
Roche

Roche Pharma Day 2024

London, 30 September 2024

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

All mentioned trademarks are legally protected.

Welcome

Bruno Eschli
Head of Investor Relations

Agenda: Pharma Day 2024

Introduction

09:30 BST Bruno Eschli, Head of Investor Relations

Strategy

Group

Thomas Schinecker, CEO Roche Group

Pharma

Teresa Graham, CEO Roche Pharmaceuticals

R&D Excellence

Levi Garraway, CMO and Global Head of Product Development

11:10-11:40 **Q&A – Strategy**

11:40-12:30 **Lunch Break**

Pipeline

Oncology/Hematology

12:30 BST Charles Fuchs, SVP and Global Head of Oncology and Hematology Product Development

Neurology

Azad Bonni, SVP and Global Head of Neuroscience & Rare Diseases at pRED

Immunology

Larry Tsai, SVP and Global Head of Immunology Product Development

Ophthalmology

Christopher Brittain, SVP and Global Head of Ophthalmology Product Development

Cardiovascular, Renal and Metabolism

Manu Chakravarthy, SVP and Global Head of Cardiovascular, Renal and Metabolism Product Development

14:00-14:30 **Q&A - Pipeline**

14:30-15:00 **Buffet reception**

Group

Thomas Schinecker
CEO Roche Group

Performance and growth outlook

Strategy update

Progress made since Pharma Day 2023

Significant progress for operational efficiency, deals and pipeline achieved

	Internal innovation	External innovation	Operational efficiency
Pharma	2 NMEs launched 11 regulatory approvals	• Telavant (anti-TL1A) • Carmot (CT-388/868/996) • Regor (CDKi portfolio) • AntlerA (Wnt agonist)	• R&D Excellence: Application of the Bar and portfolio prioritization • REDs/ PD: Systems and processes harmonization; structure alignment with 5 Therapeutic Areas • Manufacturing network optimization, incl. Vacaville divestment
Diagnostics	5 instruments launched 39 assays launched >50% of FDA PMA/BLA approvals*	• LumiraDx (PoC testing platform)	• Diabetes Care & PoC integration into Near Patient Care • Shift of FMI to Diagnostics

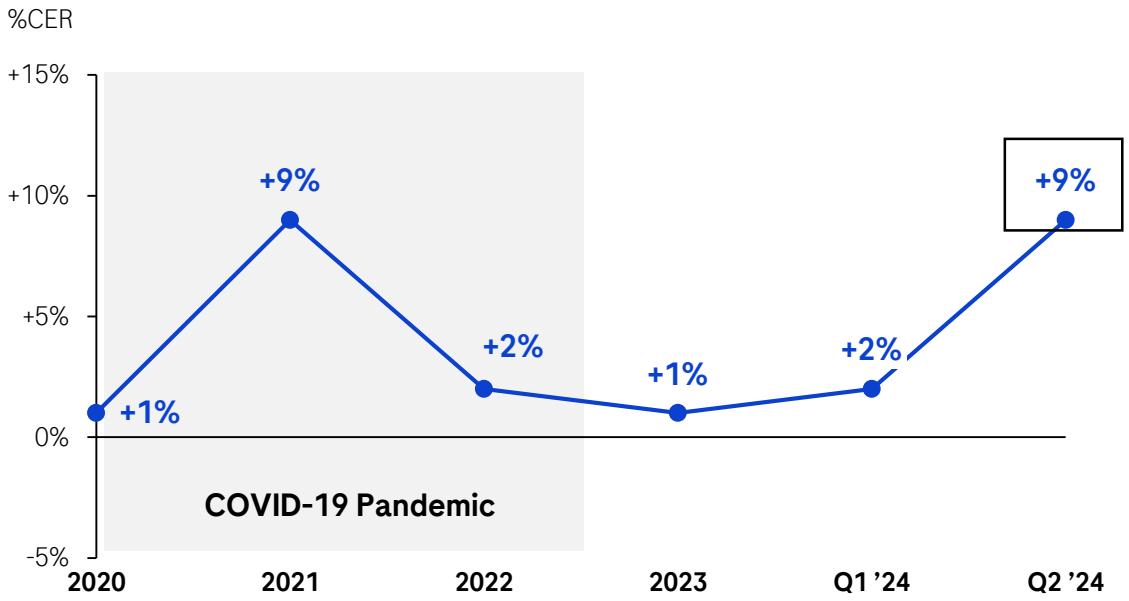
HY 2024 results prove our commitment to cost control and financial stability

*From 2019 to YTD 2024; CDK=Cyclin-dependent kinase; TL1A=TNF-like protein 1A; PoC=point of care

Sales momentum expected to continue into 2025

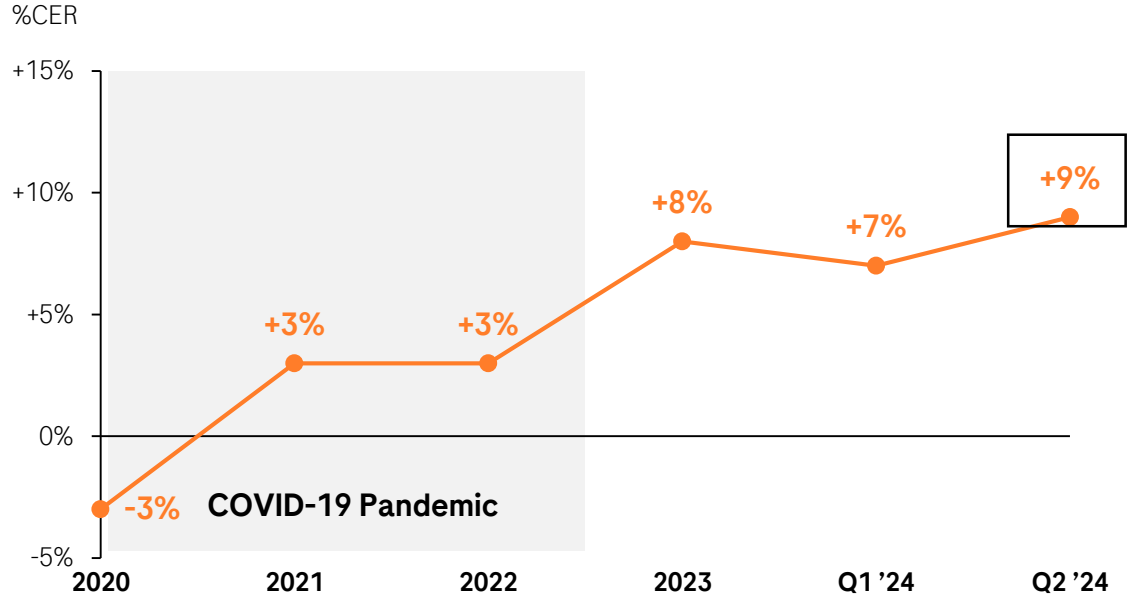
Strong growth by both divisions: Pharma and Diagnostics

Group sales growth



Total COVID-19 sales of CHF ~19bn[2]

Group base business sales growth excluding COVID related sales[1]



No significant COVID-19 impact going forward

All growth rates at CER of the respective year; 1. Base business=Pharma excluding Ronapreve and Diagnostics excluding COVID-19-related products; 2. COVID-19 sales referring to COVID-19 diagnostic tests, Ronapreve and Actemra sales

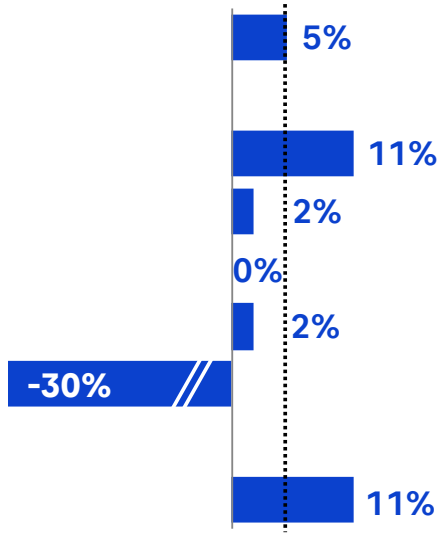
Positive Core Operating Profit momentum

Higher sales and effective cost management resulting in strong performance

	HY 2024 CHFm	HY 2024 abs. CER
Sales	**29,848**	**+1,515**
Other revenue	908	+94
Cost of sales	-7,300	-168
R&D	-6,268	-21
SG&A	-6,376	-96
OOI&E	481	-212
Core operating profit	**11,293**	**+1,113**
Core OP in % of sales	*37.8%*	
At CER	*38.2%*	
	(HY 2023: 36.3%)	

HY 2024 vs. HY 2023

CER growth

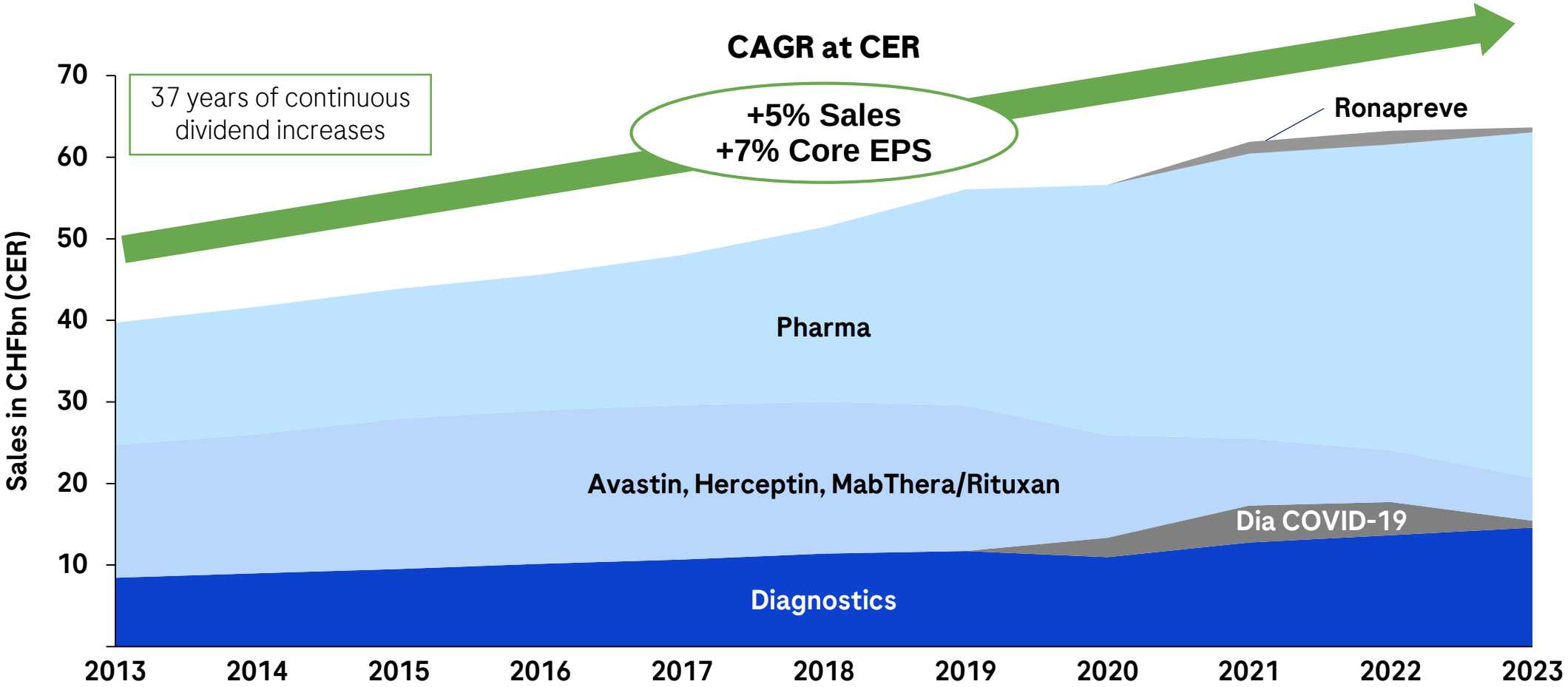


+4% in CHF

CER=Constant Exchange Rates (avg full year 2023); OP=Operating Profit; R&D=Research & Development; SG&A=Selling, General & Administration; OOI&E=Other Operating Income & Expense

Roche delivered consistent growth through biosimilar erosion

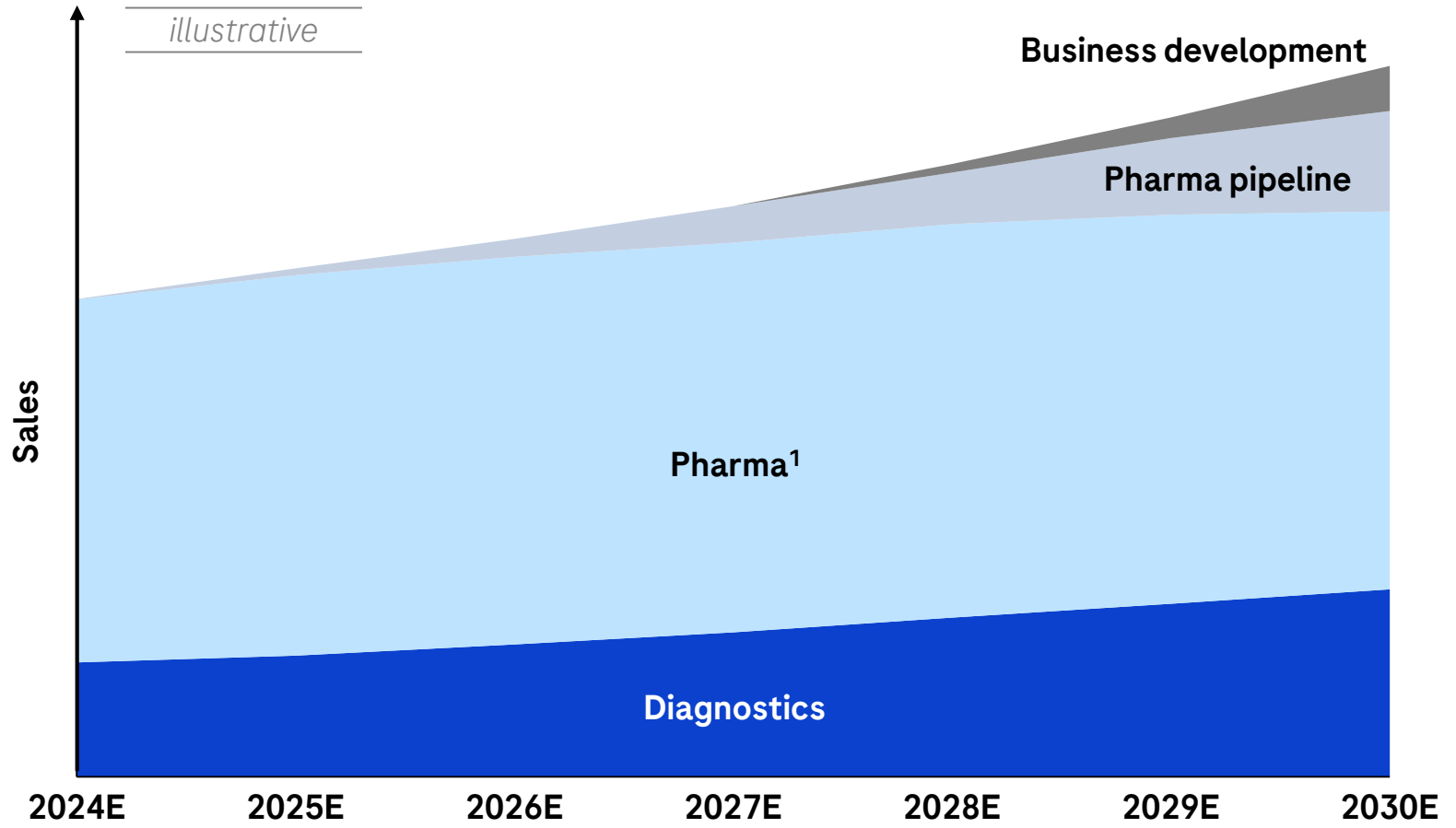
Successful diversification driven by young portfolio with 16 blockbusters in Pharma



Note: FMI sales with Pharma Division for all years; CAGR based on CER growth rates of each year; CAGR=Compound Annual Growth Rate; CER=Constant Exchange Rates (avg full year 2022);
Source: Roche Finance Report 2013-2023

A solid base to deliver future growth

Pipeline and business development to add significant upside potential



- BD to accelerate pipeline portfolio
- In-house pipeline with upside potential

- On-market Pharma portfolio to deliver growth until 2027
- No patent cliff ahead
- COP margins at least stable

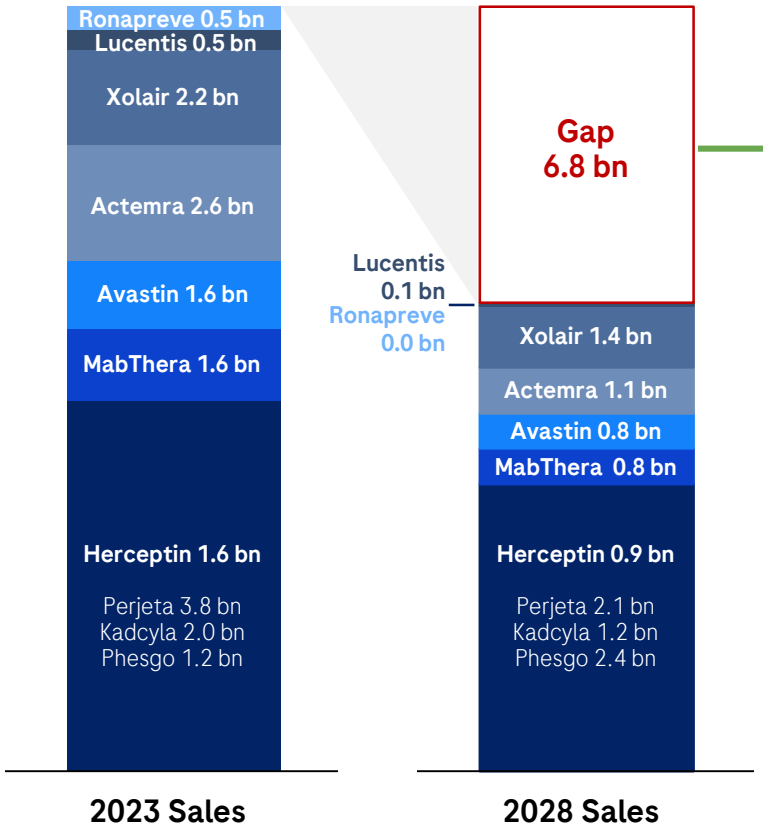
- Diagnostics growth driven by on-market portfolio and key launches
- Mid- to high-single digit sales growth
- COP growth ahead of sales growth

Note: Graph is purely conceptual to outline portfolio trends; [1] Pharma: On-market portfolio including young portfolio (products launched since end of 2015); COP=core operating profit

Consensus outlook 2023-28*

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

Biosimilar gap (23-28)



Consensus sales growth (23-28)

Vabysmo	4.6 bn
Ocrevus	1.5 bn
Polivy	1.3 bn
Columvi	1.1 bn
Hemlibra	0.9 bn
Evrysdi	0.9 bn
Elevidys[1]	0.6 bn
Lunsumio	0.6 bn
Gazyva	0.6 bn
Tecentriq	0.5 bn
Alecensa	0.4 bn
PiaSky	0.3 bn
Susvimo	0.3 bn
Enspryng	0.3 bn
Other in-market[2]	(0.1) bn
Pipeline Ph III[3]	**3.7 bn**
thereof giredestrant	*1.0 bn*
thereof inavolisib	*0.8 bn*
thereof tiragolumab	*0.6 bn*
thereof fenebrutinib	*0.5 bn*
thereof anti-TL1A mAb	*0.3 bn*
thereof astegolimab	*0.3 bn*
thereof SPK-8011	*0.3 bn*
Total	**17.5 bn**

Potential up-side 2025+

Assets with low to no coverage in current sell side models (first assets could launch as early as 2025):

Oncology/Hematology: divarasib in NSCLC; NXT007 in HemA; P-BCMA-ALLO1 in r/r MM; P-CD19 x CD20 - ALLO1 in heme tumors; autogene cevumeran in solid tumors

Neurology: prasinezumab in PD; anti-latent myostatin mAb in SMA & FSHD; trontinemab in AD; gamma-secretase modulator in AD

Immunology: Gazyva in LN; ASO Factor B in IgAN

Ophthalmology: vamikibart in DME & UME; satralizumab in TED

Cardiovascular & Metabolism: CT-388/868/996 in diabetes & obesity; zilebesiran in hypertension

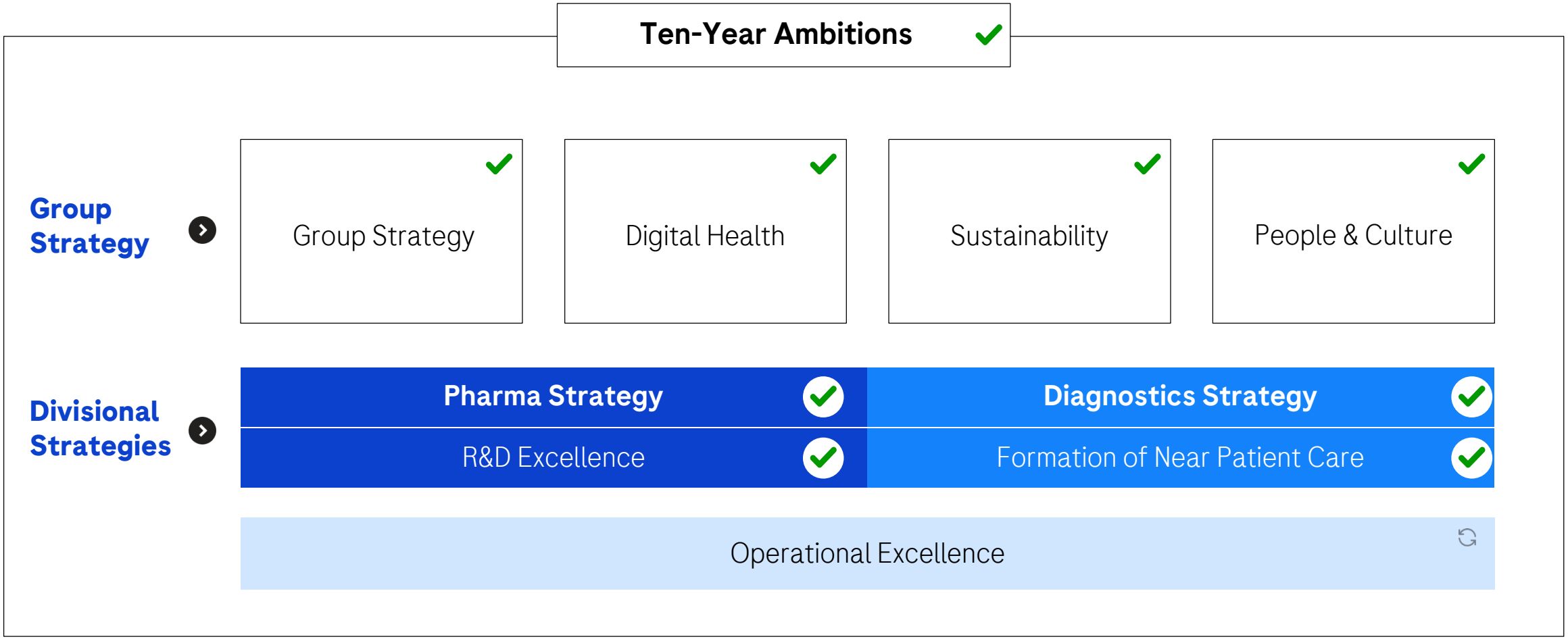
*All estimates are based on Post HY 2024 consensus collected by FTI Consulting on behalf of Roche (n=20); [1]Elevidys consensus sales growth ex-US; [2]Activase/TnKase, Pulmozyme, CellCept, Xofluza, Rozlytrek, Mircera; [3]included in >50% of sell-side models

Performance and growth outlook

Strategy update

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✓ Defined

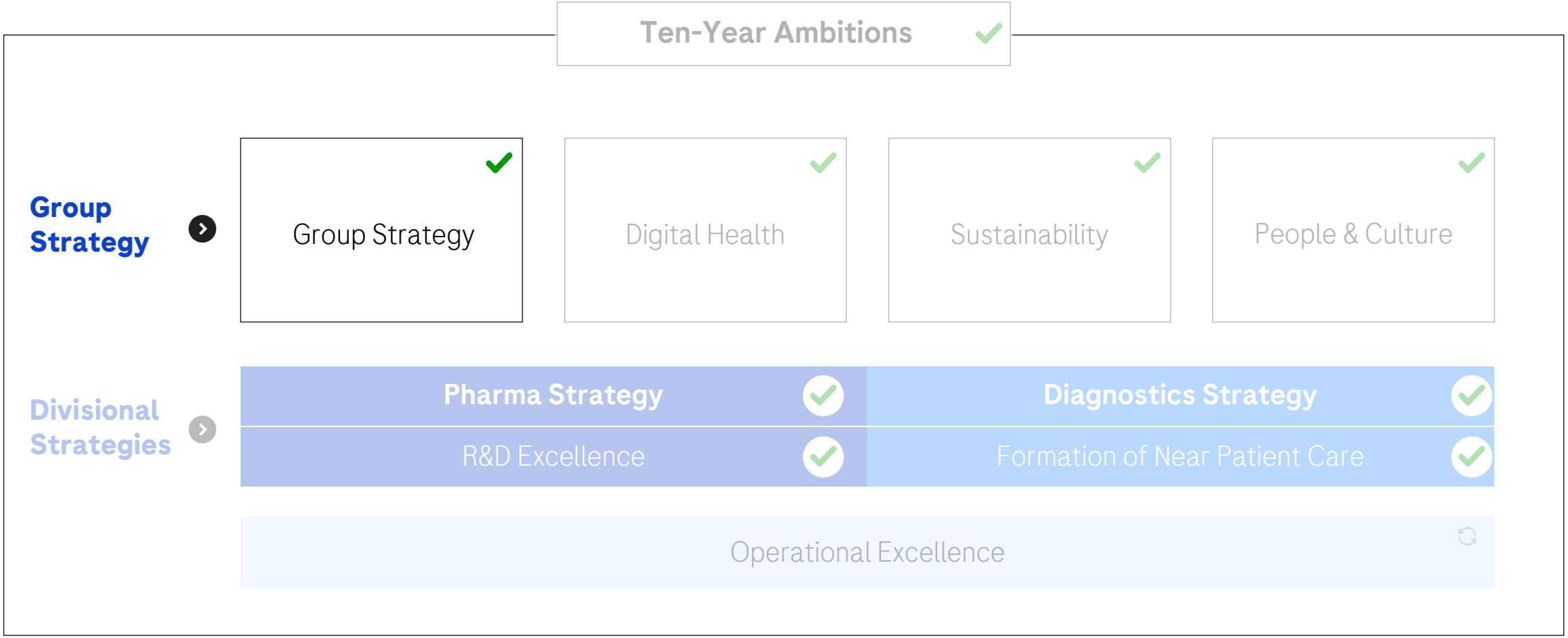
The future of healthcare: Our Ten-Year Ambitions 2020-2029

Updated ambitions outline our aspirational long-term objectives

	Ten-Year Ambitions	Long-term objectives
Group	**Innovate across the patient journey to improve outcomes** *Updated*	• Combine Diagnostics & Pharma strengths to address unmet needs along the entire patient journey • Realize synergies in every part of the value chain
Pharma	**Deliver 20 transformative medicines addressing diseases with the highest societal burden** *Updated*	• Launch 2 transformational medicines p.a. • Build industry leading R&D engine and pipeline
Diagnostics	**Double patients access to novel, high-medical-value diagnostics solutions**	• Launch 75 novel, differentiated medical value assays; 7-8 per year on average • Double the amount of patients tested
Data & Digital	**Transform our business with data and digital solutions** *Updated*	• Increase efficiency along value chain • Differentiate our Pharma and Diagnostics offering with digital products

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

The future of healthcare

Disease burden and system pressures increase, while care delivery becomes more decentralized

Increasing disease burden

50% of disease burden in cardiovascular-metabolism, oncological, and neurological diseases in ~10 years

Healthcare system pressures

Average **healthcare cost grew above GDP growth** the last 20 years

Decentralized care delivery

Care provision in outpatient settings will **grow on average 3x**[1] over next 10 years

Early detection, monitoring and intervention

Earlier detection and therefore **earlier medical interventions** result in significant outcome improvements

Access to healthcare

Half of the world's population lacks access to essential healthcare services

Transformative technologies

Transformative technologies such as **AI influence healthcare science, systems, and companies**

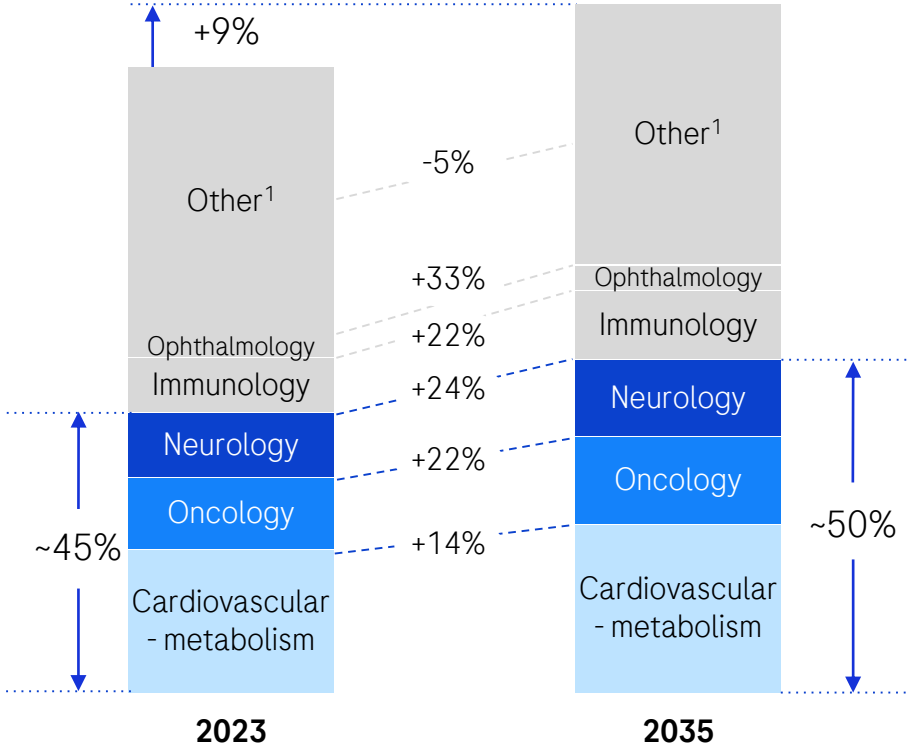
1 vs. in-patient growth | Source: OECD, Sg2 Report; ASCO "New Directions for Cancer Care: Major Trends in U.S. Health Policy"; Institute for Health Metrics and Evaluation (IHME) at the University of Washington

