] Hauser S.L. et al, ACTRIMS-ECTRIMS 2020; *Source: IQVIA claims data and IQVIA NSP (Dec 2022 – May 2023); Tx=treatment, MS=multiple sclerosis; IV=intra-venous; SC=Subcutaneous; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; Q6M=dosing every 6 months

Evrysdi: Becoming a global SMA market leader

>11,000 patients treated worldwide

Worldwide SMA sales*



Evrysdi performance update

- Significant population of untreated adults remain in key markets
- >40% of patients in the US are not on any DMT
- Nearly half of Evrysdi new patients starts are treatment naïve
- Patients continue to switch to Evrysdi for the following reasons: tolerability concerns and lack/loss of efficacy (Spinraza) and hope of additional benefit (Zolgensma)[1]
- EU label expansion for infants under 2 months achieved in August

Outlook

- Continued global market share gains driven by switch and naïve
- Access driving growth; Evrysdi approved in >100 countries globally

Further potential to grow our SMA franchise:
Ph II/III combination trial with anti-latent myostatin mAb (GYM329) ongoing

*Evaluate pharma; 1. Chiriboga et al, CureSMA 2023; SMA=spinal muscular atrophy; DMT=disease modifying therapy; Evrysdi in collaboration with PTC Therapeutics and SMA Foundation

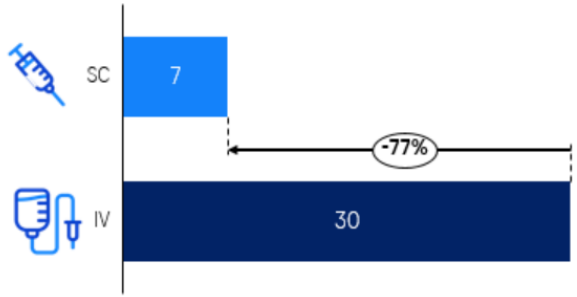
Tecentriq: First PD-1/L1 with subcutaneous formulation

Improving convenience for patients, saving resources for healthcare systems

Roche

TECENTRIQ® atezolizumab

SC administration time (in minutes)



News | August 30, 2023

Roche wins first approval for subcutaneous Tecentriq

The subcutaneous formulation of Tecentriq has been approved in the UK for all indications that its intravenous counterpart has received approval.

By Phalguni Deswal

Tecentriq performance update

- Reaching peak share in first-in-class indications (SCLC, HCC)
- US/EU launch in adjuvant NSCLC ongoing
- Tecentriq SC: Great Britain approval in August

Outlook

- Tecentriq SC: CHMP opinion expected in Q4; US approval delayed to 2024
- Ph III (IMvoke010) Tecentriq in adj SCCHN results expected in Q4
- Ph III (SKYSCRAPER-01) Tecentriq + tiragolumab final OS results in 1L PD-L1+ NSCLC expected in Q4 / Q1
- Ph III (SKYSCRAPER-14) Tecentriq + tiragolumab in 1L HCC initiated
- Ph III (IMbrave050) in adj. HCC met primary endpoint RFS, OS immature

Potential for LEs:
Ph III in adjuvant SCCHN and pivotal tiragolumab combination program ongoing

CER=Constant Exchange Rates; SC=subcutaneous; NSCLC=non-small cell lung cancer; HCC=hepatocellular cancer; SCLC=small cell lung cancer; SCCHN=squamous cell carcinoma of head and neck; OS=overall survival; LE=line extensions; SC with Halozyme's rHuPH20/ Halozyme's human hyaluronidase

Growing portfolio in breast cancer: Expanding beyond HER2+ BC

Breast cancer cases by subtype[1]

On-market portfolio

- Herceptin
- PERJETA pertuzumab
- PHESGO PERTUZUMAB-TRASTUZUMAB
- Kadcyla ado-trastuzumab emtansine for injection
- TECENTRIQ atezolizumab

Unknown
TNBC
HR−/HER2+
HR+/HER2−
HR+/HER2+

Pipeline molecules

- **giredestrant** (SERD)
- **inavolisib** (PI3Kα inhibitor)
- **runimotamab** (HER2xCD3)
- **ZN-1041** (HER2 TKI)

Ph III clinical development overview

Ph I	Ph II	Ph III
Giredestrant + palbociclib (perservERA) in 1L ER+/HER2- mBC		
Giredestrant + CDK4/6 (pionERA) in 1L ER+/HER2- mBC		
Giredestrant (lidERA) in adjuvant ER+ BC		
Giredestrant + Phesgo (heredERA) in 1L maint ER+/HER2+		
Inavolisib + palbo + fulv (INAVO120) in 1L HR+/HER2-/PI3Km mBC		
Inavolisib + fulv (INAVO121) post CDK4/6i HR+/HER2-/PI3Km BC		
Inavolisib + Phesgo (INAVO122) in 1L HER2+/PI3Km BC		

Further potential to grow our breast cancer franchise:
Expanding into HR+ with two NMEs in Ph III, including in combination with Phesgo

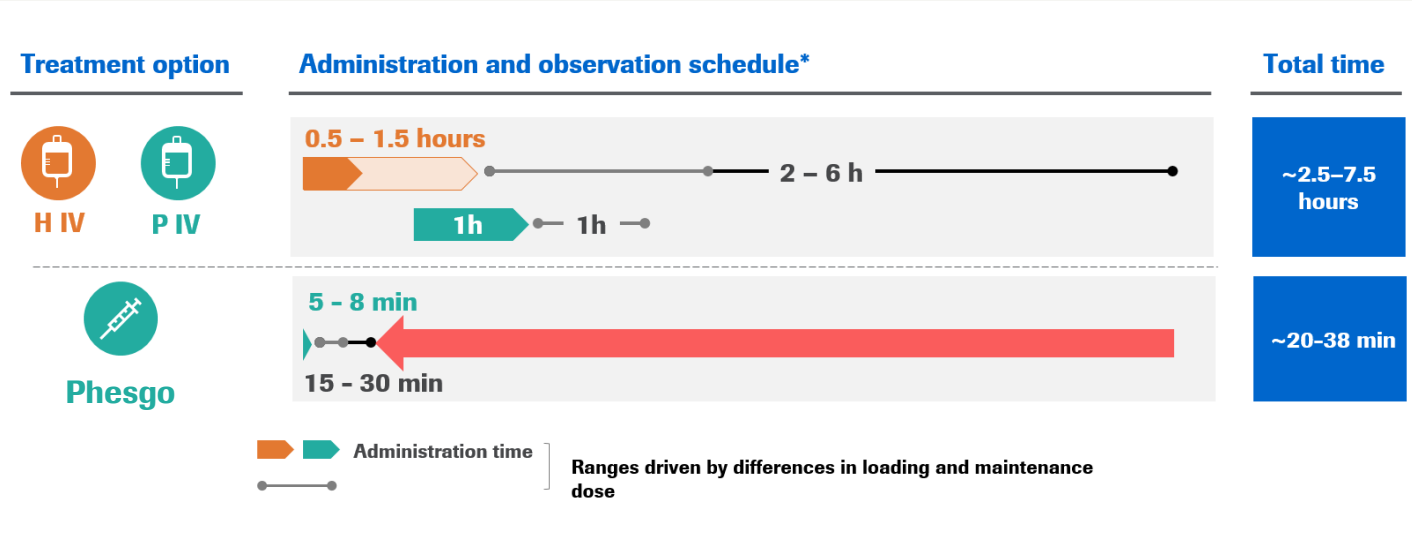
[1] Cancer Stats Facts: Female Breast Cancer Subtypes. National Cancer institute. Available at: https://seer.cancer.gov/statfacts/html/breast-subtypes.html (Access date: May 24, 2022; HER2=Human Epidermal growth factor Receptor 2; HR=Hormone receptor; TNBC=Triple negative breast cancer; SERD=Selective estrogen receptor degrader; ER=Estrogen receptor; PI3K=Phosphoinositide 3-Kinase; TKI=Tyrosine kinase inhibitor

Phesgo: Rapid conversion in early launch countries

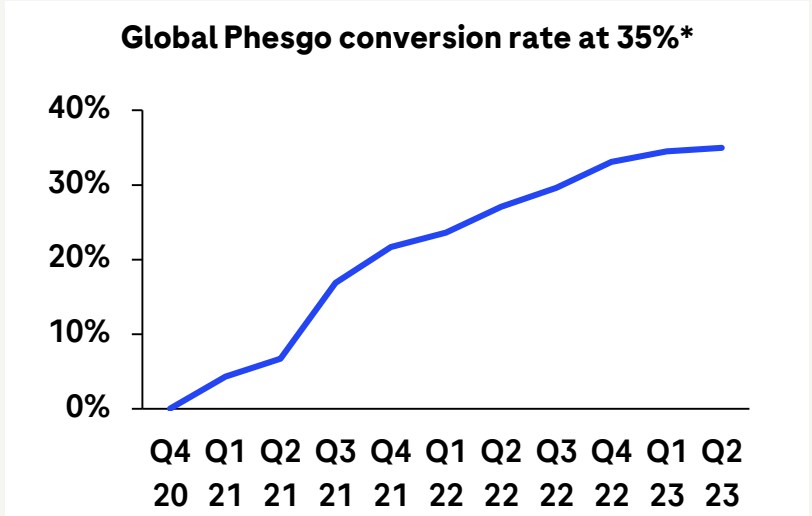
Significantly reducing healthcare costs and resource use

PHESGO®

Phesgo reduces administration time & costs



Strong global launch

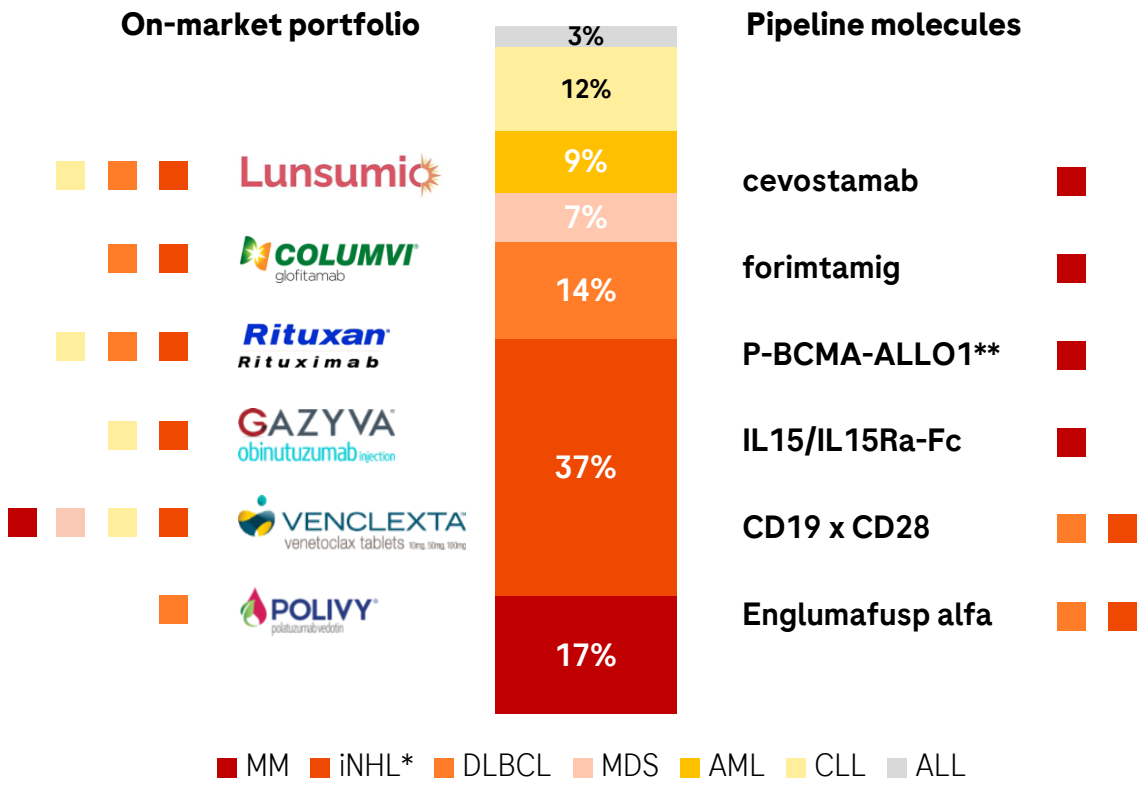


- 85% of patients preferred Phesgo for subcutaneous administration over the intravenous formulation of Perjeta and Herceptin
- Phesgo conversion rate at 35% in early launch countries; conversion in key markets: UK 92%, France, 59%, US: 19%, Germany 16%
- Phesgo expanding eBC market share
- Pivotal Phesgo on-body-injector (OBI) development ongoing

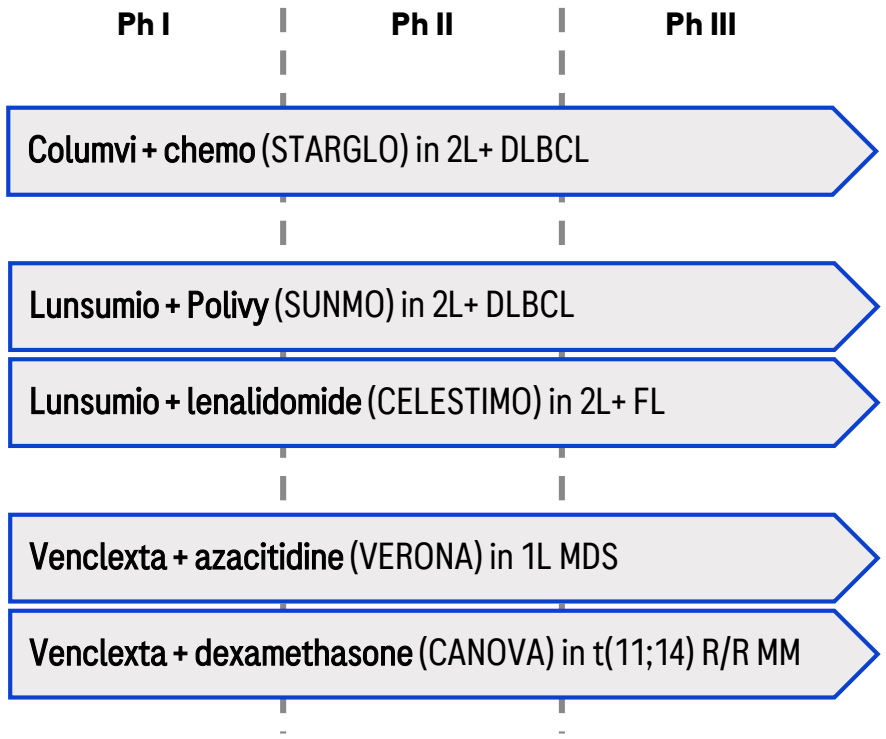
Source: O'Shaughnessy J, et al. ESMO 2020 (Abstract 165MO); H=Herceptin; P=Perjeta; IV=Intravenous; *Ranges driven by differences in loading and maintenance dose; *Perjeta/Phesgo conversion rate is based on volumes (vials) and includes all launch countries after the 2nd quarter after the launch (38 countries); Phesgo in collaboration with Halozyme

Growing portfolio in malignant hematology

Hematologic tumor cases by subtype[1]



Ph III clinical development overview



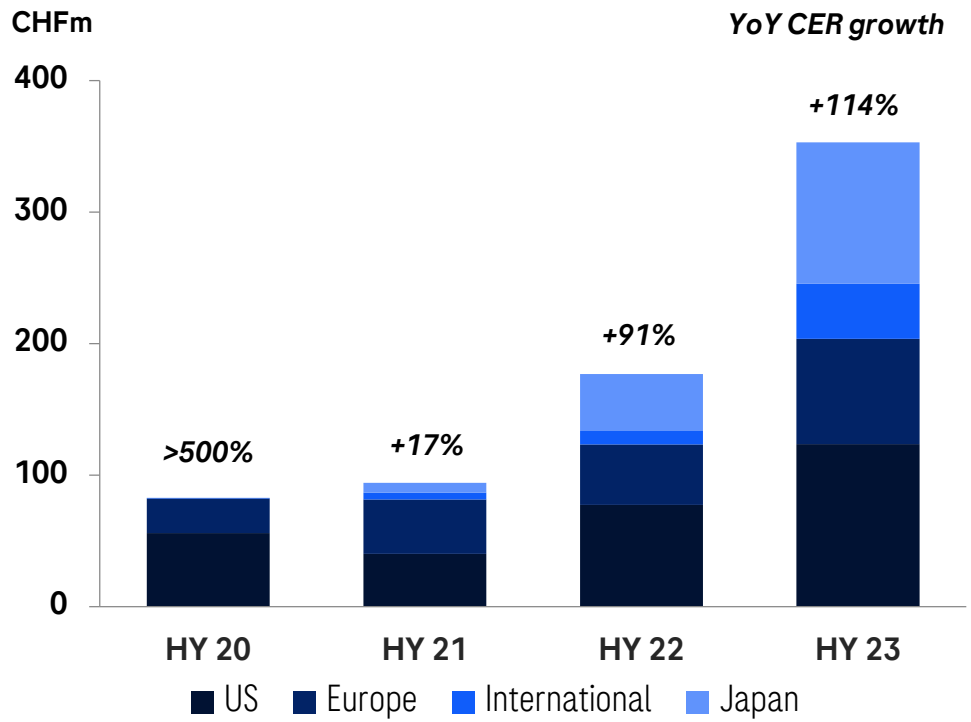
Further potential to grow our hematology franchise:
Taking Columvi and Lunsumio into earlier lines, as well as 6 NMEs into new indications

1 Datamonitor: incidence rates includes the 7 major markets (US, Japan, France, Germany, Italy, Spain, UK); *including FL; **In collaboration with Poseida Therapeutics; MM=Multiple myeloma; iNHL=indolent non-hodgkin's lymphoma; DLBCL=Diffuse large B-cell lymphoma; MDS=Myelodysplastic syndromes; AML=Acute myeloid leukemia; CLL=Chronic lymphocytic leukemia; NHL=Non-hodgkin's lymphoma; FL=Follicular Lymphoma

Polivy: Accelerated growth following 1L DLBCL approval

Transforming the standard of care in 1L DLBCL again after 20 years

Global Polivy sales



Polivy performance update

- Currently approved in >80 countries in 1L DLBCL
- Strong 1L DLBCL uptake especially in US, EU and JP
- Growing patient shares in 1L DLBCL (IPI 0-5), US 13%, Germany 21%, UK 26% and Japan 32%
- Updated treatment guidelines established Polivy as standard of care in 1L DLBCL in key markets such as US (NCCN category 1), Germany and Japan

Outlook

- Further growth expected driven by additional approvals and positive reimbursement decisions in EU and international markets
- Comprehensive development program, including Polivy combinations in 1L / 2L+ DLBCL with first-in-class bispecifics Lunsumio and Columvi

CER=constant exchange rates; DLBCL=diffuse large B-cell lymphoma; IPI=International prognostic index; NCCN=National Comprehensive Cancer Network; Polivy in collaboration with Seagen

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

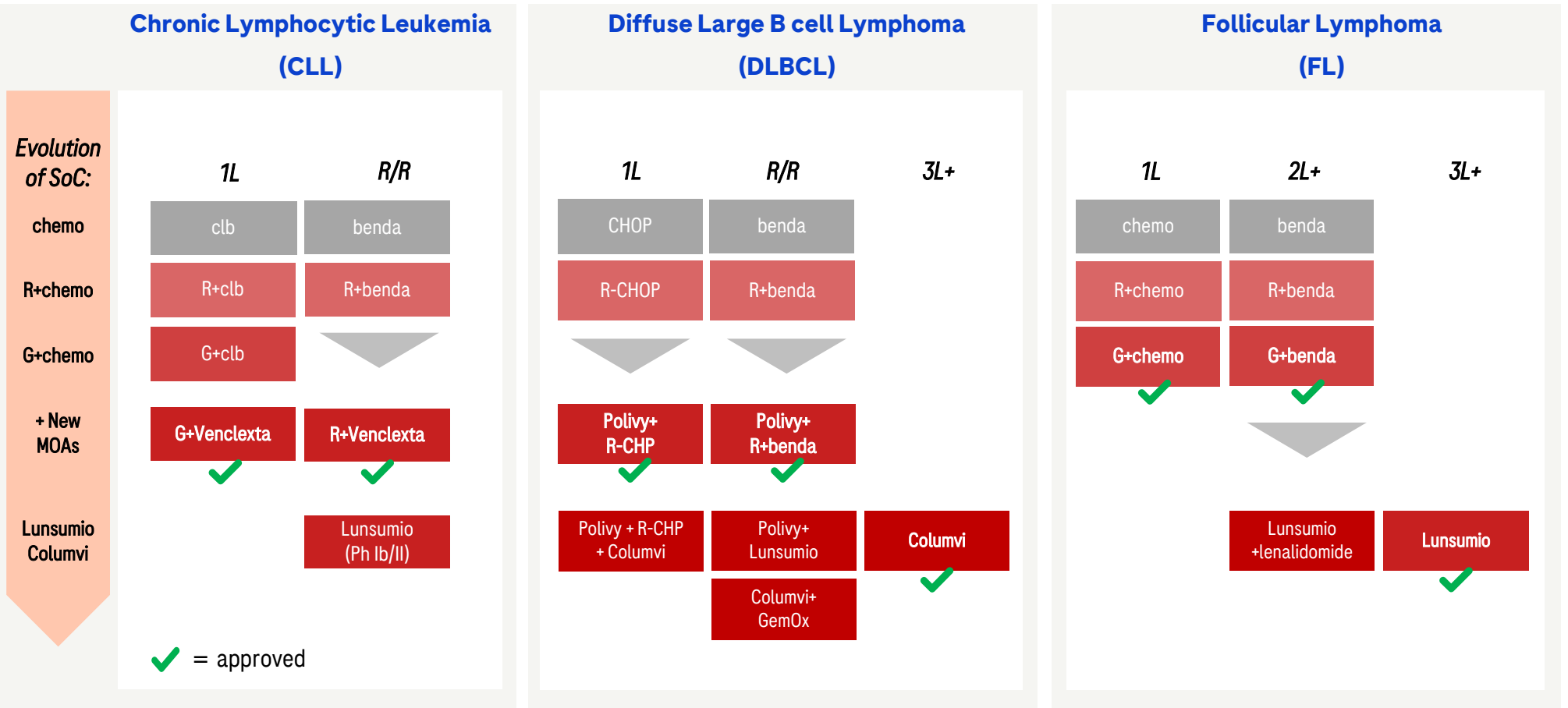
chemotherapy

1997 Rituxan Rituximab / MabThera Rituximab

2013 GAZYVA obinutuzumab injection

2019 POLIVY polatuzumab vedotin / VENCLEXTA venetoclax tablets

2022/23 Lunsumio / COLUMVI glofitamab



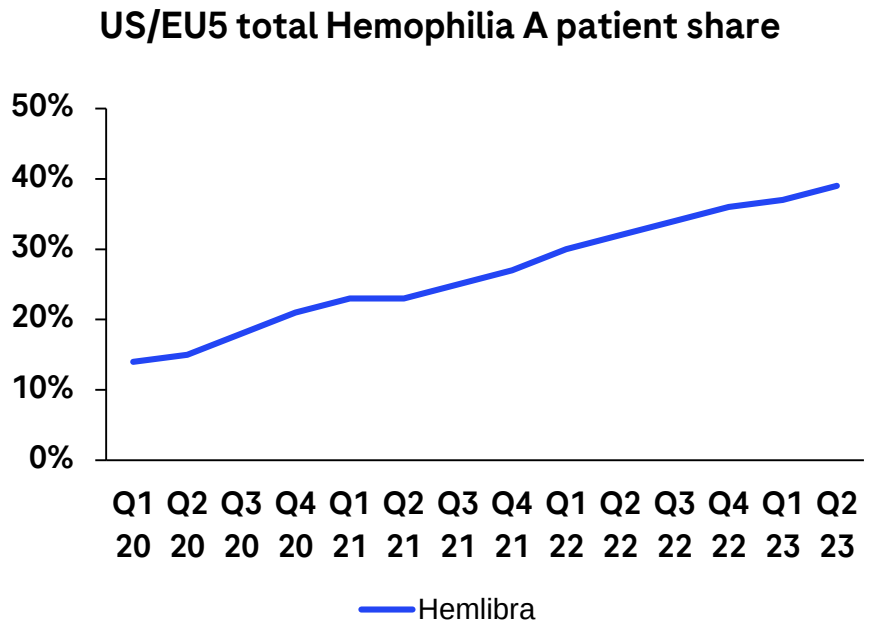
Building on the standard of care with new best-in-class and/or first-in-class combinations

CLL=chronic lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; R=Rituxan; CHP=cyclophosphamide, doxorubicin, prednisone; R/R=relapsed/refractory; GemOx=gemcitabine, oxaliplatin; G=Gazyva; benda=bendamustine; SoC=standard of care; MOA=mechanism of action; Venclexta in collaboration with AbbVie

Hemlibra: Expecting continued market share gains globally

*The global standard of care with ~40% patient share reached in US/EU5**

Steady patient share gains in US and globally



Hemlibra performance update

- ~21,000 patients treated globally
- Outstanding profile with >2/3 of patients on monthly or Q2W SC dosing and zero risk of developing inhibitors over time
- Non-inhibitor approved in >100 countries and reimbursed in 58
- Further penetration among moderate/severe patients who remain uncontrolled on FVIII ongoing; high satisfaction amongst switchers

Outlook

- Focus on access opportunities in non-inhibitors (severe and moderate); some countries already with ~70% non-inhibitor patient share (CA, UK, FR)
- Driving growth in key accounts which are below peak share potential
- Increasing international access

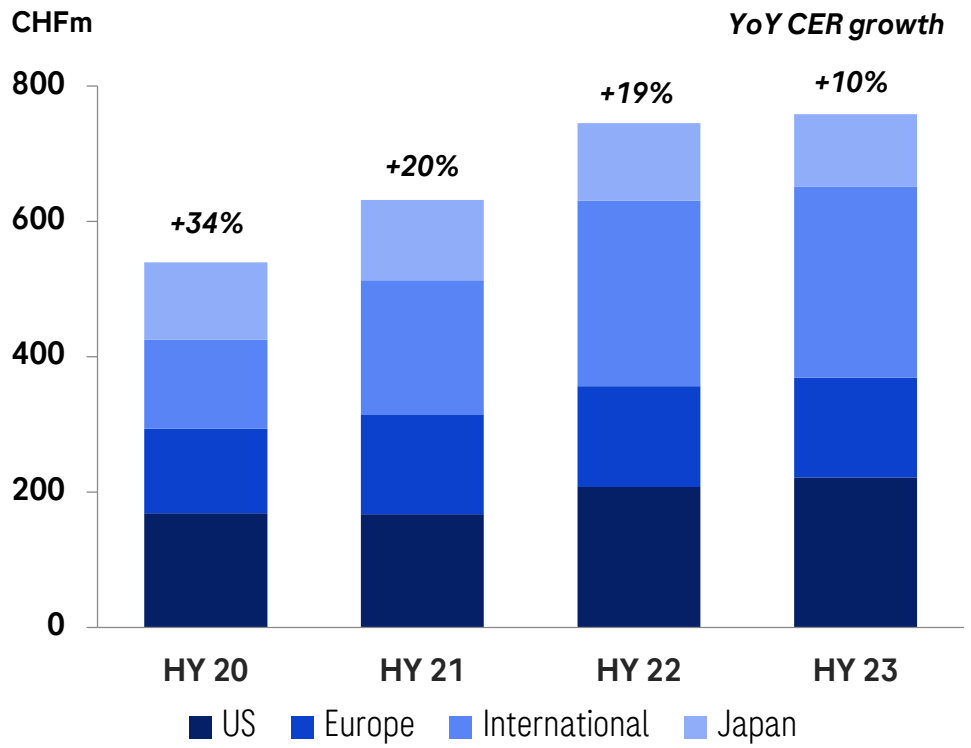
Further growth potential in our Hemophilia A franchise:
SPK-8011 gene therapy program and NXT-007 bispecific development ongoing

* US/EU5 Patient Share within Hemlibra labelled population, source: affiliate data (UK NHS Providers, US sales volume triangulated with IQVIA claims data, DE, ES, IT field force, France volumes); Q2W= every two weeks dosing

Alecensa: Unprecedented Ph III results in adjuvant ALK+ NSCLC

Continued >70 market share with further growth potential

Global Alecensa sales



Alecensa performance update

- Market leadership in 1L ALK+ NSCLC globally established
- Growth driven by International markets