Disease burden increase and decentralization trend

Shared priority areas to account for ~50% of disease burden; care delivery growing faster in outpatient setting

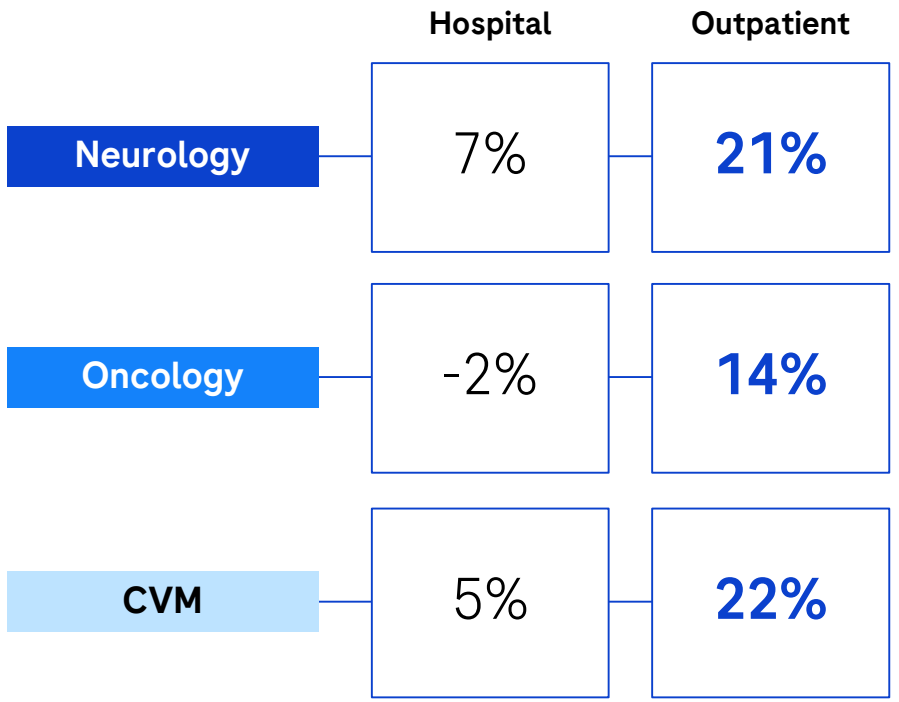
~50% of disease burden in shared priority areas by 2035

Increase of Disability-adjusted life years (DALY)[1]



Outpatient setting to grow 3x faster vs. hospital setting

Projected 10 year growth by site of care[2]



1 Other includes: all other diseases excluding transport injuries, unintentional injuries, and self-harm/ interpersonal violence, 2 Definition of DALYs by WHO: DALY represents the loss of the equivalent of one year of full health| Source: Institute for Health Metrics and Evaluation (IHME) at the University of Washington, accessed on: 08/27/2024. Used with permission.; 2 In United States | Source: Sg2 Report; ASCO "New Directions for Cancer Care: Major Trends in U.S. Health Policy"; CVM=cardiovascular-metabolism

The future of healthcare: Business implications

How we address these trends through our strategy

Increasing disease burden

Prioritize **disease areas with high societal burden**

Healthcare system pressures

Innovate and offer holistic solutions to **improve outcomes and reduce cost**

Decentralized care delivery

Develop **near patient care** diagnostics solutions and drug delivery systems for **decentralized settings**

Early detection, monitoring and intervention

Focus on **early detection and preventing & curing diseases**; enable **monitoring**

Access to healthcare

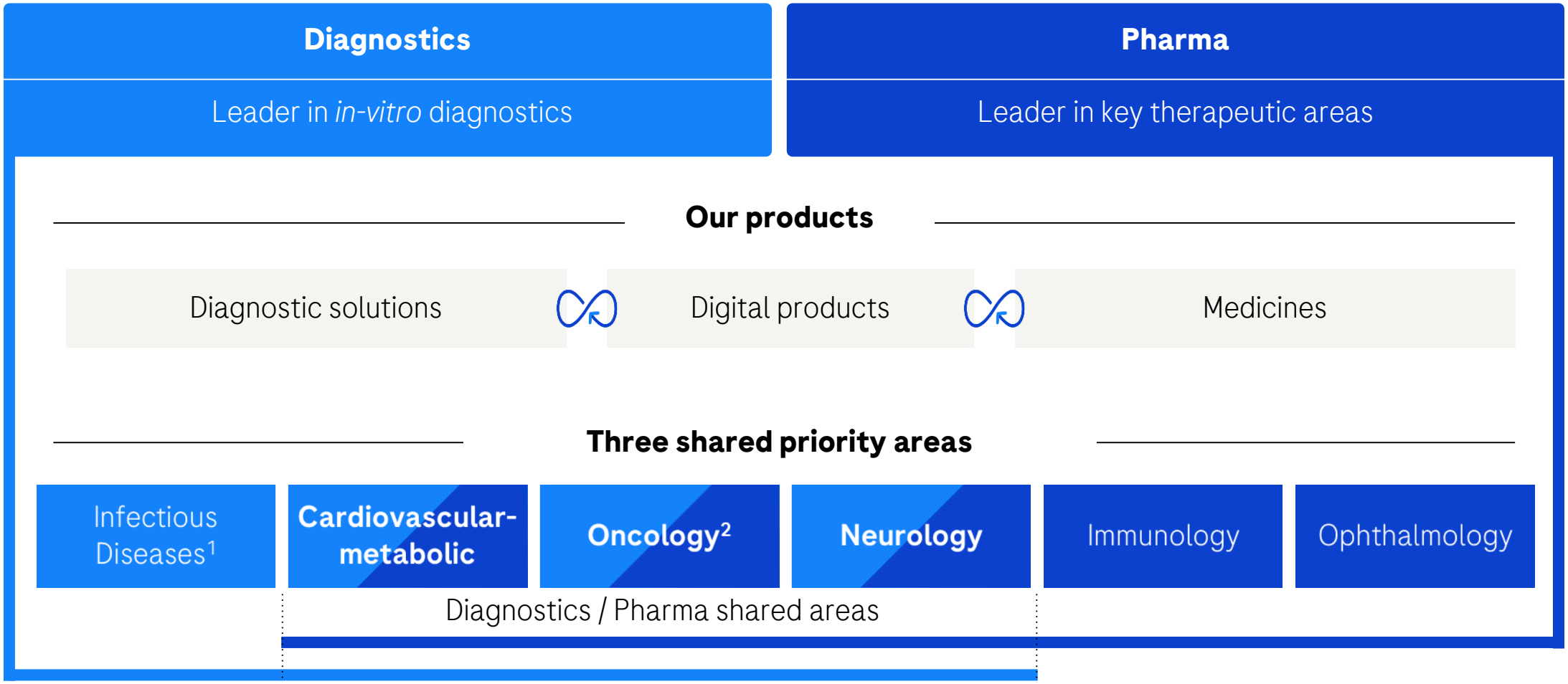
Maximize access to innovative medicines & diagnostics solutions and **advance health equity**

Transformative technologies

Invest in **breakthrough technologies**

Two divisions working together to address healthcare needs

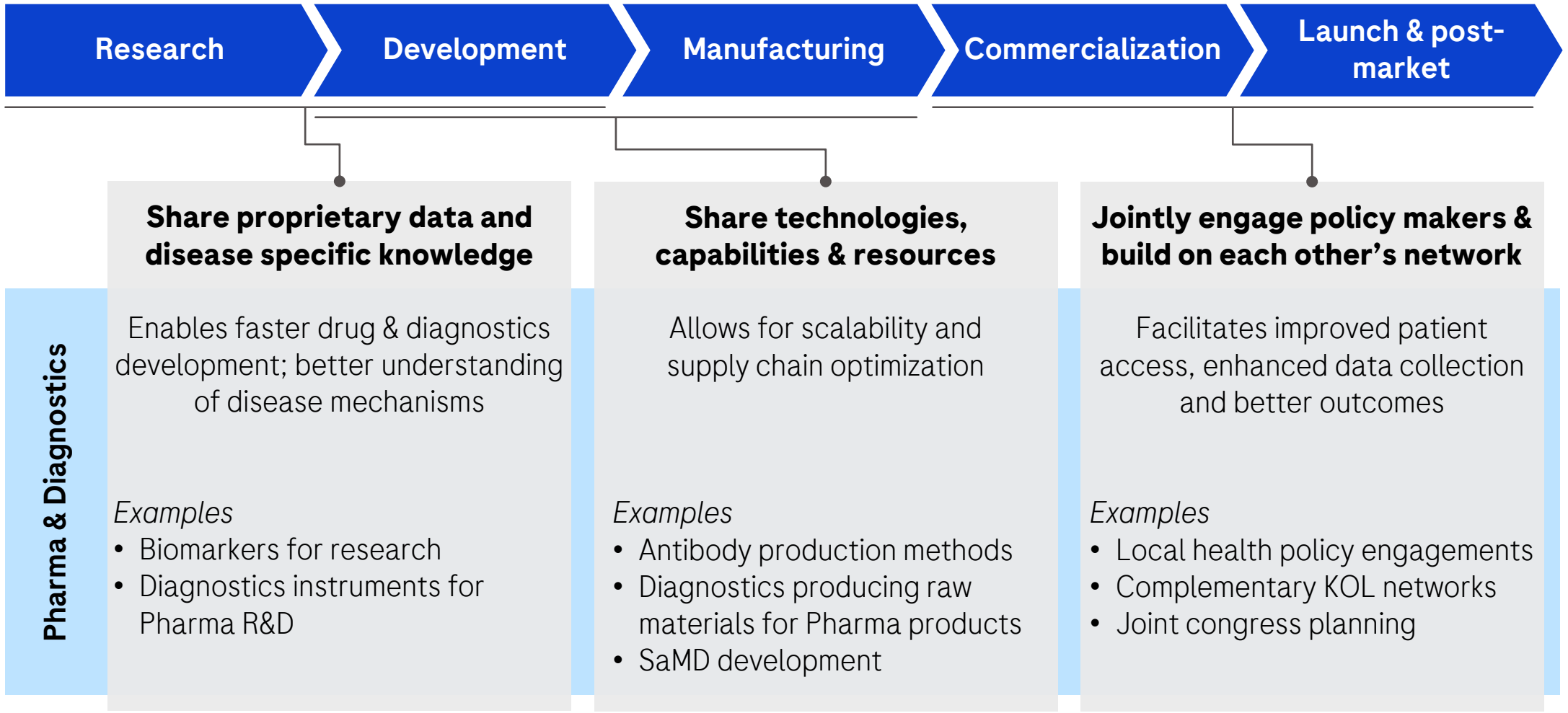
Three shared priority areas between Diagnostics and Pharma



1 Also relevant for Antimicrobial Resistance in Pharma; 2 Includes Hematology in Pharma

Two divisions with synergy potential across the value chain

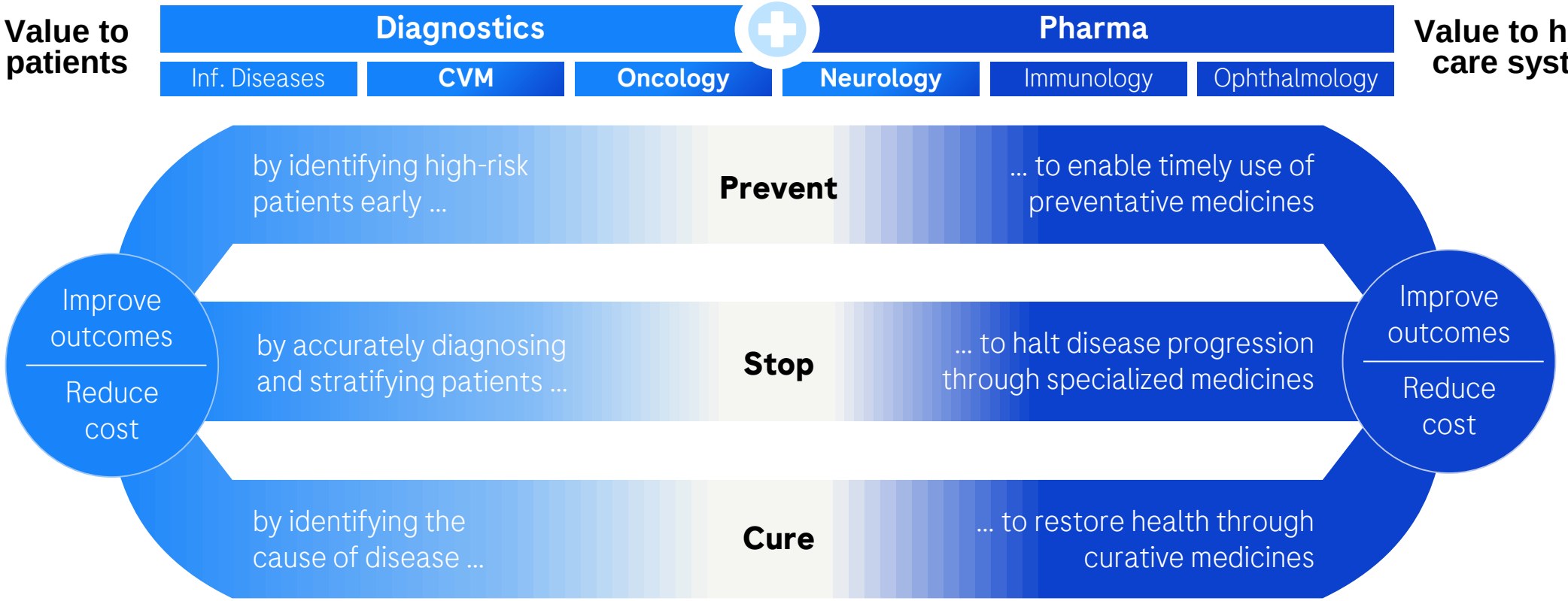
Key enabler of our strategy is the collaboration across our two divisions



SaMD=Software as a Medical Device; KOL=Key opinion leaders

Creating a healthier future, together

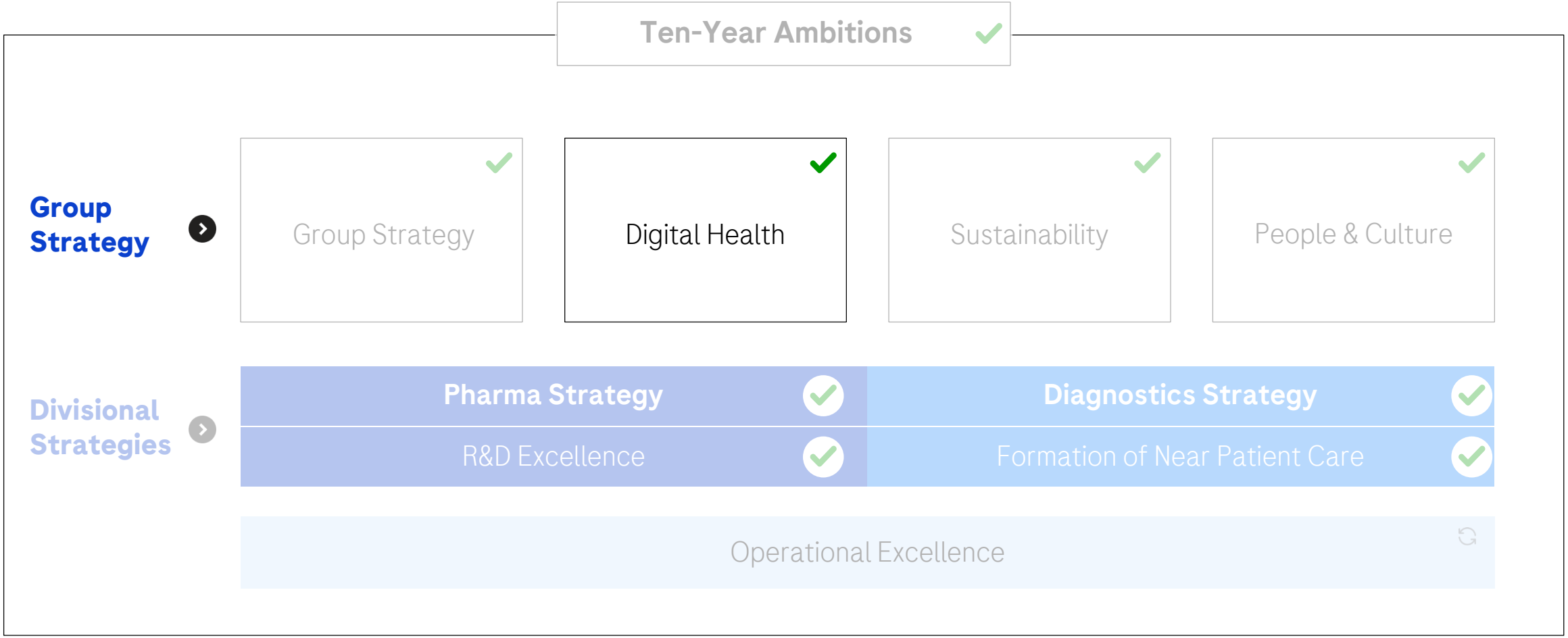
Roche is uniquely positioned to address patient and healthcare system needs across the patient journey



Innovate across the patient journey to improve outcomes
for diseases with the highest societal burden, meeting patients where they are

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

Updated Digital Health Strategy

Focus on four product segments enabled by one technology stack and one operating model

Where to play

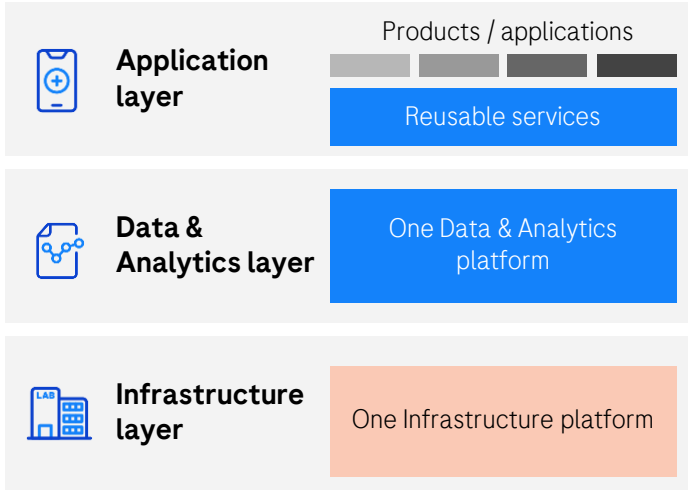
Four Product Segments

- Lab Insights
- Clinical Decision Support
- Clinical Workflow Optimisation
- Remote Patient Management

4 product segments complementing the Pharma and Diagnostics businesses

How to win

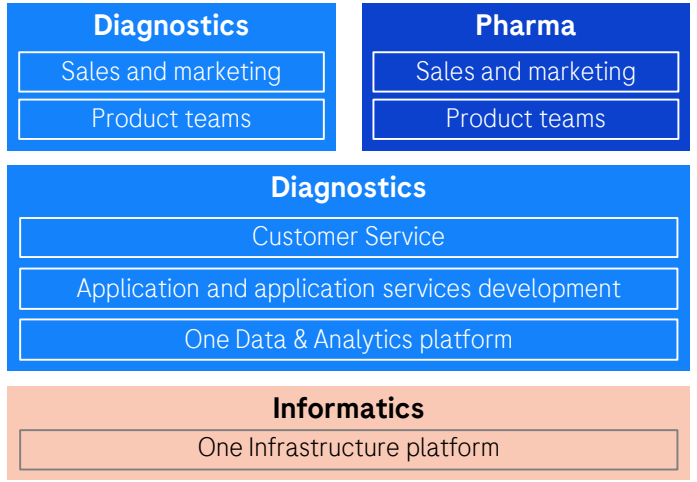
One Technology Stack



Drives data/digital asset reuse, improves customer experience and accelerates innovation

How to win

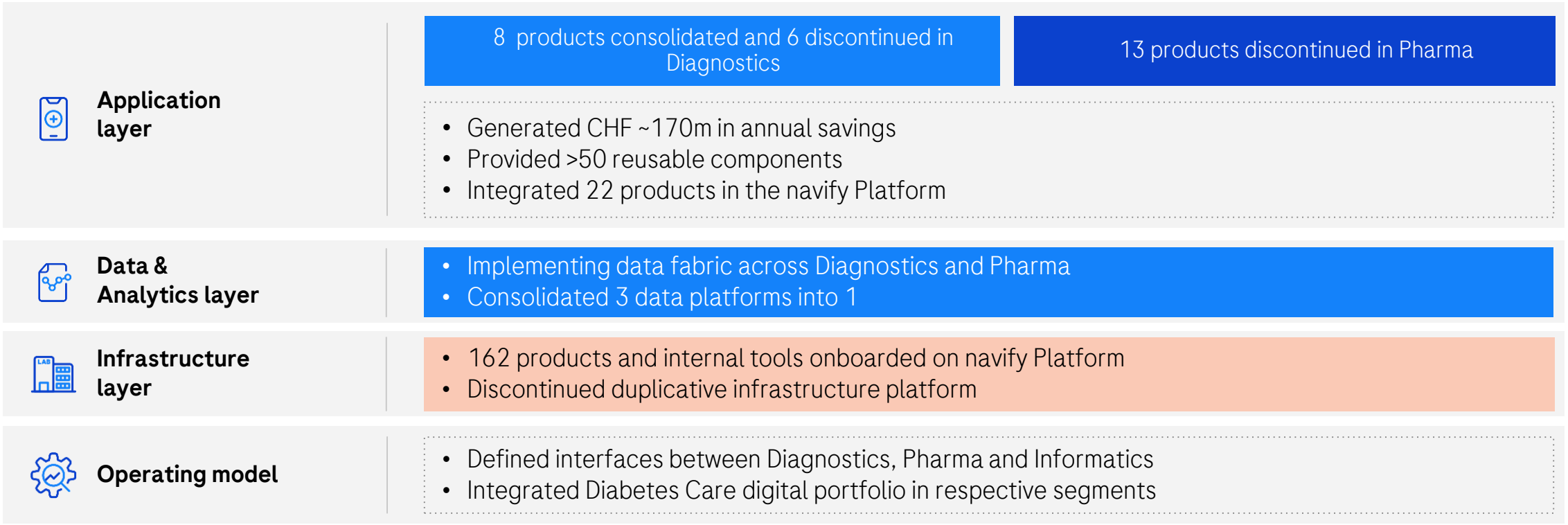
One Operating Model



Clear responsibilities across the Group to maximize synergies and build strong functional expertise

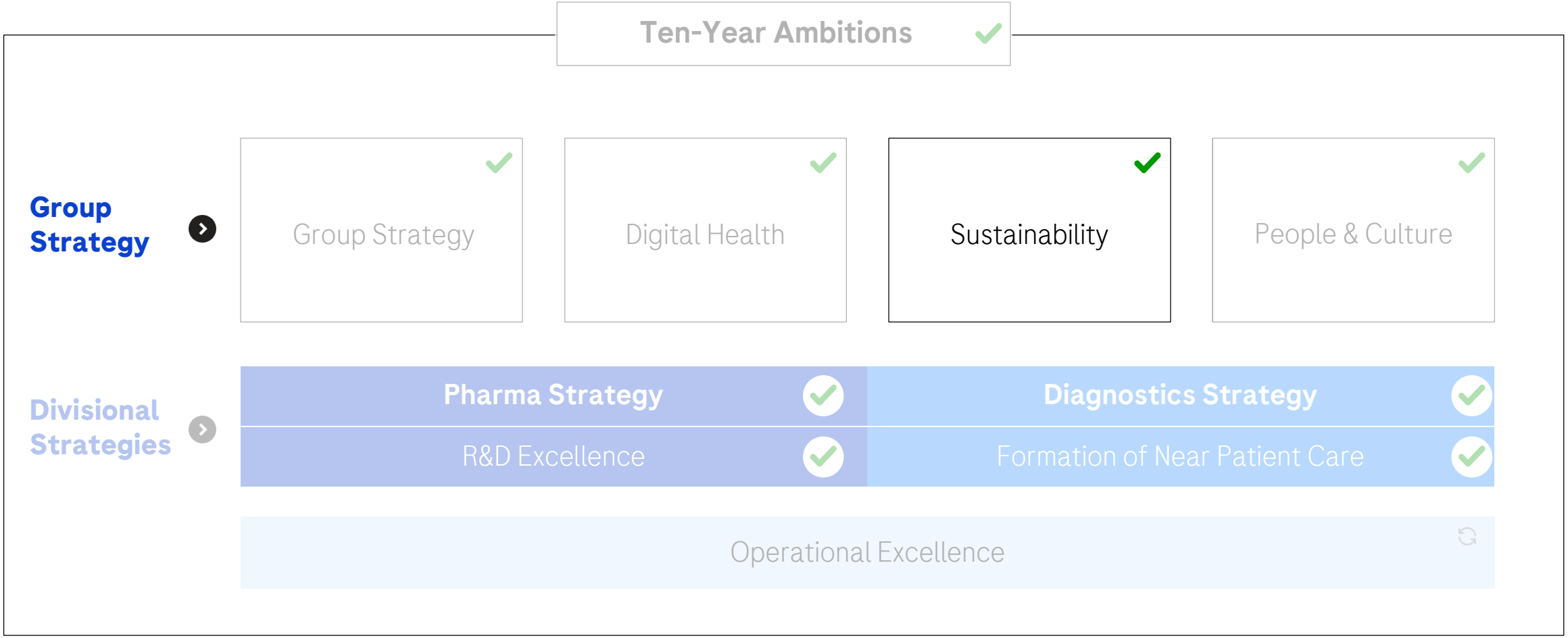
Strategy implementation: Prioritization and consolidation

Recent example of significant synergies realized



Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

Roche's strengthened sustainability commitment

Our strategy contributes to the long-term success of Roche and society, focusing on six priorities

Creating value for all stakeholders

Access to innovation

- Maximize access to our innovative medicines and diagnostics solutions
- Advance health equity for patients

People

- Foster an inclusive work environment where people can thrive

Environment

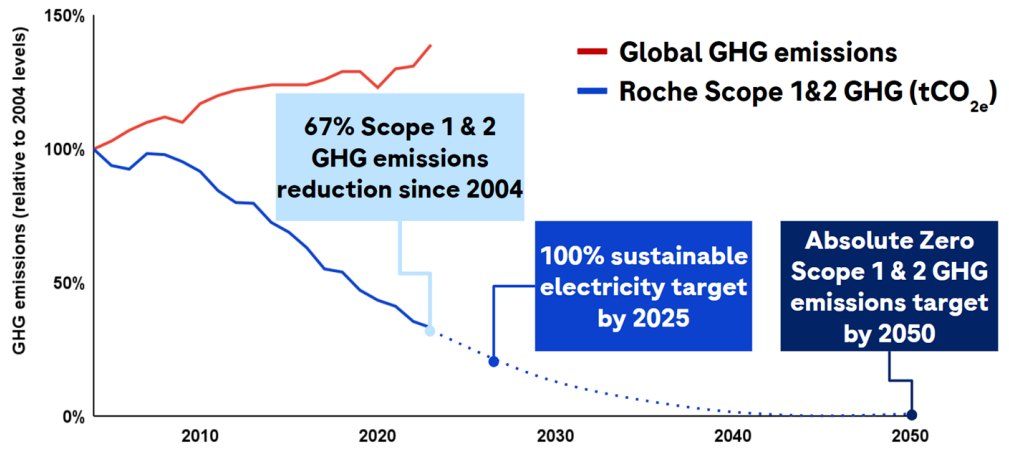
- Achieve Net Zero emissions
- Minimize the environmental footprint of our products
- Protect biodiversity and water resources

On track to meet our new Net Zero target

Submitted to SBTi in Sep

Reducing Scope 1 & 2 GHG emissions for nearly 20 years

Our commitment to absolute zero : 67% reduction since 2004



We commit to net zero for scope 1, 2 & 3 by 2045[1] and to absolute zero for scope 1 & 2 by 2050

1 Pending SBTI approval; 2022 base year; the target boundary includes land-related emissions and removals from bioenergy feedstock

Roche's exceptional commitment to Global Health Security

Diagnostics and Pharma taking a leading role to address antimicrobial resistance (AMR) crisis

Diagnostics: Rapid identification of pathogens

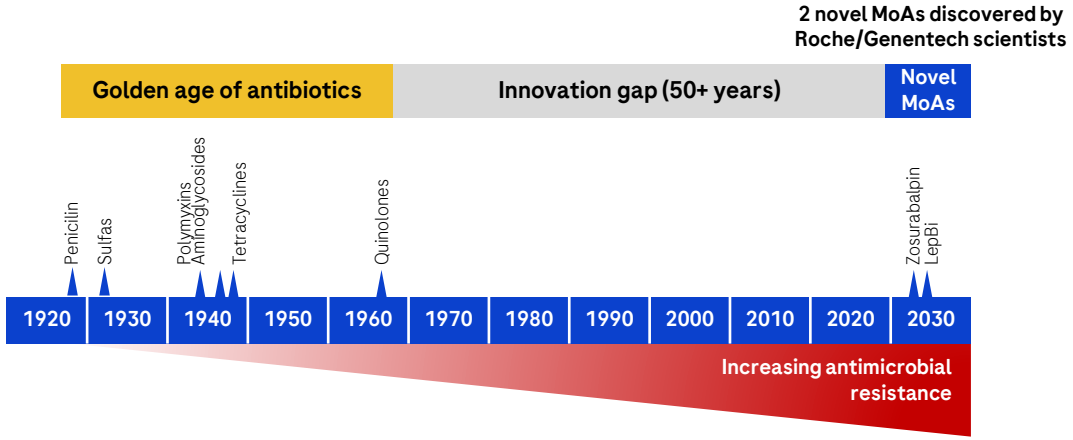
Focus indications in Infectious Diseases

not exhaustive

Hepatitis	Respiratory	Tuberculosis	Sepsis	Others		
HCV PSC	Respiratory flex MPLX	TB IGRA	Prenosis (US)	Gastro flex MPLX	STI Panel	BV/CV
HBsAg III	ePlex Respiratory Panel 3	Active TB	IL-6 (US)	ePlex Gastro Panel	Lyme Panel	Strep B
Anti-HBc qt	Liat RSV, Flu A/B & Covid			Lesion Panel	NG resistance	Malaria
Anti-HDV	Atyp Pneum.			Dengue Panel	HIV DUO II	

- Broad test portfolio and Global Surveillance Program for quick response to emerging pathogens
- Infection prevention and antimicrobial stewardship, including syndromic testing and point-of-care diagnostics

Pharma: First novel classes of antibiotics in 50 years



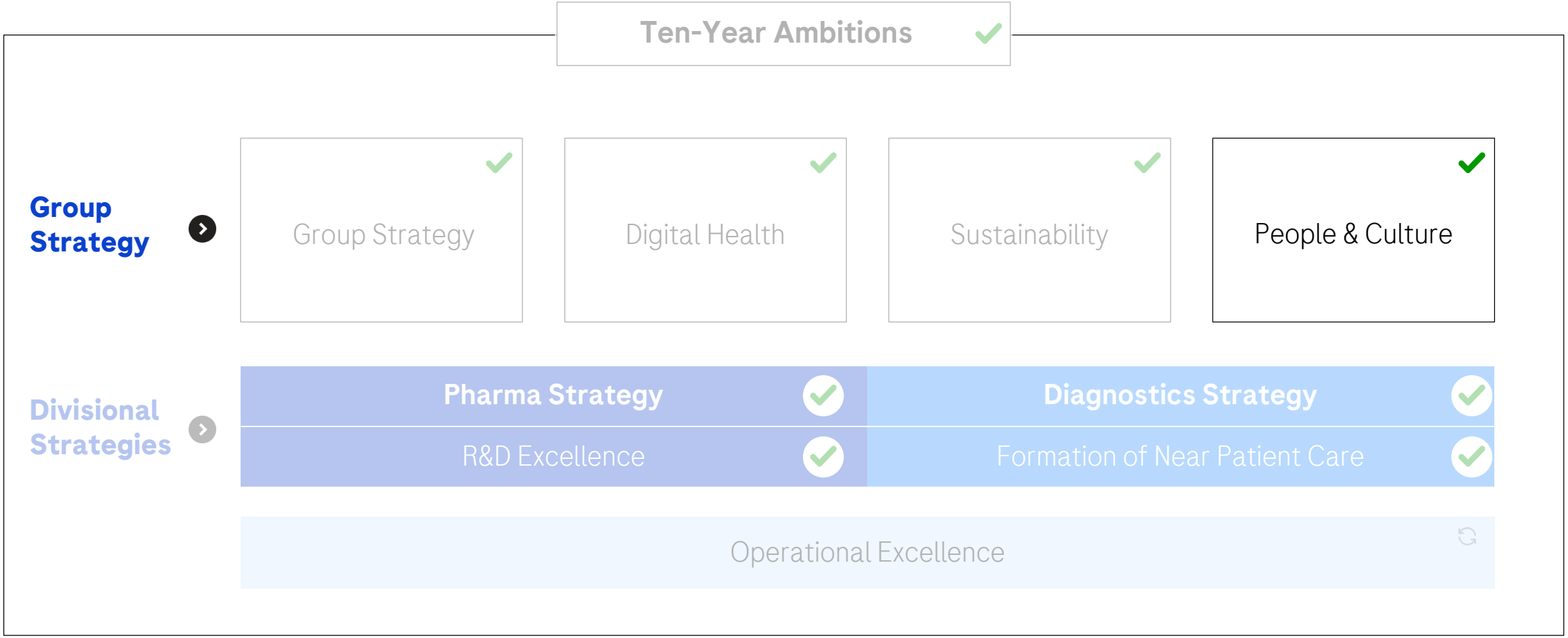
- Global Health Security program in place, aligned with WHO and CDC
- Zosurabalpin and LepBi represent the first new classes of antibiotics against gram negative bacteria

Using our scientific capabilities and unique strengths to deliver a long-standing societal impact

AMR=antimicrobial resistance; MoA=mechanism of action; WHO=World Health Organization; CDC=Centers for Disease Control and Prevention

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

Our people and culture

Fostering and rewarding high performance

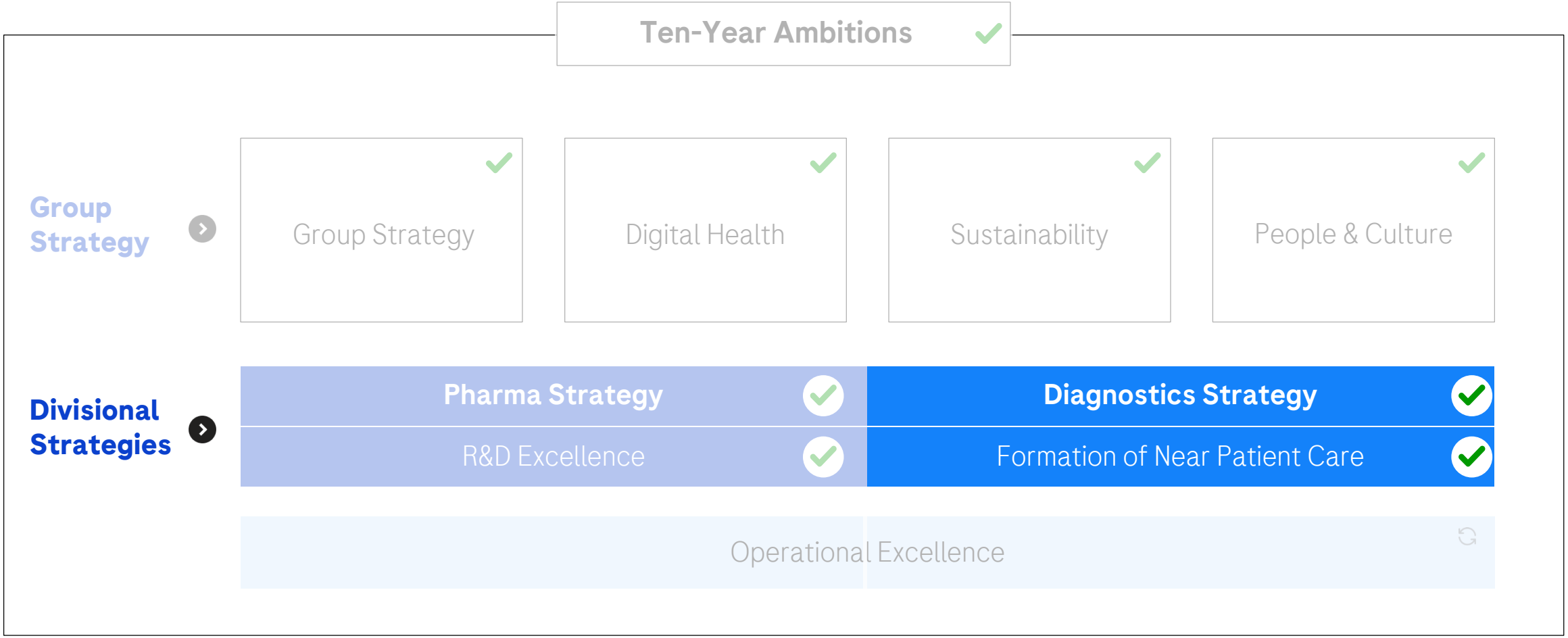
Roche Framework (selection)

Focus areas

- **Talent:** Strengthened talent management and succession planning (internal/external), building critical capabilities
- **Diversity, Equity & Inclusion:** Embedded across the organization to foster an inclusive work environment and diverse perspectives
- **Leadership:** Drive urgency, effective decision making, as well as empowerment and accountability
- **New performance & reward practices:** Strengthened feedback & debate culture, performance focus

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

Transformation of Roche Diagnostics 2020-2021

Simplified operating model and shift of investments; increased employee engagement

Innovation & financial success

- Increased R&D investments by 500m CHF
- Mid- to high-single digit sales growth
- Core OP growth ahead of sales growth

Operating model

- Simplified processes and systems
- Reduced organizational complexity

Culture

- Updated operating principles
- Created culture of empowerment and accountability

Engagement & diversity

- Increased employee engagement
- Increased diversity in senior leadership

R&D
8 units to 2

Business Areas
5 to 1

Quality Management
48 systems to 1

Hierarchy layers
9 to 5

The Diagnostics Strategy was co-created with the entire organization of 35,000 employees

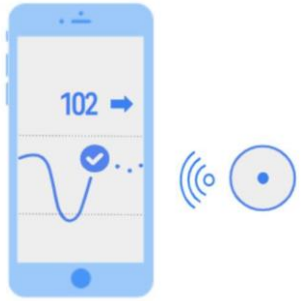
Accelerated momentum driven by key launches

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

LumiraDx

- Consolidate PoC testing on a single platform (clinical chemistry, immunoassay and potentially molecular)
- Room temperature storage of tests
- Drive access in LMIC

Continuous glucose monitoring (CGM)



- 14 day real-time glucose sensor
- One-step application with initial calibration
- Predictive algorithms for 2 hours and night-time hypo

Mass spectrometry

- First fully integrated and automated mass spectrometry
- Launch menu complimentary to immunoassay offering, >40 key biomarkers
- Approvals: CE (2024), FDA (2025)

Next generation sequencing (NGS)

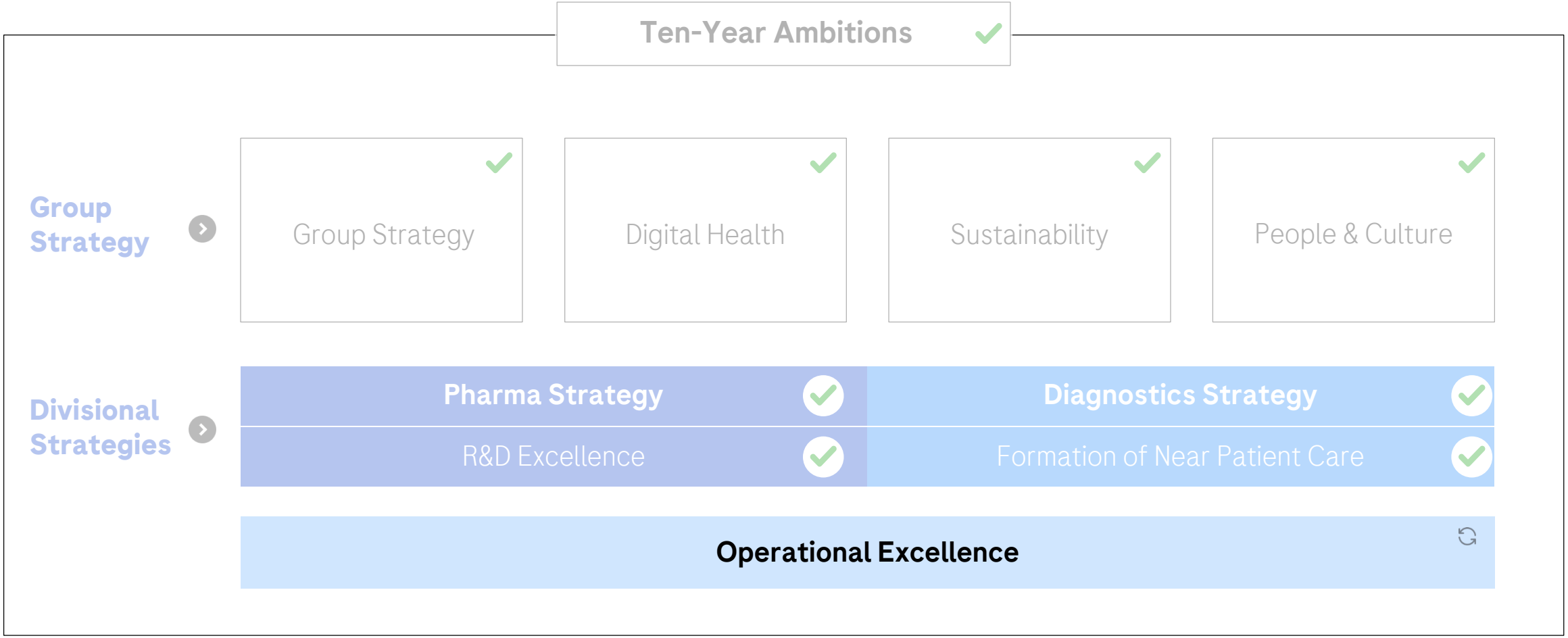
- Unique sequencing by expansion technology, significantly improving nanopore performance
- Nanopore system offers flexible run size at competitive cost

Innovative Diagnostics technologies enable joint development opportunities and synergies with Pharma

PoC=Point of Care; LMIC=Low- and middle-income countries; CVM=cardiovascular & metabolism

Overview of key strategic initiatives

Significant progress made across the entire organization

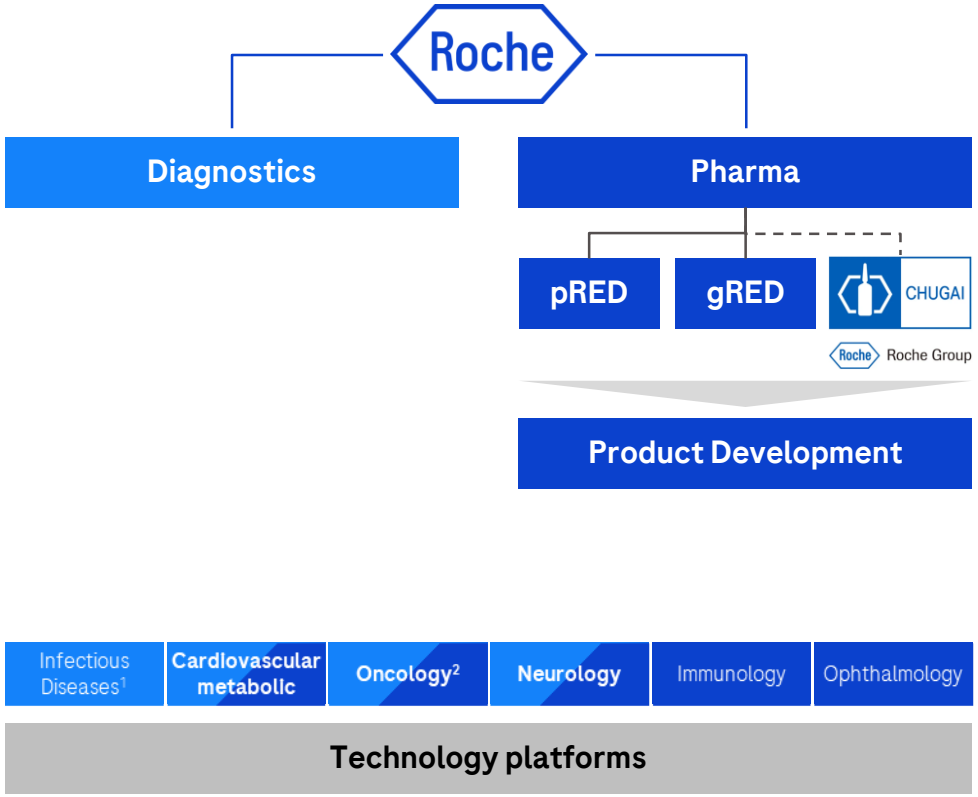


Status: Ongoing ✔ Defined

Balancing centralization and decentralization

Improving operational performance and realizing synergies across the Group

Maximize benefit of two divisions with streamlined structures



Pharma

Decentralized

- Independent early research units aligned to drive innovation with focus on unique expertise and platform technologies
- Local go to market approaches

Centralized

- Centralized late-stage development and E2E portfolio management
- Harmonized systems, processes and governance

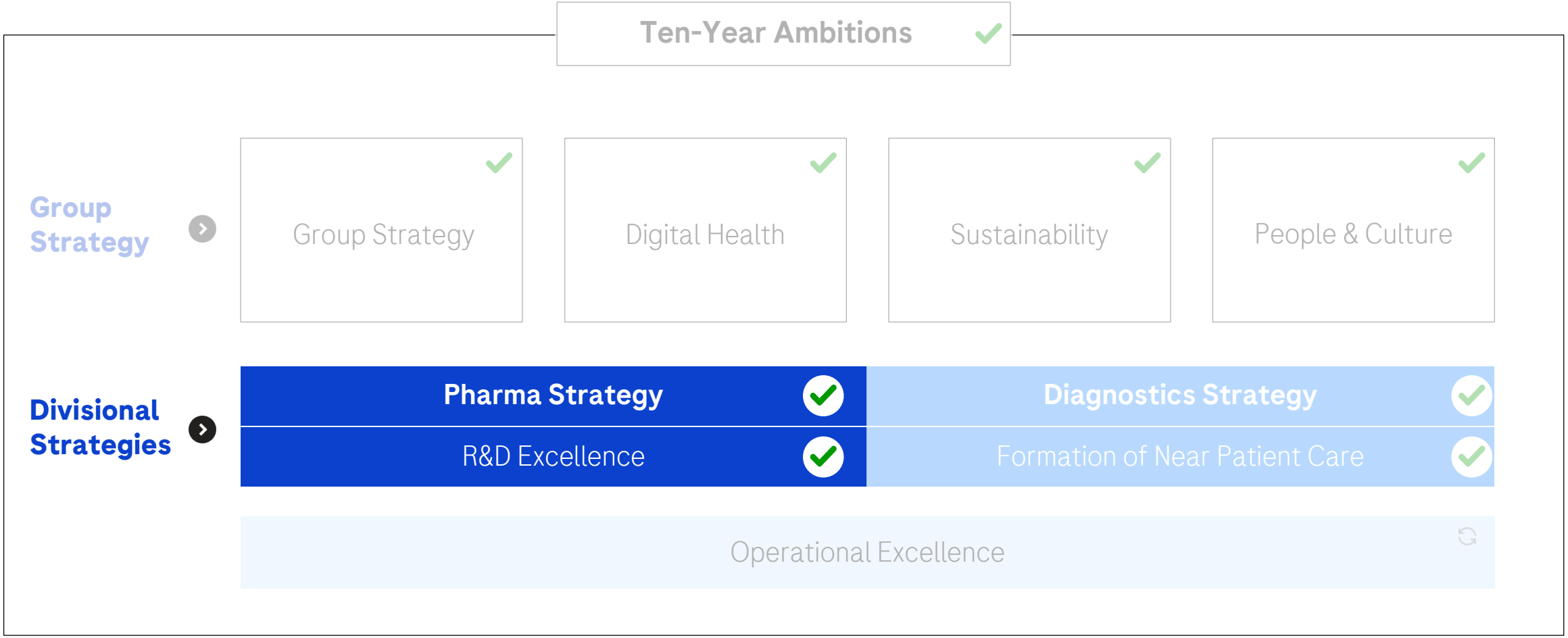
Group

- Shared proprietary data, disease knowledge and KOL networks
- Build holistic patient solutions in shared priority areas across Diagnostics/Pharma
- Leverage digital technologies, capabilities and resources

1 Also relevant for Antimicrobial Resistance in Pharma; 2 Includes Hematology in Pharma; E2E=end-to-end; KOL=key opinion leader

Overview of key strategic initiatives

Significant progress made across the entire organization



Status: Ongoing ✔ Defined

Pharma

Teresa Graham
CEO Roche Pharmaceuticals

Pharma Strategy

Therapeutic Areas & focus diseases

Our core capabilities

Significant future growth opportunities

Today, Roche Pharma leads in multiple Therapeutic Areas

Diversified portfolio of innovative medicines

Number 1 in key Therapeutic Areas

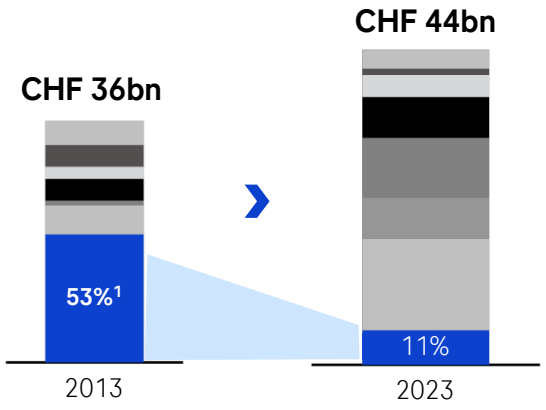
#1 in Neurology, a leader in Ophthalmology and Oncology/Hematology

Pipeline

72 NMEs in clinical development

Portfolio

Roche Sales per therapeutic area



Young portfolio driving growth, incl.16 blockbusters vs. 8 in 2013

Innovation

26 NMEs launched since 2013

43 FDA Breakthrough Therapy Designations since 2013[2]

#1 Pharma in AI readiness[3]

1 Includes Avastin, Herceptin and MabThera/Rituxan (AHR); 2 Includes molecules coming from acquisitions and partnerships; 3 CBInsight, 2023

Our updated Ten-Year Pharma Ambition

Focus on delivering transformative medicines, enabled by R&D and business objectives

Pharma Ambition 2020-2029

Deliver 20 transformative medicines[1] addressing diseases with the highest societal burden[2]

Value

+40%

in avg. pipeline peak sales

Innovation

80%

of pipeline has best-in-disease potential

Access

3x

more patients treated[3]

1 Transformative medicines: Medicines that deliver significant or transformative clinical benefit in at least one indication or bring a significant benefit to the healthcare system; 2 Addressing the highest societal burden: high burden in terms of patient unmet need and the population affected; 3 Excludes LOE products and pandemic stockpiling

Defining our portfolio focus

Purposeful balance between exploration and focus

Follow the science

with emphasis on breakthrough innovation and patient value

Intentional focus

in end-to-end disease areas where we develop depth of experience and operational scale to deliver transformative medicines

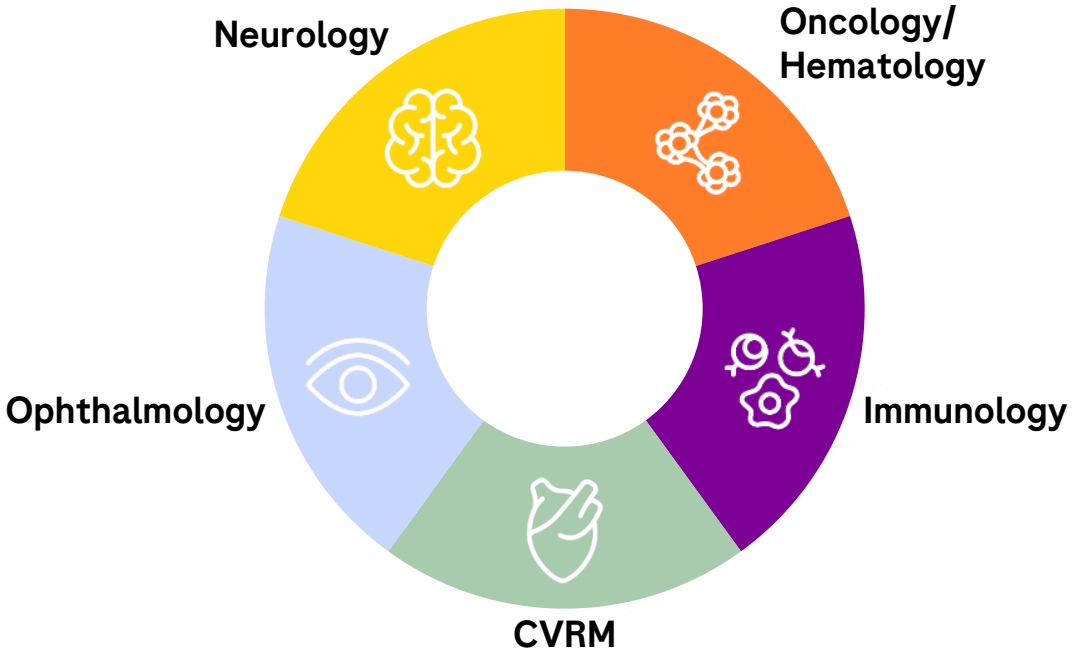
The Bar

defines transformative medicines and is applied rigorously to each asset entering and progressing in the portfolio, across all stages of R&D (including Partnering and M&A)

Our new Pharma Strategy

Providing clarity and intentional focus to leverage our scientific strengths and impact patients globally

Where we play: Priority Therapeutic Areas



How we succeed: Core capabilities

- Modalities & Technologies
- Devices
- Manufacturing
- Customer Experience & Access
- Data & AI
- Our People

Pharma Ambition: Deliver 20 transformative medicines addressing diseases with the highest societal burden

CVRM=cardiovascular, renal and metabolism; AI=artificial intelligence

Pharma Strategy

Therapeutic Areas & focus diseases

Our core capabilities

Significant future growth opportunities

Selecting our therapeutic areas and focus disease areas

Our focus considers societal burden and transformational potential, as well as Roche's current capabilities

External drivers ⟷ **Internal drivers**

Burden of disease and societal costs

- Disease prevalence, incidence, mortality and morbidity
- Unmet need (SoC and gaps in treatment)

Potential to yield transformative medicines

- Scientific maturity
- Biological understanding
- Innovation potential

Roche's strengths

- Pipeline with best-in-disease potential
- Leadership and existing capabilities in Neurology, Ophthalmology and Oncology/Hematology

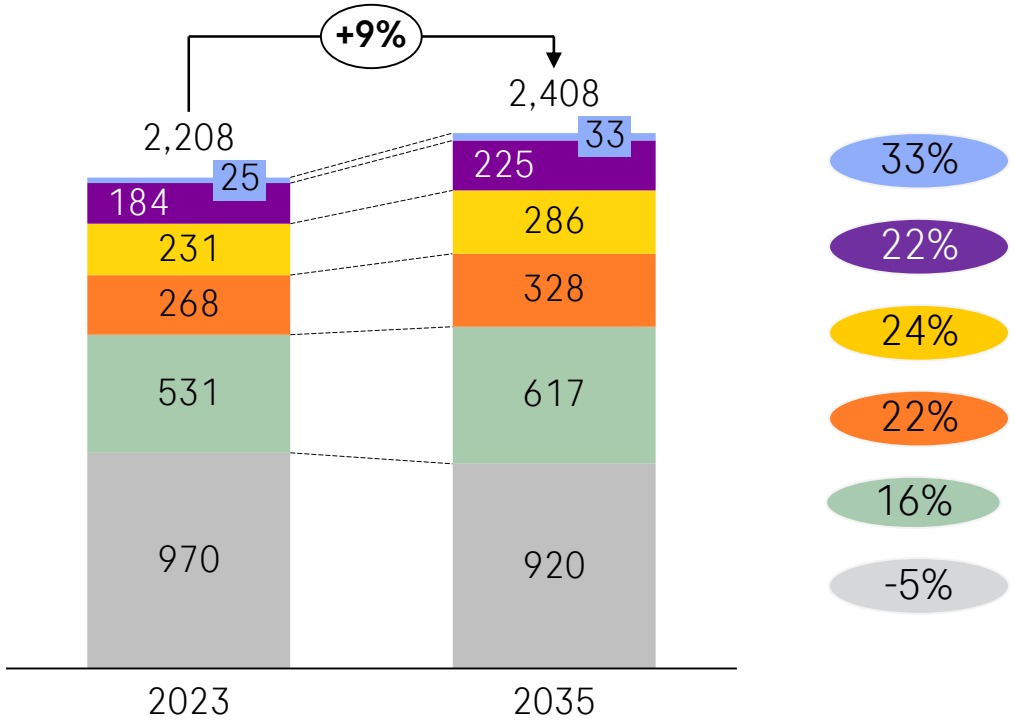
Our Therapeutic Areas: ~60% of total Global Burden of Disease and ~80% of potential growth

SoC=Standard of care

Global burden of disease by Therapeutic Area

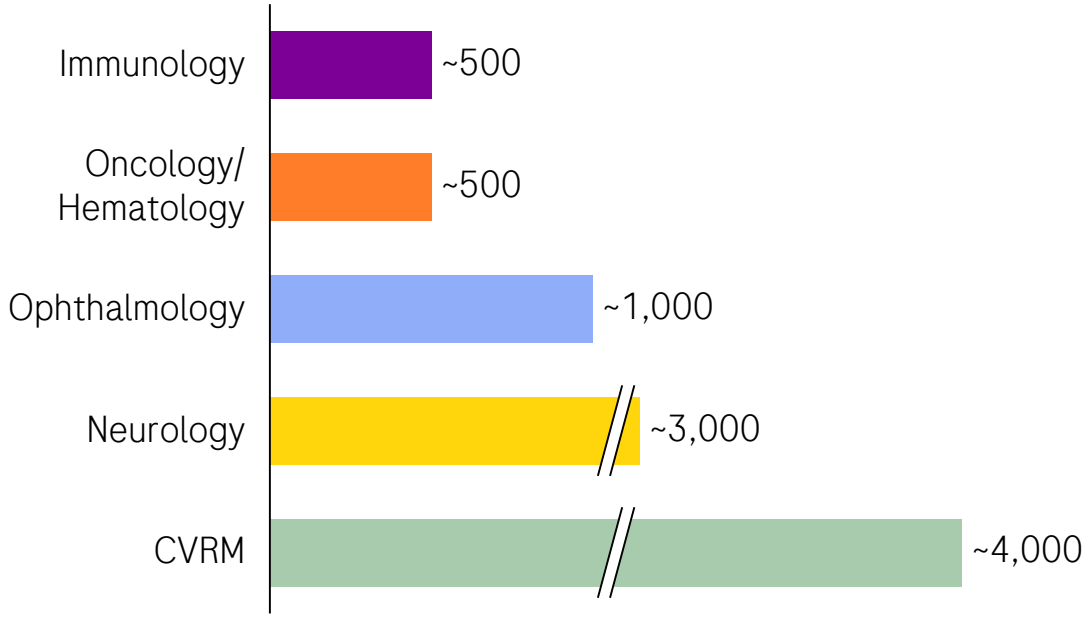
Our focus therapeutic areas address ~60% of the global burden of disease and millions of patients worldwide