Outlook

- Continued leadership and growth in 1L ALK+ NSCLC globally
- Expanding into early disease with ~45% of all ALK+ eNSCLC patients being tested at this stage*
- Positive Ph III (ALINA) results of Alecensa in adjuvant ALK+ NSCLC results to be presented at upcoming conference; first-in-class filing ongoing
- Ph III (TAPISTRY) tumor-agnostic multi-cohort study including Alecensa ongoing

* US data; ZS Primary Market Research, August 1st Release; CER=constant exchange rates; ALK=anaplastic lymphoma kinase; NSCLC=non-small cell lung cancer

2023: Key late-stage newsflow*

	Compound	Indication	Milestone	
Regulatory	**Hemlibra**	Moderate hemophilia A	EU approval	✓
	Polivy + R-CHP	1L DLBCL	US approval	✓
	Vabysmo	RVO	US approval/EU filing	✓ EU filing
	Tecentriq	Subcutaneous administration	US approval/EU filing	*US 2024 /* ✓ EU filing
	Columvi (glofitamab)	3L+ DLBCL	US/EU approval	✓
	Xofluza	Influenza (paediatric 1+ yrs.)	EU approval	✓
Phase III / pivotal readouts	**Tecentriq + Avastin**	Adjuvant HCC	Ph III IMbrave050	✓
	Tecentriq + chemo	Neoadjuvant / adjuvant TNBC	Ph III GeparDouze/NSABP B-59	*2024*
	Tecentriq	Adjuvant SCCHN	Ph III IMvoke010	
	Tecentriq + chemo	Adjuvant TNBC	Ph III IMpassion030	✗
	Tiragolumab + Tecentriq	1L PDL1+ NSCLC	Ph III SKYSCRAPER-01	*Q4 2023 / Q1 2024*
	Tiragolumab + Tecentriq + chemo	1L esophageal cancer	Ph III SKYSCRAPER-08 (China only)	*2024*
	Venclexta + dexamethasone	t(11;14) R/R MM	Ph III CANOVA	
	Venclexta + azacitidine	1L high risk MDS	Ph III VERONA	
	Alecensa	Adjuvant ALK+ NSCLC	Ph III ALINA	✓
	Phesgo OBI (on body injector)	HER2+ BC	Ph I *(pivotal)*	
	Crovalimab	PNH	Ph III COMMODORE 1/2	✓
	Columvi + GemOx	2L+ DLBCL	Ph III STARGLO	*2024*
	Lunsumio + Polivy	2L+ DLBCL	Ph III SUNMO	*2024*
	Elevidys (Delandistrogene moxeparvovec)	DMD	Ph III EMBARK	
	Ocrevus 6m SC	RMS / PPMS	Ph III OCARINA II	✓
	TNKase	Stroke patients 4.5-24h	Ph III TIMELESS	✗
	Susvimo	DME	Ph III PAGODA	✓
	Susvimo	DR	Ph III PAVILION	✓
	Xolair	Food allergy	Ph III OUtMATCH	

Additional 2023 newsflow:

- **Fenebrutinib**: Positive Ph II (FENopta) results in RMS
- **Elevidys** US approval in DMD for 4 and 5 years old (Sarepta)
- **Tiragolumab + Tecentriq + Avastin**: Positive Ph I/II (MORPHEUS) results in 1L HCC
- **Inavolisib + palbociclib + fulvestrant** Ph III (INAVO120) data expected Q4 2023

* Outcome studies are event-driven: timelines may change

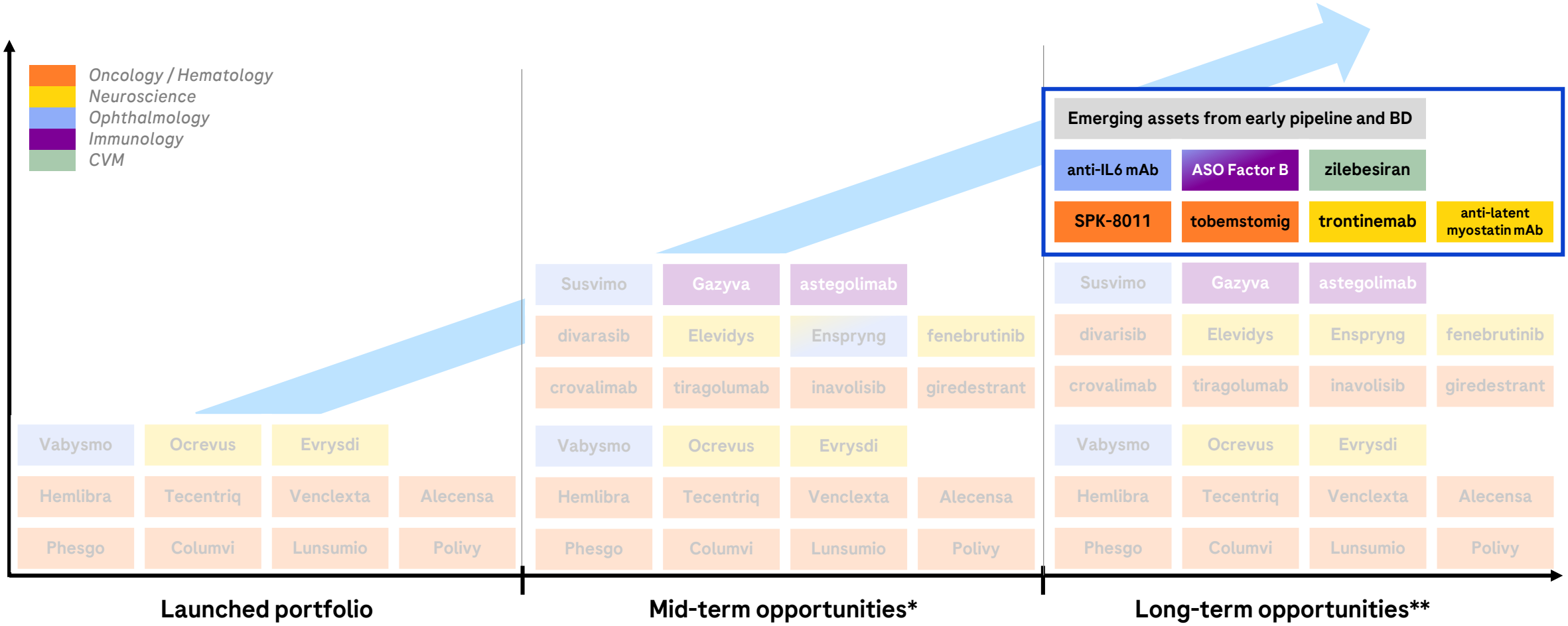
Pharma Update

On-Market Portfolio With Further Growth Potential

Significant Growth Opportunities Ahead

Building blocks for future growth through 2030

Several mid-term in-house late-stage projects that can deliver upside

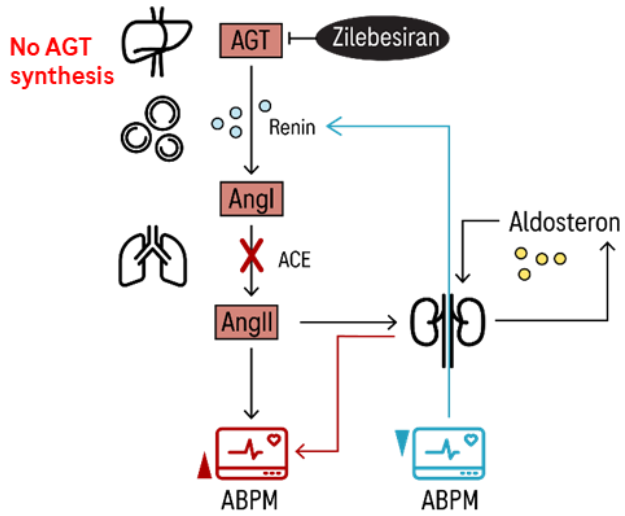


CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

Adding to in-house opportunities through BD

Successful track record of disrupting the SoC and building new franchises

Zilebesiran (siRNA targeting AGT)



- siRNA targeting AGT, the precursor protein of all angiotensin peptides
- Consistent + durable BP control with potential for improved adherence
- Ph II (KARDIA-1/2) development program ongoing; positive KARDIA-1 results to be presented at upcoming scientific conference; KARDIA-2 data expected in early 2024

Our proven strengths

- Strong track record of entering new therapeutic areas and disrupting established markets
- Expertise in advancing inclusive research to address health equity in CVM
- Strong Pharma & Diagnostics partnerships with health systems allow for integrated disease management solutions
- Integrated commercialization expertise utilizing an innovative customer engagement model
- Prowess in access and policy shaping differentiates Roche in the industry

In collaboration with Alnylam Pharmaceuticals
siRNAi=small interfering RNA; AGT=angiotensinogen; SoC=standard of care; CVM=cardiovascular & metabolism; BP=blood pressure

Key late-stage pipeline assets with 1bn+ sales potential*

Oncology, Hematology	*Neuroscience, Cardiometabolic*	*Immunology, Ophthalmology*
tiragolumab NSCLC, HCC, ESCC, SCCHN ●●	**Elevidys** DMD ●●	**astegolimab** COPD ●●
giredestrant HR+ BC ●●	**fenebrutinib** RMS, PPMS ●●	**ASO Factor B** IgAN, GA ●●
divarasib KRAS+ NSCLC, CRC ●	**anti-latent myostatin mAb** SMA, FSHD ●	**anti-IL-6** UME, DME ●●
inavolisib Pi3Km BC ●	**zilebesiran** hypertension ●●	
crovalimab PNH, aHUS, SCD, LN ●		
Tecentriq Adj. SCCHN / HCC, tira combo ●●	**Ocrevus** SC, high dose ●●	**Gazyva** LN, SLE, MN ●
Columvi 2L DLBCL, 1L DLBCL ●	**Enspryng** gMG, MOGAD, AIE, TED ●	
Lunsumio 2L DLBCL, R/R FL, 1LFL ●		

● *1bn+ sales potential* ●● *2bn+ sales potential*

8 late-stage NMEs with CHF>2 bn each in peak sales potential

4 late-stage NMEs with CHF >1bn each in peak sales potential

2 marketed products with LEs that could add CHF>2 bn each in peak sales potential

4 marketed products with LEs that could add CHF>1 bn each in peak sales potential

Trial populations listed in appendix table

*8 with 2bn+ opportunities; LE=line extensions

Late Stage Pipeline Oncology (Solid Tumors)

Levi Garraway |
EVP, Head of Global Product Development and Chief Medical Officer

Product Development

Continued commitment to delivering the worlds most impactful medicines

Selected Product Development Leaders

Head of PD/CMO
Levi Garraway

Clinical Science
Oncology & Hematology
Charlie Fuchs

Clinical Science
Neuroscience & Rare Diseases, Immunology, Infectious Disease & Ophthalmology
Paulo Fontoura

Medical Affairs
Stefan Frings

R&D Excellence

1. Set ambitious R&D objectives
2. Strengthen portfolio framework
3. Transform portfolio management & governance
4. Access the best external innovation
5. Optimize R&D engines and invest in emerging technologies
6. Evolve talent, culture and mindset to achieve objectives

R&D productivity

$$\text{R\&D productivity} = \frac{\text{Success rate} \times \text{Value} \times \text{Volume}}{\text{Costs} \times \text{Cycle time}}$$

Success rate × Value × Volume → Effectiveness

Costs × Cycle time → Efficiency

R&D=Research and development

Strategic pillars of oncology

Precision medicine	Early disease	Novel immunotherapy	Rational combinations	New modalities
Right medicines at the right patient	*Early diagnosis and treatment increases the chance for cure*	*Need more options for patients who have progressed on prior treatment*	*Leverage breadth of oncology portfolio to explore new combinations*	*Invest in potentially transformative science*
Recent/emerging examples				
inavolisib *INAVO120 (1L HR+ Pi3Km BC) data expected 2023* ***divarasib*** *Recently published data in NEJM*	***Alecensa*** *ALINA (adj ALK+ NSCLC) positive data* ***giredestrant*** *Potential to replace ET in eBC (and mBC)*	***tiragolumab + Tecentriq*** *Ph III in 1L HCC initiated* ***Tombestomig (PD1 x LAG3)*** *Multiple Ph II trials initiated (e.g. mUC, NSCLC, RCC)*	***Polivy + Columvi +R-CHP*** *Ph III trial in 1L DLBCL to be initiated* ***giredestrant + Phesgo*** *HeredERA (1L HER2+/HR+ BC)*	***AR Degrader*** *Ph I trial in mCRPC with FPI in Q2* ***PROTAB*** *Recent paper published in Nature*

HCC=Hepatocellular carcinoma; NSCLC=Non-Small Cell Lung Cancer; R-CHP=Rituxan + cyclophosphamide + hydroxydaunorubicin + prednisone; DLBCL=Diffuse large B-cell lymphoma; Pi3K=Phosphoinositide 3-Kinase; NEJM=New England Journal of Medicine; ET=Endocrine therapy; eBC=Early breast cancer; mBC=Metastatic breast cancer;HR=Hormone receptor;adj=adjuvant; mUC=Metastatic urothelial carcinoma; RCC=Renal cell carcinoma; HER2=Human epidermal growth factor receptor 2; mCRPC=Metastatic castration-resistant prostate cancer

Oncology – solid tumor pipeline

A leading portfolio differentiated on targets and modalities

Ph I (26 NMEs)

RG6156	EGFRvIII x CD3
RG6185	belvarafenib (pan-RAF inh)
RG6189	FAP-CD40
RG6194	runimotamab (HER2 x CD3)
RG6279	eciskafusp alfa (PD1-IL2v)
RG6286	undislcosed
RG6292	CD25 MAb
RG6323	IL15/IL15Ra-Fc
RG6344	BRAF inhibitor (3)
RG6353	HLA-G x CD3
RG6411	undisclosed
RG6433	SHP2i
RG6440	TGFβ (SOF10)
RG6524	DLL3 trispecific
RG6526[1]	camonsertib
RG6537	AR Degrader
RG6596[2]	ZN-1041 (HER2 TKI)
RG6614[3]	KSQ-4279 (USP1 inh)
RG7802	cibisatamab
RG7827	FAP-4-1BBL
CHU	glypican-3 x CD3
CHU	codrituzumab
CHU	CD137 switch antibody
CHU	RAS inhibitor
CHU	SPYK04
CHU	SAIL66

Ph II

RG6058	**tiragolumab** Multiple indications
RG6139	**tobemstomig** Solid tumors
RG6180	**autogene cevumeran** 1L melanoma

- Small molecule
- Antibody
- Bispecifics/Trispecifics
- Neoantigen vaccines
- Fusion protein
- Antibody drug conjugate
- Cyclic peptides

Ph III

RG6058	**tiragolumab** Multiple indications
RG6114	**inavolisib** HR+ mBC
RG6171	**giredestrant** HR+ BC
RG7440	**divarasib** 2L NSCLC
RG3502	**Kadcyla** HER2+ eBC high risk
RG7446	**Tecentriq** Multiple indications
RG6058	**Alecensa** ALK+ NSCLC adj

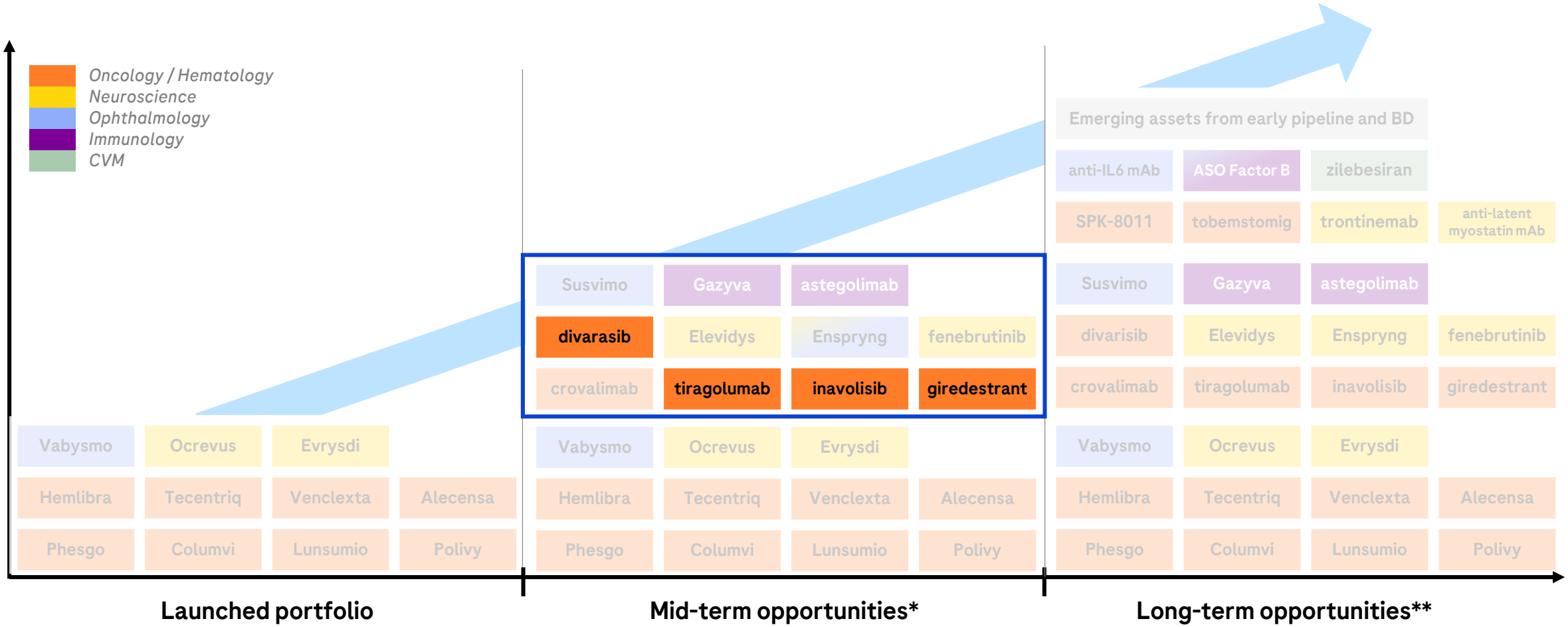
Launched

RG6058	**Alecensa** 1L ALK+ NSCLC
RG3502	**Kadcyla** HER2+ BC
RG1273	**Perjeta** HER2+ BC
RG6264	**Phesgo** HER2+ BC
RG7446	**Tecentriq** Multiple indications
RG6268	**Rozyltrek** ROS1+ & NTRK+ NSCLC

NME=new molecular entities; [1]managed by Repare Therapeutics; [2]managed by Zion Pharma; [3]managed by KSQ Therapeutics

Building blocks for future growth through 2030

4 NMEs in oncology with FIC/BIC potential in late stage development

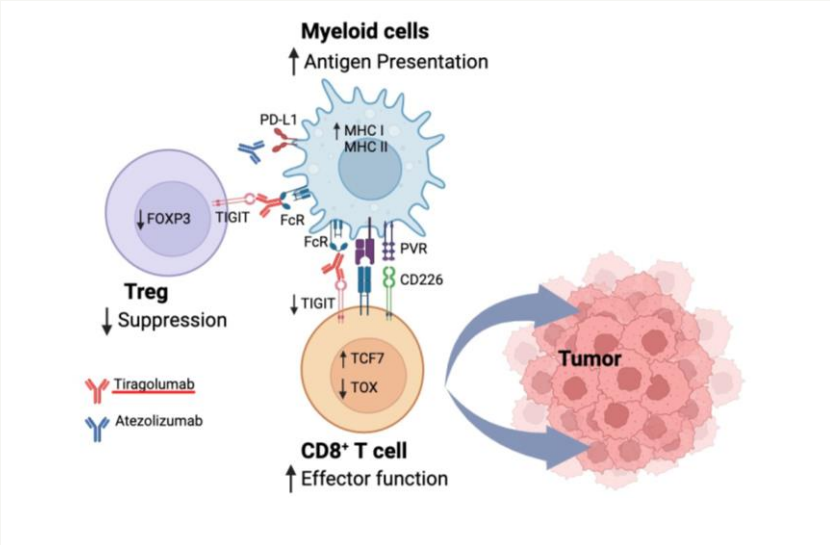


CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

Tiragolumab development program continues to expand

Continued confidence in anti-TIGIT biological activity based on numerous evidence to date

First-in-class anti-TIGIT mAb



- Tiragolumab blocks the binding of TIGIT to its ligand PVR
- Tiragolumab activates T-cells and also modifies the tumor microenvironment by decreasing suppressive T-regs and activating myeloid cells via its intact Fc region
- This could lead to an enhanced anti-tumor immune response when combined with PD-L1 blockade

Clinical development program

	Indication	Ph I / Ph II / Ph III	
Lung cancer	1L NSCLC: PD-L1 high	SKYSCRAPER-01	Results in Q4/Q1
	Stage III unres. NSCLC	SKYSCRAPER-03	
	Neoadj / Adj NSCLC	SKYSCRAPER-05	
	1L NSq NSCLC	SKYSCRAPER-06	
GI/GU cancer	1L uHCC	SKYSCRAPER-14 / IMbrave152	
	Locally advanced ESCC	SKYSCRAPER-07	LPI in Q3
	1L ESCC	SKYSCRAPER-08	Results in H1 2024
Other solid tumors	2L+ PD-L1+ Cervical Ca	SKYSCRAPER-04	Results in H2 2023
	1L SCCHN	SKYSCRAPER-09	
Formulations	Fixed Dose Combination	SKYSCRAPER-11	
	Subcutaneous		

- Comprehensive development program ongoing
- Ph III SKYSCRAPER-14/IMbrave152 in 1L unresectable HCC initiated
- Ph III SKYSCRAPER-01 continues to the final OS analysis expected in Q4/Q1 (event-driven)

mAb= monoclonal antibody; NSCLC=Non-Small Cell Lung Cancer; ESCC=esophageal squamous cell carcinoma; NSq=non-squamous; HCC=hepatocellular carcinoma; uHCC=unresectable hepatocellular carcinoma; SCCHN=squamous cell carcinoma of head and neck; OS=Overall survival; LPI=last patient in; PVR=Poliovirus receptor

Tiragolumab in 1L NSCLC and 1L HCC

SKYSCRAPER-01 continues to final OS analysis; Ph III in HCC initiated

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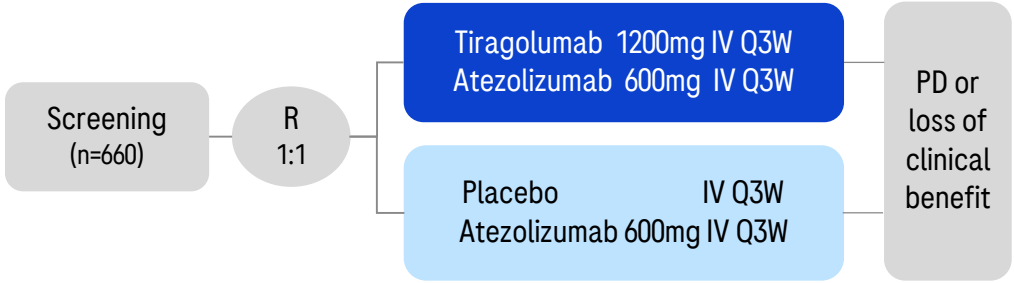
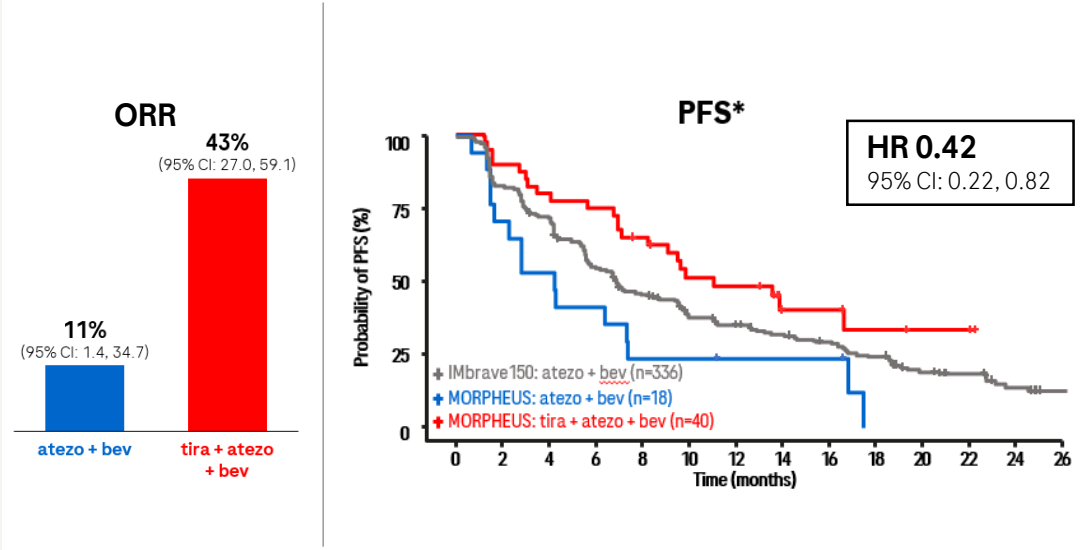
Ph III (SKY-01) trial design in 1L PDL1+ NSCLC



- At the 1st interim primary PFS endpoint not met; however, a numeric improvement was observed in both PFS and OS and curves were separating
- Inadvertent disclosure of 2nd interim analysis of SKYSCRAPER-01: study is ongoing and remains blinded to patients and investigators
- We are continuing the study as planned until the final analysis for overall survival
- At the 2nd interim OS was immature with a mOS of 22.9m for tiragolumab + Tecentriq vs 16.7m for Tecentriq (HR=0.81); no new safety signals

Ph I/II (MORPHEUS) results in 1L HCC



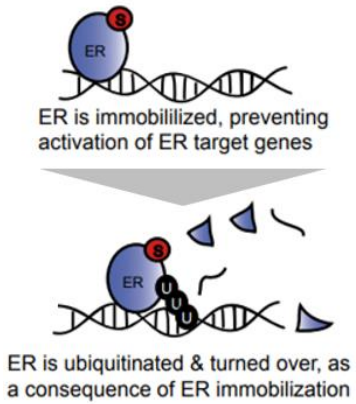
- Tiragolumab + Tecentriq + Avastin with an ORR of 43% and a PFS benefit of 58% (HR=0.42)
- Treatment benefit supported by benchmarking vs Ph III IMbrave150 data
- No new safety signals

Finn R, et al. ASCO 2023; NSCLC=non-small cell lung cancer; HCC=hepatocellular carcinoma; PFS=Progression-free survival; OS=Overall survival; mOS=median overall survival; m=month; CI=confidence interval; ORR=overall response rate; HR=hazard ratio; PD=progressive disease; IV=intravenous; Q3W=every 3 weeks

Giredestrant in HR+ breast cancer

Potential new endocrine backbone potential across eBC and mBC

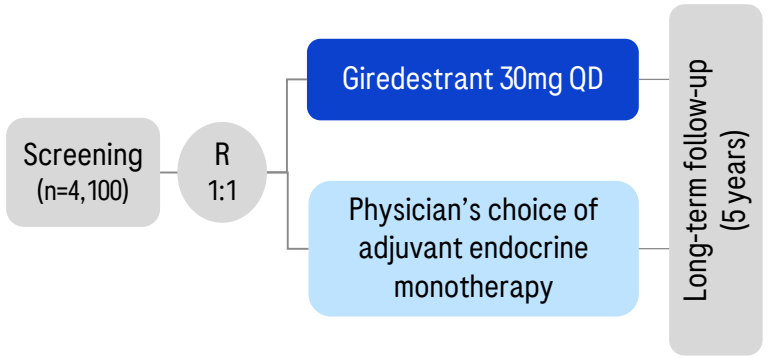
Selective ER degrader (SERD)



- Highest preclinical potency vs. other oral SERDs in development
- Combinable with all CDKis including: palbociclib, abemaciclib, ribociclib
- Well tolerated at all doses, with no dose-limiting toxicity

Broad development program in eBC and mBC

Ph III (lidERA) trial design in adjuvant ER+/HER2- BC



Clinical development program

Indication regimen	Ph I	Ph II	Ph III
1L ER+/HER2- mBC giredestrant + palbociclib	*persevERA*		
1L ER+/HER2- mBC giredestrant + CDK4/6 of choice	*pionERA*		
Adjuvant ER+/HER2- BC giredestrant	*lidERA*		
1L maintenance ER+/HER2+ mBC giredestrant + Phesgo	*heredERA*		