Global Burden of Disease in 2023 and 2035 (million DALYs)



Growth, p.p %

Number of people living with diseases in our committed therapeutic areas globally [3] (million)



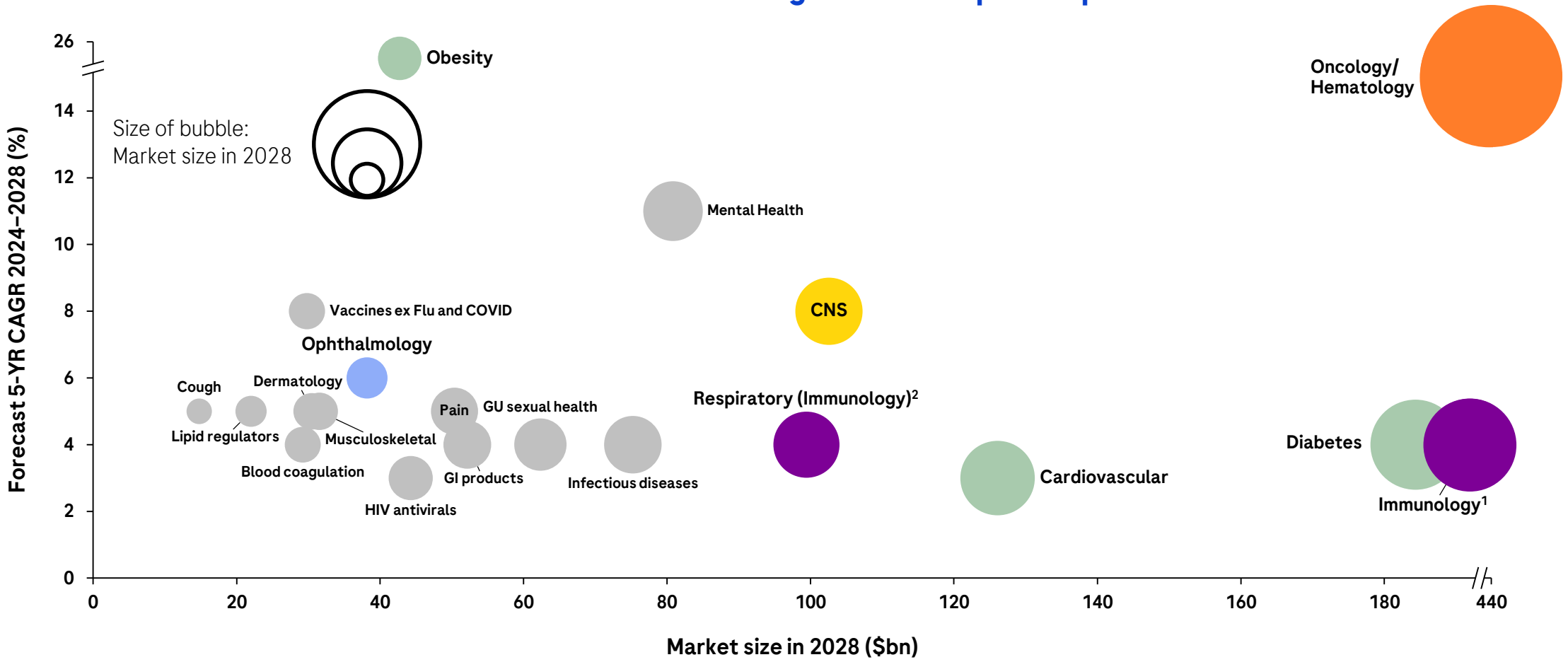
Ophthalmology | Immunology[1] | Neurology | Oncology/ Hematology | CVRM | Others[2]

Source: IHME, Clarivate (DRG); 1 Immune-mediated diseases includes selection of diseases across TAs, i.e., COPD, IBD, CSU, CF, RA, urticaria, idiopathic interstitial pneumonia (incl. ILD), chronic cough, glomerulonephritis, LN/SLE, asthma, IgAN; 2 Others include Infectious Diseases, Reproductive Health including neonatal and maternal health, non-immunological gastrointestinal diseases, vitamin deficiencies, among others; 3 Estimated from sum of prevalence of different diseases - could include double counting; TA=Therapeutic area; DALYs= disability adjusted life years; CVRM=Cardiovascular, renal and metabolism; CAGR=Compound annual growth rate

Significant future growth potential in focus Therapeutic Areas

Our focus TAs account for ~80% of future growth

Global market size and forecast growth for top Therapeutic Areas



All Roche NMEs from Ph I to Registration included; Note: Immunology includes auto-immune and allergic inflammation. Grouping of diseases are specific to Analytics Link classifications; 1 Psoriasis, psoriatic arthritis, atopic dermatitis, rheumatoid arthritis, ankylosing spondylitis, systemic lupus, Chron's disease, ulcerative colitis, erythematosus 2 COPD, cystic fibrosis, allergic rhinitis, acute pharyngitis, idiopathic pulmonary fibrosis, other diseases of the respiratory system; Source: IQVIA Forecast Link, Dec 2023 Global Use of Medicines 2024: Outlook to 2028. Report by the IQVIA Institute for Human Data Science.

E2E disease areas: Focus on delivering transformative medicines

Discovery, R&D and commercialization resources concentrated on our end-to-end disease areas

Selection

Burden of disease/societal cost

Potential to yield transformative medicines

Roche's capabilities

End-to-end disease areas

Implications

Discovery	Dedicated research teams to drive novel scientific innovation
R&D	Significant early and late stage development investments
Commercial	Full-scale commercial investment to realize meaningful market value

Continued investment in emerging areas with breakthrough potential, regardless of disease areas

E2E=End-to-end

Currently, 11 disease areas where we ‘invest end-to-end’

We focus at scale, end-to-end, in these disease areas to bring transformative medicines to patients

Oncology/ Hematology	Neurology	Immunology	Ophthalmology	CVRM
Breast cancer	**Multiple sclerosis**	**IBD**	**Retinal vascular disorders[1]**	**Obesity**
Lung cancer	**Alzheimer’s disease**	**COPD**	**GA / intermediate AMD**	
Malignant heme				
Hemophilia				
Broad portfolio and pipeline in Breast cancer, with potential to develop unique combinations	*Ocrevus a leading asset in MS market, with SC launch ongoing & fenebrutinib in Ph III*	*Ph III anti-TL 1A and Ph II vixarelimab development in IBD*	*Establishing Vabysmo as new SoC in nAMD and DME, Susvimo as low dosing frequency option, and broad NME pipeline*	*CT-388/-868/-996 development in Obesity and exploring combinations*

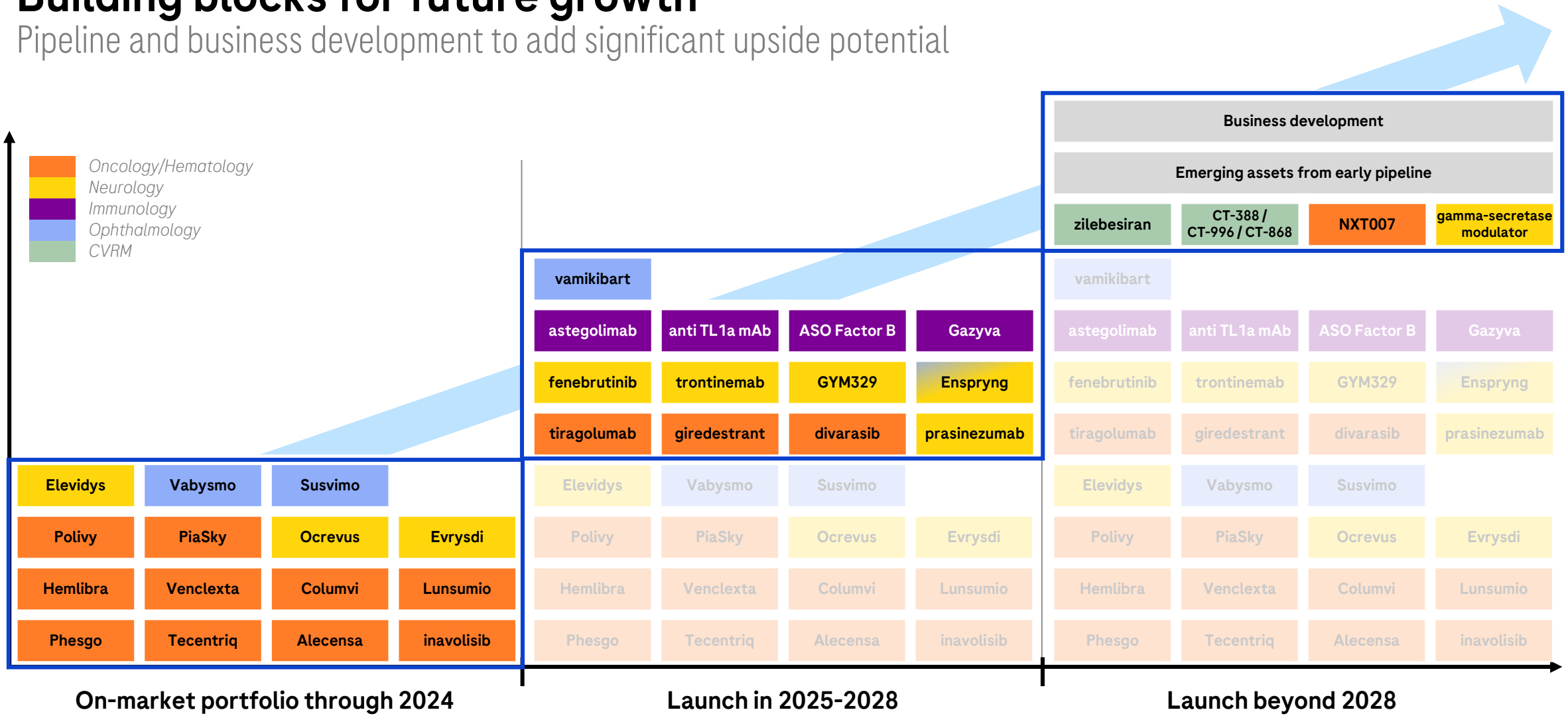
End-to-End examples

Categorization is dynamic and disease areas will be reprioritized, using consistent and objective criteria, when scientific and/or commercial inflection points are reached

1 Includes Diabetic Macular Edema, Age-related Macular Degeneration, Retinal Vein Occlusion, Diabetic Retinopathy; GA = geographic atrophy; (n)AMD = neovascular age-related macular degeneration; IBD=inflammatory bowel disease; COPD=chronic obstructive pulmonary disease; MS=multiple sclerosis; SC=subcutaenoues; SoC=standard of care; DME=diabetic macular edema; TL1A=TNF-like protein 1A

Building blocks for future growth

Pipeline and business development to add significant upside potential



Note: Outcome studies are event-driven, timelines may change; inavolisib pending US PDUFA 27th November 2024; CVRM=cardiovascular, renal and metabolism

Pipeline acceleration through partnering and acquisitions

Key deals completed to complement our pipeline across the Pharma focus therapeutic areas

ANTLERA	Sangamo THERAPEUTICS	Monte Rosa THERAPEUTICS / ORIONIS™ BIOSCIENCES	MediLink Therapeutics	Regor Therapeutics Group *	CARMOT THERAPEUTICS	Alnylam PHARMACEUTICALS	Telavant
Wnt agonist in retinopathies	**Zinc finger molecules** in Alzheimer's	**Molecular glue degraders** in oncology and neurology	**ADCs** in solid tumors	**CDKi portfolio** in breast cancer	**Dual GLP-1/GIP RA & PYY analogue** in obesity ±diabetes	**siRNA targeting AGT** in hypertension	**Anti-TL1A** in inflammatory bowel disease
Ophthalmology	**Neurology**	**Onco & Neuro**	**Oncology**	**Oncology**	**CVRM**	**CVRM**	**Immunology**
Pre-clinical	**Pre-clinical**	**Pre-clinical**	**Ph I ready**	**Ph I**	**Ph II**	**Ph II**	**Ph III ready**

*pending deal closure; CVRM=cardiovascular, renal & metabolism; siRNA=small interfering RNA; AGT=angiotensinogen; TL1A=Tumor necrosis factor-like cytokine 1A; GLP-1=glucagon-like peptide-1; GIP=glucose-dependent insulinotropic polypeptide; RA=receptor agonist; CDKi=cyclin dependent kinase inhibitor; ADC=antibody-drug conjugate; WNT=wingless-related integration site

Breast Cancer: Sustained growth in HER2+ and expanding into HR+

Inavolisib in 1L *PIK3CA*-mut HR+ HER2- mBC (Nov 27th PDUFA); additional indications in development

Breast cancer portfolio

PHESGO™ Kadcyla®

	Ph I	Ph II	Ph III	
inavolisib	**INAVO120** (1L *PIK3CA*-mut HR+HER2- mBC (AI resistant))			✓
inavolisib	**INAVO121** (post-CDK4/6 *PIK3CA*-mut HR+/HER2- BC)			
inavolisib + Phesgo	**INAVO122** (1L *PIK3CA*-mut HER2+ BC)			
inavolisib	**INAVO123** (1L *PIK3CA*-mut HR+/HER2- mBC (AI sensitive))			
giredestrant + palbociclib	**persevERA** (1L ER+/HER2- mBC (endocrine sensitive))			2025
giredestrant + everolimus	**evERA** (post CDKi ER+/HER2- mBC)			2025
giredestrant + any CDK4/6i	**pionERA** (1L ER+/HER2- mBC (endocrine resistant))			
giredestrant	**lidERA** (adjuvant ER+/HER2- mBC)			
giredestrant + Phesgo	**heredERA** (1L maintenance ER+/HER2+ mBC)			
HER2 TKI	HER2+ BC			
RGT-419B* (CDK4/2i)	HR+ BC			
runimotamab (HER2xCD3)	HER2+ BC			✓ Filed

Expanding beyond HER2+ breast cancer (new cases by subtype[1])

On market

PHESGO™
Kadcyla®
PERJETA®
Herceptin® trastuzumab
TECENTRIQ™ atezolizumab

Pipeline

- **giredestrant** (SERD)
- **inavolisib** (PIK3CAi)
- **RGT-419B** (CDK4/2i)
- **runimotamab** (HER2xCD3)
- **ZN-1041** (HER2 TKI)

HR+/HER2- | TNBC | HR+/HER2+ | HR-/HER2+ | Unknown

- HER2 franchise expected to grow through 2026; Mid-term tail of ~40% of peak sales expected
- Moving into HR+ BC, with key giredestrant Ph III (persevERA/evERA) readouts expected in 2025
- Positive and transformative results for inavolisib in 1L PIK3CAm HR+ mBC - filed in US and EU; FDA BTD granted and PDUFA set for Nov 27th
- Complementing pipeline via Regor deal, adding CDK4/2 (Ph I) and CDK4 (Ph I-ready)

*Pending deal closure; 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); PIK3CA-mut=phosphatidylinositol 3-kinase, catalytic, alpha polypeptide mutated; HR+=hormone-receptor positive; ER+=estrogen receptor positive; HER2=human epidermal growth factor receptor 2; e/mBC = early/metastatic breast cancer; AI=aromatase inhibitor; CDKi=cyclin dependent kinase inhibitor; PDUFA = prescription drug user fee act; TKI=tyrosine kinase inhibitor

Breast Cancer: Inavolisib filed in 1L *PIK3CA*-mut HR+ BC

Inavolisib with BIC potential in breast cancer and beyond

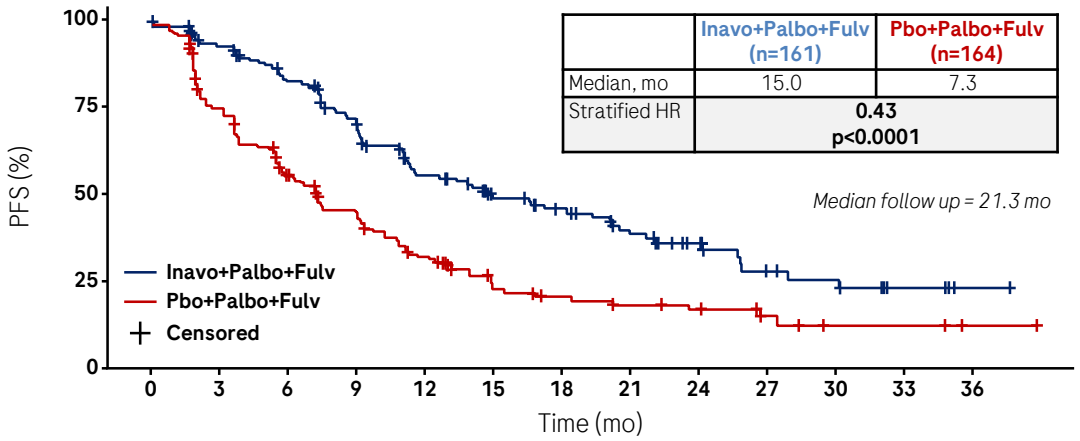
Breast cancer portfolio

PHESGO™ Kadcyla®

		Ph I	Ph II	Ph III	
inavolisib	**INAVO120** (1L *PIK3CA*-mut HR+HER2- mBC (AI resistant))				✓
inavolisib	**INAVO121** (post-CDK4/6 *PIK3CA*-mut HR+/HER2- BC)				
inavolisib + Phesgo	**INAVO122** (1L *PIK3CA*-mut HER2+ BC)				
inavolisib	**INAVO123** (1L *PIK3CA*-mut HR+/HER2- mBC (AI sensitive))				
giredestrant + palbociclib	**persevERA** (1L ER+/HER2- mBC (endocrine sensitive))				2025
giredestrant + everolimus	**evERA** (post CDKi ER+/HER2- mBC)				2025
giredestrant + any CDK4/6i	**pionERA** (1L ER+/HER2- mBC (endocrine resistant))				
giredestrant	**lidERA** (adjuvant ER+/HER2- mBC)				
giredestrant + Phesgo	**heredERA** (1L maintenance ER+/HER2+ mBC)				
HER2 TKI	HER2+ BC				
RGT-419B (CDK4/2i)	HR+ BC				
runimotamab (HER2xCD3)	HER2+ BC				✓ Filed

Inavolisib

Ph III (INAVO120) in 1L *PIK3CA*-mut HR+ BC - PFS results[1]



	Inavo+Palbo+Fulv (n=161)	Pbo+Palbo+Fulv (n=164)
Median, mo	15.0	7.3
Stratified HR	0.43 p<0.0001	

***PIK3CA* mutation frequency**

Tumor type	*PIK3CA*mut prevalence
HR+ BC	40%
HER2+ BC	30%
Ovarian Clear Cell	~33%
Endometrial	22-31%
Colorectal	13-20%
Bladder	14-20%
Cervical	11-24%
HNSCC	11-16%
Gastric	5-9%

- PFS primary endpoint met with OS immature but clear positive trend
- Manageable safety and tolerability profile for inavolisib + palbo + fulvestrant with very low discontinuation rates due to hyperglycemia AEs (~1%)
- *PIK3CA* testing well-established; INAVO120 targeting AI-resistant patients, with INAVO123 designed to expand addressable patient pool to AI-sensitive
- Potential to initiate eBC trials; 12 signal-seeking Ph Ib/II trials ongoing in various tumour types

1 Jhaveri KL et al., SABCS 2023; PIK3CA-mut=phosphatidylinositol 3-kinase, catalytic, alpha polypeptide mutated; HR+=hormone-receptor positive; ER+=estrogen receptor positive; HER2=human epidermal growth factor receptor 2; e/mBC = early/metastatic breast cancer; AI=aromatase inhibitor; CDKi=cyclin dependent kinase inhibitor; PDUFA = prescription drug user fee act; TKI=tyrosine kinase inhibitor; PFS=progression-free survival; OS=overall survival; HNSCC=head and neck squamous cell carcinoma

Malignant hematology: Diverse portfolio and a broad pipeline

Columvi Ph III (STARGLO) in 2L+ DLBCL: positive results have been filed with global health authorities

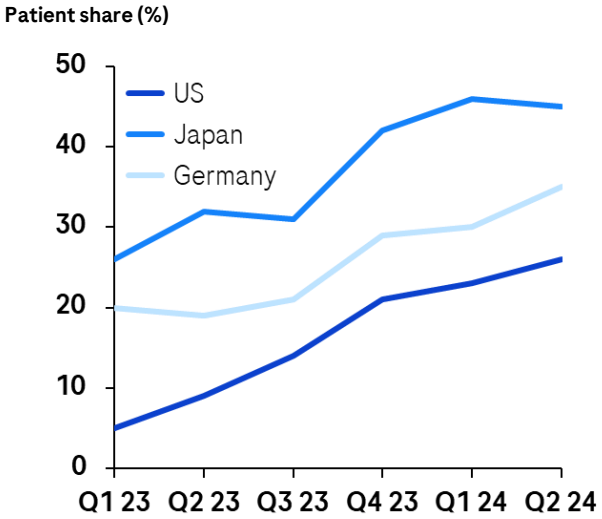
Malignant hematology portfolio

	Ph I	Ph II	Ph III	
Lunsumio SC	3L+ FL			✓ 2025
Lunsumio SC + Polivy	**SUNMO** (2L+ DLBCL (SCT-ineligible))			
Lunsumio + lenalidomide	**CELESTIMO** (2L+ FL)			
Lunsumio SC + lenalidomide	**MorningLYTE** (1L FL)			
Lunsumio + Polivy	1L DLBCL (elderly/unfit)			
Columvi + GemOx	**STARGLO** (2L+ DLBCL (SCT-ineligible))			✓
Columvi + Polivy + R-CHP	**SKYGLO** (1L DLBCL)			
Columvi	**GLOBRYTE** (R/R MCL (post-BTKi))			
P-CD19XCD20-ALLO1	R/R B-Cell malignancies			
P-BCMA-ALLO1	R/R MM			

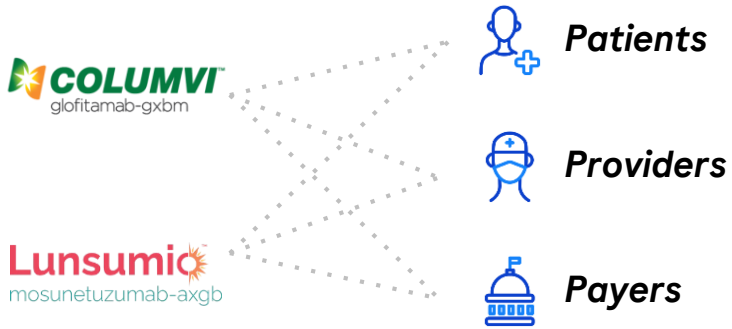
✓ Filed/primary endpoint met

Polivy

Market share trend (1L DLBCL, IPI 0-5)



Columvi/Lunsumio



Differentiated product profiles to meet the diverse needs of patients with NHL

- Polivy strong 1L DLBCL uptake (>33k pts treated globally); Included as 1L DLBCL SoC comparator in >15 Ph I & II studies*; POLARIX 5yr data submitted to upcoming medical congress
- Comprehensive Columvi/Lunsumio development program; Positive Columvi Ph III (STARGLO) in 2L+ DLBCL have been filed with global regulators; Positive pivotal trial of Lunsumio SC in 3L+ FL
- Broad hematology pipeline in DLBCL and FL; expanding into additional disease areas, including allogeneic CAR-Ts in B-cell malignancies & MM

Note: Venclexta sales booked by AbbVie; *Only studies not sponsored by Roche and listed as active on clinicaltrials.gov (accessed September 2024); FL=follicular lymphoma; DLBCL=diffuse large B-cell lymphoma; MCL=mantle cell lymphoma; MM=multiple myeloma; R/R=relapsed/refractory; CAR=chimeric antigen receptor; CR=complete response; CRS=cytokine release syndrome; SoC=standard of care; NHL=Non-Hodgkin's lymphoma; IPI=international prognostic index; P-CD19CD20-AllO1 and P-BCMA-ALLO1 in collaboration with Poseida Therapeutics

Hemophilia A: Hemlibra the global SoC with extensive real-world data

Achieving ~80% zero treated bleeds with a convenient administration

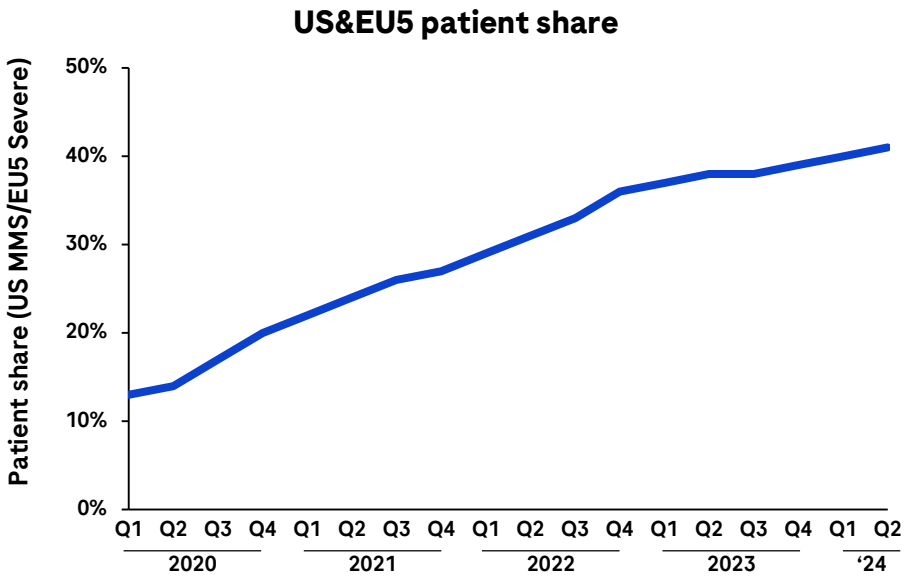
Hemophilia A portfolio

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

	Ph I	Ph II	Ph III	Ph IV	
Hemlibra				**Ph IV: BEYOND ABR** (moderate/severe Hemophilia A)	IA 2025
NXT007 (FIXa x Fx)			Hemophilia A		2025
SPK-8011			Hemophilia A		Re-evaluation

- BEYOND ABR evaluating overall health, physical activity, and joint outcomes
- NXT007 with the potential to achieve zero treated bleeds for Hem A pts, without need for additional FVIII treatment
- SPK-8011 Ph III trial paused and HemA gene therapy approach being re-evaluated

Hemlibra



New vial options
More choices & less wastage

Updated admin kit
Simplified prep & smaller needle

Autoinjector (in development)
non-visible needle & improved comfort

- Global SoC in Hemophilia A with 41% pts share in US&EU5; Further penetration among moderate/severe patients who remain on FVIII
- Outstanding profile with >2/3 pts on Q2W or Q4W SC dosing, ca. 80% zero bleeds* and without inducing FVIII inhibitor development
- Continuous improving convenience, including autoinjector development; Roche working on expedited timeline with regulators to bring the device to patients as fast as possible

*Based RWD from McCary I, et al. Haemophilia 2020, Wall C, et al. ISTH 2020, Poon M-C, et al. ASH 2022 and Khairnar R, et al. ASH 2021; SOC=standard of care; Q2W/Q4W=once every 2/4 weeks; SC=subcutaneous; MMS=mild-moderate-severe; IA=interim analysis

Multiple sclerosis: Ocrevus Zunovo™ (SC) US approval achieved

Ocrevus Zunovo™ with strong US label; Positive fenebrutinib Ph II (FENopta) relapse data presented at ECTRIMS

Multiple sclerosis portfolio

OCREVUS® ocrelizumab

	Ph I	Ph II	Ph III	
Ocrevus SC	**OCARINA II** (RMS & PPMS)			✓
Ocrevus HD	**MUSETTE/GAVOTTE** (RMS & PPMS)			2025
fenebrutinib	**FENhance 1/2** (RMS)			2025
fenebrutinib	**FENtrepid** (PPMS)			2025
fenebrutinib	**FENopta** (RMS)			
BrainShuttle™ CD20	MS			

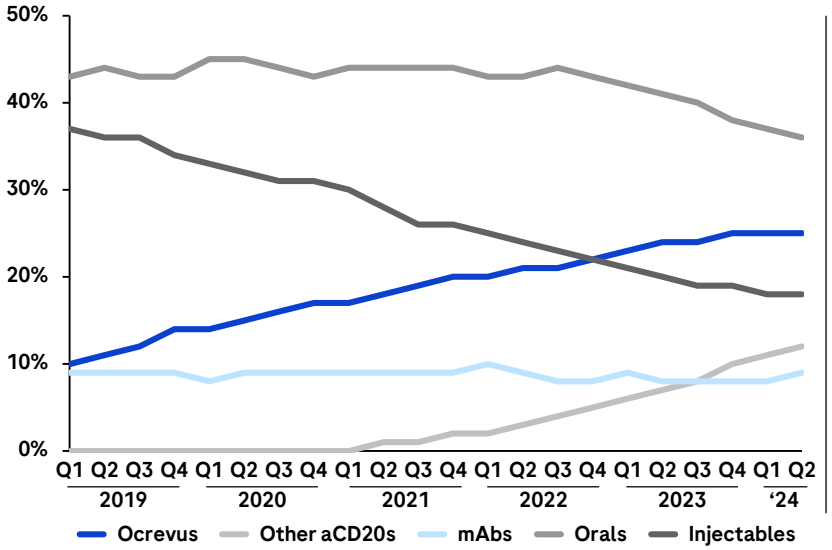
✓ Approved

- Ph III readouts expected in 2025 for Ocrevus HD (RMS & PPMS) and fenebrutinib in (RMS & PPMS)

Ocrevus

ECTRIMS 2024

MS total patient share (global)*



Ph IV (MINORE/SOPRANO) results for family planning

- Negligible Ocrevus transfer through placenta and breast milk
- No increased adverse impact to infant B-Cell levels or health outcomes
- Safety in pregnant/breastfeeding women consistent with well-established safety profile in RMS and PPMS

- Ocrevus Zunovo™ markedly reduces administration time to 10 min; retains Q6M dosing that has demonstrated high compliance and strong patient preference
- Ocrevus Zunovo™ with potential to drive market expansion in IV constraint settings and overcome non-preference for IV in SC/oral segment
- Positive Ph IV (MINORE/SOPRANO) show potential for Ocrevus to become the treatment of choice for patients considering family planning

*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; RMS=relapsing MS; PPMS=primary progressive MS; SC=subcutaneous; HD=high dose; IV=intravenous; HE/LE=high/low-efficacy; Ocrevus Zenuvo with Halozyme's rHuPH20/ Halozyme's human hyaluronidase

Immunology kidney: Positive Ph III for Gazyva in lupus nephritis

New Immunology strategy, including bispecifics moving into autoimmune diseases

Immunology kidney portfolio

GAZYVA* obinutuzumab injection

	Ph I	Ph II	Ph III	
Gazyva	**REGENCY** (LN)			✓
Gazyva	**MAJESTY**(MN)			
Gazyva	**ALLEGORY**(SLE)			2025
Gazyva	**INShore**(INS)			
ASO Factor B	**IMAGINATION** (IgAN)			
Lunsumio	SLE			
CD19xCD3	SLE			

✓ Primary endpoint met

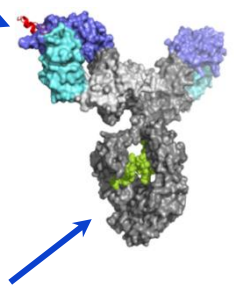
- MN, SLE and INS: Complementary indications of the Gazyva program
- Gazyva with BID potential in MN, SLE and childhood onset INS

Gazyva

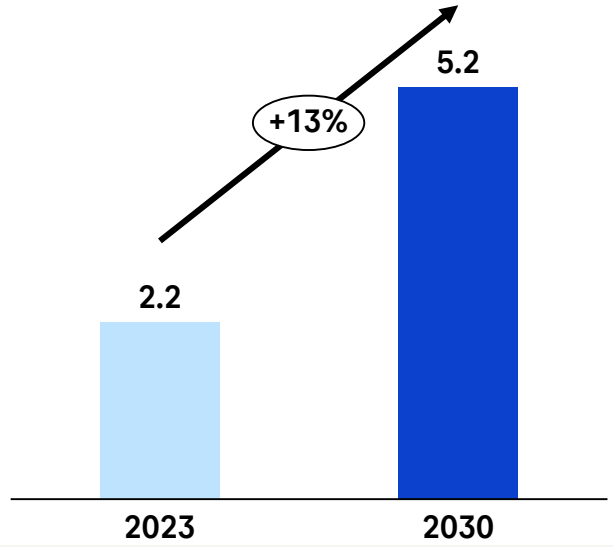
Glycoengineered anti-CD20 mAb

Type II anti-CD20 region
- Increased direct cell death
- Decreased CDC
- Reduced internalization

Glycoengineered Fc region
- Higher FcγR affinity
- Increased ADCC/ADCP



LN market[1] (USD$ bn, CAGR in %)



- Phase III (REGENCY) of Gazyva in LN met its primary endpoint of CRR, showing superiority over SoC; results to be shared with global health authorities and to be presented at a future medical conference
- Safety was in-line with the well-characterized safety profile of Gazyva; no new safety signals
- Global lupus nephritis market is expected to grow at a CAGR 2023-30 of 13%

1 Evaluate Pharma; LN=lupus nephritis; MN=membranous nephropathy; SLE=systemic lupus erythematosus; INS=Idiopathic nephrotic syndrome (Childhood onset INS also known as PNS=Pediatric nephrotic syndrome); BID=best-in-disease; ASO=anti-sense oligonucleotide; IgAN=IgA Nephropathy; CRR=complete renal response; SoC=standard of care; *pending approval of Gazyva in LN; ASO Factor B in partnership with Ionis Pharmaceuticals

Retinal vascular disorders: Vabysmo US market shares continuing to grow

Vabysmo pre-filled syringe launched in the US; Susvimo US commercial relaunch in nAMD commencing

Retinal vascular disorders portfolio

VABYSMO

susvimo ranibizumab injection 100 mg/mL For Ocular Implant

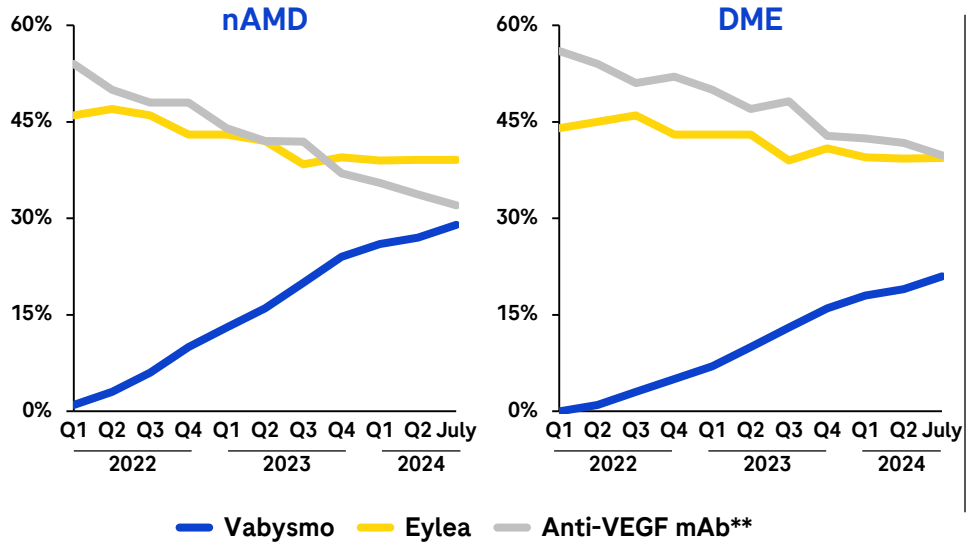
	Ph I	Ph II	Ph III	
Vabysmo	**POYANG** (CNV)			
Susvimo	**PAGODA/PAVILION** (DME/DR)			✓
vamikibart	**SANDCAT/MEERKAT** (UME)			2025
vamikibart	**BARDENAS/ALLUVIUM** (DME)			2025
satralizumab	**SatraGO-1/2** (TED)			
OpRegen	GA			
zifibancimig VEGF-Ang2 DutaFab	**BURGUNDY** (nAMD)			

✓ Filed

- Vabysmo in RVO: EU approval achieved
- Susvimo in DME/DR: US filing accepted

Vabysmo

US patient share since launch*



Pre-filled syringe launch

Simple, one-handed dose adjustment for fast administration

Potential to broaden uptake, including in the 1L setting

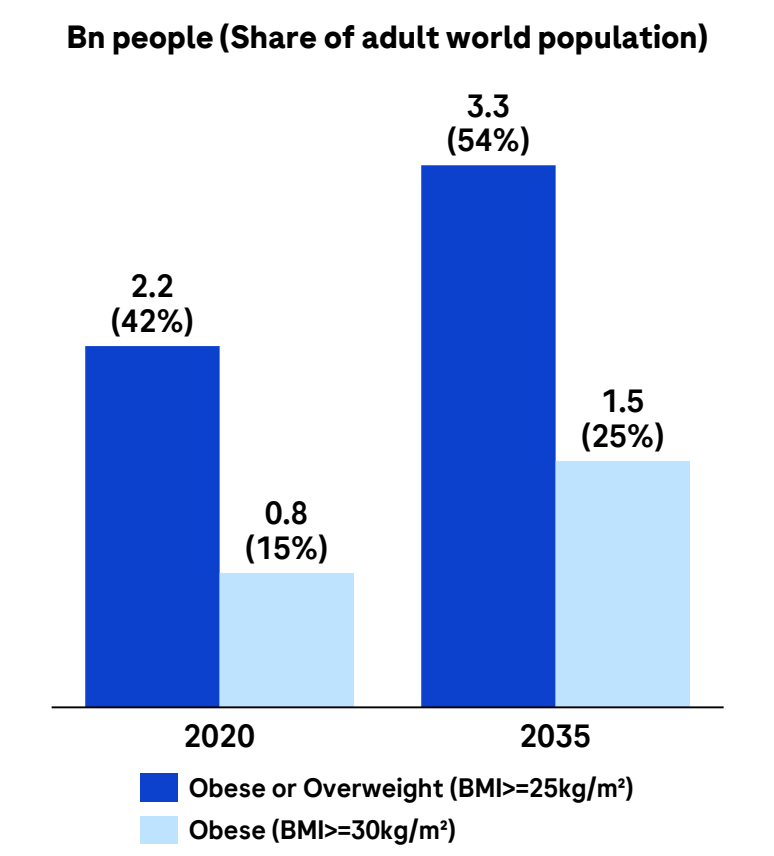
- Vabysmo with continued market share gains and increasing penetration in naive patients
- Growing body of RWD with >50k pts substantiates treatment benefits seen in clinical trials
- Vabysmo first and only bispecific antibody for the eye available in a pre-filled syringe in the US; EU filing ongoing
- Susvimo US commercial relaunch in nAMD commencing; ex-US 2025+

*Claims data based on Verana shares through July 2024; **Avastin, Lucentis and biosimilars; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; DR=diabetic retinopathy; RVO=retinal vein occlusion; TED=thyroid eye disease; GA=geographic atrophy; CNV=choroidal neovascularization; RWD=real-world data; OpRegen in collaboration with Lineage Cell Therapeutics

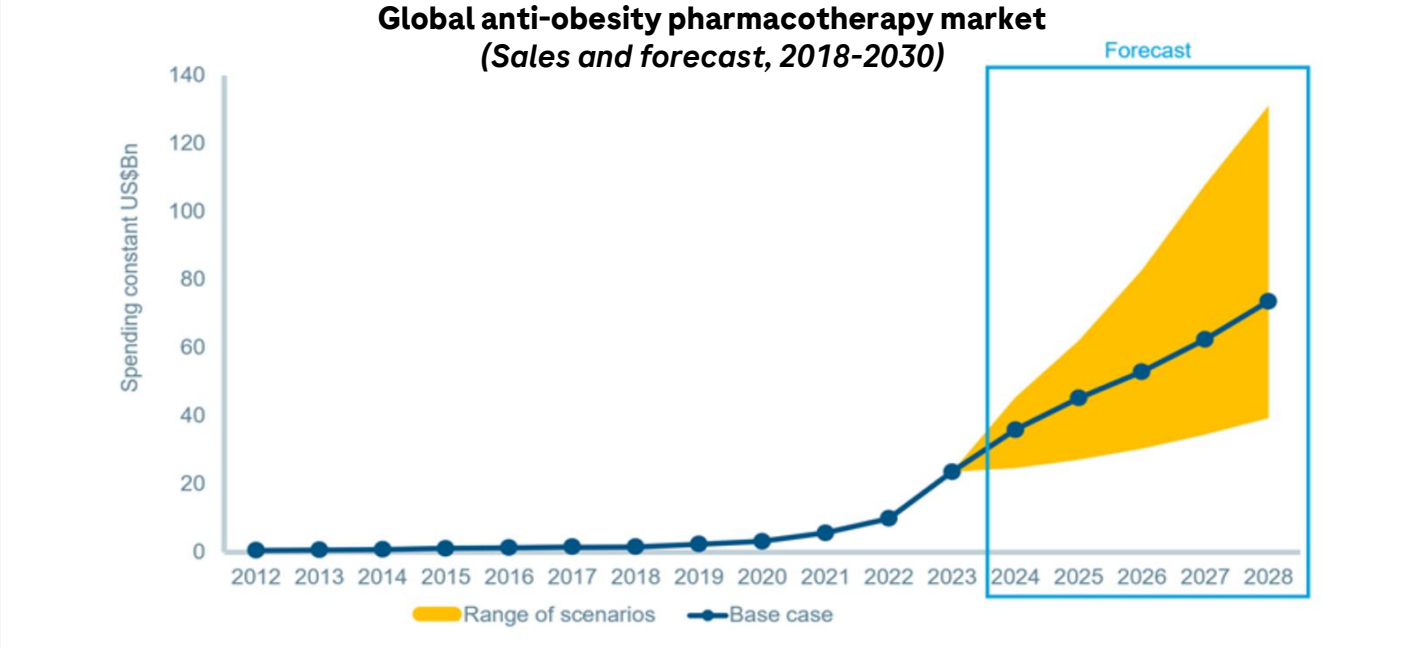
Anti-obesity market is expanding significantly

> 50% of global population expected to be obese/overweight by 2035

Global obese/overweight population[1]



Obesity market could grow beyond 100bn US$ by 2030[2]



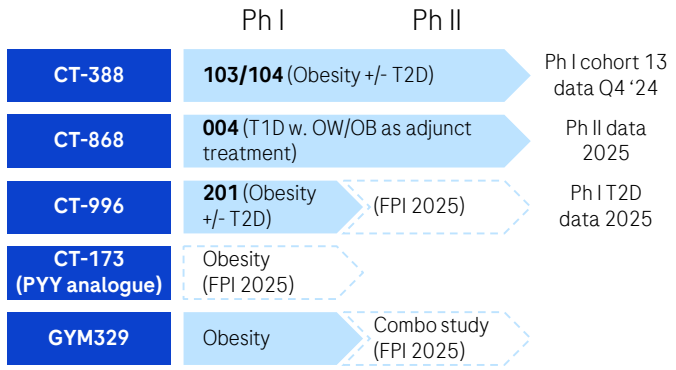
- Growth in prevalence combined with the launch of innovative treatments for diabetes and obesity are expected to grow the overall market for metabolism Rx
- Obesity one of the fastest growing market segments

1. World Obesity Federation. World Obesity Atlas 2024. Accessed August 14, 2024. https://data.worldobesity.org/publications/WOF-Obesity-Atlas-v7.pdf, 2. 2024: The obesity market's inflection point?, IQVIA

Obesity: Pipeline with potentially unique combination opportunities

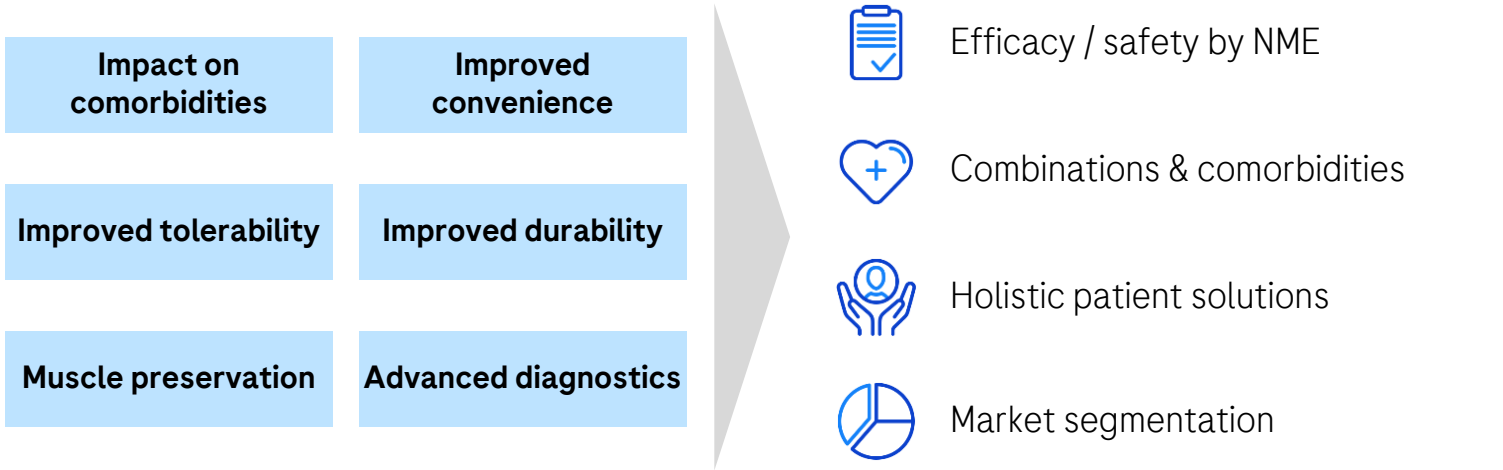
Despite numerous approved treatments, unmet need remains; Roche set up to leverage Obesity opportunity

Obesity portfolio



- Pipeline of potentially differentiated assets
- Positive Ph I data for CT-388 & CT-996 shared at EASD
- CT-868 Ph II data expected in 2025
- CT-173 Ph I in obesity to initiate in 2025

Roche's obesity pipeline



- CT-388 and CT-996 with BIC potential, as well as CT-868 with BIC/FIC potential in OW/OB patients with T1D, based on Ph I results
- Obesity market expected to segment by e.g. comorbidities, weight loss goal or oral vs SC
- Combination potential with Roche assets in several TAs; Expansion into adjacent indications
- SC devices in development; synergies with Roche DIA Diabetes and Digital Health solutions

T2D=type-2 diabetes; T1D=type-1 diabetes; QW=once weekly; QD=once daily; OW=overweight; OB=obese; FPI=first patient in; BIC/FIC=best-/first-in-class; SC=subcutaneous

Pharma Strategy

Therapeutic Areas & focus diseases

Our core capabilities

Significant future growth opportunities

How we succeed: Our Core Capabilities

Modalities & Technologies

Focus on approaches with breakthrough potential in focus TAs & diseases

Devices

Making devices an integral part of our assets, from R&D to commercialization

Manufacturing

Optimizing and future-proofing our manufacturing network

Customer Experience & Access

Providing a holistic customer experience & enabling rapid, broad & sustainable access

Data & AI

Leveraging data and generative AI to improve process efficiency

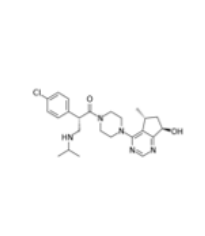
Our People

Creating a culture that allows our people to thrive in our Pharma division

AI=artificial intelligence

Diversified portfolio of technologies and modalities

Newest platform technologies brain shuttle and cyclic peptides have entered the pipeline

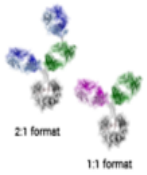


Small molecules

- divarasib
- inavolisib
- giredestrant
- fenebrutinib
- CT-996
- zosurabalpin
- AR degrader
- BRAF inh. (3)
- HER2 TKI[2]
- SPYK04
- USP1 inh.
- WRN covalent inhibitor
- selnoflast
- LepB inhibitor

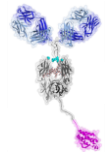
Monoclonal antibodies

- IL-6mAb
- vixarelimab
- GYM329
- anti-TL1A[3]
- astegolimab
- prasinezumab
- tiragolumab
- anti-latent TGFβ1 (SOF10)
- CD137 switch antibody



Bispecifics / trispecifics

- anti-CLDN6 trispecific
- glypican-3 x CD3a
- runimotamab (HER2 X CD3)
- cevostamab
- FIXa x FX
- VEGF-ANG2 DutaFab



Fusion proteins

- eciskafusp alfa (PD1-IL2v)
- efbalropendekin alfa (IL15/IL15Ra-Fc)
- FAP-4-1BBL

Antibody Drug Conjugates (ADC)

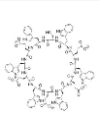
- cMET [5]
- pre-clinical

Brain Shuttle

- trontinemab
- Brain shuttle CD20

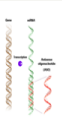
Peptides

- CT-388
- CT-868



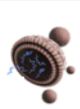
Cyclic peptides

- LUNA18



RNA molecules

- ASO factor B
- tominersen
- zilebesiran[4]

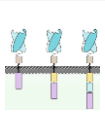


Neoantigen vaccines

- autogene cevumeran

Gene therapy

- Elevidys



Allogeneic CAR-T cells

- P-BCMA-ALLO1[1]
- P-CD19CD20-ALLO1[1]

Stem Cell therapy

- OpRegen

Strong legacy of pioneering new drug modalities, e.g. mAbs, ADCs and bispecifics

*list is not extensive; 1. Poseida Therapeutics managed; 2. Zion Pharma managed; 3. Telavant managed; 4. Alnylam Pharmaceuticals managed; 5. MediLink managed; CAR=chimeric antigen receptor

Increased focus on drug delivery devices

Significant investments in device development excellence will be critical to support our future portfolio

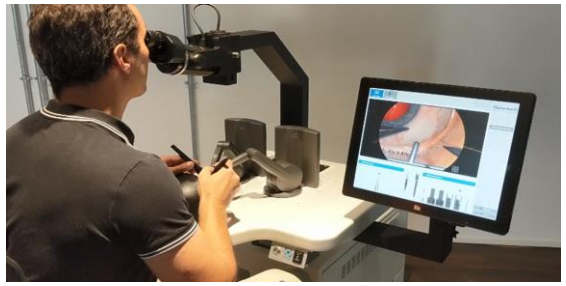
Intravitreal delivery

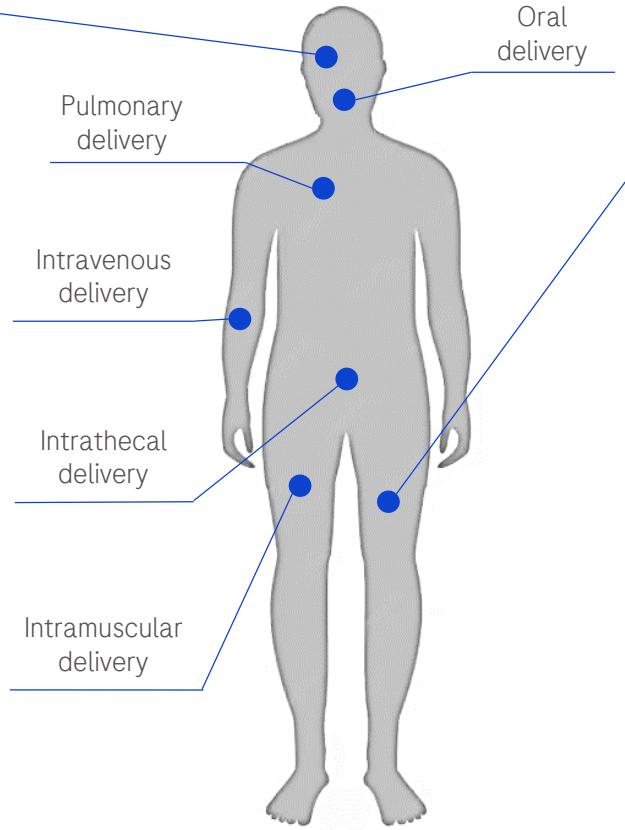
VABYSMO faricimab-svoa injection 6 mg

susvimo ranibizumab injection 100 mg/mL For Ocular Implant

Pre-filled syringe for ophthalmic use

Intravitreal drug delivery implants





Subcutaneous delivery

OCREVUS ocrelizumab

TECENTRIQ atezolizumab

PHESGO pertuzumab/trastuzumab/hyaluronidase-zzxf SUBCUTANEOUS INJECTION

Xolair Omalizumab

ACTEMRA tocilizumab

Pre-filled syringe/ needle safety device

(High-volume) autoinjector

On-body injector

~60% of current pipeline NMEs and LEs will launch with a device

Establishing our resilient manufacturing network of the future

Global network investments to enable portfolio evolution

	Network of the future	Milestones achieved
Biologics	Modular technology & optimized capacity	Single-use technology, modular filling & process intensification; Vacaville divestment
Small molecules	State of the art clinical development and launch capabilities	Basel modernization investment (CHF 0.6bn new small molecule facility)
Cell and gene therapy	Pioneer new capabilities	Hillsboro and Penzberg Cell & Gene Therapy capability build-up
Peptide	Pioneer new capabilities; Pivot to internal at later stage	Manufacturing strategy for GLP-1s established
Oligo	Fit-for-purpose network leveraging external capabilities	Strategic partnership established for oligo
ADC	Internal capacity drug substance and drug product filling	E2E value chain for ADC established
Geographical footprint	Global manufacturing footprint (North America, Europe, Asia)	China manufacturing footprint initiated

Process development and supply chain optimization work ongoing, with goal to drive down COGS

ADC=antibody drug conjugate; E2E=end-to-end; COGS=cost of goods sold

Leeway to invest in new drug modalities, including peptides

Enabled by manufacturing network optimization and ongoing productivity improvement

Incretin manufacturing strategy

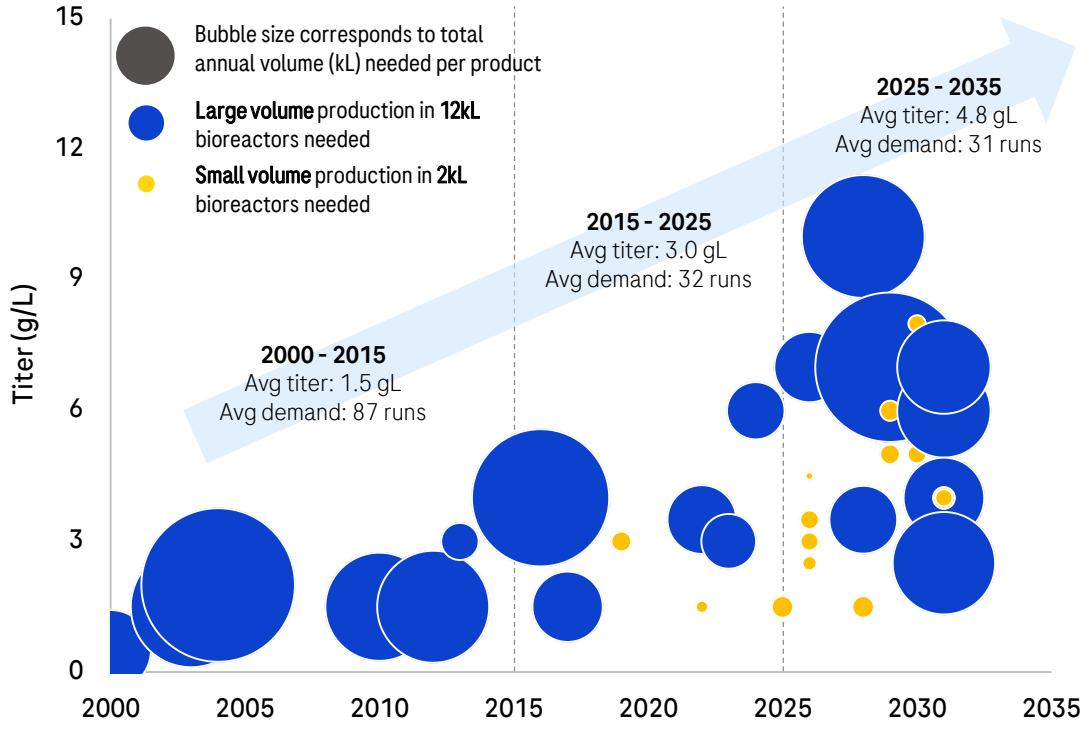
CT-388 / CT-868: Injectable peptides

- Clinical supply secured at CDMOs (no near-term capacity constraints)
- Commercial production will require a mix of in-house and external manufacturing
  - Build requirements could be managed within existing Roche CAPEX budget (p.a. ~3.5-4bn)
  - CDMO network expected to add capacity by time of launch
- In-house device development capabilities & strategic partnerships for devices to support obesity portfolio

CT-996: Oral, small molecule

- CT-996 is a small molecule with streamlined chemical synthesis
- Production will be supported by Roche manufacturing network

Biologics portfolio evolution with 5-fold productivity increase from 2000 to 2030



NME=new molecular entity; Small volume=less than 10 runs at 12kL scale; *Expected from 2000-2030; Volumes referring to drug substance volumes

Roche has a track record in reaching leadership in new markets

Leveraging learnings from successful launches for upcoming expansion into IBD and CVRM

	Market at time of launch	Commercialization approach	Result
OCREVUS® ocrelizumab **Multiple sclerosis**	• Highly competitive market with >10 available DMTs • Unmet need for high efficacy DMT	• Pre-launch market shaping • Responsible US pricing strategy • Tailored patient navigation support	**A global market leader in MS[1]** **>350,000 patients treated**
HEMLIBRA emicizumab-kxwh **Hemophilia A**	• Highly competitive market; companies with decades of experience • Critical success factor: company trust	• Strong KOL & advocacy relationships • Rare diseases-focused field teams • Innovative mechanisms for access	**A global market leader in Hem A[1]** **>26,000 patients treated**
VABYSMO **nAMD/DME/RVO**	• Strong entrenched competitor • First Lucentis biosimilars approved • Roche new to ophthalmology ex-US	• Rapid access secured in major markets within 6 months of launch • DTC empowering patients in the US • Integrated RWD generation	**Rapid market share gains** **Increasing penetration in naïve patients**

1 In all must win markets (US, CN, JP, DE, UK, FR, IT, ES, CA); IBD=inflammatory bowel disease; CVRM=cardiovascular, renal and metabolism; DMTs=disease-modifying therapies