- Girdestrant has the potential to be best-in-class backbone endocrine agent in HR+ BC, either used alone or in combination, replacing standard of care (aromatase inhibitor, fulvestrant or tamoxifen)
- A single-arm lidERA substudy will investigate giredestrant + abemaciclib in high risk eBC patients; lidERA is ~1 yr ahead of other oral SERD competition in eBC
- Initiated additional Ph III (pionERA) trial in 1L mBC (girdestrant + CDK4/6 of choice vs. fulvestrant + CDK4/6 of choice)
- First results from Ph III persevERA (1L mBC) expected in 2025

SERD=Selective estrogen receptor degrader; HR=Hormone receptor; ER=Estrogen receptor; HER2=Human epidermal growth factor receptor 2; BC=Breast cancer; mBC=metastatic breast cancer; eBC=early breast cancer; CDKi=Cyclin-dependent Kinase Inhibitor; CDK4/6=CDKI=Cyclin-dependent Kinase 4/6

Giredestrant data support potential in 1L and adj HR+ BC

Tumor response is correlated with higher tumor ER activity

In eBC , 1L, and ESR1m patients, the tumor is ER pathway dependent

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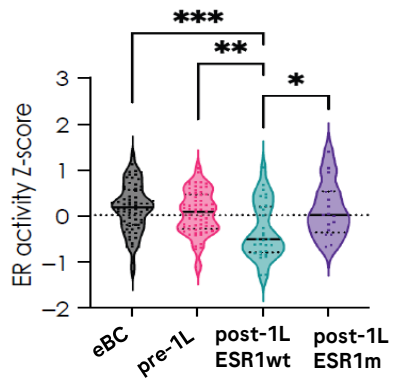
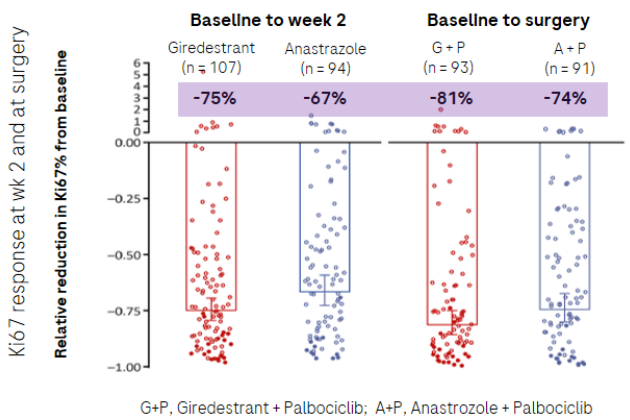
Tumor ER pathway activity by time of sample collection



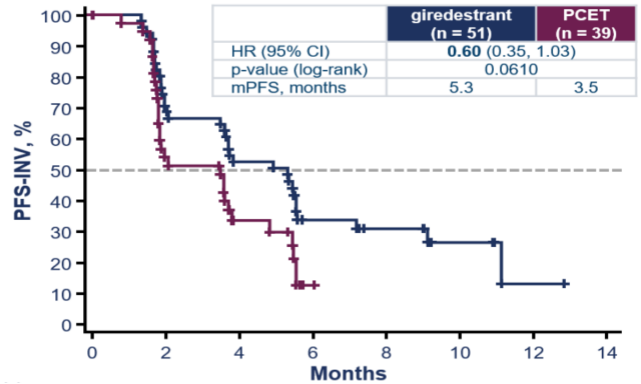
2022 ASCO ANNUAL MEETING

Ph II (coopERA) results in neoadj setting



PARIS 2022 ESMO congress

Ph II acelERA results in 2/3L setting PFS-INV: ESR1m subgroup



- Exploratory biomarker analysis of acelERA: Post 1L treatment, ER activity was maintained in patients with ESR1m tumors at levels similar to early BC and pre-1L, while activity was significantly lower in late-line patients with no ESR1 mutation
- Ph II (coopERA) in neoadjuvant setting: Final analysis confirmed greater suppression of Ki67 and rates of complete cycle arrest with giredestrant vs. anastrazole at time of surgery; Ki67 is a biomarker of proliferation associated with improved long-term efficacy outcomes in early stage disease
- Ph II (acelERA) in 2/3L setting: PFS benefit more pronounced in patients with baseline ESR1 mutations (HR 0.61 in ESR1m patients vs. HR 0.81 in all-comers)
  - Majority of 2L/3L patients appear to be no longer sensitive to endocrine inhibition but ESR1m patients' tumors are still dependent on ER signaling

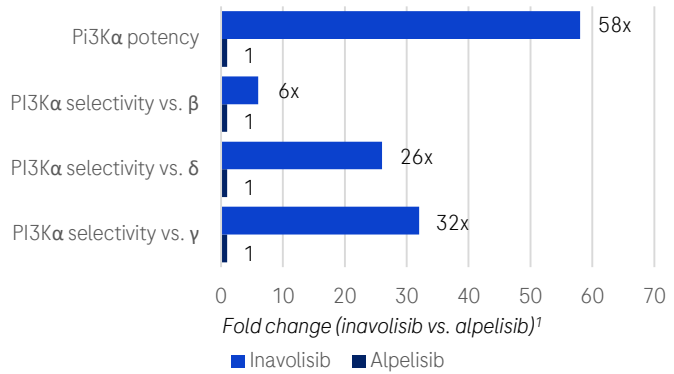
Collier A. et al., ASCO 2023; Fasching P. et al., ASCO 2022; Martin M. et al., ESMO 2022; adj=adjuvant; ORR=objective response rate; PFS=progression-free survival; HR=hazard ratio; HR+=Hprmone receptor positive; ER=estrogen receptor; eBC=early breast cancer; m=months; CI=confidence interval; ESR1=estrogen receptor 1

Inavolisib in *PI3K*-mutant breast cancer

H2H trial vs alpelisib initiated; Ph III (INAVO120) results in 1L expected Q4 2023

Potential best-in-class PI3Kα inh

Potency/selectivity (inavolisib vs. alpelisib)

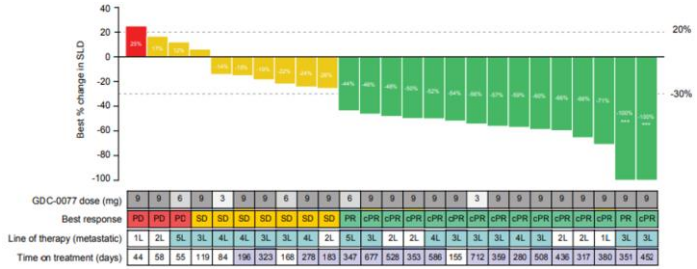


- Differentiated from existing PI3K inhibitors:
  - More potent and selective for PI3Kα subunit
  - Better in vivo efficacy
  - Greater safety margins allow for combination with ET and palbociclib at standard doses
- 40% of HR+/HER2- patients with *PI3K* mutations

Potential for differentiated safety, efficacy, and combinability

Ph I dose escalation and expansion cohort:

Inavolisib + palbociclib + letrozole



Clinical development program

Indication regimen	Ph I	Ph II	Ph III
1L HR+/HER2- PI3Km mBC inavolisib + palbociclib + fulvestrant	INAVO120		
Post CDK4/6i HR+/HER2- PI3Km mBC inavolisib + fulvestrant	INAVO121		
1L PI3Km and HER+ mBC inavolisib + Phesgo	INAVO122		

- Strong efficacy and favorable safety as single agent or in combination with ET +/- CDK4/6i in patients with *PI3K*-mutant HR+ breast cancer
- Ph III INAVO120 in 1L HR+/PI3Km mBC data expected in Q4 2023
- Ph III INAVO121 post-CDKi (head-to-head vs. alpelisib) achieved FPI in Q2
- Ph III INAVO122 in 1L HER2+/PI3Km BC (combination with Phesgo) achieved FPI in Q3

Kalinsky K. et al., AACR 2017; Jhaveri, K., et al, SABCS 2019; H2H=head-to-head; inh=inhibitor; ET=endocrine therapy; HR=hormone receptor; mBC=metastatic breast cancer; FPI=first patient in; PI3K=Phosphoinositide 3-Kinase; ET=Endocrine therapy; HR=Hormone receptor; HER2=Human Epidermal growth factor Receptor 2; CDK4/6i=Cyclin-dependent kinase 4 and 6 inhibitors; BC=Breast cancer

ZN-1041 in HER2+ BC with brain metastases

Building on HER2+ breast cancer franchise, exploring novel combinations

2023 ASCO ANNUAL MEETING

Potential best-in-class HER2 TKI

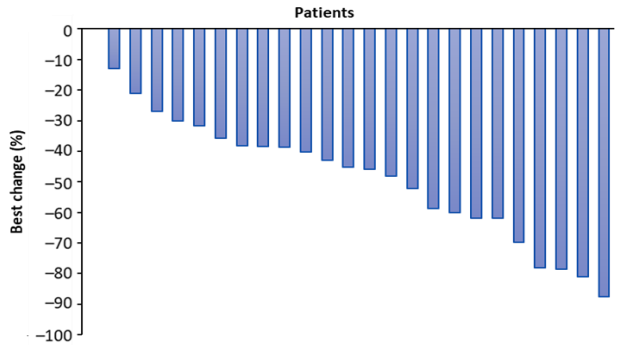
TKI	$AUC_{br,u}/AUC_{pl,u}$	Efflux transporter (P-gp/BCRP) substrate?
Tucatinib	0.004	Yes
Lapatinib	0.010	Yes
Neratinib	0.013	Yes
Pyrotinib	0.024	Yes
Epertinib	0.080	Yes
ZN-1041	**0.470–0.770**	**No**

- Differentiated by high blood-brain-barrier permeability and CNS retention
- ZN-1041 is not effluxed by P-gp and BCRP transporters, resulting in better CNS retention (>100-fold vs. tucatinib)[1]

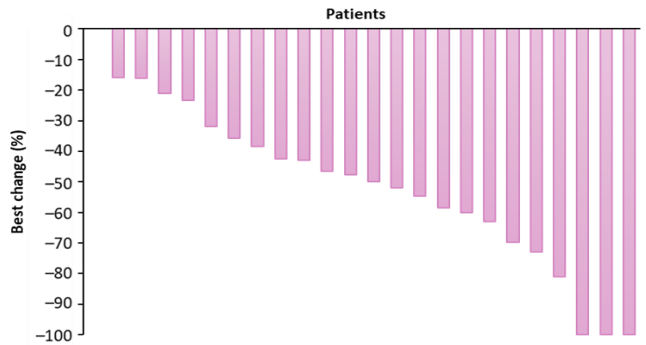
Encouraging preliminary activity and safety

Ph Ic combination results with trastuzumab and capecitabine results[1]

Overall tumor size changed from baseline



CNS tumor size changed from baseline



- Well tolerated and promising GI safety profile observed compared to other HER2 TKIs
- May be combined with other established anti-HER2 backbones (e.g., Phesgo, Kadcyla, Enhertu) to improve efficacy outcomes, for both prevention and treatment of brain metastases
- Ph I trial in patients with HER2+ breast cancer ongoing

[1] Ma F, et al., ASCO 2023; BC=breast cancer; TKI=tyrosine kinase inhibitor; CNS=central nervous system; AUC=area under the curve; BCRP=breast cancer resistance protein; P-gp=P-glycoprotein; GI=gastrointestinal; HER2=Human Epidermal growth factor Receptor 2

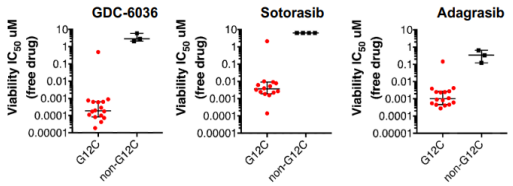
Divarasib in KRAS G12C-mutant tumors

Potential best-in-class molecule; Ph II/III in 2L NSCLC ongoing

FDA BTD

KRAS G12C inhibitor

Proliferation potency/selectivity



- Divarasib is an irreversible covalent inhibitor of mutant KRAS G12C protein resulting in a locked inactive conformation
- Best-in-class potential being more potent and selective *in vitro* than sotorasib and adagrasib

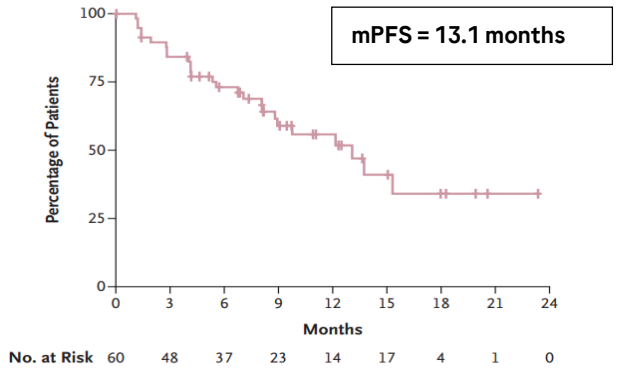
Best-in-class potential supported by early clinical data

The NEW ENGLAND JOURNAL of MEDICINE

Overall response rates

Indication Regimen	Confirmed ORR
2L+ NSCLC Monotherapy	53% (all doses) 56% (400mg dose)
2L+ CRC Monotherapy	29% (all doses) 36% (400mg dose)
2L+ CRC Divarasib + cetuximab	62%

PFS (all doses) in 2L+ NSCLC monotherapy



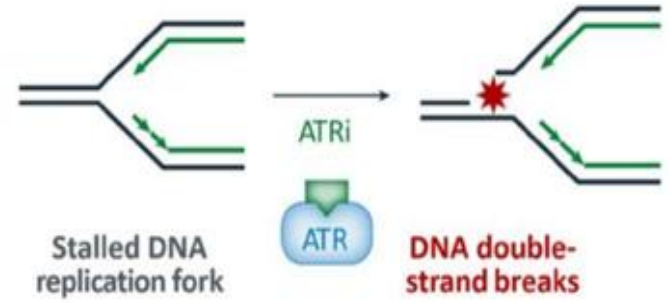
- Robust clinical benefit in patients with KRAS G12Cm NSCLC and CRC as monotherapy and in combination
- Manageable safety with reversible adverse events across tumor types
- Pivotal Ph II/III trial in 2L NSCLC (BFAST) with divarasib cohort ongoing
- Ph Ib trials in 1L NSCLC (KRASCENDO) in combination with pembrolizumab and in 1L, 2L CRC (INSTRINSIC) in combination with cetuximab +/- FOLFOX/FOLFIRI) initiated

Purkey H. et al., AACR 2022; Sacher A. et al., NEJM Aug 2023; Desai J, et al., AACR 2023; NSCLC= non-small cell lung cancer; CRC=colorectal cancer; PFS=progression free survival; mPFS=median progression free survival; FOLFOX=folinic acid, fluorouracil and oxaliplatin; FOLFIRI=folinic acid, fluorouracil and irinotecan; ORR=Overall Response Rate

DNA Damage Response (DDR)

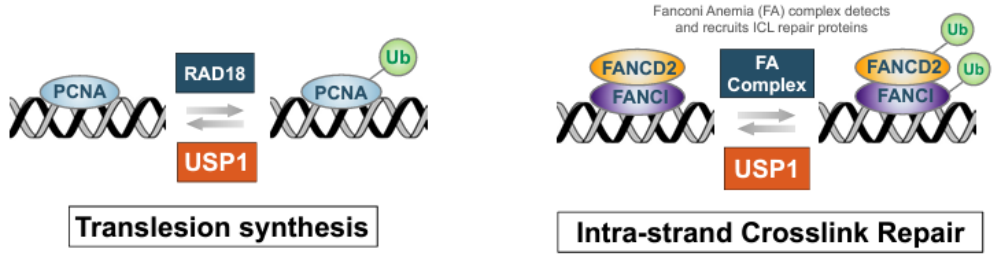
Building a diversified and differentiated portfolio in DDR

Camonsertib (ATR inhibitor)



- ATR is a key mediator of cellular DDR and is activated in response to DNA replication stress
- Preclinical studies suggest camonsertib to be more selective and potent vs. other ATRi in development with best-in-class potential
- Ongoing PhI/II (TRESR) demonstrated monotherapy responses in multiple tumors (ovarian, breast, prostate) including patients who received prior PARPi and prior platinum chemotherapy
- Currently investigated as monotherapy and in combo with various agents

KSQ-4279 (first-in-class USP1 inhibitor)



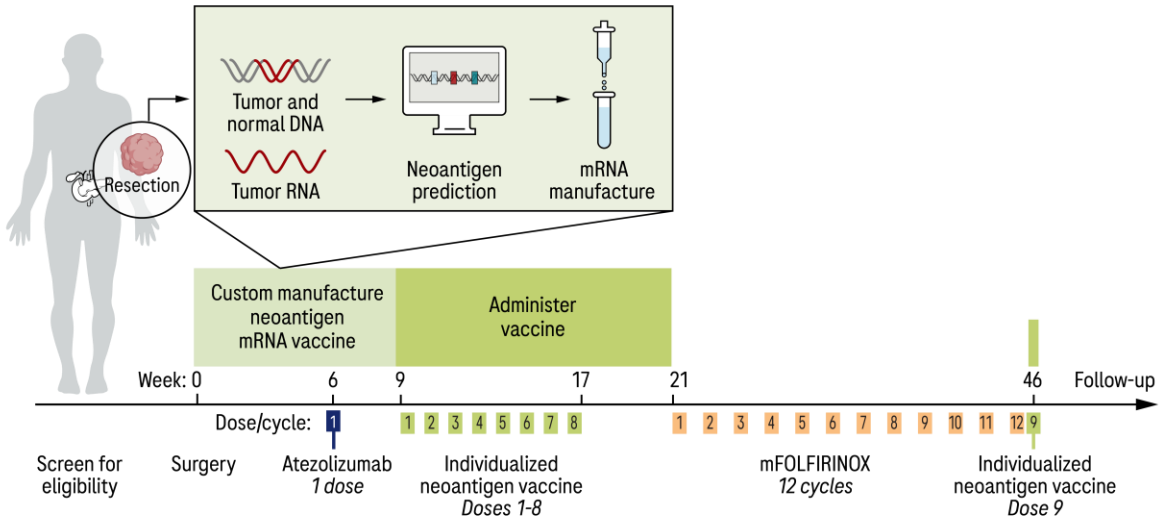
- USP1 is involved in DNA damage repair processes through mechanisms distinct from both PARPi and other targeted therapies
- KSQ-4279 is a first-in-class small molecule inhibitor of USP1
- Combination with PARPi demonstrated strong activity in PARP naïve and PARP resistant mouse models
- Ph I trial in patients with advanced solid tumors ongoing

Camonsertib in partnership with Repare Therapeutics; KSQ-4279 in partnership with KSQ Therapeutics; DDR=DNA Damage Response

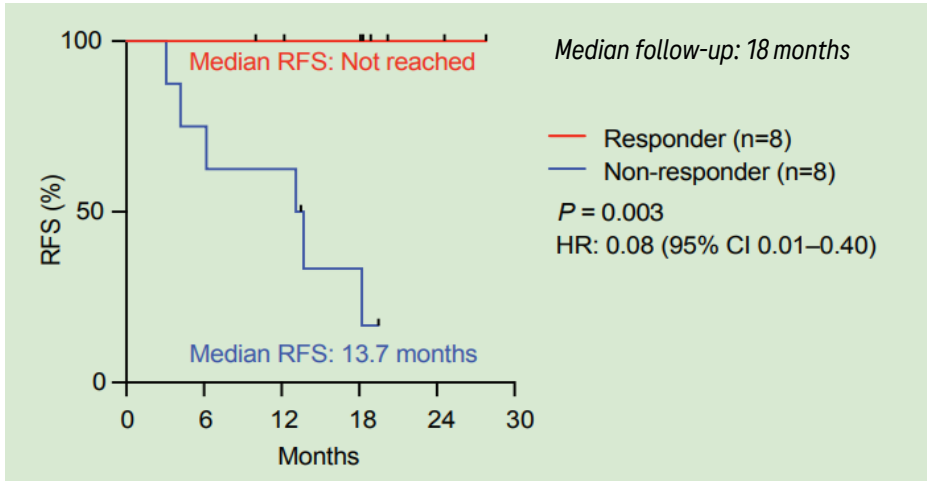
Neoantigen vaccine: Autogene cevumeran

Substantially and durably expanded T-cells, correlating with delayed recurrence

Phase I results in surgically resectable PDAC (target n=20)



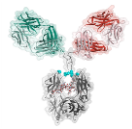
Vaccine induced T-cell response associated with longer RFS



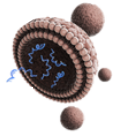
- Autogene cevumeran expanded polyclonal IFNγ-producing neoantigen-specific CD8 + T-cells in 50% (n = 8/16) of patients from undetectable levels to large fractions (median 2.9%) of all blood T-cells
- Randomized trial in PDAC initiated, FPI expected Q3 2023
- Planning to initiate additional studies in other tumors

Autogene cevumeran in partnership with BioNtech; Balachandran V et al., ASCO 2022; PDAC=pancreatic ductal adenocarcinoma; RFS=relapse free survival

Advancing new modalities across key oncology pathways

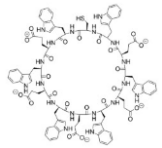


Bispecifics / trispecifics

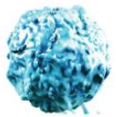


Neoantigen vaccines

Degraders

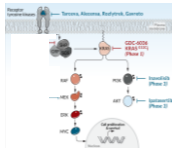


Cyclic peptides



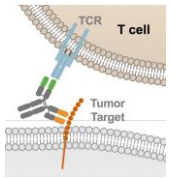
Cell Therapies

PROTABS
(Proteolysis-targeting antibody)



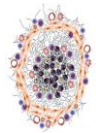
Oncogenic pathways/drivers

Synthetic lethality/DNA damage response



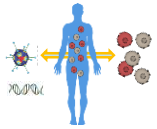
T-cell redirection

Synthetic immunity



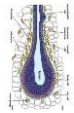
Tumor microenvironment

Immunomodulation



Adaptive immunity

T-cell generation



Lineage dependencies

Explore biology of early disease and transform treatment of cancer

Late Stage Pipeline Hematology

***Charles Fuchs* |**

SVP – Global Head of Hematology and Oncology Product Development

Roche: A leader in malignant and non-malignant hematology

Launching new standards of care

- *Hemlibra in hemophilia A*
- *Polivy + R-CHP in 1L DLBCL*
- *Lunsumio in 3L+ FL*
- *Columvi in 3L+ DLBCL*

Investing in growing & new indications

- *Established leader in DLBCL, FL, CLL and hemophilia A*
- *Expansion potential in malignant (AML, MM, MDS, MCL) and in non-malignant hematology (PNH, aHUS, SCD)*

Broad portfolio enables novel combinations

- *7 medicines on the market and 10 NMEs in clinical development*
- *Novel combinations in NHL (e.g. Polivy + CD20xCD3 bispecifics; Columvi + costimulatory molecules)*

Exploring different modalities

- *Bispecific antibodies*
- *Antibody drug conjugates*
- *Recycling antibody technology*
- *Gene therapy*
- *Allogeneic CAR-T*

Improving patient / provider experience

- *Fixed duration*
- *Simple dosing schedule*
- *Off-the-shelf availability*
- *Outpatient administration*

DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; CLL=chronic lymphocytic leukemia ; MM=multiple myeloma; AML=acute myeloid leukemia; MDS=myelodysplastic syndromes; MCL=mantle cell lymphoma; CAR-T=chimeric antigen receptor T- cell; R-CHP=rituxan + cyclophosphamide + doxorubicin + prednisone; PNH=Paroxysmal Nocturnal Hemoglobinuria; aHUS=atypical Hemolytic Uremic Syndrome; SCD=Sickle Cell Disease; NHL=Non-Hodgkins lymphoma; NME=New Molecular Entity

Broad hematology pipeline enabling novel combinations

A pioneer in bispecific antibodies and antibody drug conjugates

Ph I

RG6076	**englumafusp alfa** Heme tumors
RG6160	**cevostamab** r/r MM
RG6234	**forimtamig** MM
RG6323	**IL15/IL15Ra-Fc** Heme tumors
RG6333	**CD19 x CD28** r/r NHL
RG6512	**FIXa x FX** Hemophilia
RG6538*	**P-BCMA-ALLO1** MM
RG6026	**Columvi** Heme tumors
RG7828	**Lunsumio** Heme tumors

Ph II

RG6026	**Columvi** 1L ctDNA high risk DLBCL
RG6107	**crovalimab** SCD
RG6357	**dirloctogene samoparvovec** Hemophilia A

Ph III

RG6026	**Columvi** 2L+ DLBCL
RG7828	**Lunsumio** 2L+ FL & 2L+ DLBCL
RG6107	**crovalimab** aHUS
RG7601	**Venclexta** r/r MM & 1L MDS

- Small molecule
- Antibody
- Bispecifics
- Gene therapy
- Fusion protein
- Antibody drug conjugate
- Allogeneic CAR-T cells

Registration

RG6107	**crovalimab** PNH

Launched

RG6026	**Columvi** 3L+ DLBCL
RG7828	**Lunsumio** 3L+ FL
RG7596	**Polivy** 1L & r/r DLBCL
RG7601	**Venclexta** CLL & AML
RG6013	**Hemlibra** Hemophilia A
RG7159	**Gazyva** CLL & FL
RG105	**MabThera** DLBCL, FL & CLL

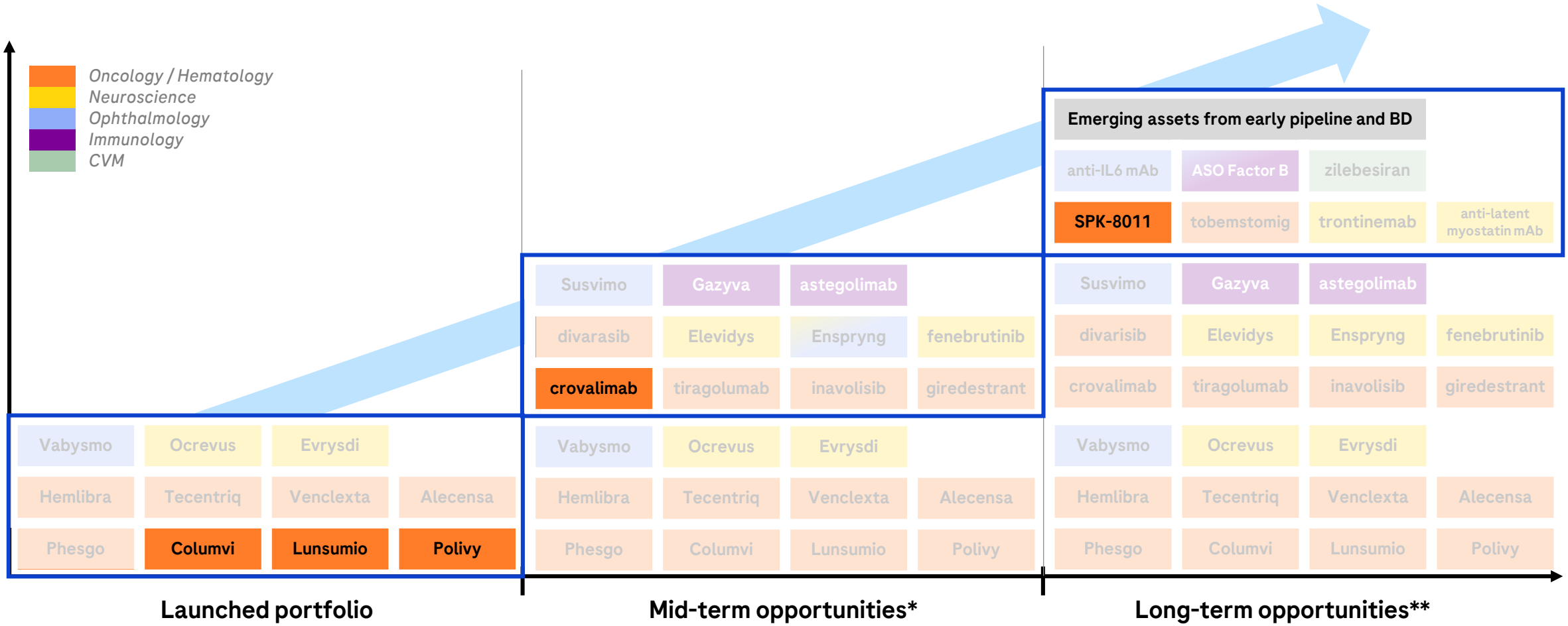
*managed by Poseida Therapeutics; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; CLL=chronic lymphocytic leukemia ; MM=multiple myeloma; AML=acute myeloid leukemia; MDS=myelodysplastic syndromes; PNH=Paroxysmal Nocturnal Hemoglobinuria; aHUS=atypical Hemolytic Uremic Syndrome; SCD=Sickle Cell Disease; NHL=Non-Hodgkins lymphoma; CAR-T=chimeric antigen receptor T- cell

Update late-stage hematology pipeline

Malignant hematology: B-cell malignancies

Non-malignant hematology: PNH, Hemophilia A

Building blocks for future growth through 2030



CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

Update late-stage hematology pipeline

Malignant hematology: B-cell malignancies

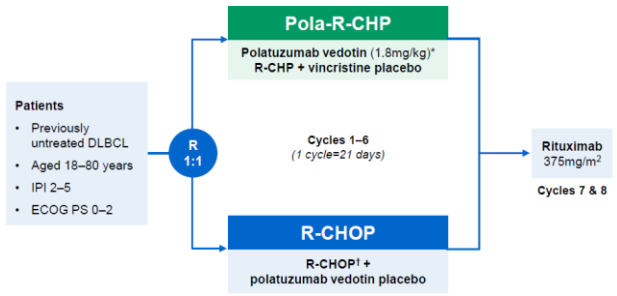
Non-malignant hematology: PNH, Hemophilia A

Polivy + R-CHP to become a new SOC in 1L DLBCL

POLARIX subgroup data confirm benefit in elderly patients

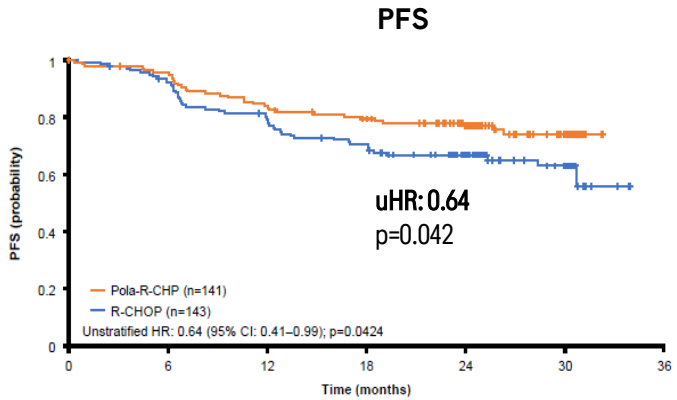
Polivy + R-CHP first new treatment in >20 years in 1L DLBCL

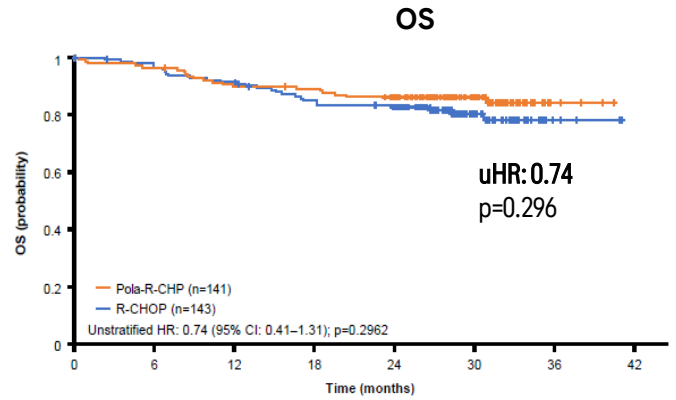
Ph III (POLARIX) trial design



- Sustained PFS benefit for Polivy+R-CHP (HR 0.76) vs. R-CHOP (mFU 39.7 mo)
- Safety comparable with that of R-CHOP
- Off-the-shelf and fixed duration treatment
- For all treatment settings, including community
- Approved in >80 countries
- Ph III Columvi+Polivy+R-CHP to initiate in 2023

Ph III (POLARIX) subgroup of ~280 patients (median age 74 yrs), similar baseline characteristics compared to ITT





- Clinically meaningful improvement in PFS with a uHR of 0.64 for Polivy+R-CHP vs R-CHOP
- OS data immature with a trend for reduction in the risk of death with a uHR of 0.74
- Similarly high treatment exposure across both treatment arms, highlights the tolerability of the Polivy+R-CHP regimen in elderly patients
- The safety profile of Polivy+R-CHP in patients aged ≥70 years with 1L DLBCL was generally similar to that of R-CHOP and consistent with that reported for the overall population aged 18-80 years

Hu B et al., ASCO 2023; Herrera et al. ASH 2022; DLBCL=diffuse large B-cell lymphoma; PFS=progression free survival; OS= overall survival; mFU=median follow-up; ITT=intent-to-treat; R-CHOP=Rituxan + cyclophosphamide + doxorubicin + vincristine + prednisone; R-CHP=Rituxan + cyclophosphamide + hydroxydaunorubicin + prednisone; HR=hazard ratio; uHR=unstratified hazard ratio; CI=confidence interval; SOC=Standard of care

Lunsumio and Columvi: Tailored to address diverse patient and healthcare system needs in off-the-shelf approach

Approved in 3L+ follicular lymphoma

Lunsumio

- High CR rate and durable responses
- Favorable tolerability with low grade CRS
- No required hospitalization

For outpatient setting, indolent disease (FL) and elderly/unfit patients

Approved in 3L+ diffuse large B cell lymphoma

Columvi

- Best in class efficacy potential, high CR rates and durable responses comparable to CAR-Ts
- Well tolerated with low grade, predictable CRS; low rate of ICANS and discontinuations
- Minimal CRS in 1L DLBCL combined with R + chemo

For aggressive disease (1L DLBCL, R/R DLBCL, MCL)

CD20 x CD3 development program moving into earlier lines

Regimen	Indication	Ph I / Ph II / Ph III
Lunsumio	3L+ FL	✓ US/EU approved
Lunsumio + Polivy	2L+ DLBCL (SCT-ineligible)	SUNMO — Readout 2024
Lunsumio + lenalidomide	2L+ FL	CELESTIMO
Lunsumio	r/r CLL	
Lunsumio	1L DLBCL (elderly/unfit)	
Lunsumio + Polivy	1L DLBCL (elderly/unfit)	

Regimen	Indication	Ph I / Ph II / Ph III
Columvi	3L+ DLBCL	✓ US/EU approved
Columvi + GemOx	2L+ DLBCL (SCT-ineligible)	STARGLO — Readout 2024
Columvi + CD19x4-1BBL	r/r NHL	
Columvi + CD19xCD28	r/r NHL	
Columvi + Polivy + R-CHP	1L DLBCL	Ph III to initiate in 2023

- Ph III readouts for Columvi + GemOx in 2L+ DLBCL (STARGLO) and Lunsumio + Polivy in 2L + DLBCL (SUNMO) expected 2024

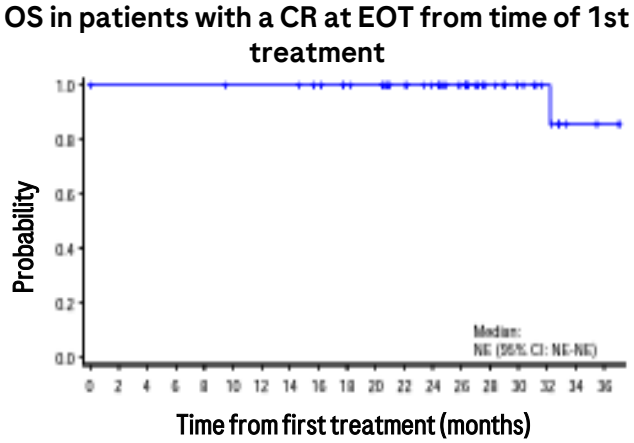
CR=complete response; CRS=Cytokine Release Syndrome; r/r=relapsed refractory; FL=follicular lymphoma; DLBCL=diffuse large B-cell lymphoma; CLL=chronic lymphocytic leukemia; SCT=stem cell transplantation; NHL=non-Hodgkin's lymphoma; GemOx=gemcitabine oxaliplatin; R-CHP=rituxan + cyclophosphamide + hydroxydaunorubicin + prednisone; ICANS=Immune Effector Cell-associated Neurotoxicity Syndrome; R=Rituximab; MCL=Mantle Cell Lymphoma

Lunsumio: Durable efficacy with a manageable safety profile in patients with 3L+ FL after > 2 years of follow-up

Roche
Lunsumio

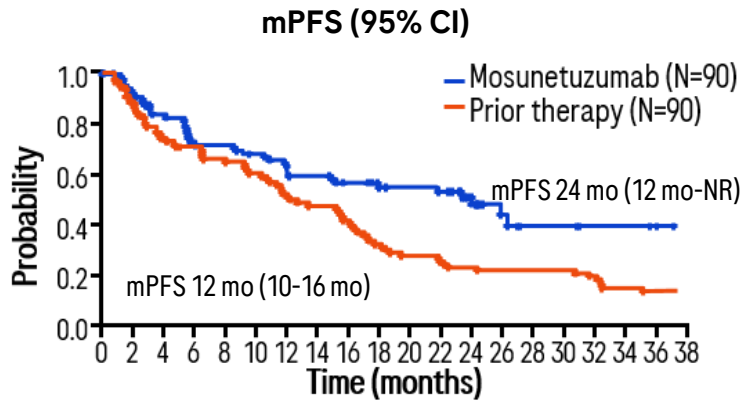
Pivotal Ph II (GO29781) in 3L+ FL

Efficacy summary	IRC N=90
CR rate, n (%)	54 (60)
ORR, n (%)	72 (80)
mPFS, mo (95% CI)	NE (26.3-NE)
Median follow-up, months (range)	28.3 (2–38)
24-mo DoCR rate, % (95% CI)	65 (39-90.5)
Median DoCR, months (95% CI)	NE (23.2–NE)



- Clinically meaningful outcomes in heavily pretreated r/r FL patients with a CR rate of 60% and median DoCR not reached; 24-month DoCR rate at 65%
- 24-month OS rate was 100% in patients with CR at EOT with mOS not reached
- No mandatory hospitalization; manageable safety and CRS (mostly low grade and during C1)
- Fixed-duration treatment: 8 cycles if CR after C8; 17 cycles if PR/SD after C8

Exploratory analysis of pivotal Ph II: Lunsumio versus last prior therapy[1]



- Exploratory analysis demonstrated a 12-month improvement in mPFS with Lunsumio vs last prior therapy in the same patients despite being treated in later lines[1]
- Similarly, DoCR was extended with mDoCR not reached with Lunsumio vs 15 months with last prior therapy

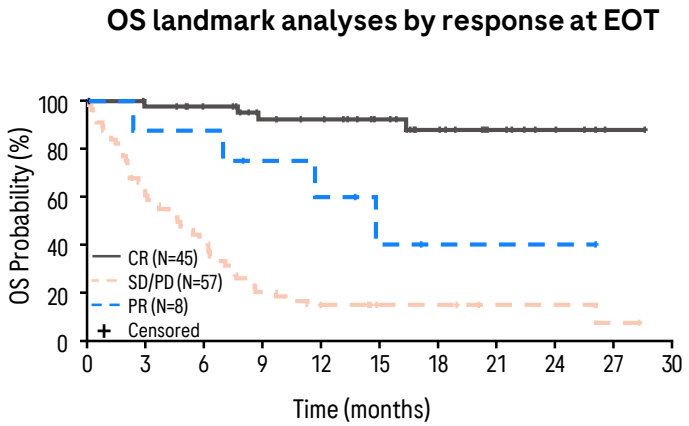
[1]Bartlett et al. ASH 2022; Sehn et al, ICML 2023 ; FL=follicular lymphoma; PR=partial response; SD=stable disease; DoCR=duration of complete response; ORR=overall response rate; CR=complete response; CRS=cytokine release syndrome; AE=adverse event; EOT=end of treatment; mPFS=median progression-free survival; OS=overall survival; mOS=median overall survival; C=Cycle; mDoCR=median duration of complete response; NE=not estimable

Columvi: Durable remissions achieved in 3L+ DLBCL with fixed-duration therapy

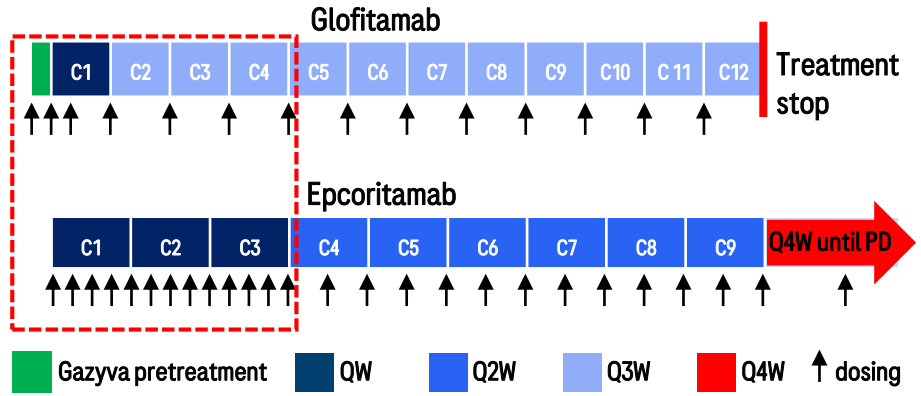
Pivotal Ph II (NP30179) in 3L+ DLBCL

Efficacy summary	IRC N=155*
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]
Median follow-up, months (range)	18.2 (0–33)
Ongoing CRs, n/N (%)	42/62 (68)
Median DoCR, months (95% CI)	26.9 (18.4–NE)

*Intent-to-treat population; CI, confidence interval; NE, not estimable.



Columvi: Fixed duration and simple dosing schedule



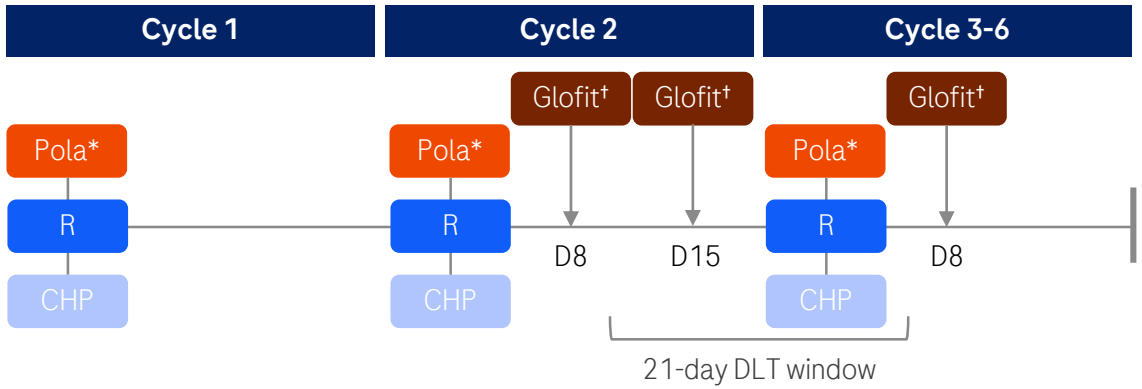
- Clinically meaningful outcomes in highly refractory r/r DLBCL patients with a CR rate of 40% and a median DoCR of 26.9 months following a fixed treatment
- Highly durable responses with 70% of patients with a CR at any time remaining in remission at 18 months post-EOT
- Majority of patients (92%, 30/45) with a CR at EOT are alive at 12 months after EOT
- Following step up dosing in C1, glofitamab is administered in a simple Q3W schedule, with fixed treatment duration of 12 cycles (= 8.5 months)
- Fixed-duration treatments help to avoid long term side effects, are convenient, and generate savings for the healthcare system

Dickinson M, et al. Hematol. Oncol. 2023;41 (S2):144-6; CR=complete response; ORR=overall response rate; DoCR=duration of complete response; CI=confidence interval; R/R=relapsed refractory; DLBCL=diffuse large B-cell lymphoma; EOT=end of treatment; CR=Complete response; SD/PD=Stable disease / Progressive disease; PR=Partial response; C=Cycle

Columvi + Polivy + R-CHP in 1L DLBCL early data encouraging

Building upon POLARIX to address remaining unmet need

Ph I study design



*Pola-R-CHP administered on D1 of each 21-day cycle (maximum 6 cycles); †Glofitamab IV administered in C2–C6, C2 SUD (2.5mg C2D8, 10mg C2D15); target dose (30mg) C3D8 onwards

Patient characteristics

- 24 patients enrolled, received study treatment**
- Median age 65.0 years
- Majority of patients had a high tumor burden

Endpoint assessment criteria

- Response rate assessed by PET-CT [1]

Key inclusion criteria

- Aged ≥18 years, ECOG PS 0-3, IPI score 2-5

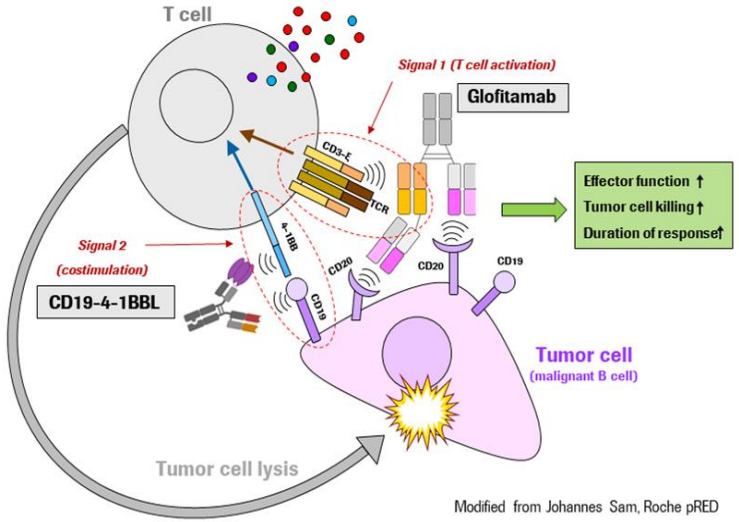
- Encouraging Ph I data with Columvi + Polivy + R-CHP demonstrating high CMR rates, irrespective of baseline IPI score, no patients had progressive disease
- Initiating treatment with Polivy + R-CHP (debulking) was associated with a low rate and mild severity of CRS (3 patients with G1 CRS only)
- More mature data to be presented at upcoming conference
- Ph III Columvi + Polivy+ R-CHP in 1L DLBCL to be initiated 2023

Dickinson M. et al., ASCO 2023; **as of November 14, 2022; 1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68; R=Rituximab; CHP=Cyclophosphamid, doxorubicin and prednison; DLBCL=Diffuse large B-cell lymphoma; PET-CT=Positron emission tomography-computerized tomography; CRS=Cytokine release syndrome; ECOG Eastern Cooperative Oncology Group performance status; IPI=International Prognostic Index; DLT=Dose-limiting toxicity; IV=Intravenous; CMR=Complete metabolic response; G1=Grade 1; D=Day

Englumafusp alfa (CD19-4-1BBL) in r/r NHL

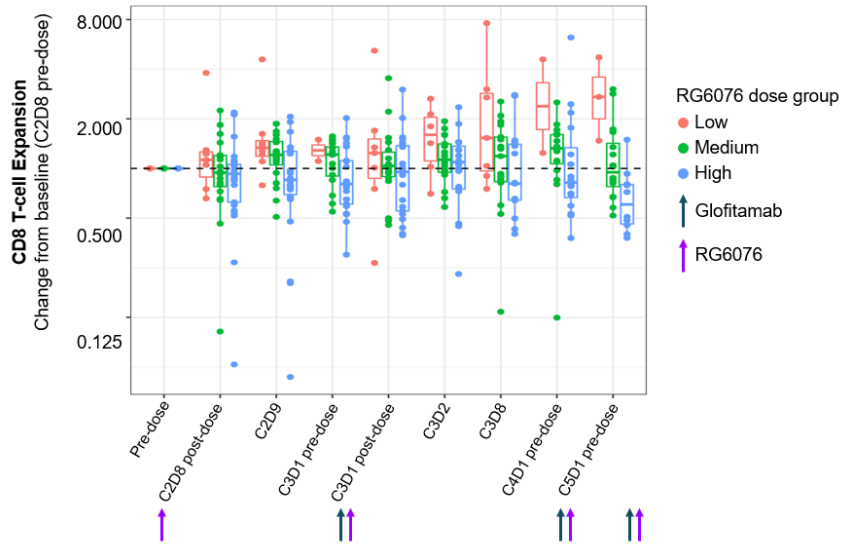
First-in-class B cell-targeted costimulatory T cell agonist

Englumafusp alfa + Columvi



- Signal 1: NK or T cell activation delivered by Columvi
- Signal 2: CD19-4-1BBL leads to enhanced NK and T cell activation and promotes a durable immune response
- First-in-class 4-1BB agonist with B cell targeted co-stimulation of T cells

Pharmacodynamic biomarker data support novel MoA



- A dose relationship with reversal of PD1+ terminally differentiated CD8 T-cell expansion in blood is emerging at the C3D8, C4D1, and C5D1 timepoints
- Data indicate that CD19-4-1BBL costimulation may lead to a more durable response to Columvi and potentially prevent disease escape
- Ph I studies for Columvi + CD19-4-1BBL or costimulatory bispecific CD19 x CD28 in r/r NHL ongoing

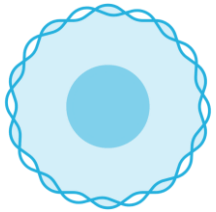
Hutchings et al. ASH 2022; TCB=T cell bispecific; NK=natural killer; R/R=relapsed refractory; NHL=non-Hodgkin´s lymphoma; MoA=Mode of action

Off-the-shelf CAR-Ts for hematologic malignancies

Highly differentiated new generation of fully allogeneic CAR-Ts

Long-lived self-renewing stem cell memory T cells

T_{SCM} Cell

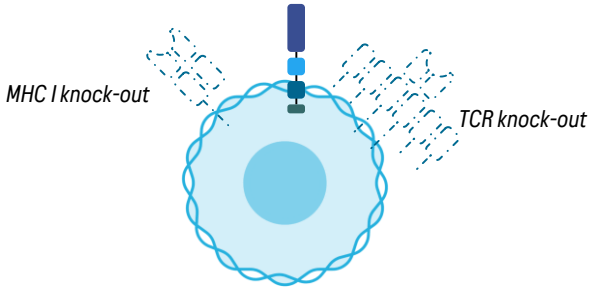


Stem cell memory

- Self-renewing
- Long-lived
- Multipotent
- Healthy donor derived

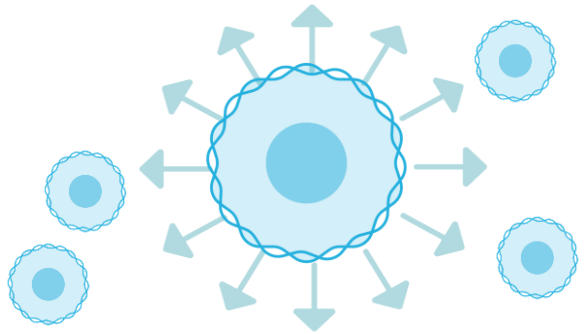
- T_{SCM} - ideal cell type for CAR-T due to greater safety and durability
- piggyBac® - superior non-viral gene insertion technology

High-fidelity, proprietary gene editing technology



- Addressing both Graft v Host and Host v Graft alloreactivity with Cas-CLOVER™ Gene Editing

Cost, scale and reach



- Proprietary booster molecule enables potential to deliver 100's of doses translating into lower cost, lower wait time and broader patient reach

- Ph I open-label dose-escalation study of P-BCMA-ALLO1 in MM ongoing: Early signs of efficacy and favorable tolerability profile
- P-CD19CD20-ALLO1 IND approved Q2 2023, Ph I in B-cell malignancies expected to start early 2024
- Additional allogeneic CAR-Ts in development for MM and AML

Program in partnership with Poseida; Kocoglu M et al., ESMO I-O 2022; IND=investigational new drug application; CAR-T=chimeric antigen receptor T- cell; MM=multiple myeloma; AML=Acute myeloid leukemia

Update late-stage hematology pipeline

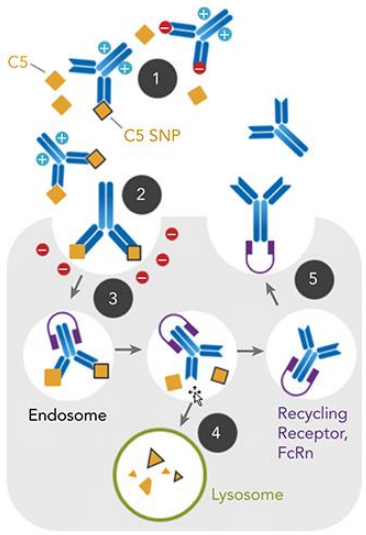
Malignant hematology: B-cell malignancies

Non-malignant hematology: PNH, Hemophilia A

Crovalimab: Expanding program in complement-mediated diseases

Positive Ph III data in PNH filed globally; US filing accepted on 1 Sep

Crovalimab (anti-C5 recycling Ab)



- Uses Chugai's recycling antibody technology (SMART-Ig)[1-6]
- Rapid, long-lasting neutralization of C5 in complement mediated diseases
- Low volume administration supports convenient SC Q4W dosing at home

Broad development program in complement mediated diseases

Indication		Ph I / Ph II / Ph III	
PNH	*Paroxysmal nocturnal hemoglobinuria*	**COMPOSER**	✓
		COMMODORE 1 (switch)	✓
		COMMODORE 2 (naïve)	✓
		COMMODORE 3 (China)	✓
aHUS	*Atypical hemolytic uremic syndrome*	**COMMUTE-a** (adults)	
		COMMUTE-p (pediatric)	
SCD	*Sickle cell disease*	**CROSSWALK-c** (chronic)	
		CROSSWALK-a (acute)	
LN	*Lupus nephritis*		✓ Filed

- Ph III (COMMODORE 2/1) results in PNH show successful disease control in naïve patients and a favorable benefit-risk profile for patients switching from other C5 inhibitors
- Clear dosing advantage over current C5 inhibitors with the majority of COMMODORE 2/1 patients preferring crovalimab over previous therapy
- Filed globally in PNH; first approvals expected in 2024

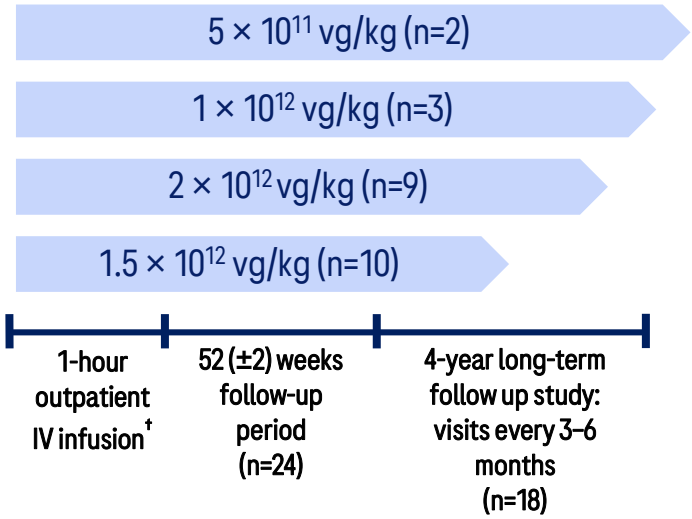
1 Röth A et al. Blood 2020;135:912–20; 2 Fukuzawa T et al. Sci Rep 2017;7:1080; 3 Sampei Z et al. PLoS One 2018;13:e0209509; 4 Röth A, Nishimura J. Centro Congressi Federico II 2019; 5 Röth A et al. ASH 2018; 6 Sostelly A et al. ASH 2019; PNH=paroxysmal nocturnal hemoglobinuria; Ab=antibody; SC=subcutaneous; Q4W=every 4 weeks; aHUS=atypical hemolytic uremic syndrome; SCD=Sickle cell disease; LN=lupus nephritis