Leveraging AI to increase overall Pharma productivity

Selected AI use cases along the value chain

Drug development	Regulatory & reimbursement	Manufacturing & distribution	Commercialization
gRED's 'Lab-in-a-loop' • AI/ML: Computational biology to integrate data and experiments • Acceleration of research, lower costs, higher success rates and more drug candidates identified	**Document writing** • Gen AI: co-author CSRs for faster regulatory submissions • Timeline reduction of 50%, for example when filing	**Digital twin** • AI-driven digital twin: predict cell-age and growth for production cell-lines • Increased product yield/ quality by 10%/ 40%	**Predictive alerts** • Predictive AI: Pts-focused, real-time predictive alerts improving relevance of HCP interactions • Incremental revenue gain of USD 0.5-0.7bn in 2024

AI-enabled solutions increasing efficiencies and productivity

(Gen) AI=(generative) artificial intelligence; ML=machine learning; HCP=healthcare professional; CSR=clinical study report; LN=lupus nephritis

Our people: Critical enablers for our new Pharma Strategy

We commit to creating a culture where our people can thrive across the Pharma Division

An attractive employer

We strive to hire, develop and retain the best people in the industry; providing an environment for talent to thrive across their career

High performing organisation

We purposefully commit to the five conditions of a High Performing Organisation - elevating our performance and delivery

People Strategy pull through

We deliver the People Strategy - a simplified and focused approach ensuring current and future activities have the greatest collective impact

Ways of working

We elevate our ways of working[1] across the Pharma Division

1 Put patients first, follow the science, act as one team, embrace differences, accelerate learning, simplify radically, make impact now, think long term

Pharma Strategy

Therapeutic Areas & focus diseases

Our core capabilities

Significant future growth opportunities

Peak sales potential of key pipeline assets (NMEs and LEs)

New Molecular Entities (NME)

giredestrant HR+ BC	**prasinezumab** Parkinson's disease	**astegolimab** COPD
inavolisib Pi3Km BC	**fenebrutinib** RMS, PPMS	**ASO Factor B** IgAN
divarasib KRAS+ NSCLC, CRC	**Elevidys**[1] DMD	**vamikibart** DME/UME
tiragolumab NSCLC, uHCC, ESCC	**GYM329** SMA, FSHD	**CT-388/CT-996/CT-868** Obesity,T1D,T2D
trontinemab Alzheimer's disease	**anti-TL1A mAb** IBD	**zilebesiran** hypertension

- 7+ NMEs with CHF >3bn peak sales potential per asset
- 4 NMEs with CHF 2-3bn peak sales potential per asset

Line Extensions (LE)

Columvi 2L DLBCL, 1L DLBCL	**PiaSky** PNH, aHUS, SCD	**Enspryng** MOGAD, AIE, TED
Lunsumio 2L DLBCL, R/R FL, 1L FL	**Ocrevus**[2] SC, high dose	**Gazyva** LN, SLE, MN, PNS

- 6 marketed products with LEs that could add CHF 1-2bn peak sales potential per asset

0.5-1bn peak sales · *1-2bn peak sales* · *2-3bn peak sales* · *>3bn peak sales*

Oncology/Hematology · *Neurology* · *Immunology* · *Ophthalmology* · *CVRM*

Please find corresponding trial populations in the appendix

Peak sales shown unadjusted; [1] Elevidys peak sales are ex-US; [2]Incremental peak sale opportunity for Ocrevus

2025: Significant key newsflow ahead*

	Compound	Indication	Milestone
Regulatory	**inavolisib + palbociclib + fulvestrant**	1L *PIK3CA*-mut HR+ BC	EU approval
	Columvi + GemOx	2L+ DLBCL	US/EU approval
	Elevidys	DMD	EU approval
	Gazyva	Lupus nephritis	US/EU filing; US approval
	Susvimo	DME/DR	US approval
	Susvimo	nAMD	EU filing
Clinical results	**giredestrant + palbociclib**	1L ER+ mBC	Ph III persevERA
	giredestrant + everolimus	ER+ BC	Ph III evERA
	Lunsumio + Polivy	2L+ DLBCL	Ph III SUNMO
	Lunsumio + lenalidomide	2L+ FL	Ph III CELESTIMO
	Venclexta + azacitidine	1L MDS	Ph III VERONA
	PiaSky	aHUS	Ph III COMMUTE-a
	Ocrevus HD	RMS/PPMS	Ph III MUSETTE/GAVOTTE
	fenebrutinib	RMS	Ph III FENhance 1/2
	fenebrutinib	PPMS	Ph III FENtrepid
	astegolimab	COPD	Ph II/III ARNASA/ALIENTO
	Gazyva	SLE	Ph III ALLEGORY
	vamikibart	UME	Ph III SANDCAT/MEERKAT
	vamikibart	DME	Ph II ALLUVIUM/BARDENAS
	trontinemab	AD	Ph Ib/IIa Brainshuttle™ AD
	Evrysdi + GYM329	SMA	Ph II MANATEE
	GYM329	FSHD	Ph II MANOEUVRE
	zilebesiran	Hypertension with high CV risk	Ph II KARDIA-3
	CT-868 (QD SC)	T1D with Obesity	Ph II
	CT-996 (QD oral)	Obesity with T2D	Ph I (*Arm 3*)

*Outcome studies are event-driven: timelines may change

R&D Excellence

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

By 2030, we aspire to

Consistently deliver many of the world's **most impactful medicines** (20 transformative medicines[1] by end 2029)

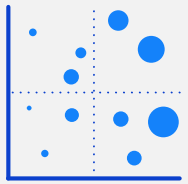
Reach **top-quartile performance** in R&D productivity across the biopharma industry

1. Reaching 'Bar' criteria: Future medicines that can have high impact for patients, higher revenue potential, and optimized risk

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework



Introduce the ‘Bar’ to recognize assets with transformative potential

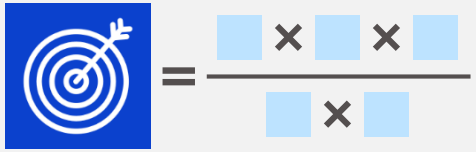
Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the ‘Bar’

Access the best external innovation

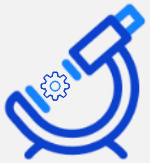
Identify and bring in exciting external assets which clear the ‘Bar’

Embrace ambitious R&D objectives



Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence



Invest in technologies and platforms that enable top-tier R&D productivity

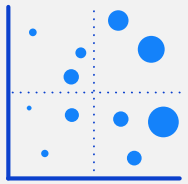
Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework



Introduce the ‘Bar’ to recognize assets with transformative potential

Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the ‘Bar’

Access the best external innovation

Identify and bring in exciting external assets which clear the ‘Bar’

Embrace ambitious R&D objectives

Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence

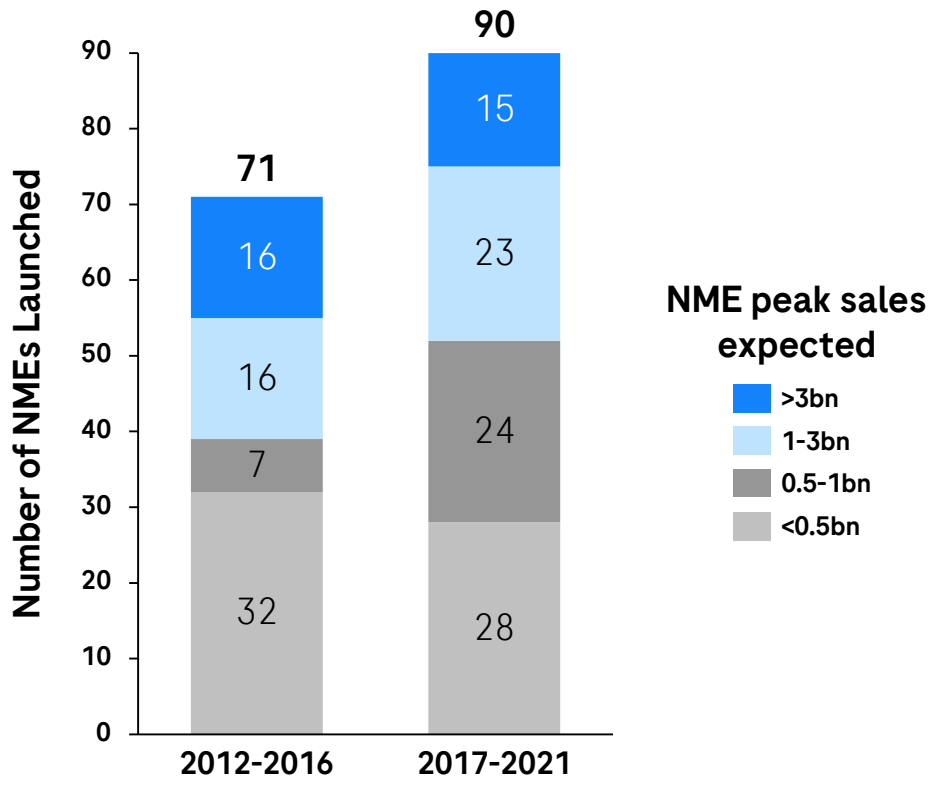
Invest in technologies and platforms that enable top-tier R&D productivity

Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

The world's most valuable medicines

NME peak sales expectations at launch for top 10 Pharma



Number of blockbusters (FY 2023 sales in USD)

Category	Count
'Unicorn' (>10bn)	8
Uber-blockbuster (5-10bn)	19
Mega-blockbuster (3-5bn)	21
Blockbuster (1-3bn)	151

Source: evaluate Pharma

Adopt a unified portfolio framework

Using the 'Bar' to identify and invest sufficiently in medicines with transformative potential

The Bar

Answers a clear & addressable unmet need	Engages a 'foundational target'	Possesses worthy pharmacologic characteristics	Achieves meaningful therapeutic differentiation	Unlocks a path to value

We have applied the 'Bar' across our entire pipeline of clinical stage assets - and it is now built-in to our governance and portfolio reviews. This has resulted in three specific accomplishments:

a. **Identification of promising, partially de-risked programs** likely to clear the 'Bar' that merit increased investment

b. **'Fast-track' of selected programs** that clear the 'Bar' and can bring exceptional value to patients and Roche

c. **Removal of projects/programs** that cannot meet the 'Bar', and re-prioritising these resources to higher impact assets

‘Fast-track’ of selected programs

Initial set of assets designated for acceleration based on exceptional potential

Asset	Acceleration
anti-TL1A Inflammatory Bowel Disease[1]	**Ph III**
Trontinemab Alzheimer’s Disease	**Ph III**
CT-388 Obesity	**Ph II & Ph III**

Examples of potential acceleration levers:

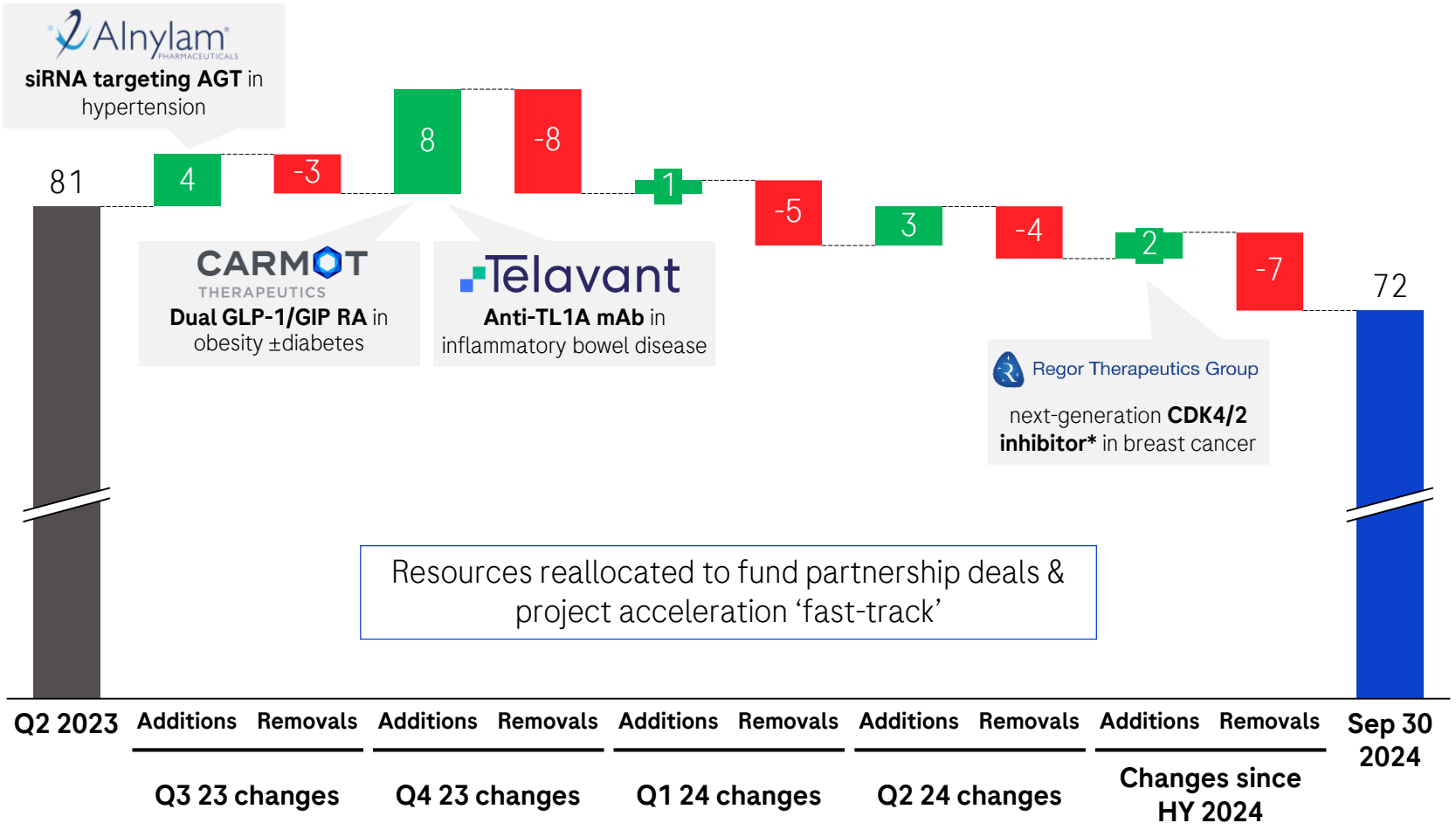
- Expediting enrollment with additional clinical trial sites
- Reallocating resources to accelerate
- Expanding into additional indications to maximize potential

These assets are only a starting point, with the option to extend the effort to more assets in the future

1 Includes both Ulcerative Colitis and Crohn’s Disease; TL1-A=tumor necrosis factor-like cytokine 1A

Pharma pipeline evolution since Pharma Day 2023

Since Pharma Day 2023, 17 NMEs were added and 26 NMEs removed, resulting in a higher impact portfolio



Pipeline changes since Q2'23

17 Additions

- 8 Ph I/Ph II NMEs acquired as part of high value partnerships
- 9 Ph I were added to the pipeline from internal feeding

26 Removals

- 9 NMEs terminated - not meeting the 'Bar'
- 17 NMEs exited the pipeline (including one approval)

*pending deal closure; siRNA=small interfering RNA; AGT=angiotensinogen; TL1A=Tumor necrosis factor-like cytokine 1A; GLP-1=glucagon-like peptide-1; GIP=glucose-dependent insulinotropic polypeptide; CDK4/2=cyclin dependent kinase-4/2; RA=receptor agonist; mAb=monoclonal antibody; NME=new molecular entity; Note: Chart Includes all assets from Ph I to Registration

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework

Introduce the 'Bar' to recognize assets with transformative potential

Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the 'Bar'

Access the best external innovation

Identify and bring in exciting external assets which clear the 'Bar'

Embrace ambitious R&D objectives

Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence

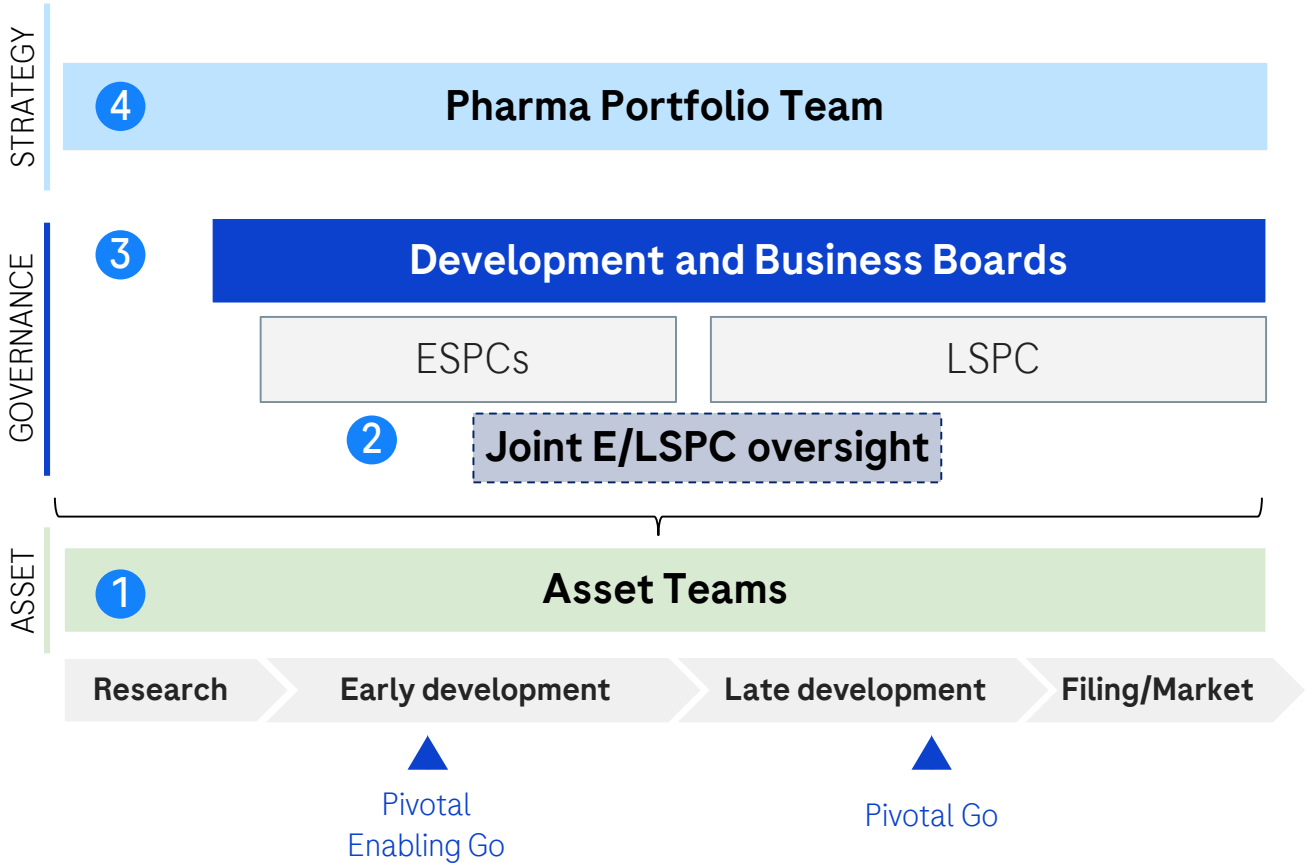
Invest in technologies and platforms that enable top-tier R&D productivity

Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

Reconfiguring governance and strategic portfolio management

Transforming our portfolio oversight and end-to-end governance to execute the 'Bar' and increase our PTS



1. Delivers end-to-end development plans to minimize whitespace
2. Ensures optimal data assessment, trial design and resourcing during transition phase
3. Comprehensive technical reviews to optimize success rates and return on investment
4. Maintains a balanced portfolio risk and value profile at enterprise level

E/LSPC=Early/Late Stage Portfolio Committee, PTS=probability of technical success

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework

Introduce the 'Bar' to recognize assets with transformative potential

Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the 'Bar'

Access the best external innovation

Identify and bring in exciting external assets which clear the 'Bar'

Embrace ambitious R&D objectives

Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence

Invest in technologies and platforms that enable top-tier R&D productivity

Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

Access the best external innovation

Partnering and acquisitions over the past year clearly met the 'Bar' criteria

Recent acquisitions

Entered high-impact partnerships since commencing R&D Excellence, e.g.,

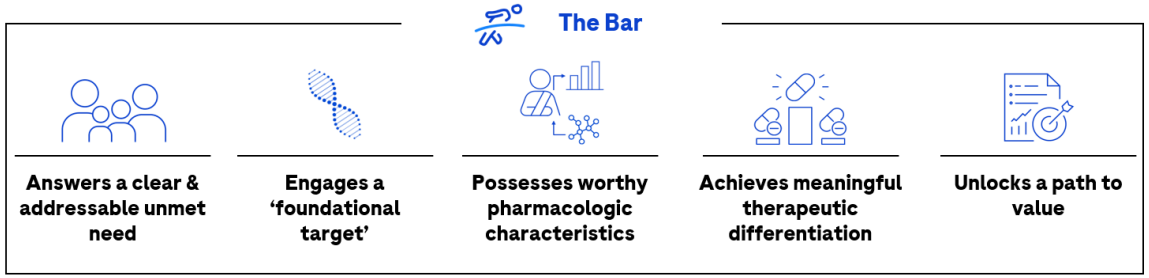
Telavant · Alnylam PHARMACEUTICALS · CARMOT THERAPEUTICS · ANTLERA

Regor Therapeutics Group

Roche announces asset purchase* with Regor Therapeutics to acquire its next-generation CDK inhibitor portfolio in breast cancer

Portfolio impact

- Business Development deals exemplify characteristics of the 'Bar'
- Assets that entered portfolio have a higher PTS



*pending deal closure; CDK=cyclin dependent kinase; PTS=probability of technical success

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework

Introduce the 'Bar' to recognize assets with transformative potential

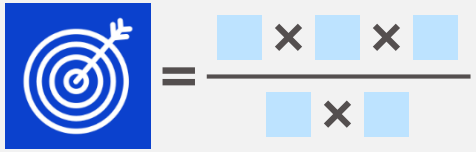
Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the 'Bar'

Access the best external innovation

Identify and bring in exciting external assets which clear the 'Bar'

Embrace ambitious R&D objectives



Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence

Invest in technologies and platforms that enable top-tier R&D productivity

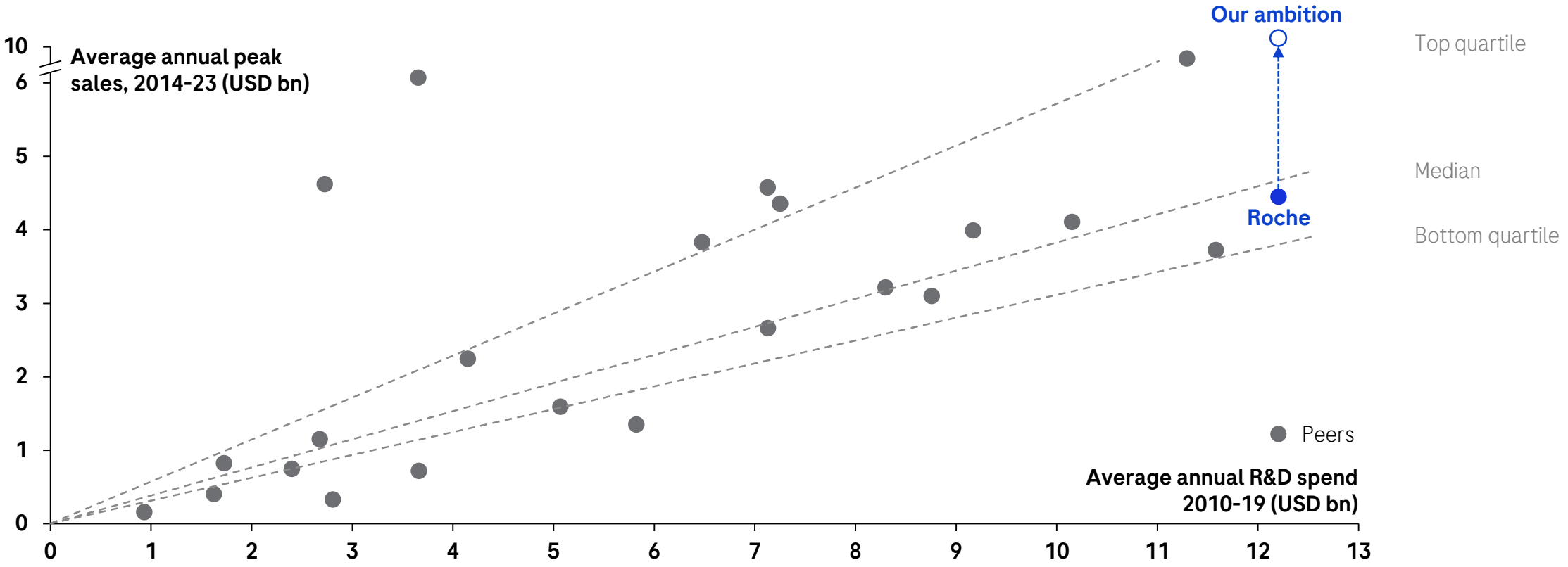
Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

R&D productivity: Comparison of leading Pharma players

We aim to be in the top quartile of all players

R&D productivity as annual peak sales vs. average annual R&D spend



Note: All numbers are inflation adjusted to 2023; Sources: Evaluate Pharma, FDA, BCG analysis (R&D Productivity Database)

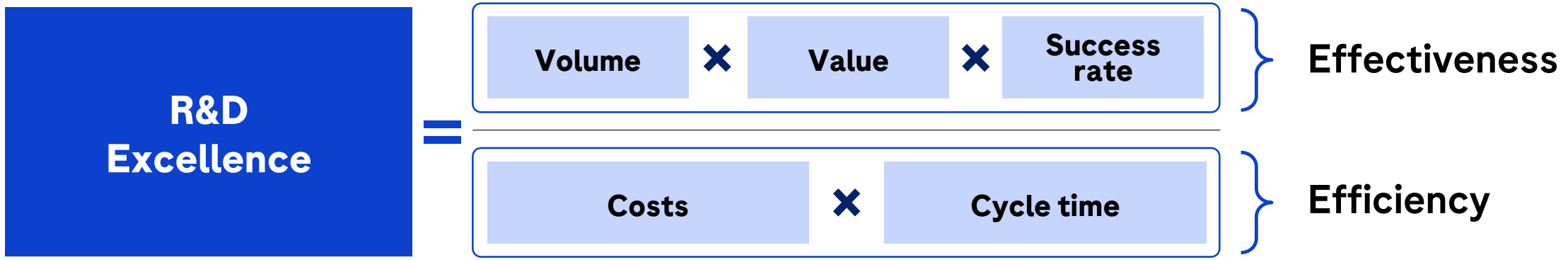
Embracing bold objectives: Our 2030 R&D ambitions

Toward top quartile industry performance

Increase Ph 0 initiations/yr[1]:
+50%

Increase average peak year sales of pipeline assets:
+50%

Increase Ph III success rate:
+22%p



Reduce R&D costs per NME launched by:
-20%

Reduce the average development cycle length[2]:
-40%

1 Initiations of projects; 2 Refers to cycle time from Lead Identification and Lead Optimization to end of Phase 3; NME=new molecular entity

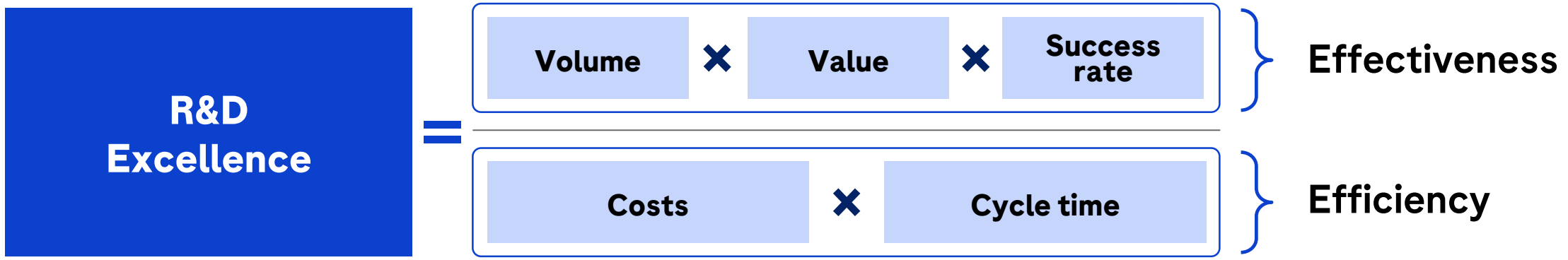
Meaningful improvements achieved in 2024

R&D Excellence enables us to reallocate resources to new projects, new deals & accelerate priority assets

Added **8 assets** through high-value partnerships and **9 assets** from early R&D

CHF +0.24bn average peak year sales per project through termination of low-value and addition of high-value projects

Recent team-assessed **PTS for PivGo's is 10%p higher** vs. historic 5 year average



Reinvest CHF 0.2bn of savings in 2024 to higher-return activities, and **keep our overall R&D spend roughly flat in the short-term**

~4 months cycle time acceleration through faster study site activation and automated content creation

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework

Introduce the 'Bar' to recognize assets with transformative potential

Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the 'Bar'

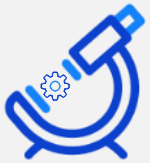
Access the best external innovation

Identify and bring in exciting external assets which clear the 'Bar'

Embrace ambitious R&D objectives

Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence



Invest in technologies and platforms that enable top-tier R&D productivity

Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

Simplifying and harmonizing our systems

Further streamlining our processes to elevate performance with AI

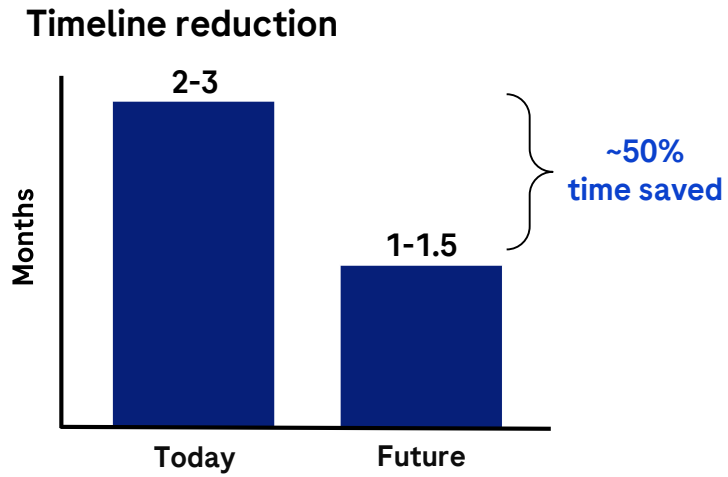
Progress in complexity reduction in several key R&D areas

	From	Moving towards
	Fragmented and complex R&D data ecosystem	Simplified and harmonized systems managed with single investment strategy
Electronic lab notebooks	8	1
Risk based quality management systems	3	1

Generative AI as Clinical Study Report co-author to enable faster regulatory submissions

Starting point:

Generation of Clinical Study Reports involves time consuming, repetitive, and often menial work



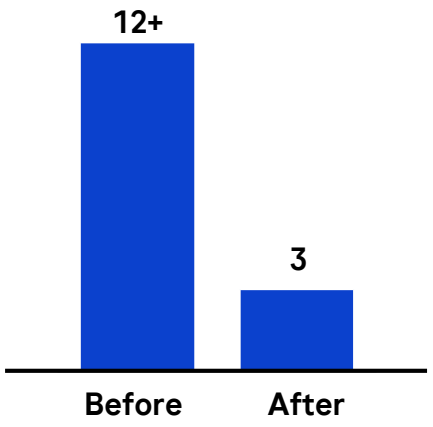
Streamlining our processes: CRO partnerships

Leveraging our scale to build long-lasting, end-to-end strategic relationships with vendors

Consolidation of vendors

Collaborative partnerships with three Contract Research Organizations

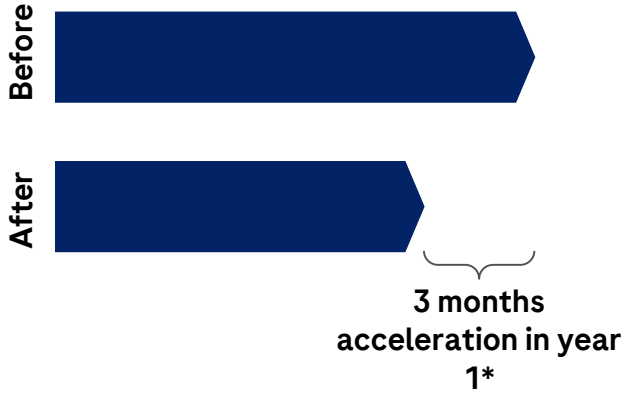
Number of CROs



Cycle time reduction

Eliminate switching and recontracting resulting in reduction in whitespace through aligning CROs by TA

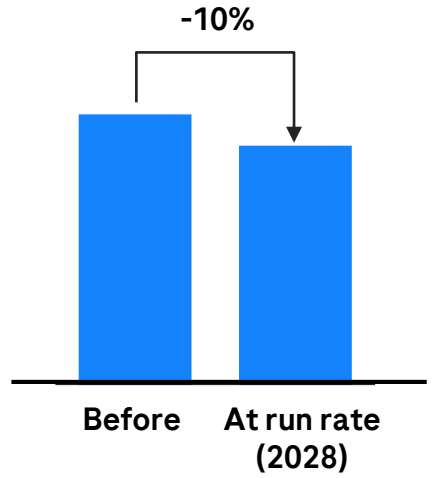
Cycle time (illustrative)



Cost reduction

Leverage economies of scale: Reducing vendor carrying costs by CHF -0.2bn over next five years

Run rate vendor costs



CRO=Contract Research Organization; TA=Therapeutic Area; *3 months acceleration in year 1 (further acceleration will result from full implementation)

R&D Excellence: Our solutions

We identified six solutions to achieve top quartile performance - with implementation ongoing

Adopt a unified portfolio framework

Introduce the 'Bar' to recognize assets with transformative potential

Transform our portfolio management & governance

Reconfigure end-to-end governance to meet the 'Bar'

Access the best external innovation

Identify and bring in exciting external assets which clear the 'Bar'

Embrace ambitious R&D objectives

Set bold R&D objectives linked to Pharma ambition

Evolve our R&D engine and invest in its excellence

Invest in technologies and platforms that enable top-tier R&D productivity

Align our incentives with the new R&D strategy

Link our R&D productivity objectives to individual and team performance

By 2030, with our ongoing efforts in R&D excellence, we will have...