SPK-8011 in hem A: Durable FVIII activity observed up to 5 years

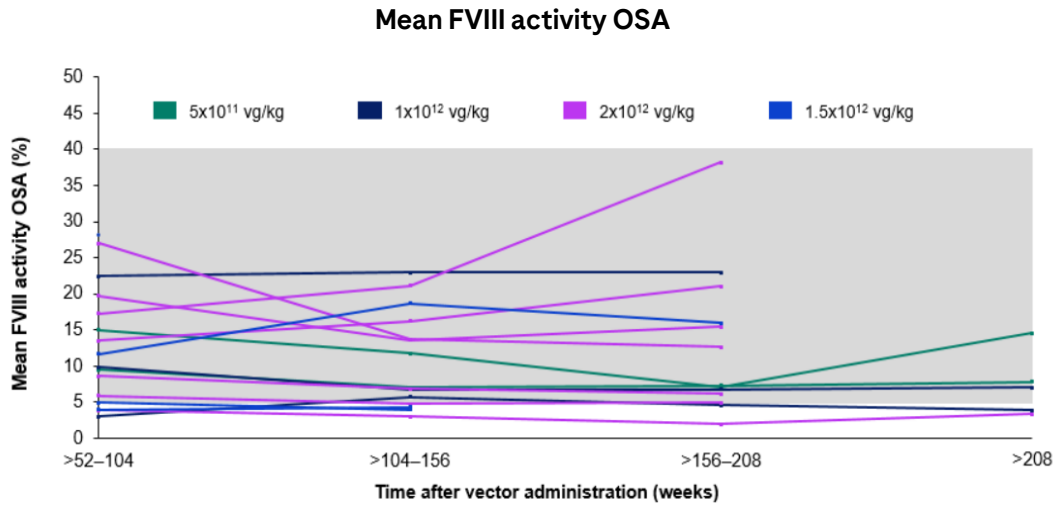
FVIII activity accompanied by durable clinical benefit in ABR, joint health and quality of life

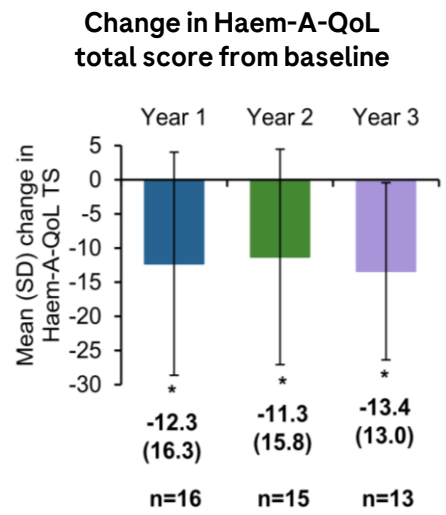
FDA BTD

Study design



Stable FVIII activity levels and improved QoL over long-term follow-up





Efficacy and safety of single SPK-8011* infusion:

- 16 participants with ≥1 year follow-up showed no apparent decrease in FVIII activity over time, with a majority expressing in the mild HA range
- 82–99% reductions in ABR and substantial reductions in FVIII consumption, no major safety signals
- Clinically meaningful improvements in joint health by total HJHS score at Year 2 and 3 and in total Haem-A-QoL at Years 1, 2, and 3
- Ph III study to open enrolment in 2H 2023

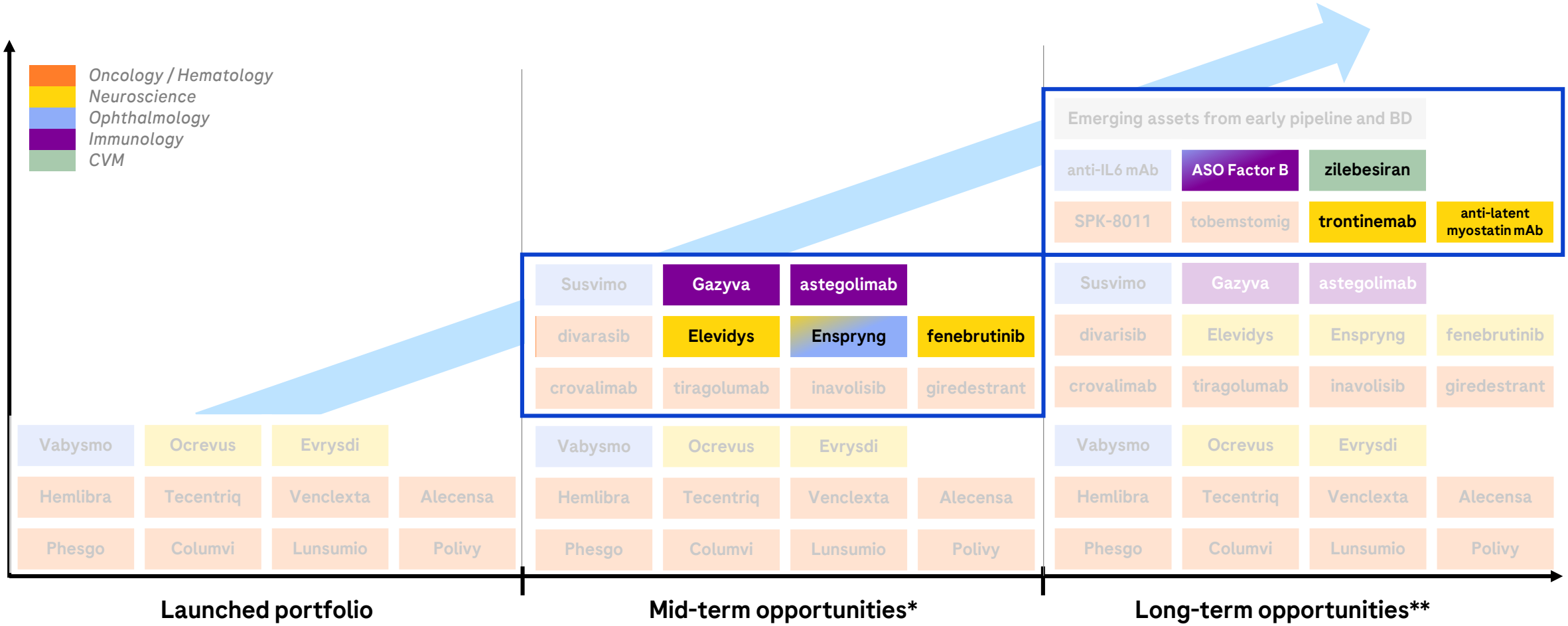
* dirloctocogene samoparvovec; Croteau et al ASH 2022; Data cut-off: Oct 4 2022; analysis includes participants with >52 weeks of follow up (n=16). Grey shaded area indicates the mild range of hemophilia A; FVIII assessments obtained within 5 days of administration of a FVIII infusion were excluded; OSA=one-stage assay; FVIII:C=FVIII coagulant activity; HA=hemophilia A; QoL=Quality of life; ABR=Annualized bleeding rate; M.V. Ragni et al., ISTH 2023, B. Samelson-Jones et al., ISTH 2023

Late Stage Pipeline Neuroscience, Immunology and Cardiovascular-Metabolism

Paulo Fontoura M.D. Ph. D. |
SVP and Global Head of Neuroscience and Immunology

Building blocks for future growth through 2030

9 NMEs in Neuroscience, Immunology and CVM with FIC/BIC potential in late stage development



CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

Neuroscience pipeline

Industry leading portfolio differentiated on targets and platform technologies

Ph I (5 NMEs)

RG6091	**rugonersen** Angelman syndrome	RD
RG6035	**brain shuttle CD20** Multiple Sclerosis	
RG6182	**MAGLi** Multiple Sclerosis	
RG6289	undisclosed Alzheimer's	
RG6163	undisclosed psychiatric disorders	

- Small molecule
- Antibody
- Gene therapy
- Brain shuttle
- Locked nucleic acid / antisense

Ph II (10 NMEs)

RG7935	**prasinezumab** Parkinson's	
RG6100	**semorinemab** Alzheimer's	
RG6100	**bepranemab*** Alzheimer's	
RG6102	**trontinemab** Alzheimer's	
RG6042	**tominersen** Huntington's	
RG6237 + RG7916	**GYM329 + Evrysdi** SMA	RD
RG6237	**GYM329** FSHD	RD
RG7906	**ralmitaront** Schizophrenia	
RG7816	**alogabat** Autism spectrum disorder	
RG7314	**balovaptan** PTSD	
RG1662	**basmisanil** Dup 15q syndrome	RD

Ph III (1 NME, 5AI)

RG6168	**Enspryng** gMG	RD
RG6168	**Enspryng** MOG-AD	RD
RG6168	**Enspryng** AIE	RD
RG7845	**fenebrutinib** Multiple Sclerosis	
RG1594	**Ocrevus high dose** Multiple Sclerosis	
RG1594	**Ocrevus SC** Multiple Sclerosis	

Launched (4)

RG1594	**Ocrevus** Multiple Sclerosis		✓
RG6168	**Enspryng** NMOSD	RD	✓
RG7916	**Evrysdi** SMA type 1/2/3	RD	✓
RG6356	**Elevidys** DMD	RD	✓

- Neuro-immunologic disorders
- Neuro-degenerative disorders
- Neuro-developmental disorders
- Neuro-muscular disorders
- Psychiatric disorders
- ✓ FDA approval
- RD = Rare disease

Upcoming readouts

- Ph III (EMBARK) Elevidys (delandistrogene moxeparvovec) in DMD data expected in Q4 2023
- Ph III (LUMINESCE) Enspryng in gMG data expected in H1 2024

NME=new molecular entity; AI=additional indication; NMOSD=neuromyelitis optica spectrum disorders; DMD=Duchenne muscular dystrophy; gMG=generalised myasthenia gravis; SMA=spinal muscular atrophy; FSHD=facioscapulohumeral muscular dystrophy; PTSD=post-traumatic stress disorder; MOG-AD=myelin oligodendrocyte glycoprotein antibody-associated disease; AIE=autoimmune encephalitis; MAGL=monoacylglycerol lipase; *Bepranemab partnered with UCB, studies are currently run by UCB

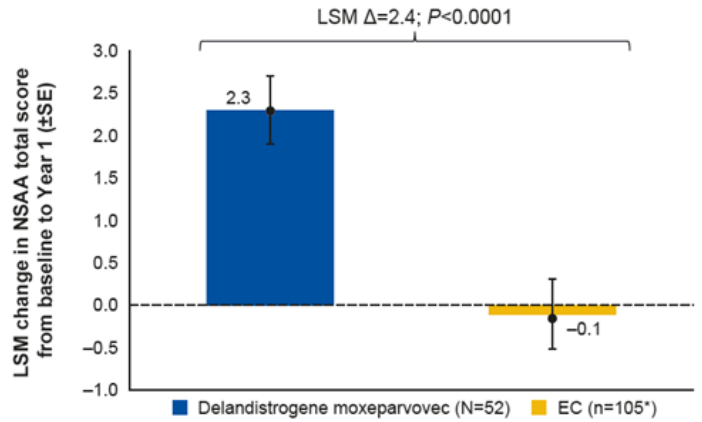
Elevidys, first FDA approved DMD gene therapy by partner Sarepta

Ph III (EMBARK) results expected in Q4

Pooled analysis of studies 101/102/103*

MDA 2023

Change from baseline in NSAA total score over 1 year**



- Positive functional and clinically meaningful results up to 4 years after treatment with consistent safety
- US accelerated approval achieved by Sarepta in Q2
- First patient treated in the US in August
- First ex-US approval in the UAE achieved

Development program

Study	DMD subgroup	Ph I / Ph II / Ph III	Comment
101	Ambulatory, 4-7 yrs.	Ph I	✓ US approval (Sarepta)
102	Ambulatory, 4-7 yrs.	Ph II	✓ US approval (Sarepta)
103 (ENDEAVOR)	Ambulatory, 3-18 yrs Non-ambulatory, all ages	Ph I	✓ US approval (Sarepta)*
301 (EMBARK)	Ambulatory, 4-7 yrs.	Ph III	EU filing and US label extension
302 (ENVOL)	Ambulatory, 0-3 yrs.	Ph I / Ph II	Expansion to younger DMD pts
303 (ENVISION)	Ambulatory, 8-18 yrs Non-ambulatory, all ages	Ph III	Expansion to older ambulatory and non-ambulatory DMD pts

- Ph III (ENVISION) in older ambulatory and all ages non-ambulatory patients started in Q2 2023
- Ph II (ENVOL) in 0-3 year old ambulatory patients to initiate in H2 2023
- Ph III (EMBARK) results in Q4 2023; data to be filed in the EU / International and to facilitate non-age-restricted expansion of the US label

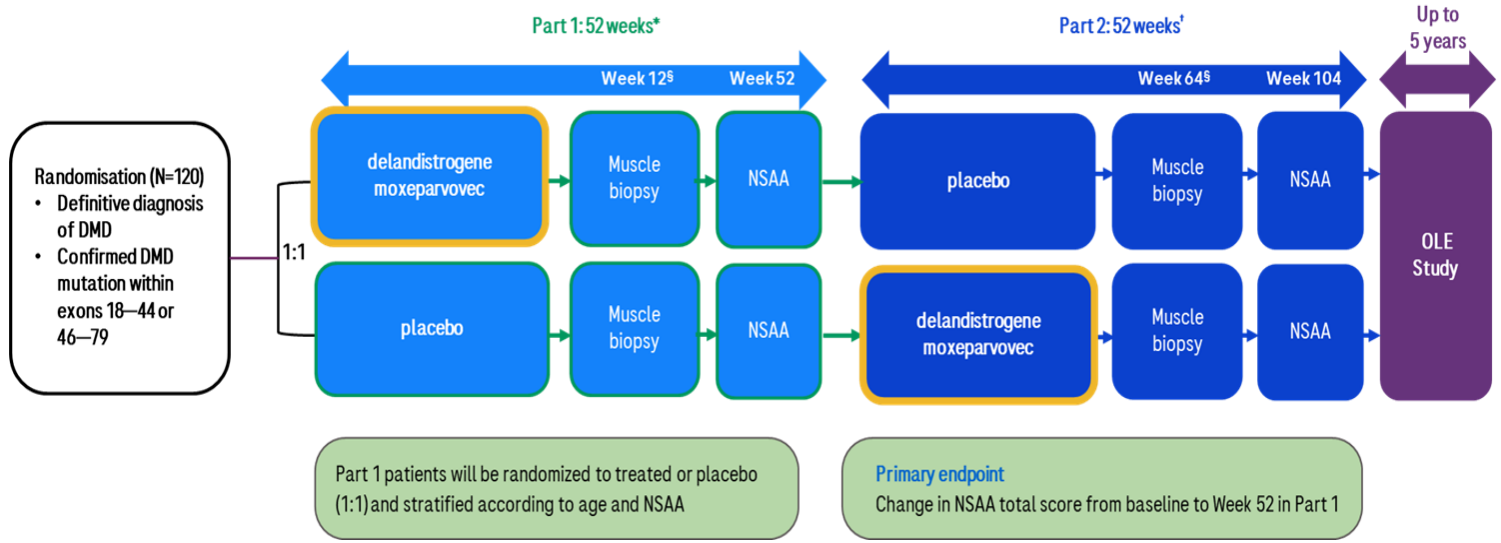
Elevidys (delandistrogene moxeparvovec) accelerated US approval by partner Sarepta Therapeutics; Zaidman, et al. MDA 2023; *For study 103 (ENDEAVOR) only cohort 1 was used; **Functional data from patients who received the 1.33x1014 vg/kg dose of delandistrogene moxeparvovec and the propensity-score-weighted EC cohort were compared; DMD=Duchenne muscular dystrophy; NSAA=North Star Ambulatory Assessment; LSM=least-squares mean; EC=external control; SE=standard error; UAE=United Arab Emirates

Elevidys development program

Largest development plans in the broadest patient population

Roche
Elevidys

Ph III EMBARK study design[1]



Additional Ph II/III studies

ENVOL

Study 302

21 patients

Ages 0-3

Open label

- *Safety (primary) and Expression (secondary)*
- *Excludes mutations 1-17*
- *EU study population*

ENVISION

Study 303

Older ambulatory (n=28) / non-ambulatory patients (n=120)

Total 148 patients

Double-blind, placebo-controlled

- *No upper age restrictions for non-ambulatory patients*
- *Ambulatory: 8-18*
- *Primary endpoint: PUL*
- *Excludes mutations 1-17*

- Pivotal Ph III (EMBARK) trail: Two part design with an OLE study of up to 5 years; primary endpoint of change in NSAA total score from baseline to Week 52 in Part 1
- Ph III (ENVOL; Study 302): Open label trial in 0-3 year olds with safety as primary endpoint and expression as secondary
- Ph III (ENVISION; Study 303): Randomized trial in older ambulatory / non-ambulatory patients without an upper age restriction
- SV95C-SYDE, first ever digital endpoint approved as primary endpoint by EMA

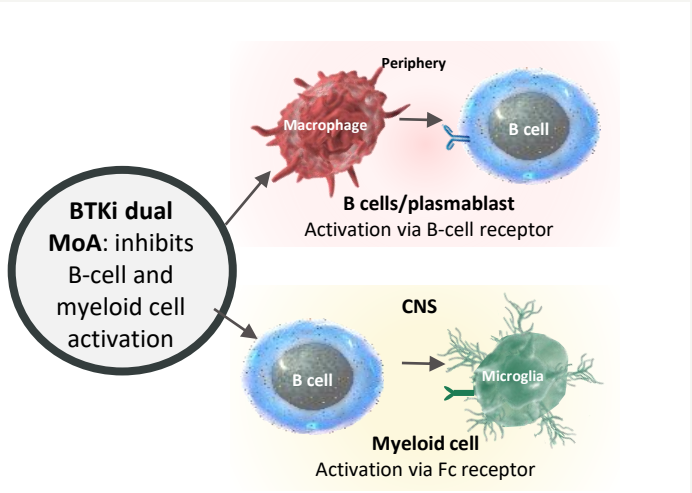
1.Muntoni et al MDA 2022; *Double-blind, placebo-controlled. †Patients, caregivers, Investigators, and site staff remain blinded. Only a subset of patients will receive a muscle biopsy for expression assessments; DMD=Duchenne muscular dystrophy; NSAA=North Star Ambulatory Assessment; PUL=performance of upper limb; OLE=Open label extension; Delandistrogene moxeparvovec in collaboration with Sarepta Therapeutics; SV95C=Stride Velocity 95th Centile; SV95C-SYDE in collaboration with Sysnav

Fenebrutinib, potential for a best-in-class BTKi in MS

Additional Ph II (FENopta) data to be presented at ECTRIMS

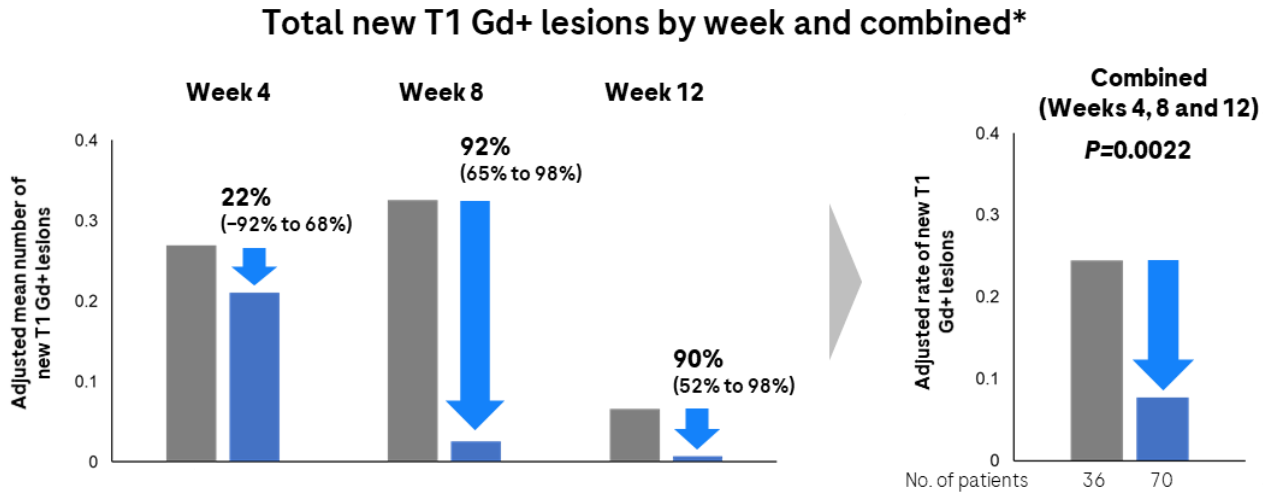
IR call on October 30

Fenebrutinib (BTK inhibitor)



- Dual MoA targeting both B cells and myeloid cells
- Oral, highly selective and only reversible non-covalent BTK inhibitor in Ph III in MS
- Excellent selectivity limits off-target effects, potential for better safety outcomes

Ph II (FENopta) results in RMS



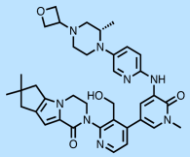
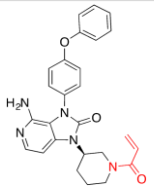
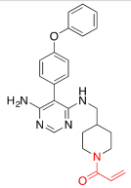
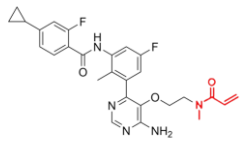
- FENopta biomarker study evaluated early impact of fenebrutinib on MRI outcomes and showed significant reductions in brain lesions in RMS patients, meeting primary and secondary endpoints
- Patients on fenebrutinib 4x likelier to have no new T1 Gd+ & N/E T2 lesions at weeks 4, 8 and 12 vs placebo
- Safety profile consistent with previous and ongoing trials
- CSF concentration data from Ph II (FENopta) trial to be presented at ECTRIMS on Oct 10-13th

Hua LH et al., EAN 2023; *Results were estimated from a negative binomial model controlling for baseline T1 Gd+ lesion status (presence or absence) and included log number of scans as an offset. Arrows indicate relative reduction (95% CI) of lesions; MS=multiple sclerosis; BTKi=Bruton's tyrosine kinase inhibitor; MoA=mechanism of action; CSF=cerebrospinal fluid; RMS=relapsing multiple sclerosis; Gd+=gadolinium-enhancing; MRI=Magnetic Resonance Imaging; RMS=Relapsing multiple sclerosis; CNS=Central nervous system

Fenebrutinib, pivotal trials in RMS and PPMS ongoing

The only BTKi in H2H Ph III trial in PPMS vs Ocrevus

BTKi competitive landscape[1]

Fenebrutinib	Tolebrutinib	Evobrutinib	Remibrutinib
			
Non-covalent Reversible	Covalent Irreversible	Covalent Irreversible	Covalent Irreversible
WB B cell IC_{50}: 8nM	10 **nM**	84 **nM**	18 **nM**
WB Myeloid cell IC_{50}: 31nM	166 **nM**	1660 **nM**	67 **nM**
Ph III	Ph III FDA partial clinical hold	Ph III FDA partial clinical hold	Ph III
RMS, PPMS (vs Ocrevus)	RMS, SPMS, PPMS (vs Placebo)	RMS	RMS

Ph III program overview

Indication	Trial design	Ph I / Ph II / Ph III	
RMS	*vs placebo*	FENopta	✓
RMS	*vs teriflunomide*	FENhance 1/2	
PPMS	*vs Ocrevus*	FENtrepid	

✓ Positive data readout, primary and secondary endpoints achieved

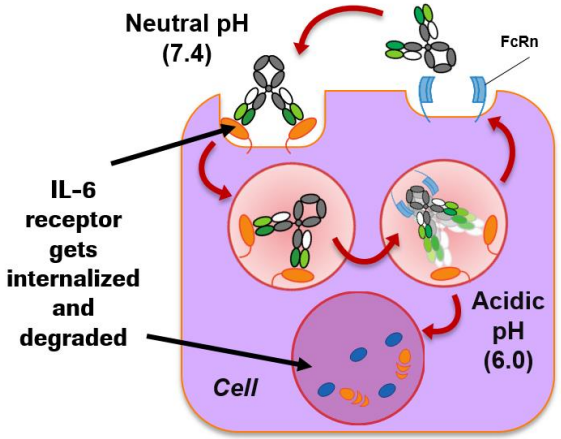
- Potential to be best-in-class given high potency, high selectivity, reversibility, and only H2H study vs Ocrevus
- Large safety database of >2,500 pts who have been dosed with fenebrutinib*
- Further solidifying commitment to MS franchise

1. Kramer, et al (2023) nature reviews neurology 289-304 ;Crawford, et al.(2018) J Med Chem 61, 2227-2245; Francesco, et al., ACTRIMS-ECTRIMS (2017) 200644. Haselmayer, et al. (2019) J Immunol 202, 2888-2906; Angst D, et al. (2020) J Med Chem 63, 5102-5118. MS=multiple sclerosis; H2H=head-to-head; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; BTK=Bruton's tyrosine kinase; nM=nanomolar; WD=whole blood; *As of Sept 2023: including non-MS Ph I/II studies

Enspryng in neurological disorders gMG, AIE, and MOG-AD

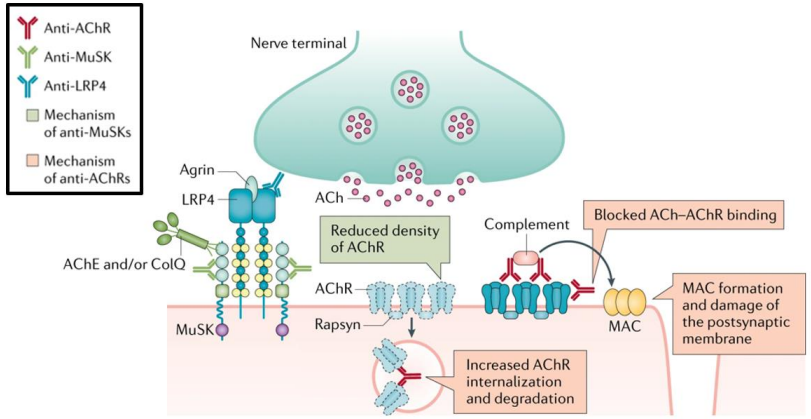
First-in-class anti-IL-6R mAB with best-in-disease potential in AcHR+ gMG

Enspryng (Anti-IL-6 receptor mAb)



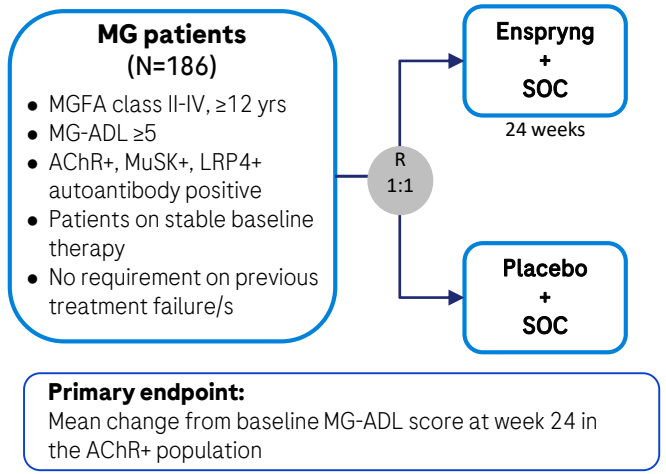
- Recycling mAb with high-affinity to soluble and membrane-bound IL-6R
- Engineered to enable maximal inhibition of IL-6 signaling
- Convenient SC Q4W home administration

gMG: Autoantibodies at the NMJ[1]



- IL-6 blockade has the potential to reduce autoantibody-mediated NMJ damage in gMG
- High unmet need: ~10-30% of patients fail SOC therapies with only up to 40% of patients on approved biologics achieve minimal symptom expression[2]
- Ph III (LUMINESCE) results in gMg expected in 2024
- Additional Ph III studies in 2 other autoantibody mediated rare neurological diseases ongoing with first-in-disease potential: Ph III (CIELO) in AIE and Ph III (METEOROID) in MOG-AD

Ph III (LUMINESCE) trial design

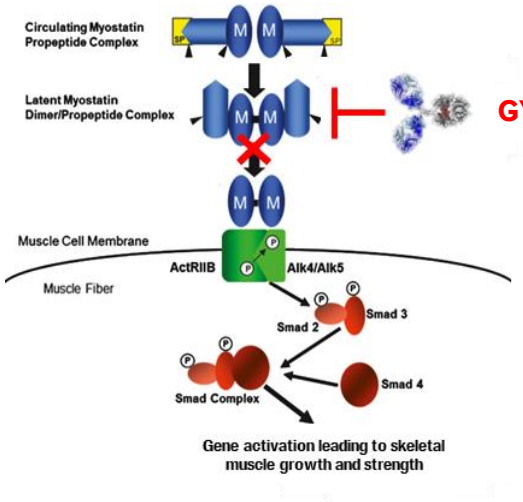


1.Gilhus N.E. et al., Nat Rev Dis Primers. 2019; 2. Howard JF Jr, et al. Lancet Neurol. 2021 IL-6R=interleukin 6 receptor; MG=myasthenia gravis; gMG= generalized myasthenia gravis; AcHR=acetylcholine receptor; NMJ=neuromuscular junction; SC=subcutaneous; Q4W=every 4 weeks; MOG-AD=myelin oligodendrocyte glycoprotein antibody-associated disease; LPI=last patient in; AIE=autoimmune encephalitis; SOC=Standard of care; MGFA=Myasthenia Gravis Foundation of America; MG-ADL=Myasthenia Gravis Activities of Daily Living

Anti-latent myostatin mAb to promote muscle growth in SMA

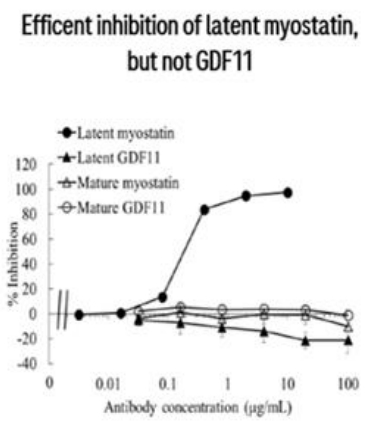
Ph II/III combination trial with Evrysdi ongoing

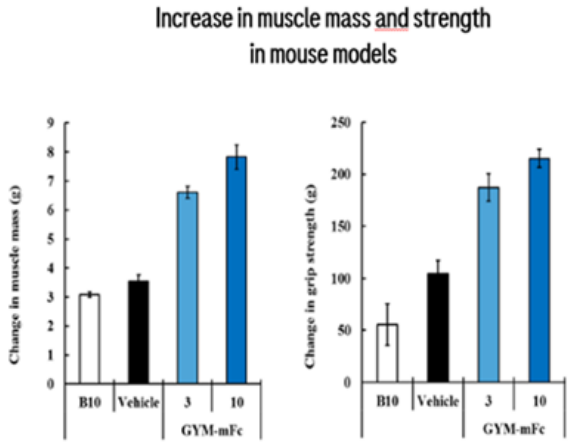
GYM329 (Anti-latent myostatin mAb)



- GYM329 binds latent myostatin, a key negative regulator of skeletal muscle growth and strength
- Unique sweeping[1] and recycling technology allows less frequent SC dosing and highly specific myostatin inhibition

Pre-clinical data in a mouse models of muscle disease





Combination rationale

- Evrysdi treats the underlying SMA disease by increasing SMN protein throughout the CNS and in peripheral tissues
- GYM329 targets skeletal muscles to increase their size and strength

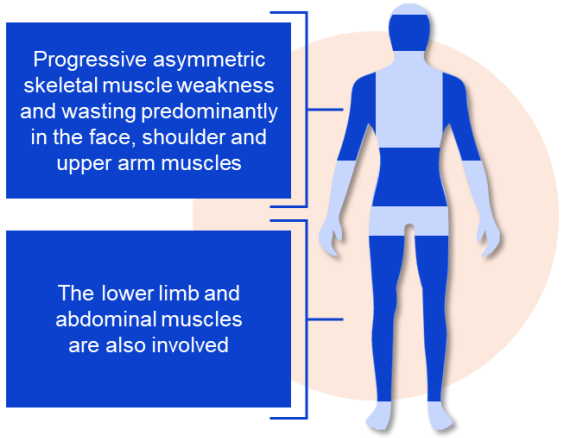
- GYM329 efficiently inhibits myostatin, but not the related muscle hormone GDF11, making it highly specific compared to other anti-myostatin Abs tested[2]
- GDF11 and myostatin act in opposite directions in muscle strength enhancement
- The combination of GYM329 + Evrysdi improved muscle size and strength in an animal model of SMA
- Ph II/III (MANATEE) of GYM329 and Evrysdi in SMA ongoing

1. A sweeping antibody is a recycling antibody that has been further engineered to bind to FcRn at neutral pH; 2.Muramatsu H. et al., Nature Scientific Reports. 2021; SC=subcutaneous; CNS=central nervous system; mAb=antibody; SMA=spinal muscular atrophy; SMN=survival motor neuron; GDF11=growth differentiation factor 11; GYM329 in collaboration with Chugai

Anti-latent myostatin mAb in the neuromuscular disorder FSHD

Ph II (MANOEUVRE) in FSHD, a disorder with high unmet need, ongoing

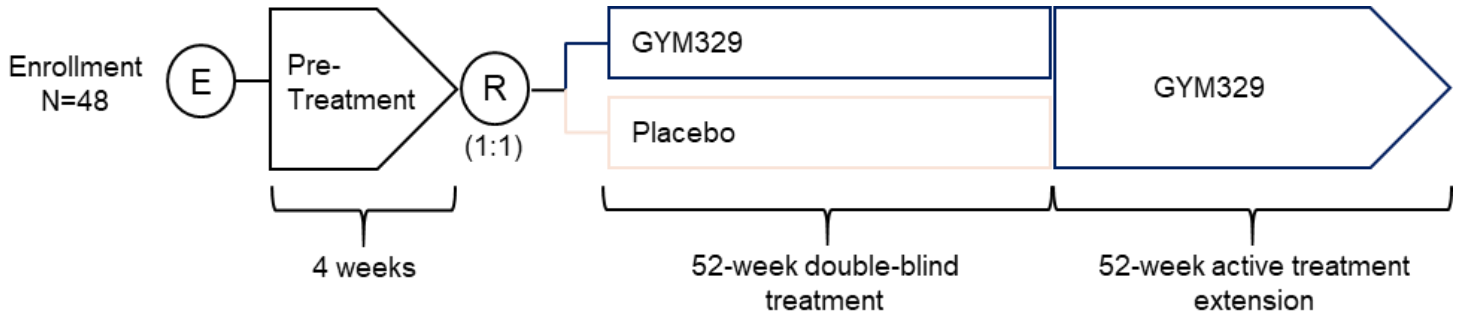
FSHD: Rare genetic disease with high unmet need



Other symptoms can include retinal vascular pathology, hearing loss and respiratory impairment

- Genetic muscle disorder driven by ectopic expression of the DUX4 transcription factor
- Estimated global prevalence of 3.2–4.6 per 100,000, affecting adults and children[1]
- Currently no DMTs against muscle wasting and weakness in FSHD

Ph II (MANOEUVRE) trial design in FSHD



Primary endpoints:

- Percent change in contractile muscle volume (CMV) of quadriceps femoris as assessed by MRI bilaterally
- Percentage of participants with adverse events (AEs)

- Preclinical studies showed that GYM329 has superior muscle strength-improvement effects in mice compared with other anti-myostatin therapies[2]
- Treatment with GYM329 also resulted in muscle growth in healthy volunteers[3]
- Best-in-Disease potential: Ph II (MANOEUVRE) of GYM329 in FSHD ongoing
- GYM329 is further explored in additional diseases and combinations

1. Faux-Nightingale A, et al. Arch Rehabil Res Clin Transl. 2021; 2. Igawa T, et al. Immunol Rev. 2016; 3. Internal data, unpublished; DMT=disease modifying therapy; E=enrollment; R=randomization; FSHD=facioscapulohumeral muscular dystrophy; MRI=magnetic resonance imaging; DUX4=double homeobox 4; DMT=Disease modifying therapy; GYM329 in collaboration with Chugai

Alzheimer's disease: Continuing to invest in high unmet need area

Leveraging key learnings to develop next generation therapies

Neurology Update
Roche IR Event
Oct 2023

AD program strategy

- Using prior experience and key learnings to develop effective clinical trials
- Leading diagnostic solutions, including screening and confirmatory tests, developing novel blood-based and digital biomarker options

Clinical development program in Alzheimer's disease

NME	MOA	Ph I	Ph II	Ph III
Bepranemab	Anti-tau mAb			
Trontinemab	Anti-Aβ mAb			
Semorinemab	Anti-tau mAb	Ph II completed		
GSM	Small molecule	Ph I completed		

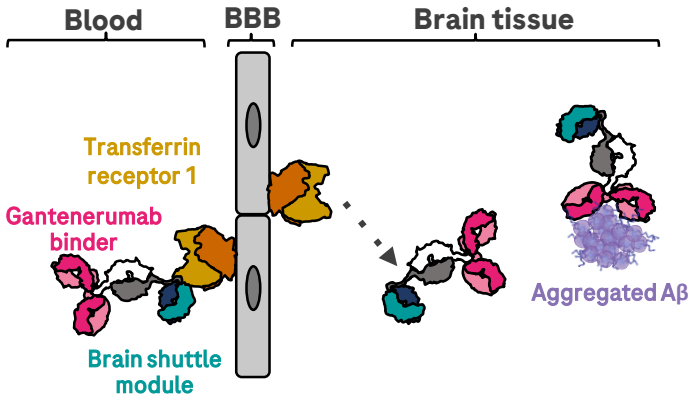
- Innovative Brain Shuttle technology to enable superior penetration of BBB, leading to deeper and faster Aβ reduction - potential for better efficacy
- Investigating MoAs to target various stages of the anti-amyloid cascade with GSM acting early in the pathological process and anti-tau mAbs acting at the end of the cascade
- Ph I dose escalation for trontinemab and FIH data for GSM to be presented at CTAD 2023 on Oct 24-27th

AD=Alzheimer's disease; BBB=blood brain barrier; mAb=monoclonal antibody; Aβ=Amyloid β; GSM=gamma secretase modulator; FIH=first in human; MoA=Mode of action

Trontinemab: First Aβ-targeting Ab brain shuttle technology

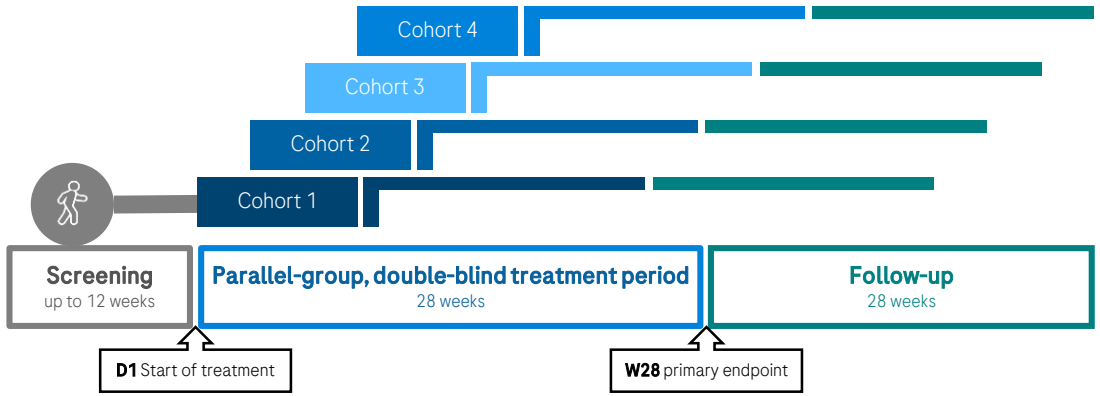
Best-in-disease potential: Fast and highly efficient plaque removal after 3-6 months

Trontinemab (Brain Shuttle TfR1-binding IgG)



- Trontinemab, brain shuttle, is an antibody format composed of gantenerumab and a linked transferrin receptor (TfR1) binding moiety
- The construct can achieve efficient transport over the blood brain barrier and target Aβ plaque in the brain[1]

Ongoing Ph I/II dose finding study in AD



- Ongoing Ph I/II study investigating four patient cohors (10-15 patients per cohort) with prodromal or mild-to-moderate AD for 7 months and with an option to expand most promising cohorts
- Faster and more efficient plaque removal, could result in a more pronounced delay in disease progression compared to first generation anti-amyloid therapies
- Updated data from the ongoing Ph I/II study to be presented at CTAD 2023 on Oct 24-27th

1 Gantenerumab brain shuttle results were compared with historical data obtained from a previous gantenerumab SAD trial (BN18726; 2.Kulic L. et al., ADPD 2021); AD=Alzheimer's disease; TfR1=Transferrin receptor protein 1; IgG=Immuno-globulin G; BBB=blood brain barrier; mAb=monoclonal antibody; Aβ=Amyloid β; Ab=Antibody

Immunology, Infectious Disease and CVM pipeline

Gazyva Ph III data in lupus nephritis expected in 2024; zilebesiran in hypertension added

Ph I (8 NMEs)

RG6107	**crovalimab** LN
RG6287	**undisclosed** aGVHD
RG6315	**undisclosed** Immunological disorders
RG6421	**TMEM16A potentiator** cystic fibrosis
RG7828	**Lunsumio (mosunetuzumab)** SLE
CHU	**anti-HLA-DQ2.5 x gluten peptides** Celiac disease
CHU	**RAY121** Immunology
RG6006	**ABx MCP** bacterial infections
RG6319	**LepB inhibitor** complicated urinary tract infection
RG6449	**HBsAg MAb** Chronic hepatitis B

Ph II (8 NMEs)

RG6299	**ASO factor B** IgA nephropathy
RG6341	**undisclosed** Chronic cough
RG6536	**Vixarelimab** IPF/SSc-ILD
RG7854/RG6346/ RG6084	**ruzotolimod/xalnesiran/PDL1 LNA** HBV
RG6359	**SPK-3006** Pompe disease
RG6615	**zilebesiran** Hypertension

Ph III (1 NMEs, 7 AI)

RG3648	**Xolair** Food allergy
RG6149	**astegolimab (Anti-ST2)** COPD
RG7159	**Gazyva** Lupus nephritis
RG7159	**Gazyva** Membranous nephropathy
RG7159	**Gazyva** SLE
RG7159	**Gazyva** Childhood onset INS
RG7159	**Xofluza** Influenza, pediatric
RG7845	**Xofluza** Influenza direct transmission

- Immunology
- Infectious diseases
- Cardiovascular & metabolism

- Small molecule
- Antibody
- Locked nucleic acid / antisense
- Gene therapy

Upcoming readouts

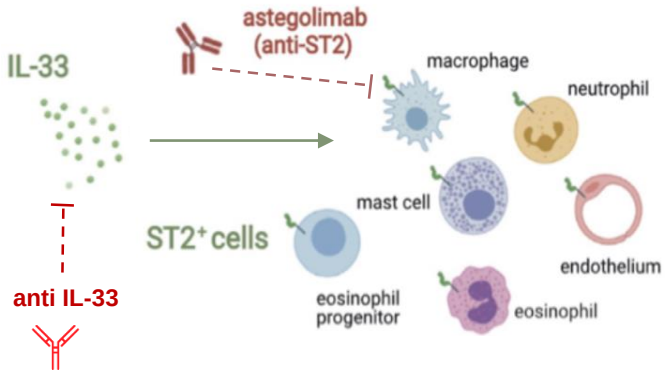
- Ph III (REGENCY) Gazyva in LN data expected in 2024
- Ph II (KARDIA-2) zilebesiran as add-on to one SoC in uncontrolled hypertension data expected early 2024

NME=new molecular entity; AI=additional indication; LN=lupus nephritis; SLE=Systemic lupus erythematosus; aGVHD=Acute graft-versus-host disease; COPD=Chronic obstructive pulmonary disease; HBV= Hepatitis B virus; INS=idiopathic nephrotic syndrome; IPF=idiopathic pulmonary fibrosis; SSC-ILD=systemic sclerosis-interstitial lung disease

Astegolimab: First-in-class anti-ST2 mAb in COPD

Early results show benefit in key endpoints throughout broad patient population

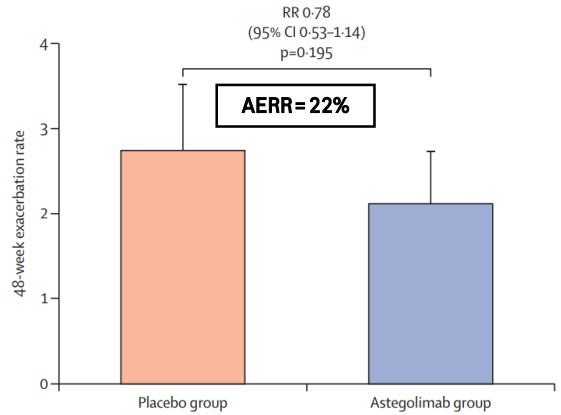
Astegolimab (anti-ST2 mAb)



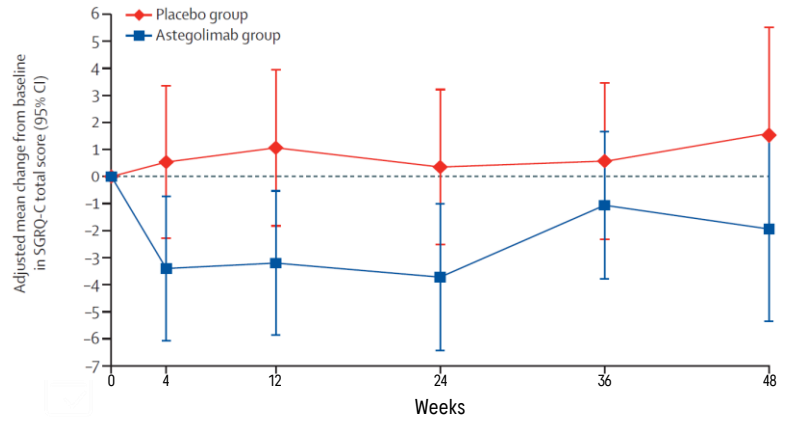
- Astegolimab binds both soluble ST2 and membrane bound ST2 (IL-33) receptor
- IL-33/ST2 blockade may impact airway remodeling in COPD patients
- #3 cause of global deaths; no biologics currently approved in COPD

Ph IIa (COPD-ST2OP) results[1]

Exacerbation rate at 48 weeks



SGRQ mean change from baseline



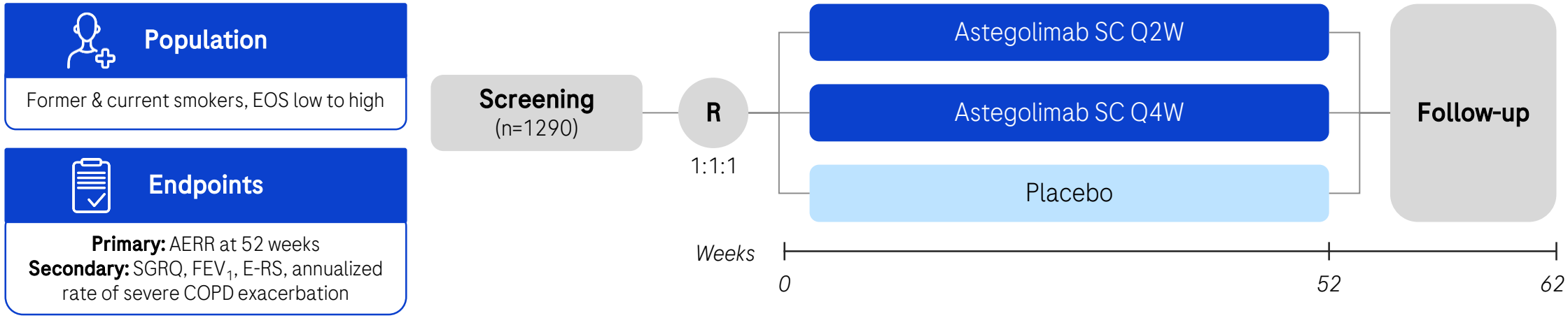
- Ph IIa (COPD-ST2OP): AER reduction of -22% (-37% in EOS low), reduction in SGRQ of -3.3 and increased FEV_1 by +40 ml
- Safe and well tolerated
- Earlier Ph II results in asthma with AER reduction of -43% (-54% in EOS low) support efficacy and safety profile in broad population, including EOS low[2]

[1] Yousuf et al. Lancet Respir. Med. 2022;10 (5):469-77; [2]Kelsen et al. J Allergy Clin Immunol 2021;148(3)790-8; mAb=monoclonal antibody; ST2=suppression of tumorigenicity 2; IL-33=interleukin-33; COPD=chronic obstructive pulmonary disease; EOS=eosinophils; RR=rate reduction; AER(R)=annualized exacerbation rate (reduction); SGRQ=St. George's respiratory questionnaire; FEV_1=forced expiratory value

Astegolimab: Pivotal program results expected in 2025

Two pivotal trials ARNASA and ALIENTO with similar design currently ongoing

PIIb (ALIENTO) / Ph III (ARNASA) trial design



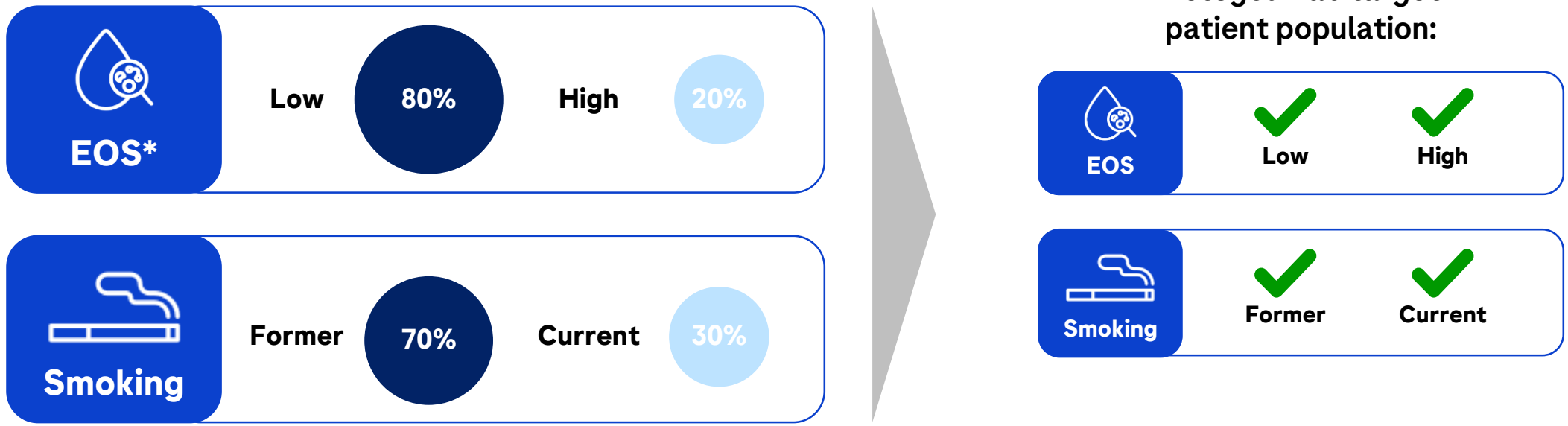
- Pivotal program includes up-scaled Ph IIb (ALIENTO) and Ph III (ARNASA); results expected in 2025
- Primary endpoint of change in AER at 52 weeks, with secondary endpoints focused on disease / health status (e.g. change in FEV_1 / SGRQ)
- Broad patient population including former and current smokers, and EOS low to high
- Filing expected to be based on combined ARNASA and ALIENTO results
- OLE for ALIENTO and ARNASA was initiated in H1 2023

COPD=chronic obstructive pulmonary disease; R=randomization; SC=subcutaneous; Q2W/Q4W=every 2/4 weeks; EOS=eosinophils; AER(R)=annualized exacerbation rate (reduction); SGRQ=St. George's respiratory questionnaire; FEV_1=forced expiratory value; E-RS=evaluating respiratory systems; OLE=open label extension

Astegolimab: Potential for biologic addressing broadest population

Aiming to address all COPD patients

COPD patient population overview[1]



- Near-term biologics in COPD are focused on EOS high or former smokers only
- Astegolimab with a unique potential to cover EOS low to high, as well as former and current smokers

1 Global strategy for prevention, diagnosis and management of COPD: 2023 report; *EOS high defined as ≥300 eosinophil cells per microliter of blood and EOS low defined as <300 eosinophil cells per microliter of blood; COPD=chronic obstructive pulmonary disease; SoC=standard of care; SC=subcutaneous; Q4W=every 4 weeks; EOS=eosinophils

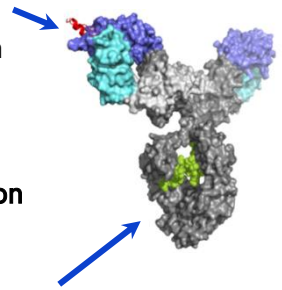
Gazyva with best-in-disease potential in lupus nephritis

Potential benefit in autoimmune diseases through sustained B cell depletion

Gazyva (glycoengineered anti-CD20 mAb)

Type II anti-CD20 region

- Increased direct cell death
- Decreased CDC
- Reduced internalization

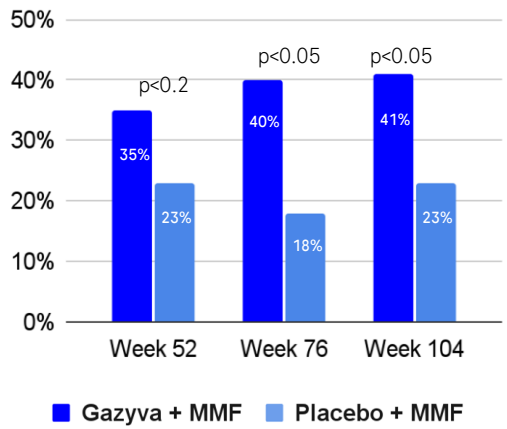


Glycoengineered Fc region

- Higher FcγR affinity
- Increased ADCC/ADCP

Ph II (NOBILITY) results in LN[1]

Complete renal response



Clinical trial program

Indication	Ph I	Ph II	Ph III
LN	REGENCY		
MN	MAJESTY		
SLE	ALLEGORY		
INS	INShore		

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

- Ph II (NOBILITY) in LN met both primary and key secondary endpoints with no new safety signals; Placebo-corrected CRR of 22% at week 76[2,3]
- Ph III (REGENCY) in LN fully recruited with results expected in 2024
- MN, SLE and INS: Complementary indications of the Gazyva program, with best-in-disease potential in MN, SLE and childhood onset INS

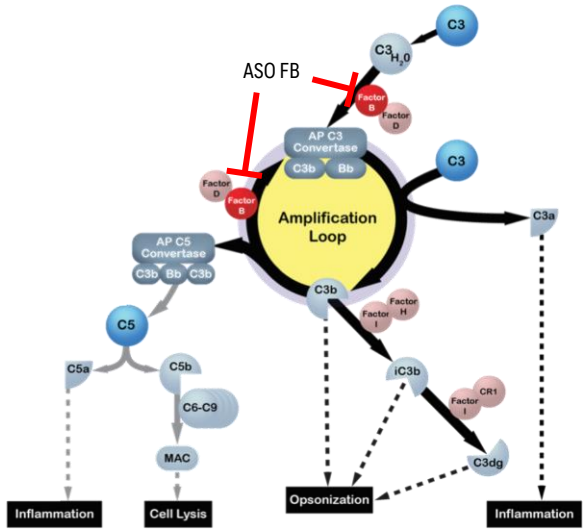
1. Furie R, et al. Ann Rheum Dis 2022; 81:100-107; 2.Furie R et al. Lupus Science & Medicine 2020;7 (Suppl 1):A27; 3.Furie R. et al; ACR 2019; mAb=monoclonal antibody; LN=lupus nephritis; MMF=mycophenolate mofetil; MN=membranous nephropathy; SLE=systemic lupus erythematosus; INS=Idiopathic nephrotic syndrome (Childhood onset INS also known as PNS=Pediatric nephrotic syndrome); CDC=complement-dependent cytotoxicity; ADCC=antibody-dependent cell-mediated cytotoxicity; ADCP=antibody-dependent cellular phagocytosis; CRR=complete renal response; IV=intravenous

Antisense oligonucleotide Factor B in IgAN

Positive Ph II UPCR results at 6 months; Ph III (IMAGINATION) initiated in Q2 2023

Antisense oligonucleotide Factor B (ASO FB)