- Adopt a unified portfolio framework
- Transform our portfolio management & governance
- Access the best external innovation
- Embrace ambitious R&D objectives
- Evolve our R&D engine and invest in its excellence
- Align our incentives with the new R&D strategy

Delivered many of the world's most impactful medicines (20 transformative medicines[1] by 2029)

Reached top-quartile performance in R&D productivity across the biopharma industry

Implementation in progress

Implemented and moving into business as usual

1 Reaching 'Bar' criteria: Future medicines that can have high impact for patients, higher revenue potential, and optimized risk

Our new product development leadership team

Aligned to our 5 focus therapeutic areas

Levi Garraway
Chief Medical Officer / Head of PD

Christopher Brittain
Head of Ophthalmology PD

Manu Chakravarthy
Head of Cardiovascular, Renal & Metabolism PD

Hideki Garren
Head of Neurology PD

Xin Li
PD Chief Operating Officer

TBD
Data Science, Analytics & Insights

Rhona O'Leary
Portfolio and R&D Excellence Implementation

Stefan Frings
Deputy Chief Medical Officer

Larry Tsai
Head of Immunology PD

Charles Fuchs
Head of Oncology/Hematology PD

PD=product development

Oncology/Hematology

Charles Fuchs
SVP and Global Head of Oncology and Hematology Product Development

Strategic pillars of oncology and hematology

Precision medicine	Novel modalities	Rational combinations	Early disease
Right medicines for the right patient	***Investing in key technologies to engage unique set of targets***	***Leverage breadth of oncology portfolio to explore new combinations***	***Early diagnosis and treatment increases the chance for cure***
inavolisib *INAVO120 (1L HR+ Pi3Km BC) US filing completed*	***Allogeneic CAR-Ts*** *Ongoing collaboration with Poseida in NHL and MM*	***Columvi + Polivy + R-CHP*** *Ph III in 1L DLBCL ongoing*	***Alecensa*** *ALINA (adj ALK+ NSCLC) approved in US and EU*
divarasib *Ph III in 2L NSCLC H2H vs sotorasib/adagrasib initiated*	***cMET ADC*** *Partnership with MediLink*	***HR+ Breast Cancer*** *Building portfolio in HR+ BC, with broad combination potential*	***giredestrant*** *Potential to replace ET in eBC*

[1] NSCLC=Non-Small Cell Lung Cancer; H2H=head-to-head; R-CHP=Rituxan + cyclophosphamide + hydroxydaunorubicin + prednisone; DLBCL=Diffuse large B-cell lymphoma; Pi3K=Phosphoinositide 3-Kinase; 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

Oncology solid tumor pipeline

A broad portfolio differentiated by targets and modalities

Ph I

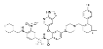
RG6194	runimotamab (HER2 x CD3)
RG6279	eciskafusp alfa (PD1-IL2v)
RG6323	efbalropendekin alfa (IL15/IL15Ra-Fc)
RG6344	BRAF inhibitor (3)
RG6411	undisclosed
RG6440	anti-latent TGF-β1 (SOF10)
RG6457	WRN covalent inhibitor
RG6468	undisclosed
RG6524	DLL3 trispecific
RG6537	AR Degrader
RG6596[1]	ZN-1041 (HER2 TKI)
RG6614[2]	KSQ-4279 (USP1 inh)
RG6648	cMET ADC
RG7827	FAP-4-1BBL
RGT-491B	CDK4/2i
CHU	glypican-3 x CD3
CHU	codrituzumab
CHU	CD137 switch antibody
CHU	RAS inhibitor
CHU	SPYK04
CHU	anti-CLDN6 trispecific
CHU	ROSE12

Ph II

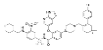
RG6180	**autogene cevumeran** multiple indications

Ph III

RG6058	**tiragolumab** multiple indications



RG6171	**giredestrant** HR+ BC

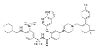


RG6330	**divarasib** 2L NSCLC

RG3502	**Kadcyla** HER2+ eBC high risk

RG7446	**Tecentriq** multiple indications

Registration



RG6114	**inavolisib** HR+ mBC


Small molecule


Antibody


Bispecifics/Trispecifics

Neoantigen vaccines


Fusion protein


Antibody drug conjugate

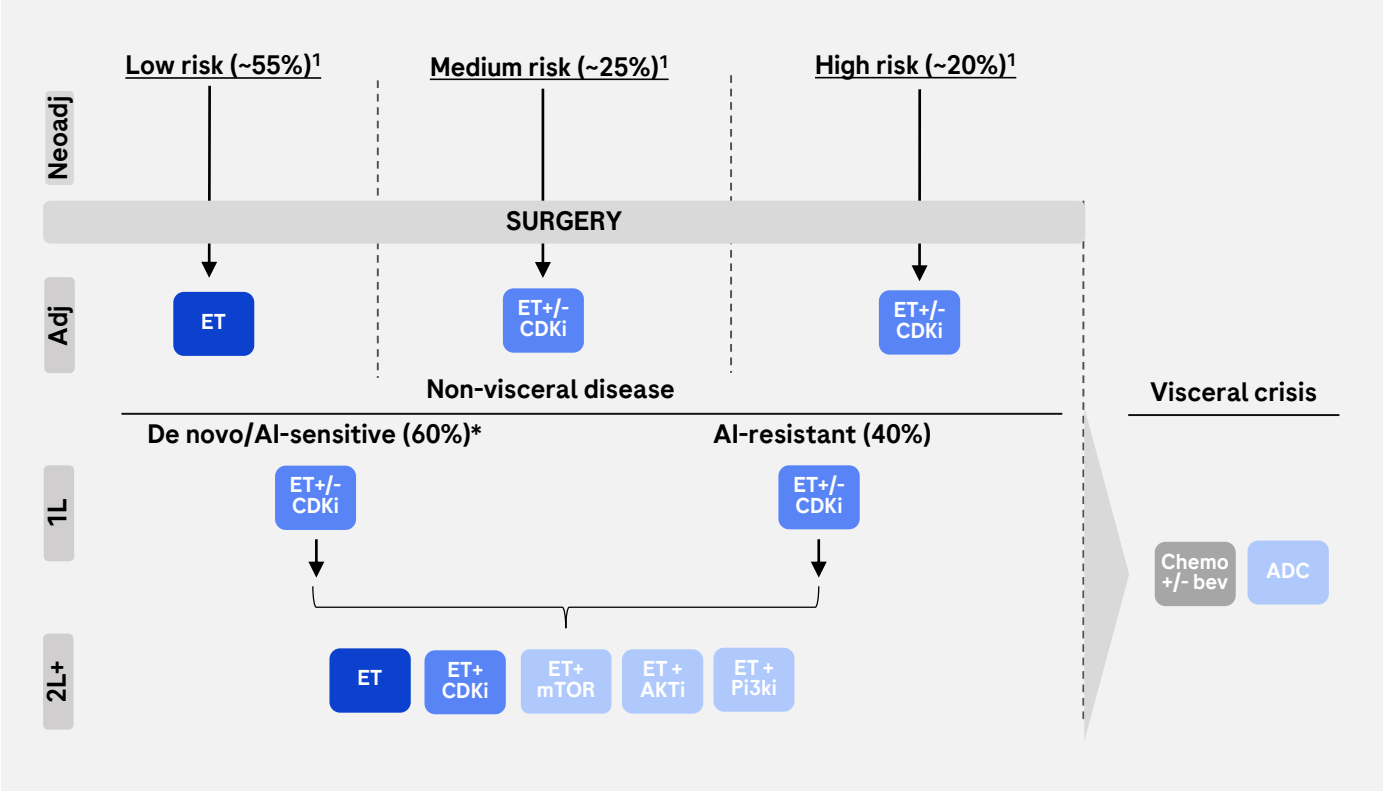

Cyclic peptides

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

HR+/HER2- BC treatment paradigm

Roche has potential to establish new standards of care across major treatment modalities

HR+ BC treatment landscape



ET Endocrine Therapy (ET)

ET is backbone treatment for ER+ BC; however, there are limitations with current ET options

ET + CDKi CDKi

ET+CDK4/6i established as backbone in HR+ mBC, and emerging in eBC, however resistance and tolerability issues remain

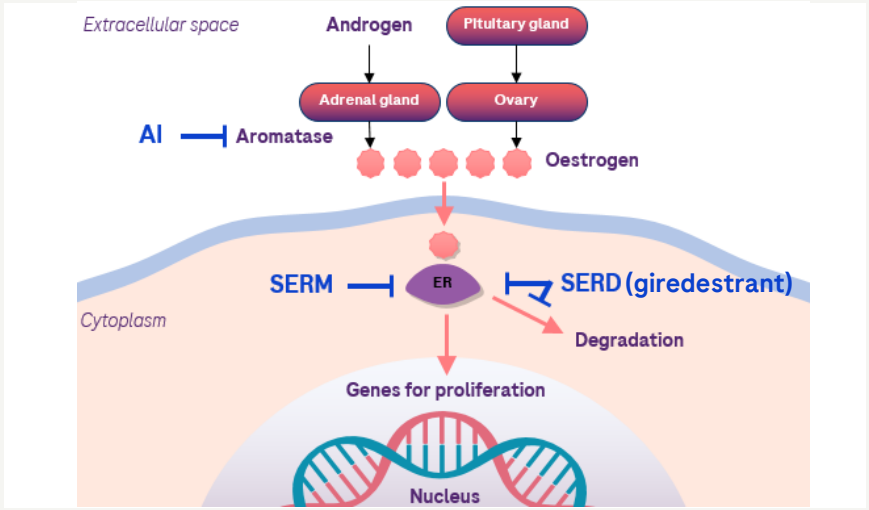
ET + tgt Targeted therapies

Currently limited to late lines

[1] Risk definitions vary according to guidelines and tools used: stage at diagnosis based on internal estimates using SEER data *AI sensitive defined as patients who relapse >1yr after completion of adjuvant therapy; HR=hormone receptor, ET=endocrine therapy, BC=breast cancer, eBC=early breast cancer, mBC=metastatic breast cancer, neoadj=neoadjuvant, adj=adjuvant

Giredestrant has the potential to overcome limitations of current ET options in 1L and eBC

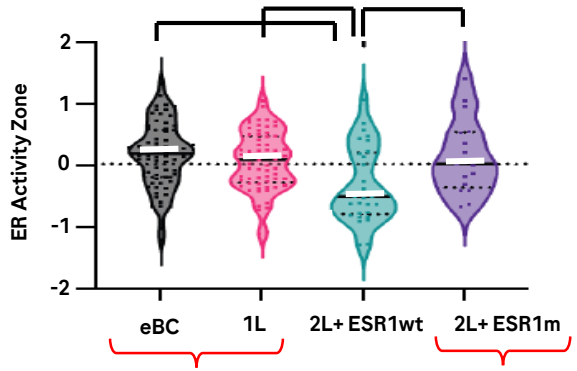
Giredestrant with best-in-class ET potential



- Highest preclinical potency vs. other oral SERDs in development
- Combinable with all CDKis including palbo, abema, ribo
- Well tolerated at all doses, with no dose-limiting toxicities
- Current SOC ET* limited by AEs leading to low adherence and mechanisms of resistance (including ESR1m)

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

Tumor ER pathway activity by time of sample collection[1]



persevERA / lidERA trials

Ph2 acelERA (ESR1m): PFS HR 0.61

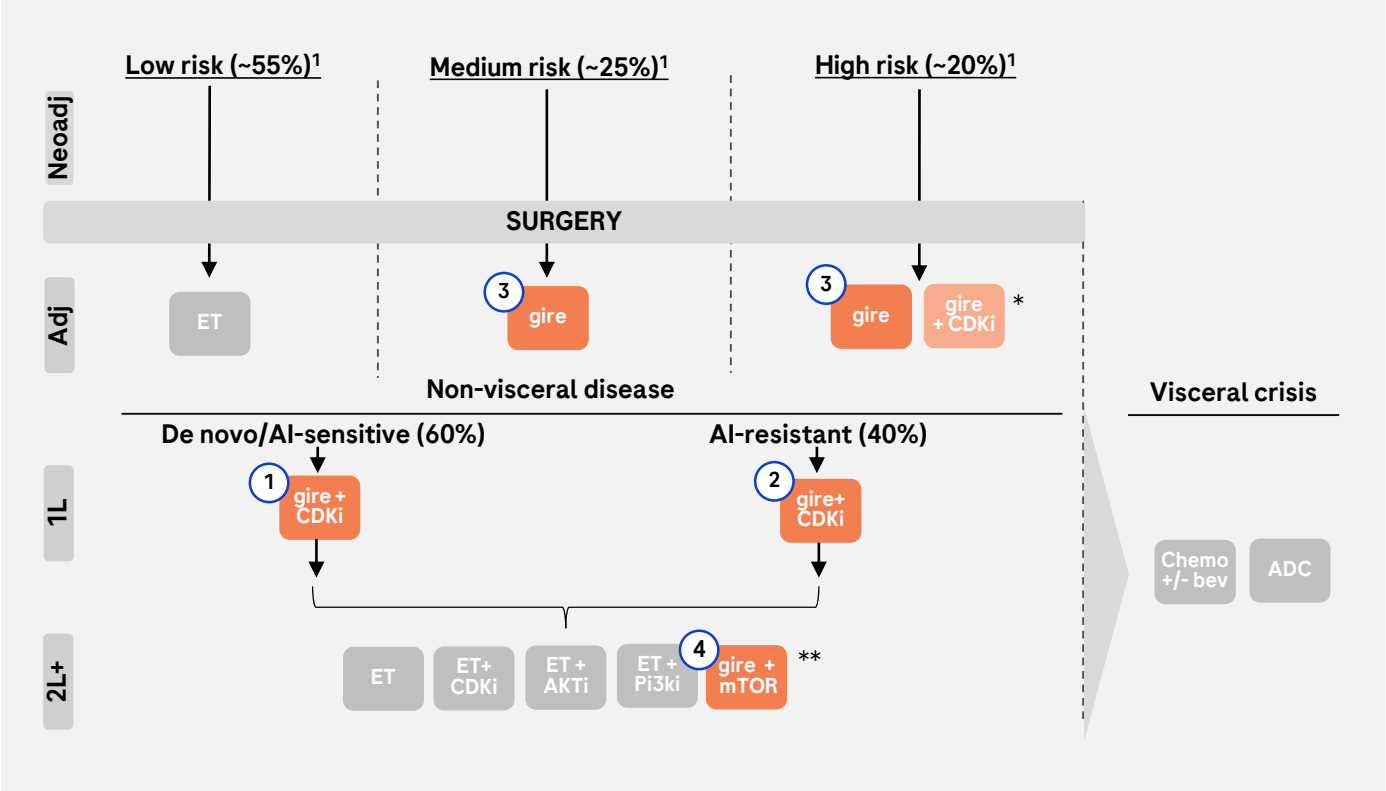
- In 2L/3L, only patients with ESR1m tumors appear to be sensitive to endocrine inhibition; in this population, giredestrant's benefit vs. fulvestrant was more pronounced with a PFS HR of 0.61
- In eBC and 1L mBC, tumors are still ER dependent, with ER activity comparable to that of 2L+ ESR1m patients.
- In earlier lines, giredestrant has potential to drive meaningful benefit in all patients, regardless of ESR1m status

Adapted from: Brufsky AM & Dickler MN. Oncologist 2018; Collier A. et al., ASCO 2023; .*Standard of care defined as aromatase inhibitors, tamoxifen and fulvestrant; AE=adverse event; eBC=early breast cancer; ER=estrogen receptor; ET=endocrine therapy; SERD=selective estrogen receptor degrader; SERM=selective oestrogen receptor modulator; palbo=palbociclib; abema=abemaciclib; ribo=ribociclib; ESR1=estrogen receptor 1

Giredestrant a new, potentially best-in-class endocrine backbone

Ph III (persevERA) 1L ER+ mBC and Ph III (evERA) 2L ER+ mBC results expected in 2025

Giredestrant aims to replace standard of care ET across eBC & mBC



gire **giredestrant**

- Initiated additional Ph III (pionERA) trial in 1L mBC with giredestrant + CDK4/6i of choice (abema, ribo, palbo)
- Leading SERD with head-to-head adjuvant trial vs. AI
- Evaluating combination with abemaciclib in eBC with single arm substudy as part of Ph III lidERA
- Plan to initiate combination with RGT-419B (CDK4/2i)

1	gire + palbo (persevERA)	1L ER+/HER2- mBC (endocrine sensitive)	2025
2	gire + any CDK4/6i (pionERA)	1L ER+/HER2- mBC (endocrine resistant)	
3	giredestrant (lidERA)	Adjuvant ER+/HER2- mBC	
4	gire + everolimus (evERA)	2L ER+/HER2- mBC	2025
	gire + Phesgo (heredERA)	1L maintenance ER+/HER2+ mBC	

[1] Risk definitions vary according to guidelines and tools used: stage at diagnosis based on internal estimates using SEER data *giredestrant + CDK4/6i in adjuvant HR+ BC being evaluated as single arm substudy as part of Ph 3 lidERA **giredestrant + everolimus in 2L+ HR+ BC is being investigated as Medical Affairs study; AI=aromatase inhibitor, ET=endocrine therapy, eBC=early breast cancer, mBC=metastatic breast cancer, neoadj=neoadjuvant, adj=adjuvant, SERD=selective estrogen receptor degrader

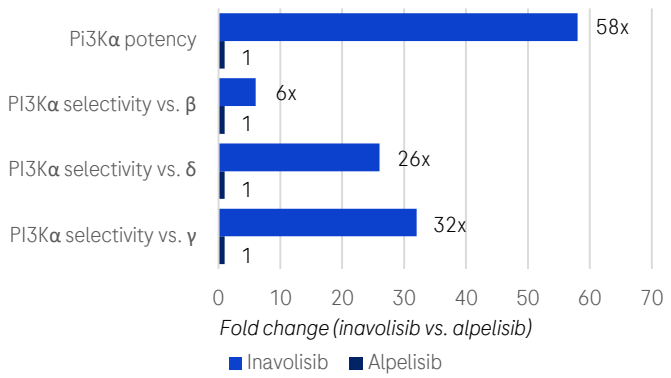
Inavolisib in *PIK3CA*m HR+ BC to define new SoC

Ph III (INAVO120) data submitted with Priority Review ongoing (PDUFA 27 Nov 2024)

FDA BTD

Inavolisib a BIC PI3Kα inhibitor

Potency/selectivity (inavolisib vs. alpelisib)[1]

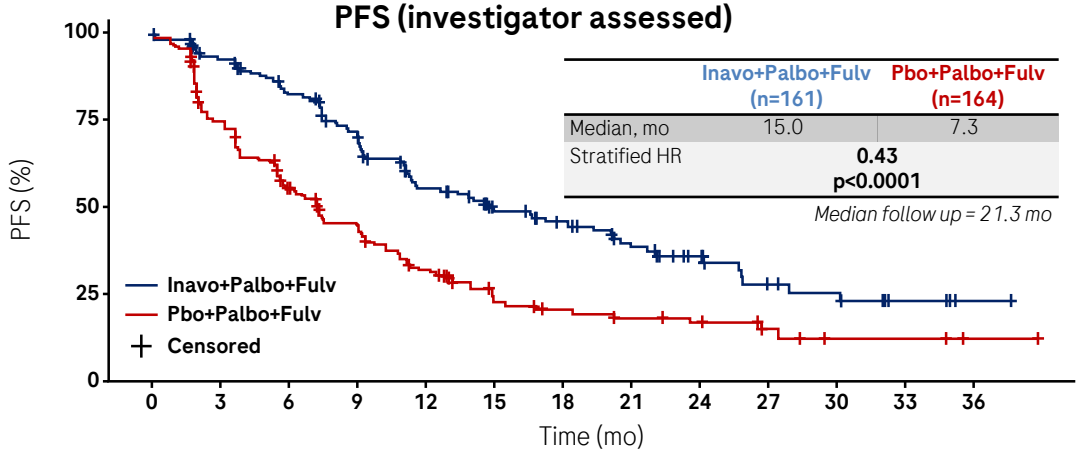


Differentiated from alpelisib:

- More potent and selective for PI3Kα subunit
- Better *in vivo* efficacy
- Greater safety margins allow for combination with ET and palbociclib at standard doses

Inavolisib more than doubles PFS in 1L *PIK3CA*m HR+ BC

PFS (investigator assessed)

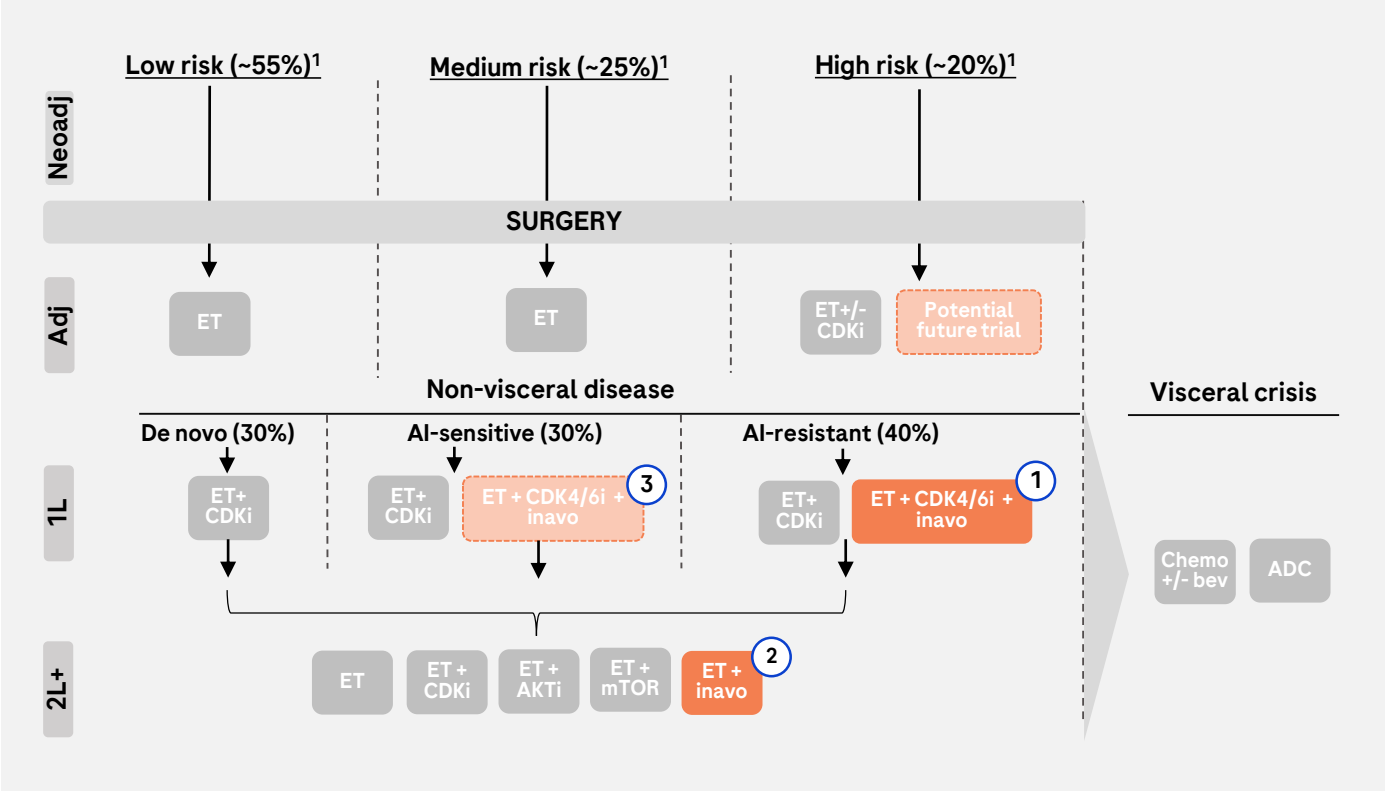


- INAVO120 met its primary endpoint, with a statistically significant and clinically meaningful improvement in PFS (15.0m versus 7.3m; HR:0.43; p<0.0001)
- OS was immature, but with clear positive trend (HR=0.64, [95% CI= 0.43, 0.97]; p=0.0338)
- Inavolisib discontinuations due to AEs were low: 6.2%, confirming the manageable safety and tolerability profile of inavolisib + palbo + fulv

[1]Jhaveri KL et al., SABCS 2023; PFS=progression-free survival; *PIK3CA*-mut=phosphatidylinositol 3-kinase, catalytic, alpha polypeptide mutated; HR+=hormone-receptor positive; ER+=estrogen receptor positive; HER2=human epidermal growth factor receptor 2; (m)BC=(metastatic) breast cancer; CDK=cyclin-dependent kinase; inavo=inavolisib; palbo=palbociclib; fulv=fulvestrant; pbo=placebo; mo=months; HR=hazard ratio; CI=confidence interval; OS=overall survival; SoC=standard of care; BIC=best-in-class

Inavolisib has potential to expand broadly in *PIK3CA*m BC

Potential for inavolisib based regimen in *PIK3CA*m HR+ BC



Ongoing study Future development plan

inavo **inavolisib**

- Ph III (INAVO123) to be initiated in 1L ET sensitive pts
- Potential to initiate additional trials in eBC
- Plan to initiate combination with RGT-419B (CDK4/2i)
- Potential to expand into other *PIK3CA*m tumors: 12 Ph Ib/II signal seeking studies ongoing across multiple tumors