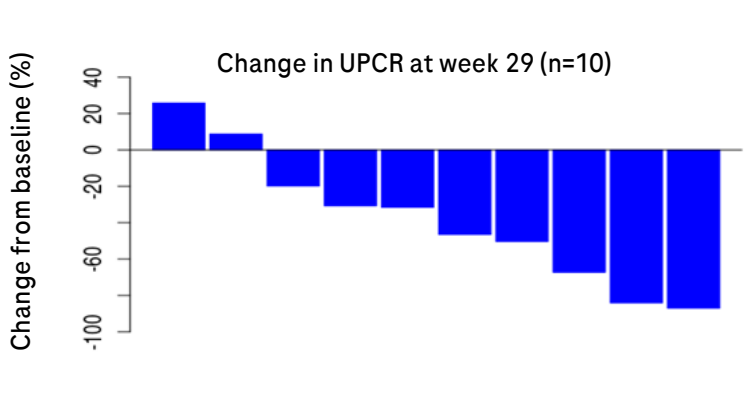
Alternative complement pathway



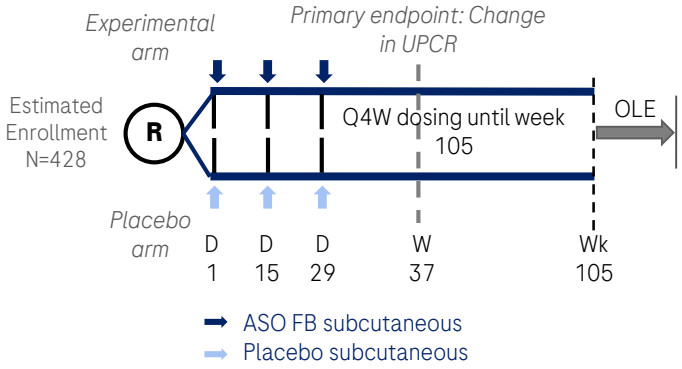
- Globally, IgAN is the most common primary GN that can progress to renal failure
- High levels of CFB are associated with IgAN[1,2]
- ASO FB downregulates CFB production by inhibiting mRNA translation

Clinical development program in IgA nephropathy

Early Ph II results[3]



Ph III (IMAGINATION) trial design



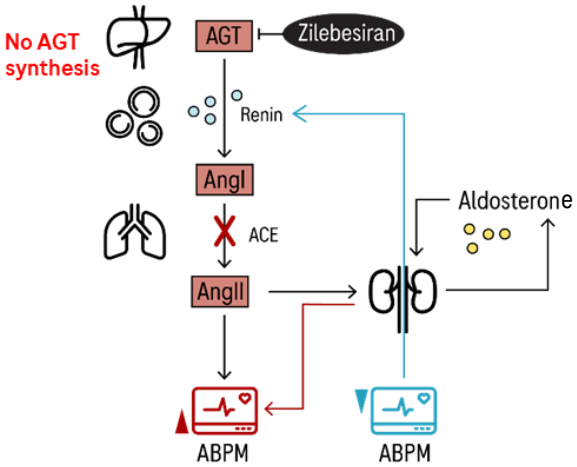
- Ph II study met its primary endpoint of change in 24-hour urinary protein, with 44% mean reduction in proteinuria from baseline to week 29[3,4]
- Achieved secondary endpoint of change in UPCR from baseline to week 29; kidney function stable during the study[3]; updated Ph II data to be shared at medical conference in Q4 2023
- Ph III (IMAGINATION) of ASO FB in IgAN initiated in Q2 2023

Figure adapted from: Barbour et al. ASN Annual Meeting 2022; 1. Chiu et al. Front Immunol. 2021; 12: 638309; 2. Yeo et al. Pediatr Nephrol 2018: 33:763-777; 3. Barbour et al. An Exploratory Trial of an Investigational RNA Therapeutic, IONIS-FB-LRx, for Treatment of IgA Nephropathy. ASN 2022 Abstract SA-PO714; 4. IONIS press release 2022: https://ir.ionispharma.com/news-releases/news-release-details/ionis-presents-positive-phase-2-data-patients-iga-nephropathy; ASO=Antisense oligonucleotide; FB=Factor B; IgAN=IgA Nephropathy; CFB=Complement factor B; mRNA=messenger RNA; MoA=Mode of action; UPCR=Urine protein/creatinine ratio; SC=Subcutaneous; Q4W=every 4 weeks; GN=Glomerulonephritis; Ph II trial: NCT04014335; Ph III (IMAGINATION): NCT05797610; ASO Factor B in partnership with IONIS Pharmaceuticals

Zilebesiran with best-in-disease potential in hypertension

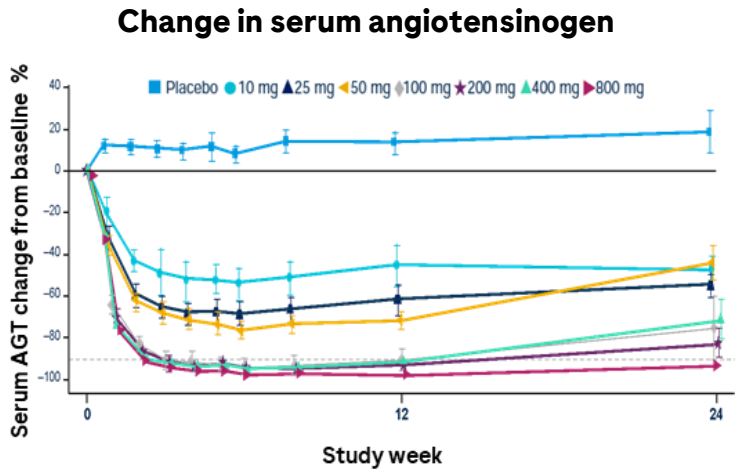
New MoA with tight upstream blockade of AGT pathway and strong early results

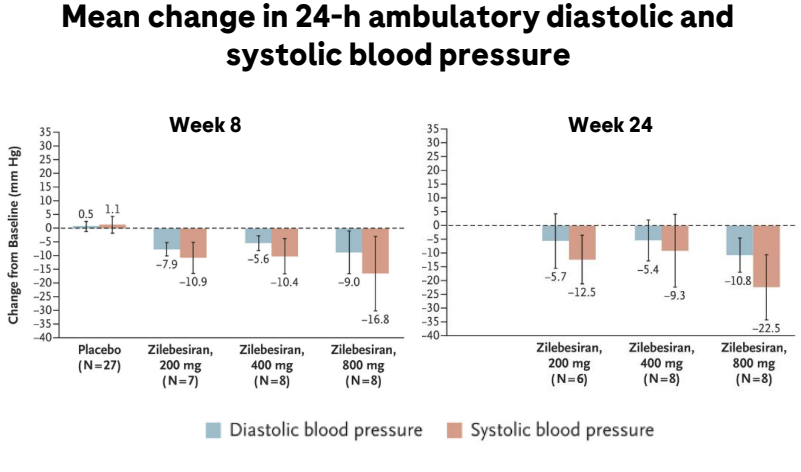
Zilebesiran (siRNA targeting AGT)



- siRNA targeting angiotensinogen, the precursor of all angiotensin peptides may avoid RAAS escape
- Consistent + durable blood pressure control with potential for improved adherence

Ph I results in hypertension[1]





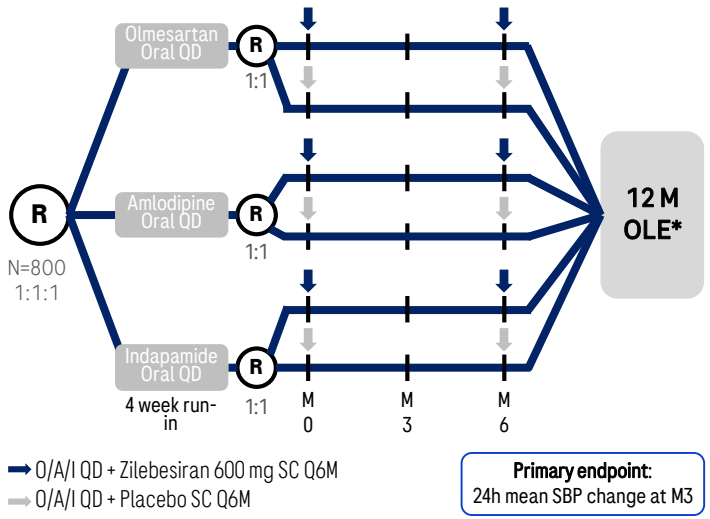
- Positive Ph I results:
  - >90% reduction of serum AGT for up to 6 months at single SC dose of zilebesiran ≥100mg
  - Decreases in systolic blood pressure (>10 mm Hg) and diastolic blood pressure (>5 mm Hg) by week 8 and sustained at 24 weeks at single SC dose of zilebesian ≥200mg
- Well tolerated, only mild-to-moderate injection site reactions and no TRAEs, hypotension or significant alterations of renal/liver function

1 Desai et al. N Engl J Med 2023;389:228-38; MoA=mode of action; siRNA=small interfering RNA; SC=subcutaneous; RAAS=renin angiotensin aldosterone system; AGT=angiotensinogen; AngI/II=angiotensin I/II; ACE=angiotensin-converting enzyme; ABPM=ambulatory blood pressure monitoring; SoC=standard of care; TRAEs=treatment related serious adverse events; zilebesiran in partnership with Alnylam Pharmaceuticals

Zilebesiran: Comprehensive development program ongoing

Positive Ph II (KARDIA-1) results to be presented at upcoming conference

Ph II (KARDIA-2) trial design[1]



Ph II (KARDIA-1) topline results

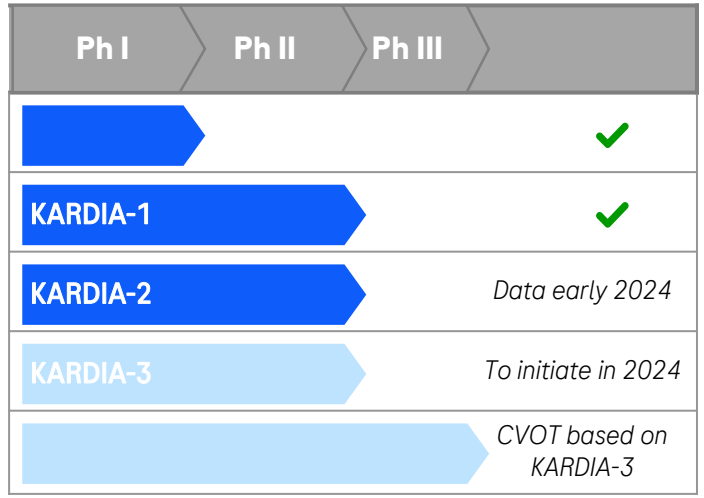
Primary endpoint

- 24h mean SBP change at month 3 ✓

Secondary endpoints

- 24h mean SBP change at month 6 ✓
- Office SBP change at month 3 & 6 ✓

Clinical development program



- Ph II (KARDIA-1): Monotherapy in mild/moderate hypertension; met all primary and key secondary endpoints; data to be presented at upcoming scientific conference
- Ph II (KARDIA-2): Add-on to one SoC in uncontrolled hypertension; data expected early 2024
- Ph II (KARDIA-3): Add-on to SoC (2+ treatments) in uncontrolled hypertension with high CV risk; to be initiated in 2024
- Ph III: CV outcomes (MACE-type endpoint) in uncontrolled hypertension with high CV risk

- Ph II (KARDIA-2) fully enrolled and ongoing
- Ph II (KARDIA-3) results will inform pivotal Ph III trial design
- Ph III to deliver robust label with CV outcomes benefits at launch
- Potential for expansion to other CV indications (e.g. heart failure)

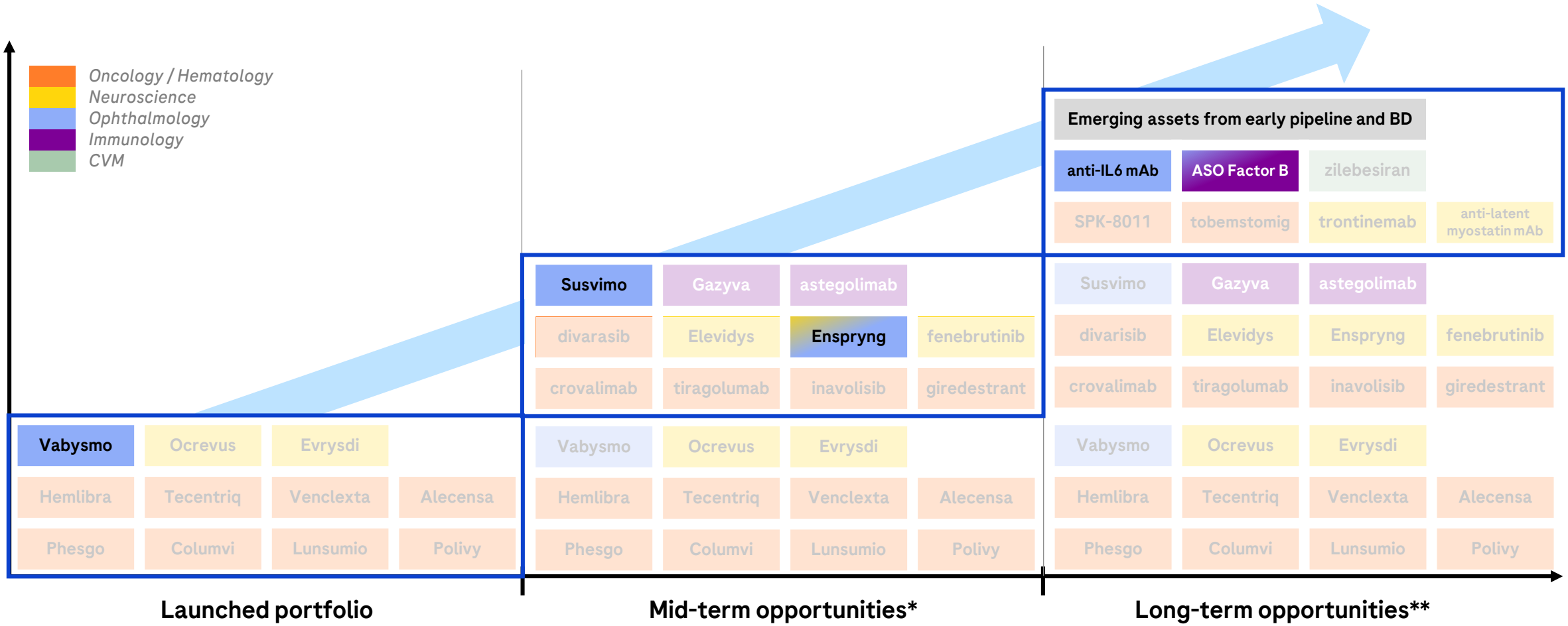
*Patients in the OLE phase receive zilebesiran 600 mg SC Q6M; [1]NCT05103332; SBP=systolic blood pressure; SoC=standard of care; CV=cardiovascular; CVOT=CV outcomes trial; MACE=major adverse cardiovascular events; R=randomization; M=month; SC=subcutaneous; Q6M=every 6 months; QD=daily; OLE=open label extension; O=olmesartan; A=amlodipine; I=indapamide; zilebesiran in partnership with Alnylam Pharmaceuticals

Late Stage Pipeline Ophthalmology

Christopher Brittain |
Vice President and Global Head of Ophthalmology Product Development

Building blocks for future growth through 2030

5 novel targets in Ophthalmology with differentiated potential in late stage development



CVM = cardiovascular / metabolism; *mid-term defined as filing 2024-2026, **long-term defined as filing after 2026, BD=business development

Roche poised for a leading role in Ophthalmology

Opportunities

- ***aVEGF therapies:*** *transformed patient outcomes over 15-years*
- ***Unmet need:*** *superior efficacy and durability*
- ***Changing landscape:*** *aging population, diabetic epidemic, fast progressing science*

Products and data

- ***Vabysmo:*** *nAMD, DME approved RVO filing completed*
- ***Susvimo:*** *nAMD approval paused DME, DR filing planned*
- ***Investment in RWE and VOYAGER study***
- ***PhII data expected '24:*** *ASO fB GA, anti-IL-6 DME*
- ***Ph III anti-IL-6 in UME***

Capabilities

- ***Leading in-house imaging data mastery:*** *AI applications, fluid & genetic biomarkers*
- ***Cell based and optogenetic gene therapy***
- ***Leverage partnering***

Leadership ambition

- ***Near-term:*** *Vabysmo as IVT SoC relaunch of Susvimo*
- ***Accelerate pipeline internally & externally:*** *lead RWE supporting value of innovation*
- ***Expand into adjacent ophthalmology areas*** *expanding with satralizumab into TED*

aVEGF=anti-vascular endothelial growth factor A; nAMD=neovascular age-related macular degeneration; DME=Diabetic macular edema; UME=Uveitic macular edema; DR=diabetic retinopathy; RVO=Retinal vein occlusion; GA=geographic atrophy; IL-6=inter-leukin-6; ASO=Antisense oligonucleotide; fB=Factor B; AI=Artificial Intelligence; IVT=Intravitreal; SoC=Standard of care; RWE=Real World Evidence; TED=Thyroid eye disease

Ophthalmology strategy

Further improving the standard of care and expanding in new indications

Update on key clinical data & outlook

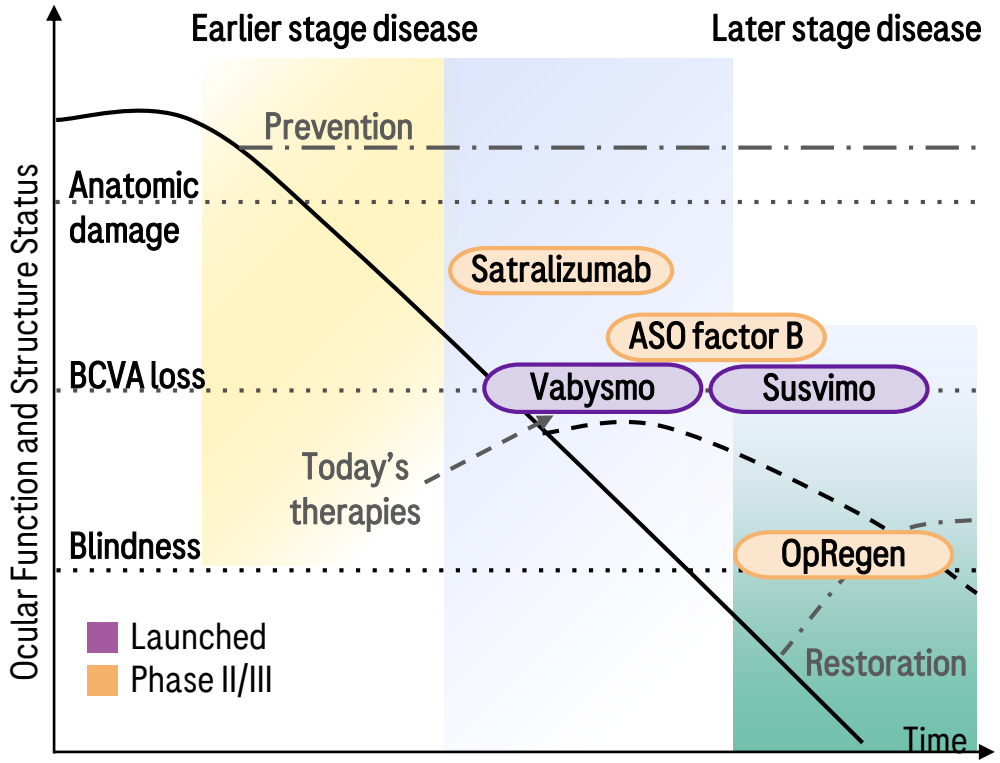
Vabysmo

- New data presented at ASRS 2023:
  - demonstrating reduced risk of epiretinal membrane (ERM) formation vs. aflibercept in patients with DME[1]
  - real-world data reinforcing 1L benefits in DME[2] and nAMD[3]
  - positive anatomical outcomes demonstrated in DME[4] and nAMD[5]
- Filed in US and EU Q2/3 2023 in RVO

Susvimo (port delivery system)

- Return to study enrollment Q4 2023 and US commercialization 2024
- Zifibancimig (VEGF-Ang2 DutaFab) with Ph1b FPI expected Q4 2023 (administration via port delivery system)

Improve outcome across all stages of ocular diseases

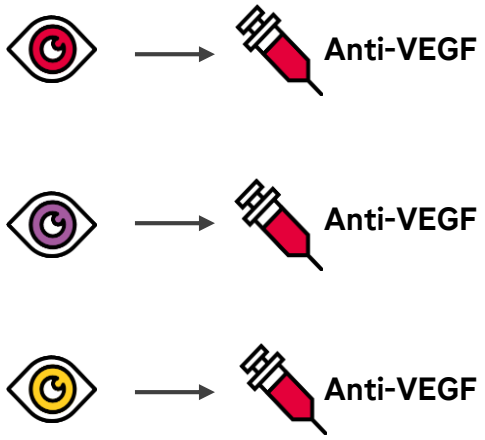


1. Glenn et al. ASRS 2023; 2. Gale et al. ASRS 2023, Poster #213; 3. Leng et al. ASRS 2023; 4. Nudleman et al. ASRS 2023; 5. London et al. ASRS 2023; BCVA=Best-corrected visual acuity; DME=Diabetic macular edema; nAMD=Neovascular age-related macular degeneration; RVO=Retinal vein occlusion; FPI=First patient in; ASO=Antisense oligonucleotide

R&D focus area ophthalmology

Better visual outcomes in the future via diagnostics and combination therapies

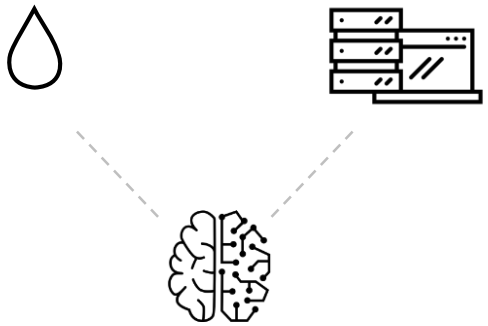
Current SoC



Future SoC

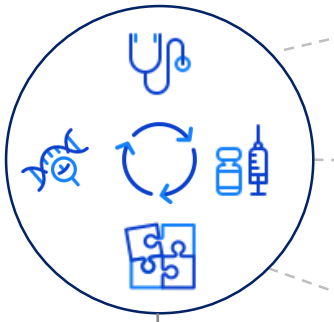
Biomarker analyses

- Aqueous humor sample
- Aqueous humor profiling
- Imaging
- Clinical data
- Genotyping



Machine learning algorithm

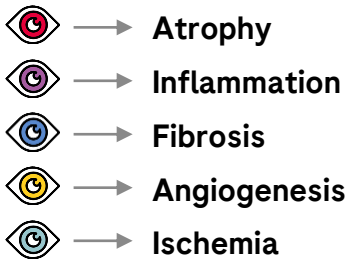
Personalized treatment options (PHC)



Clinical diagnosis support

- Prognosis
- Early diagnosis
- Drug choice
- Dosing regimen

New combination therapies



Increased value for Healthcare ecosystems by delivering better care, improving efficiencies and optimizing resource utilization

SoC=standard of care; VGEF=vascular endothelial growth factor; PHC=personalized healthcare

Ophthalmology pipeline gaining momentum

Expanding into new disease areas with satralizumab initiating Ph III in TED

Phase I		Phase II		Phase III		Launched		
RG6351	NME Retinal disease	RG6179	anti-IL-6 DME	RG7716	Vabysmo ★ BRVO	RG7716	Vabysmo nAMD	✓
RG6209	NME Retinal disease	RG6501	OpRegen[1] GA	RG7716	Vabysmo ★ CRVO	RG7716	Vabysmo DME	✓
RG7921	NME RVO	RG6299	ASO factor B[2] GA	RG6321	Susvimo DME	RG6321	Susvimo nAMD	✓
RG6120	Zifibancimig (VEGF-Ang2 DutaFab) nAMD			RG6321	Susvimo DR			
				RG6179	anti-IL-6 UME			
				RG6168	satralizumab TED			

nAMD · RVO · DME/UME · Retinal disease · GA · FDA approval · DR · Filed in US & EU · TED

Antibody · Antisense oligonucleotide · DutaFab · Stem cell therapy · PDS

Upcoming readouts:

- Data expected for ASO factor B in GA in 2024
- Data expected for anti-IL-6 in DME in 2024 and UME in 2025

[1] In collaboration with Lineage Cell Therapeutics (LCTX); [2] In collaboration with Ionis; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; UME=Uveitic macular edema; DR=diabetic retinopathy; BRVO=branch retinal vein occlusion; CRVO=central retinal vein occlusion; GA=geographic atrophy; DutaFabs=dual targeting fragment antigen-binding; VEGF=vascular endothelial growth factor; Ang-2=angiopoietin-2; IL-6=inter-leukin-6; TED=Thyroid eye disease; PDS=Port delivery system; ASO=Antisense oligonucleotide

Susvimo: Adding new indications

Positive Ph III results in DME and DR with filing in 2024

Roche

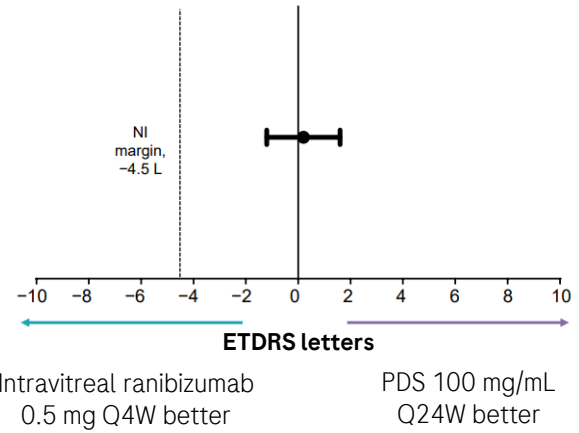
susvimo™ ranibizumab injection 100 mg/mL For Ocular Implant

Angiogenesis Feb 10-11

Ph III in DME (PAGODA)[1]

Adj. mean change from baseline in BCVA score, (95% CI)	Averaged over weeks 60 and 64
PDS 100 mg/mL Q24W	9.6 (8.7, 10.5)
IVT ranibizumab 0.5 mg Q4W	9.4 (8.3, 10.5)
Difference in adj. means	0.2 (−1.2, 1.6)

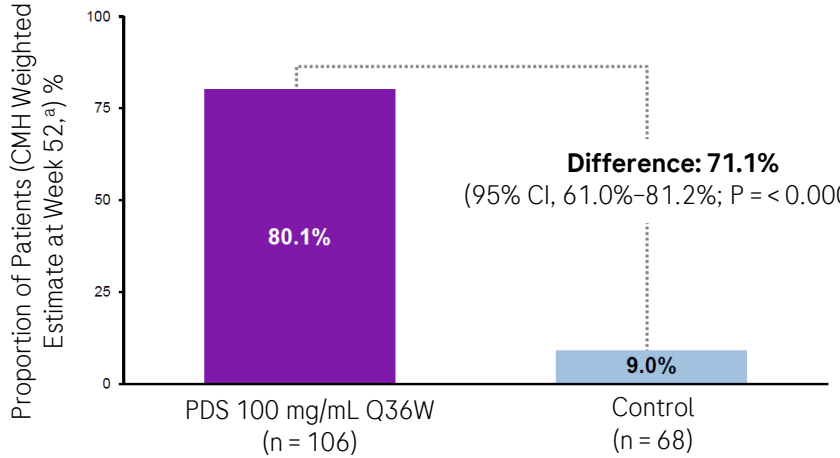
Difference in adjusted means for BCVA change averaged over weeks 60 and 64, 95% CI



Primary endpoint: BCVA score change from baseline averaged over weeks 60 and 64 as measured via ETDRS chart

Ph III in DR (PAVILION)[2]

Patients with ≥ 2-step improvement from baseline on ETDRS-DRSS, ITT population



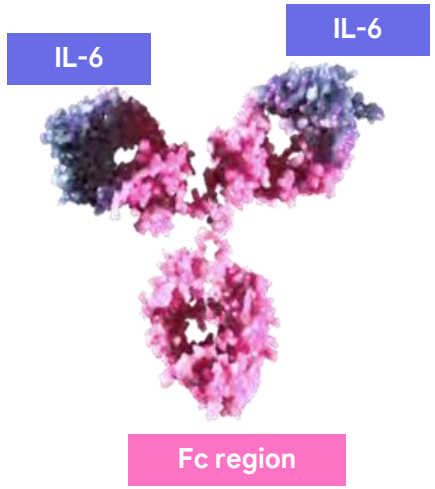
Primary endpoint: Percentage of patients with a ≥2-step improvement from baseline on the ETDRS-DRSS at week 52

1. Khanani et al. Angiogenesis 2023; 2. Pieramici et al. Angiogenesis 2023; [a]The weighted estimate based on CMH method was stratified by baseline ETDRS-DRSS level (47 vs 53) and baseline intraretinal or subretinal fluid status (present vs absent).Missing ETDRS-DRSS is imputed using the last observed outcome prior to week 52. Patients with missing baseline outcomes are excluded. [b]CMH test; DME=Diabetic macular edema; DR=Diabetic retinopathy; BCVA=Best corrected visual acuity; ETDRS=Early treatment of diabetic retinopathy study; DRSS=Diabetic retinopathy severity scale; PDS=Port delivery system with ranibizumab; CI=Confidence interval; IVT=Intravitreal; ITT=Intention to treat; Q24W=Every 24 weeks; Q4W=Every 4 weeks; Q36W=Every 36 weeks

RG6179: Novel anti-IL-6 mAb for intraocular use

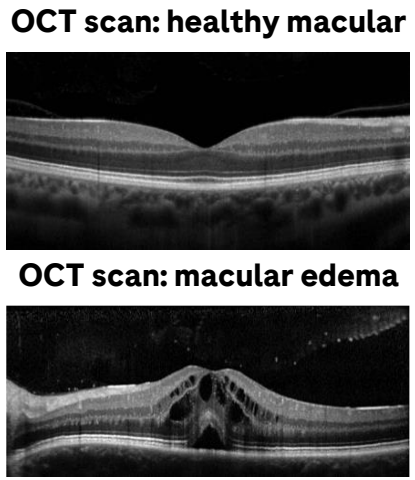
New data investigating anti-IL-6 in uveitic macular edema shared at ARVO 2023

Anti-IL-6 mAb



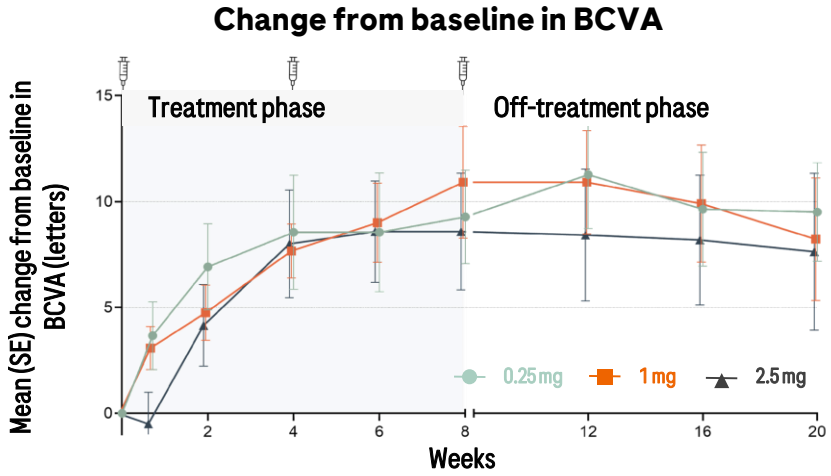
- Anti-IL-6 mAb binds IL-6 and inhibits all known forms of IL-6 signaling
- Specifically designed for intraocular use and optimized for a rapid systemic clearance

Uveitic macular edema



- UME is a common result of intraocular inflammation, with only limited treatment options
- Inflammation causes vascular leakage & fluid accumulation within the retina[2]

Ph I data (DOVETAIL) presented at ARVO 2023[1]



Preliminary clinical data in UME indicating:

- Improved vision and absence of retinal fluid in all dosing cohorts
- 25 - 36% of patients gained 15 letters or more at week 12
- All doses of anti-IL-6 were well tolerated across all patients, with no treatment-related serious AEs, sustained IOP increase, or new cataracts

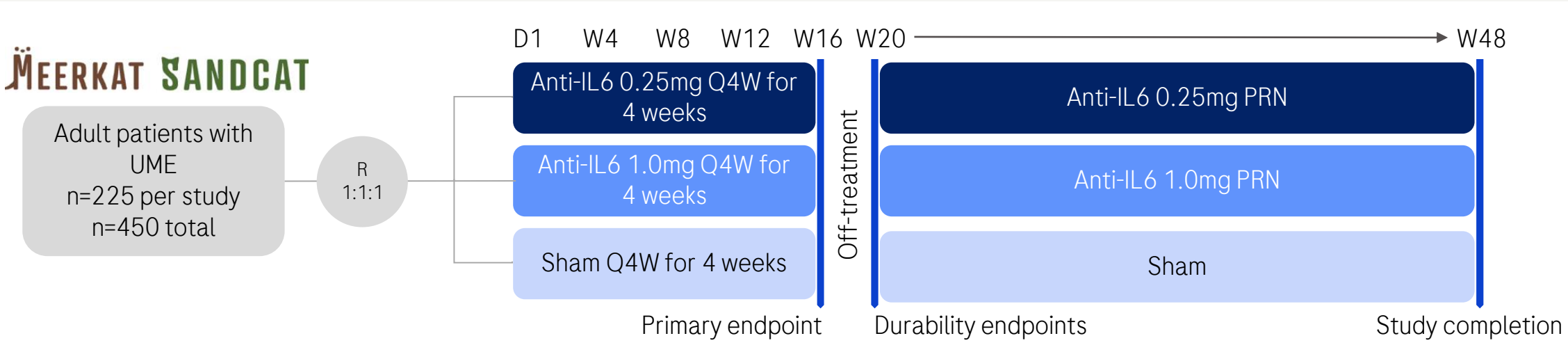
- Based on these Ph I findings, a Ph III clinical trial program is ongoing

1. Sharma et al. ARVO 2023; 2. Koronis et al. Drug Des Devel Ther. 2019 Feb 19;13:667-680. doi: 10.2147/DDDT.S166092; UME=uveitic macular edema; IOP=intraocular pressure; IL-6=interleukin-6; AE=Adverse event; BCVA=Best-corrected visual acuity; SE=Standard error; OCT=Optical coherence tomography; mAb=Monoclonal antibody

RG6179: Novel anti-IL-6 mAb in UME and DME

Two identical Ph III studies in UME initiated Q1 2023

Ph III (Sandcat/Meerkat) trials in UME



- Based on the Ph I (DOVETAIL) findings, and supported by PK/PD results, a Ph III study program investigating anti-IL-6 in UME (SANDCAT, MEERKAT) was initiated with FPI in Q1 2023 and data expected 2025
- Primary endpoint: Proportion of patients with ≥15 letters BCVA gain from baseline at week 16
- Ph II studies in DME (BARDENAS, ALLUVIUM) also ongoing

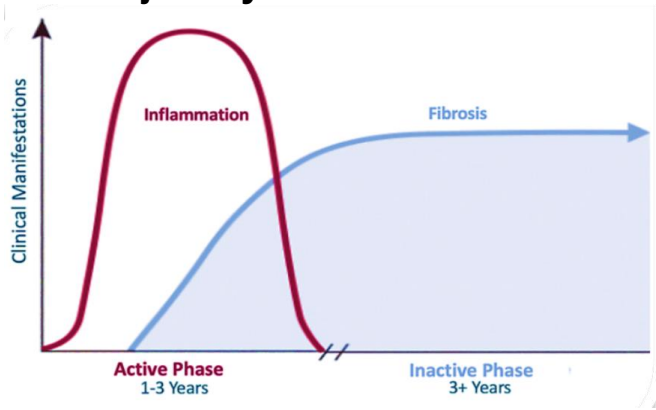
PK/PD=Pharmacokinetics/Pharmacodynamics; UME=Uveitic macular edema; DME=Diabetic macular edema; PRN=Pro re nata; BCVA=Best-corrected visual acuity; Q4W=Every 4 weeks; IL-6=Interleukin-6; W=Week

Satralizumab in thyroid eye disease

Potential disease-modifying treatment option with a well-established safety profile

Thyroid eye disease

Disease process of TED usually follows the trajectory of Rundle's curve*

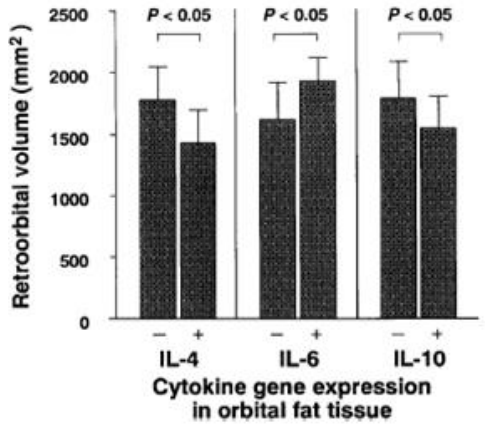


- Complex orbital inflammatory autoimmune disease[1]
- Most common orbital disease in adults, with symptoms such as redness, dry eye, double vision, protrusion of the eye with periorbital swelling and vision loss[1]
- Treatment options limited; faster and durable disease modification needed to prevent downstream fibrosis

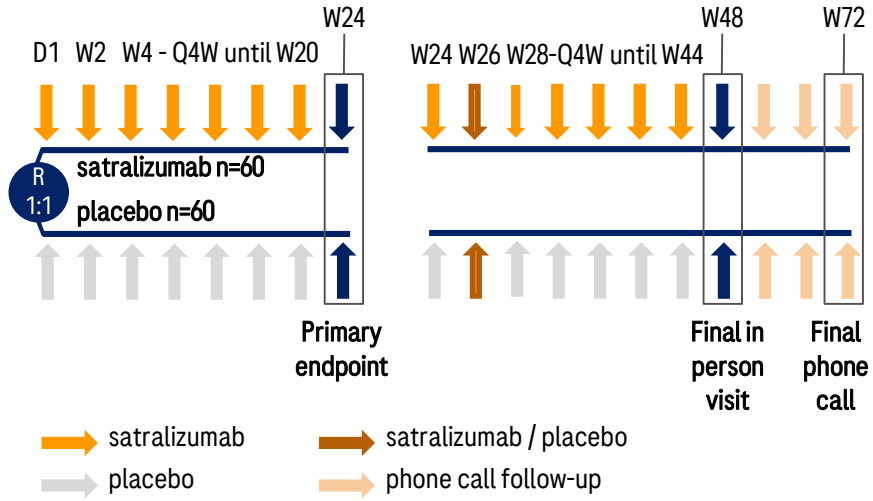
IL-6 as a potential target for treating TED

IL-6 in TED[2]

Orbital volume (CT) in TED patients with or without detectable IL-6 mRNA expression in OF (RT-PCR)



Ph III (SatraGo-1/SatraGo-2) trial design

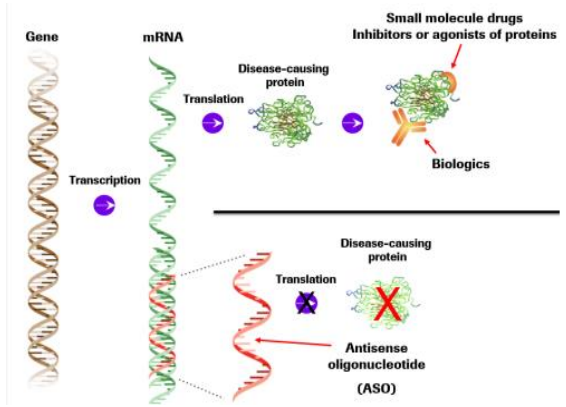


- IL-6 is a pleiotropic cytokine produced by orbital fibroblasts, macrophages and adipocytes of TED patients, mediating inflammation and fibrosis
- Satra binds to the IL-6R, preventing IL-6 from binding, inhibiting inflammatory signalling pathways[3,4]
- Two identical Ph III studies investigating Satra in TED (SatraGo-1/SatraGo-2) initiated Q3 2023

* Rundle's curve depicts schematically the typical course of thyroid eye disease severity with time; 1. https://eandv.biomedcentral.com/counter/pdf/10.1186/s40662-014-0009-8.pdf; 2. Hiromatsu et al. J Clin Endocrinol Metab. 2000 Mar;85(3):1194-9; 3. Traboulsee A, et al. Lancet Neurol 2020;19:402–412; 4. Yamamura T, et al. N Engl J Med 2019;381:2114–2124; TED=Thyroid eye disease; CT=Computed tomography; OF=Orbital fat; IL-6=interleukin-6; IL-6R=Interleukin-6 receptor; RT-PCR=Reverse transcriptase polymerase chain reaction; Satra=Satralizumab; W=week; IL-4(10)=Interleukin 4(10)

ASO factor B in GA: Targeting hyperactive alternative complement pathway via SC delivery

ASO factor B

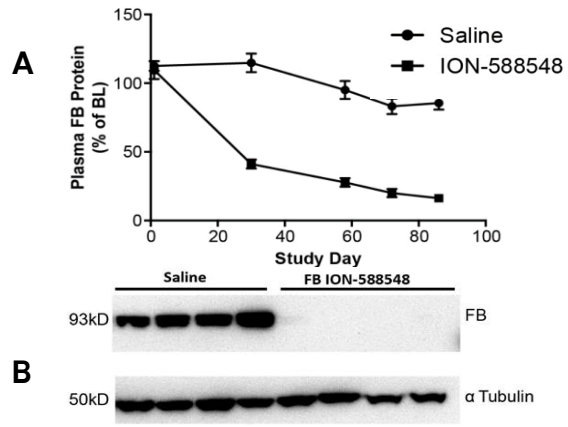


- Complement Factor B (CFB): key component of alternative complement pathway; associated with complement hyperactivity seen in GA
- Inhibits CFB gene expression & reduces the production of factor B protein

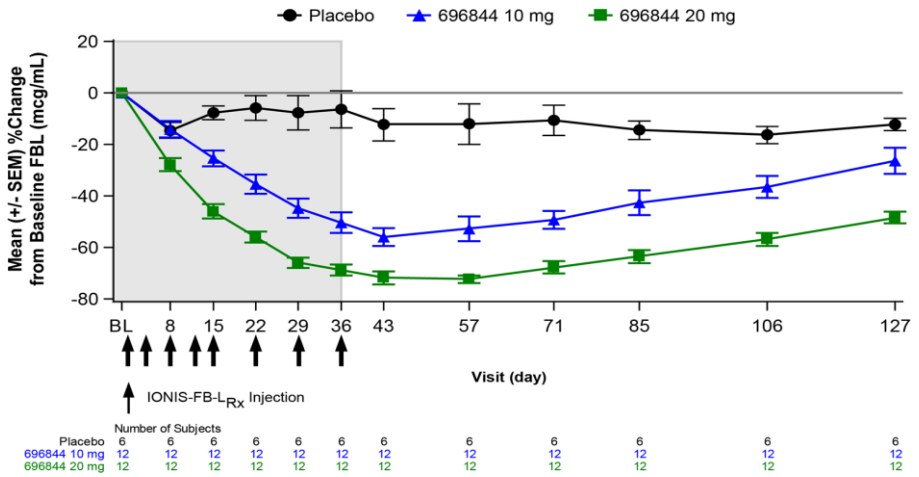
Preclinical and Ph I data

Preclinical results in monkeys[1]

Systemic (A) and ocular (B) ASO FB protein knockdown achieved with RG6299 SC



Ph I: Significant dose-dependent reductions in plasma FB levels[2]



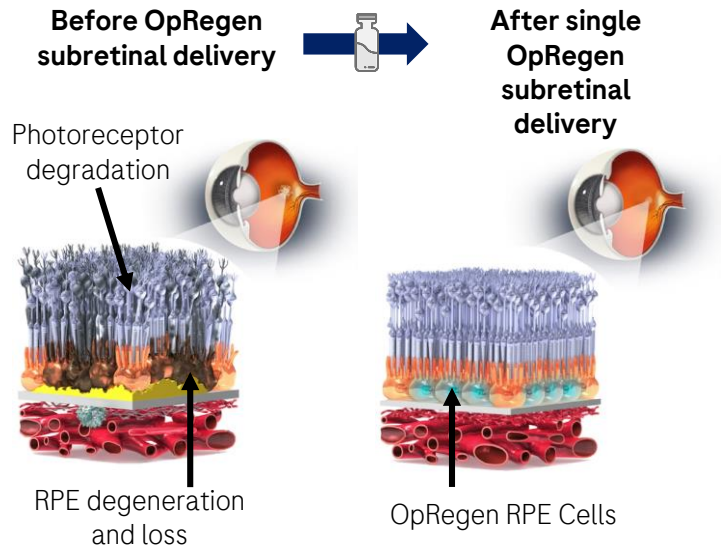
- Advantages of ASO factor B:
  - Potential for systemic Q4W SC administration, simultaneous treatment of bilateral GA and self-administration at home
  - More suitable option for treatment of early stage disease (e.g. iAMD)
- Ph II GOLDEN ongoing* with data expected 2024; pivotal study in planning stage

*Managed by IONIS; 1. Grossman et al., Mol Vis 2017; 2. Guymer RG, et al. Presented at EURETINA 2020; ASO=antisense oligonucleotide; FB=Factor B; GA=geographic atrophy; CFB=Complement factor B; iAMD=intermediate age related macular degeneration; SC=Subcutaneous; Q4W=Every 4 weeks; SEM=Standard error of the mean; ASO factor B in-licenced from IONIS pharmaceuticals

OpRegen in GA: Replenishing the retinal pigment epithelium

Encouraging early clinical data presented at ARVO 2022 and 2023

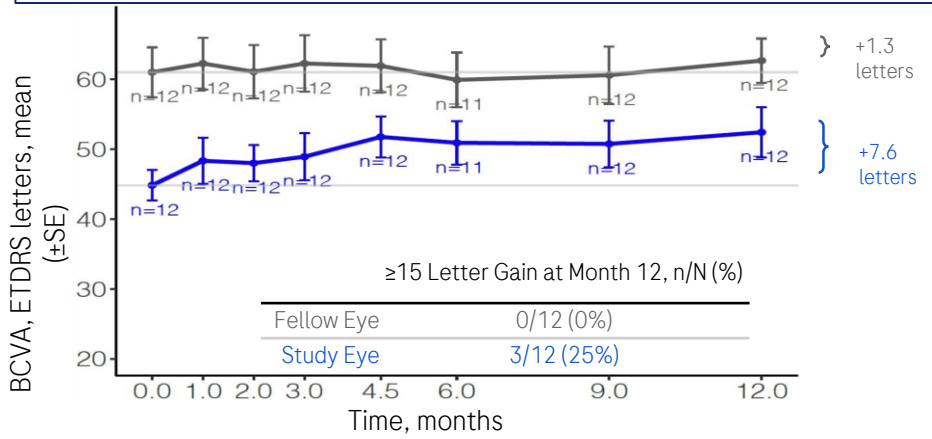
Potential to counteract RPE cell loss in GA

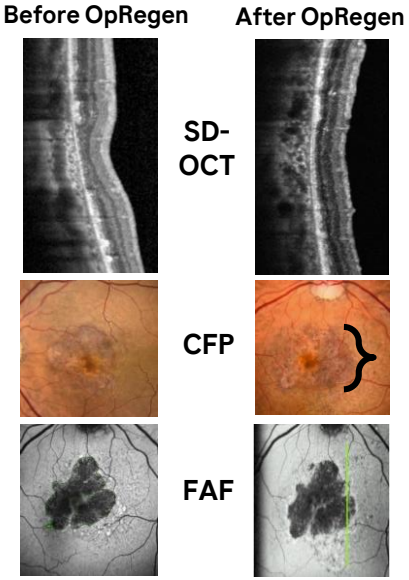


- OpRegen has the potential to counteract RPE cell loss in areas of GA by supporting retinal structure and function
- Ph IIa trial initiated Q1 2023, continuing to optimize subretinal surgical delivery

Ph I/IIa data: Outer retinal structure and visual function improvements in patients with impaired vision[1,2]

Cohort 4 (n=12):
Patients with bilateral GA secondary to AMD with BCVA ≥20/250 and ≤20/64 and GA area ≥4 and ≤11mm2





- Preliminary evidence of outer retinal structure and visual function improvements with OpRegen was observed in patients with GA and impaired vision (Cohort 4 [n=12])
- Average 7.6 letter gain and 25% of patients with ≥15 Letter gain in Cohort 4
- OpRegen well tolerated in Ph I/IIa GA study with an acceptable safety profile and mostly mild AEs

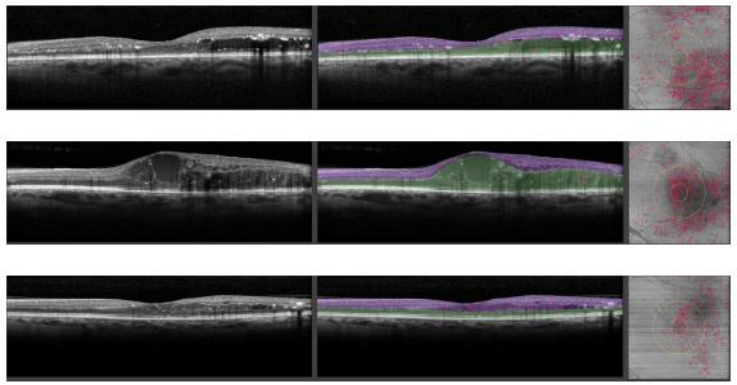
In collaboration with Lineage Cell Therapeutics, Inc. (LCTX); 1. Ho et al. ARVO 2022; 2. Banin et al. ARVO 2023; RPE=Retinal pigment epithelium; GA=Geographic atrophy; AMD=Age-related macular degeneration; BCVA=Best-corrected visual acuity; ETDRS=Early treatment of diabetic retinopathy study; SD-OCT=Spectral-domain optical coherence tomography; CFP=Color fundus photography; FAF=Fundus autofluorescence; AEs=Adverse events; SE=Standard error

Roche application of deep learning in ophthalmology

Vabysmo reduces HRF volumes more vs. aflibercept, indicating better disease control

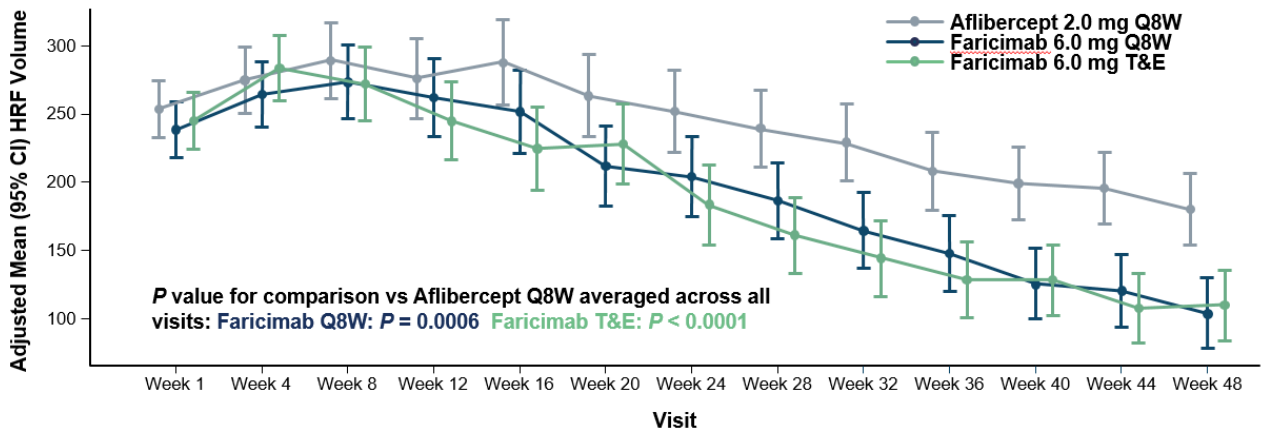
The application of deep learning to segment hyperreflective foci

Representative predictions on YOSEMITE and RHINE (3 separate study eyes, all baseline)



- HRF are small bright objects in the retina in patients with DME and may be imaging biomarkers for inflammation and disease progression
- DL was used to segment HRF, which were compared with HRF drawn by expert graders
- HRF model predictions were consistent with expert assessments

Vabysmo shown to reduced HRF volumes significantly more compared to aflibercept



- A post hoc analysis of YOSEMITE and RHINE demonstrated greater retinal HRF volume reductions in Vabysmo- vs. aflibercept-treated eyes at week 48
- Volume reductions indicate suppression of pathways that mediate inflammation
- Better resolution of the pathological manifestations of DME with Vabysmo support the therapeutic potential of dual Ang-2/VEGF-A inhibition in retinal diseases

Maunz et al. ARVO 2023, Poster # 2697 -B0519; HRF=Hyperreflective foci; DME=Diabetic macular edema; nAMD=Neovascular age-related macular degeneration; DL=Deep learning; Ang-2=Angiopoietin-2; VEGF-A=Vascular endothelial growth factor A; Q8W=Every 8 weeks; T&E=Treat and Extend; CI=Confidence interval

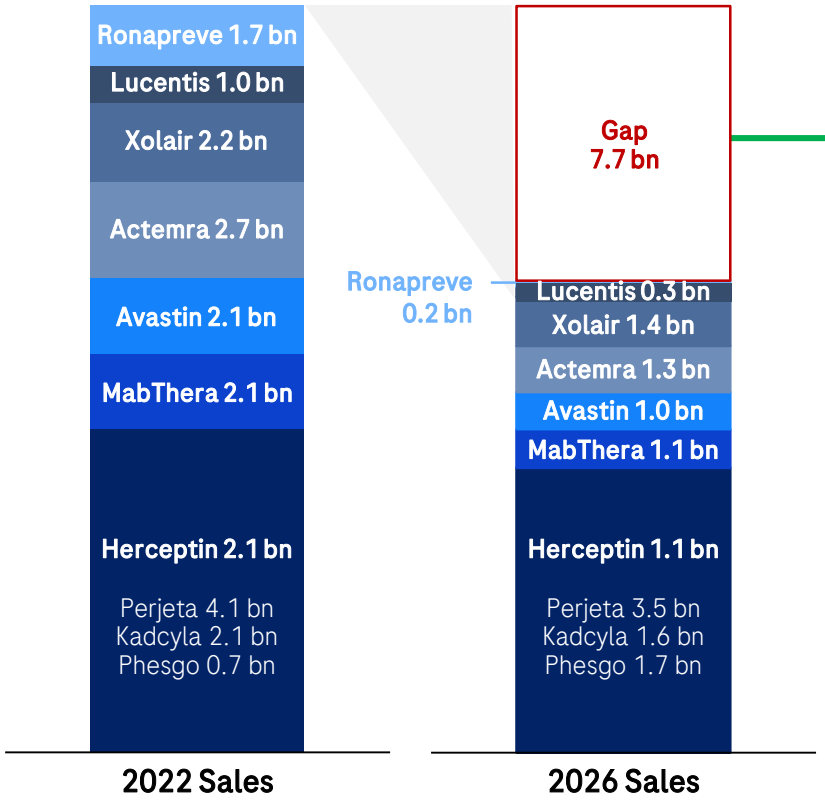
Closing remarks

Thomas Schinecker |
CEO Roche Group

Consensus outlook 2022-26*

Growth driven by our young on-market portfolio; potential pipeline up-side

Biosimilar gap (22-26)



Consensus sales growth (22-26)

Post-HY 2023 consensus survey

Vabysmo	4.3 bn
Tecentriq	1.7 bn
Hemlibra	1.6 bn
Ocrevus	1.5 bn
Polivy	1.4 bn
Evrysdi	1.2 bn
Lunsumio	0.7 bn
Columvi	0.5 bn
Gazyva	0.4 bn
Alecensa	0.3 bn
Enspryng	0.3 bn
Susvimo	0.2 bn
Other in-market[1]	(0.5) bn
Pipeline Ph III[2]	**2.4 bn**
thereof Elevidys	*0.8 bn*
thereof tiragolumab	*0.7 bn*
thereof giredestrant	*0.3 bn*
thereof crovalimab	*0.3 bn*
thereof fenebrutinib	*0.2 bn*
Total	**16.1 bn**

Potential up-side[3]

Additional up-side by late-stage NMEs / LEs poorly or not yet covered:

Oncology (inavolisib, divarasib, tobemstomig, autogene cevumeran), **Hematology** (SPK-8011), **Ophthalmology** (ASO factor B in GA, anti-IL-6 mAb, Enspryng in TED), **Neuroscience** (Enspryng in gMG, anti-latent myostatin mAb, trontinemab, prasinezumab), **Immunology** (Gazyva in LN, astegolimab, ASO Factor B in IgAN), **Cardiovascular & Metabolism** (zilebesiran)

*All estimates are based on Post HY 2023 consensus collected by FTI Consulting on behalf of Roche (n=18); [1] Activase/TnKase, Esbriet, Pulmozyme, CellCept, Erivedge, Cotellic, Gavreto, Xofluza, Rozlytrek; Luxturna
[2] included in >50% of the sell-side models; [3]Assets covered on average by only 17% of the sell side models; NME=new molecular entity; LE=line extensions

Doing now what patients need next