1	**inavolisib (INAVO120)**	1L *PIKC3A*m HR+/HER2- mBC (AI resistant)
2	**inavolisib (INAVO121)**	Post-CDK4/6i *PIKC3A*m HR+/HER2- BC
3	**inavolisib (INAVO123)**	1L *PIKC3A*m HR+/HER2- mBC (AI sensitive)
	inavolisib (INAVO122)	1L *PIKC3A*m HER2+ BC

✔ US/EU filing completed

[1] Risk definitions vary according to guidelines and tools used: stage at diagnosis based on internal estimates using SEER data; AI=aromatase inhibitor, ET=endocrine therapy, eBC=early breast cancer, mBC=metastatic breast cancer, neoadj=neoadjuvant, adj=adjuvant

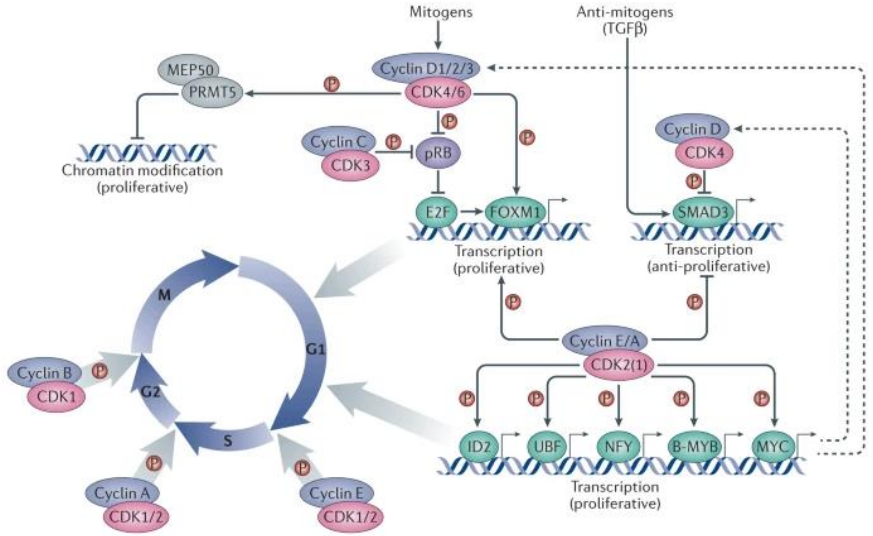
Roche

Regor Therapeutics Group

Next generation CDKi portfolio acquired from Regor

RGT-419B is the most advanced CDK4/2 inhibitor in the clinic

CDKi are critical regulators of cell cycle progression



- Side effects of 1st gen CDK4/6i and intermittent dosing limit the therapeutic benefit; AEs include neutropenia, diarrhea, and QT prolongation
- CDK4/6i resistance remains a challenge; nearly all patients progress
- Data suggest that CDK2 activity is a potential mechanism of resistance with first generation CDK4/6i having weak or no CDK2 activity

Next generation CDKi portfolio

Potent CDK4 inhibition with activity on CDK2[2]

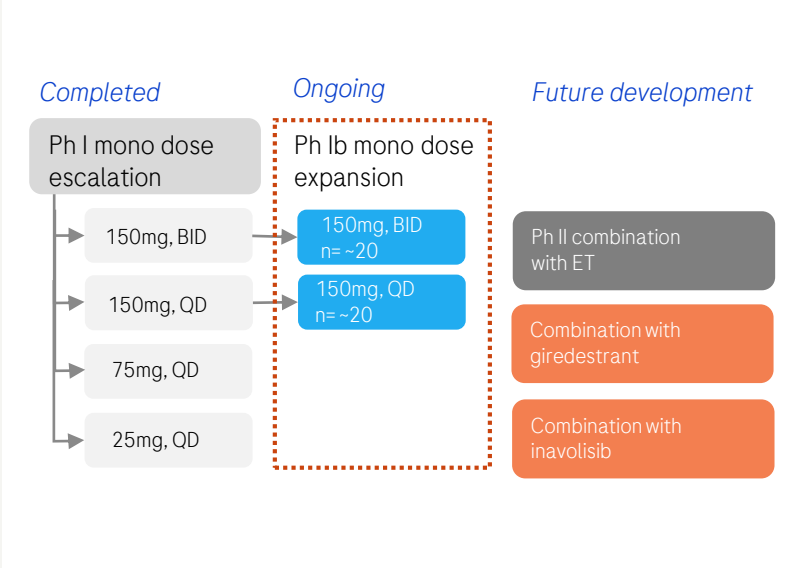
Biochemical Ki (nM)	CDK4/ Cyclin D1	CDK2/ CyclinE1
RGT-419B[1]	0.3	4.6
Abemaciclib	0.8	270
Palbociclib	2.3	>10[3]
Ribociclib	6.7	>10[3]

- RGT-419B is a potent CDK4 inhibitor with increased activity on CDK2 addressing a key mechanism of resistance to existing therapies
- RGT-587 is a Ph I ready brain-penetrant selective CDK4i

Hydbring et al. Nature Reviews, Molecular Cell Biology 2016; [1]Wander et al SABCS 2023 [2]Regor data on file; AEs=adverse events

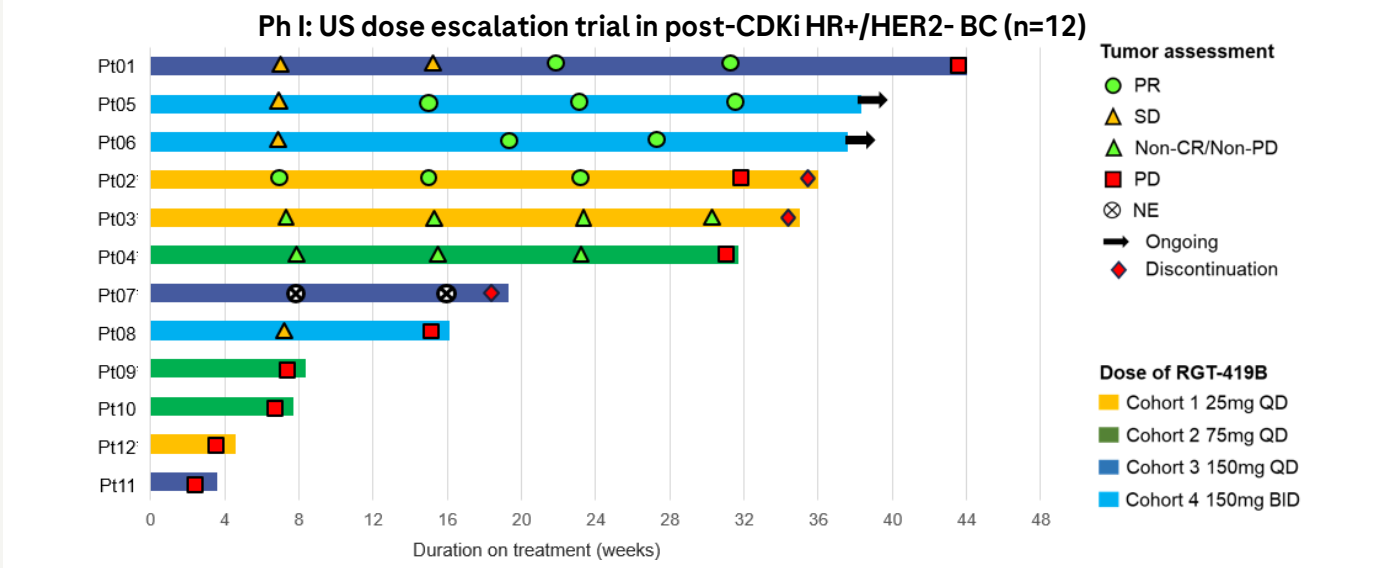
RGT-419B has best-in-class potential as next-gen CDKi in HR+ BC

Targeting expansion into 1L and eBC



- Ph Ib dose expansion ongoing in post-CDKi pts
- Ph II in combination with ET to be initiated in 2025
- Plan to initiate combinations with giredestrant and inavolisib in HR+ BC

Durable single agent activity in pts who have progressed on CDK4/6i



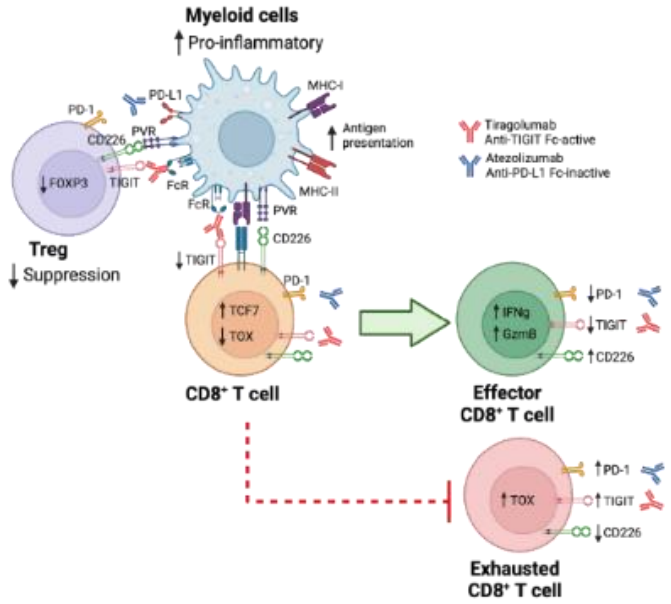
- RGT-419B can be dosed continuously with acceptable tolerability[1]
- Favorable PK profile with sustained target coverage
- Demonstrated monotherapy activity in post-CDK4/6i setting with durable responses

CDKi market expected to grow to USD >15bn by 2030, including expansion into eBC[2]

[1]Regor Therapeutics preliminary data on file, data cutoff date: Dec 22, 2023; [2] Evaluate Pharma; ET=endocrine therapy; eBC=early breast cancer; HR+ BC=hormone receptor positive breast cancer; CR=complete response; NE=not evaluable; QD=once daily; BID=twice daily; PD=progressive disease; PR=partial response; SD=stable disease; PFS=progression free survival; PK=pharmacokinetic

Multiple upcoming readouts for tiragolumab

Final OS results for Ph III (SKYSCRAPER-01) in 1L PD-L1 high NSCLC expected in Q4 2024



Tiragolumab development program

	Indication	Ph I	Ph II	Ph III	
Lung cancer	1L NSCLC: PD-L1 high	SKYSCRAPER-01			2024
	Stage III unres. NSCLC	SKYSCRAPER-03			2025
GI cancer	Locally advanced ESCC	SKYSCRAPER-07			
	1L uHCC	SKYSCRAPER-14/IMbrave152			
Others	Fixed-dose combination	SKYSCRAPER-11			

- Following negative results of Ph II/III (SKYSCRAPER-06), Ph II (SKYSCRAPER-05) and Ph III (SKYSCRAPER-15) in early NSCLC have been discontinued
- Ph III (SKYSCRAPER-01) in 1L PD-L1 high NSCLC final OS results expected in Q4 2024
- Ph III (SKYSCRAPER-03) in Stage III unresectable NSCLC, Ph III (SKYSCRAPER-07) in locally advanced ESCC, and Ph III (SKYSCRAPER-14) in 1L HCC results expected in 2025/26

Guan et al., Nature 2024; NSCLC=non-small cell lung cancer; PD-L=programmed death ligand; (Neo)Adj=(neo) adjuvant; ESCC=esophageal squamous cell carcinoma; uHCC=unresectable hepatocellular cancer; SCCHN=squamous cell cancer of the head and neck; OS=overall survival

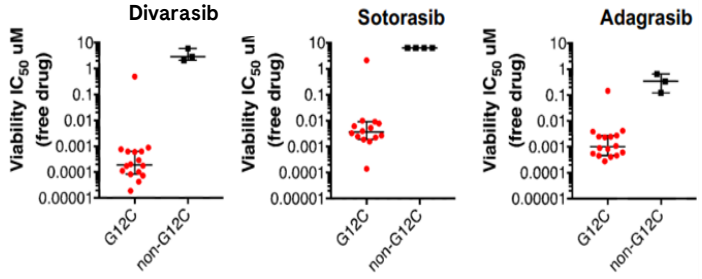
Divarasib with best-in-class potential in KRAS G12C-mutated tumors

Ph I data in 2L+ mNSCLC show improved mPFS with longer follow-up

FDA BTD

KRAS G12C inhibitor

Proliferation potency/selectivity[1]

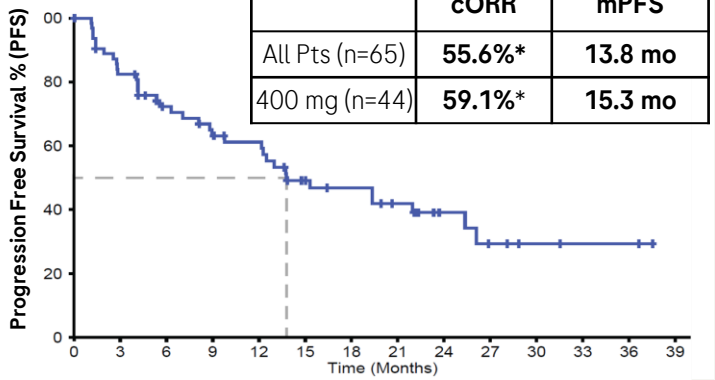


- Divarasib is an irreversible covalent inhibitor of mutant KRAS G12C resulting in a locked inactive conformation
- Divarasib is 5 to 25 times more potent and 10 to 50 times more selective *in vitro* than sotorasib and adagrasib[1]

Updated data at WCLC 2024

Ph I results in 2L+ mNSCLC[2]

	cORR	mPFS
All Pts (n=65)	**55.6%***	**13.8 mo**
400 mg (n=44)	**59.1%***	**15.3 mo**



- With additional follow-up, divarasib continued to demonstrate durable clinical activity with confirmed ORR of 59.1% and mPFS of15.3 months at 400 mg dose
- Divarasib + PD-L1 demonstrated promising clinical activity and tolerable safety with low rates of Grade ≥3 LFT abnormalities

Development program

Indication	Regimen	Ph I	Ph II	Ph III
1L mNSCLC	Divarasib +/- IO +/- chemo**	FPI exp 2025		
2L+ mNSCLC	divarasib vs sotorasib/adagrasib	Krascendo 1		
CRC	divarasib	Ph II		

- Ph III H2H trial vs. sotarasib/adagrasib in 2L NSCLC initiated (FPI Q3 2024); granted FDA BTD in 2L NSCLC
- Ph III in 1L NSCLC to be initiated in 2025
- Additional combinations ongoing including: pembrolizumab, inavolisib

[1] Purkey H. et al., AACR 2022; 2 Sacher et al., WCLC 2024; *Patients with measurable disease (all patients n=63, 400mg n=44); **Ph III 1L NSCLC regimen to be disclosed at a later stage
mNSCLC=metastatic non-small cell lung cancer; (m)PFS=(median) progression free survival; ORR=objective response rate; LFT=liver functional test; BTD=Breakthrough Therapy Designation

Hematology pipeline

A broad portfolio enabling unique combinations

Ph I

RG6076	**englumafusp alfa** Heme tumors
RG6160	**cevostamab** r/r MM
RG6323	**efbalropendekin alfa** Heme tumors
RG6538[1]	**P-BCMA-ALLO1** MM
RG6540[1]	**P-CD19xCD20-ALLO1** Heme tumors
RG7828	**Lunsumio SC** 3L+ CLL

Ph II

RG6107	**PiaSky** SCD
RG6512	**NXT007** Hemophilia A
RG6357[2]	**dirloctocogene samoparvovec** Hemophilia A
RG7828	**Lunsumio SC** 3L+ FL

Ph III

RG6026	**Columvi** 1L DLBCL, r/r MCL
RG7828	**Lunsumio** 1L & 2L+ FL & 2L+ DLBCL
RG6107	**PiaSky** aHUS
RG7601	**Venclexta** 1L MDS

Registration

RG6026	**Columvi** 2L+ DLBCL

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

[1] managed by Poseida Therapeutics; [2] Ph III trial paused and HemA gene therapy approach being re-evaluated; CLL=chronic lymphocytic leukemia; SCD=sickle cell disease; FL=follicular lymphoma; DLBCL=diffuse large B-cell lymphoma; MCL=mantle cell lymphoma; aHUS=atypical hemolytic uremic syndrome; MDS=myelodysplastic syndrome

Comprehensive development program across B-cell malignancies

Ph III trials for Lunsumio and Columvi in 1L FL and DLBCL initiated

POLIVY polatuzumab vedotin

- Strong 1L DLBCL uptake with >33k pts treated globally; treatment guidelines as 1L DLBCL SoC in 18 countries
- POLARIX 5y data submitted to an upcoming medical congress

Lunsumio mosunetuzumab

- For outpatient setting, indolent disease (FL) and elderly/unfit pts
- Approved in 3L+ FL: 20% US patient share, ~1,200 patients treated to date

COLUMVI glofitamab

- For aggressive disease (1L DLBCL, R/R DLBCL, MCL)
- Approved in 3L+ DLBCL: 17% US patient share, ~1,400 patients treated to date

Regimen	Indication	Ph I / Ph II / Ph III	
Polivy + R-CHP	1L DLBCL	POLARIX	✓ US/EU approved
Lunsumio	3L+ FL		✓ US/EU approved
Lunsumio SC	3L+ FL		✓ Co-PEP met
Lunsumio SC	3L+ CLL		
Lunsumio SC + POLIVY	2L DLBCL (SCT-ineligible)	SUNMO	Readout 2025
Lunsumio + lenalidomide	2L + FL	CELESTIMO	Readout 2025
Lunsumio SC + lenalidomide	1L FL	MorningLYTE	
Lunsumio + POLIVY	1L DLBCL (elderly/unfit)		
COLUMVI	3L + DLBCL		✓ US/EU approved
COLUMVI + GemOx	2L+ DLBCL (SCT-ineligible)	STARGLO	✓ PEP of OS met
COLUMVI + Polivy + R-CHP	1L DLBCL	SKYGLO	
COLUMVI	R/R MCL (post-BTKi)	GLOBRYTE	FDA BTD
COLUMVI + englumafusp alfa	r/r NHL		
P-CD19xCD20-ALLO1	r/r B-cell malignancies		
P-BMCA-ALLO1	r/r Multiple myeloma		

[1] NHL=Non-hodgkin lymphoma; 1L=first line; 2L+=second line or later; 3L+=third line or later; FL=follicular lymphoma; (Co)-PEP=co-primary endpoint; DLBCL=diffuse large B-cell lymphoma; MCL=mantle cell lymphoma; CRS=Cytokine release syndrome; CR=complete response; CAR=chimeric antigen receptor; P-CD19CD20-ALLO1 and PBCMA-ALLO1 in collaboration with Poseida Therapeutics

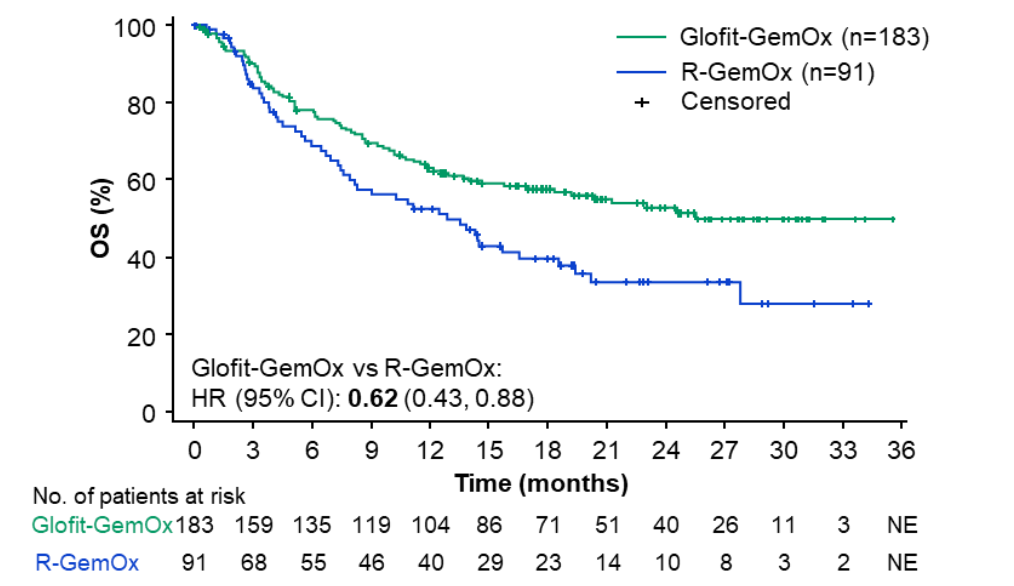
Ph III (STARGLO) Columvi + GemOx reduces risk of death by 41% in 2L DLBCL[1,2]

Columvi is the first CD20xCD3 bispecific to demonstrate an OS benefit in DLBCL

Columvi + GemOx significantly improved PFS and CR rates[1,3,4]

	R-GemOx (n=91)	Columvi + GemOx (n=183)
Median OS, months[3]	12.9	25.5
OS HR	0.62 (p=0.006)	
Median PFS, months[4]	3.6	13.8
PFS HR	0.40 (p<0.000001)	
ORR	40.7%	68.3%
CR	25.3%	58.5%
ΔCR rate	33.2% (p<0.0001)	

Median OS for Columvi + GemOx was nearly double that of R-GemOx[1,3]



- Columvi + GemOx was tolerable, with AEs consistent with study drugs; CRS generally occurred in cycle 1 and was mostly low grade
- Ph III (STARGLO) has been submitted to health authorities including FDA and EMA

[1]Abramson et al, EHA 2024. Oral presentation LB3438. [2]Data from primary analysis (median follow-up: 11.3 months); [3]Data from updated analysis (median followup 20.7 months); [4]Data from updated analysis (median follow.up 16.1 months). CI=confidence interval; HR=hazard ratio; NE=not evaluable; CR=complete response; ORR=overall response rate; OS=overall survival; R=Rituxan; GemOx=gemcitabine+oxaliplatin; PFS=progression free survival

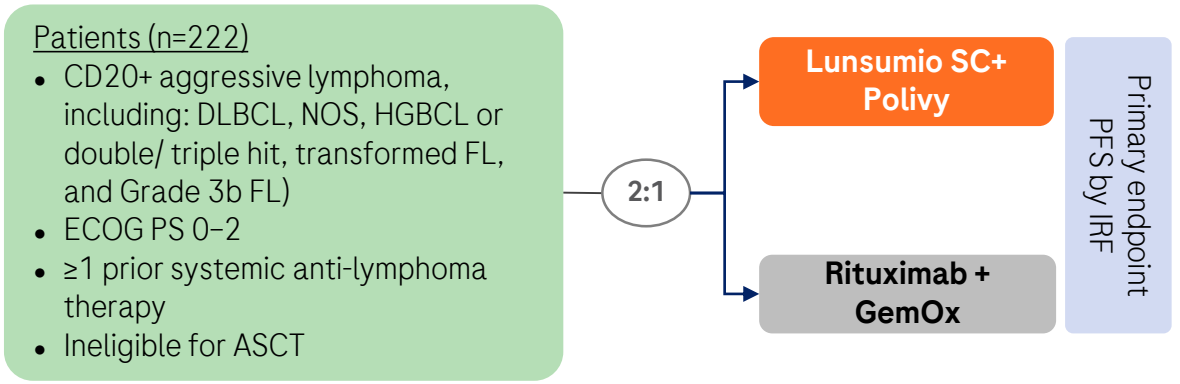
Ph III (SUNMO) chemo-free combo of two unique MoAs in 2L DLBCL

High activity and durable responses for patients unable to tolerate chemo

Ph Ib/II (GO40516): Lunsumio + Polivy with durable ORR and CR rates in R/R LBCL[2]

Efficacy endpoints	Overall population[1] (n=98)
ORR, %	59%
CR, %	46%
Median DOR, months	20.8 (14.2-NE)
Median PFS, months	11.4 (6.2-18.7)
Median OS, months	23.3 (14.8-NE)

Ph III (SUNMO): Lunsumio SC + Polivy in 2L+ R/R aggressive LBCL[3]



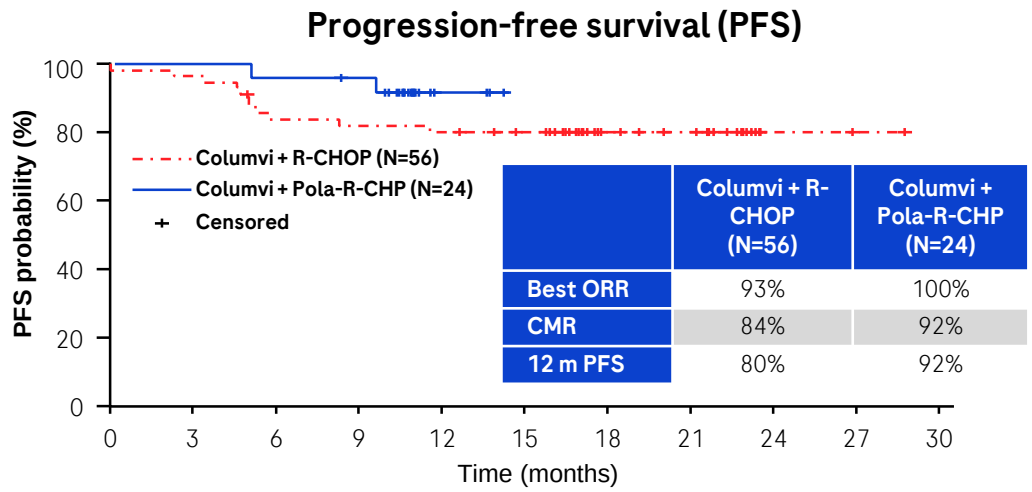
- Durable ORR and CR benefits despite poor response to 1L[1,2]; combination could offer benefit for R/R DLBCL pts ineligible for chemo
- Potential synergistic effects via different mechanisms of action and cell-surface targets
- Ph III (SUNMO) results expected to readout in 2025

[1] Budde et al. 2024; Nature Medicine 30, 229–239; [2]Assouline et al., ASCO 2024; [3]Pavlovsky et al., ICML 2023. *Refractory was defined as SD, PD, PR, or CR with relapse <3 months after first-line therapy. Relapse was defined as CR with relapse ≥3 and ≤12 months after 1L therapy. CR=complete response; ORR=overall response rate; DOR=duration of response; PFS=progression free survival; OS=overall survival; NE=not evaluable; LBCL=large B-cell lymphomas; DLBCL=diffuse large B-cell lymphoma; NOS=not otherwise specified; HGBCL=high grade B-cell lymphoma; FL=follicular lymphoma; GemOx=gemcitabine + oxaliplatin; ASCT=autologous stem cell transplant; R/R=relapsed/refractory; SC=subcutaneous; ECOG PS=Eastern Cooperative Oncology Group Performance Status

Ph III (SKYGLO) Columvi + Polivy-R-CHP in 1L DLBCL

Early data support potential for Columvi in combination with current SoC

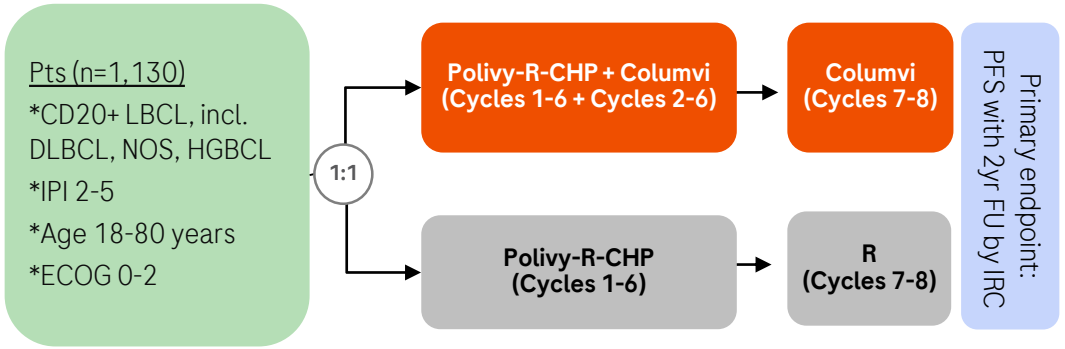
Ph Ib (NP40126): Columvi in + Pola-R-CHP and Columvi + R-CHOP with high response rates & promising PFS[1]



	Columvi + R-CHOP (N=56)	Columvi + Pola-R-CHP (N=24)
Best ORR	93%	100%
CMR	84%	92%
12 m PFS	80%	92%

Median follow-up: 20.3 months for Columvi + R-CHOP; 12.1 months for Columvi + Pola-R-CHP

Ph III (SKYGLO): Columvi + Polivy-R-CHP in 1L DLBCL



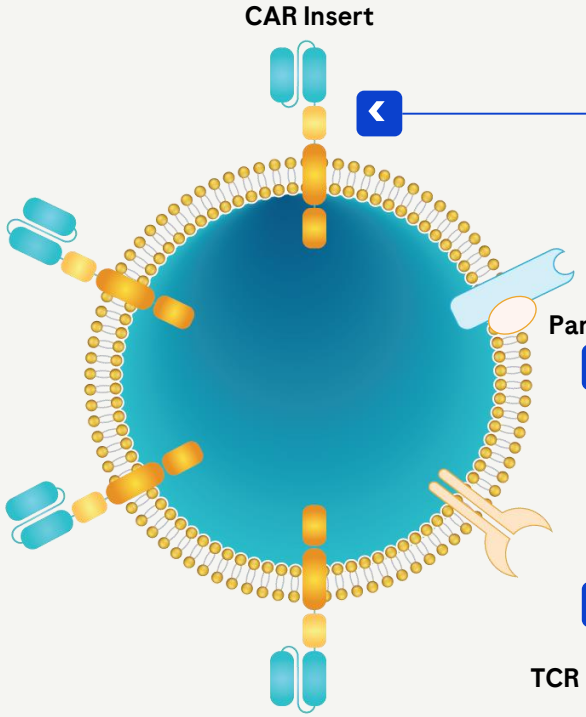
- Columvi + Pola-R-CHP demonstrate durable responses with high ORR and CMR rates; manageable safety profile (CRS any Grade:11.3 %, Grade 1: 8.8%, Grade 2: 2.5%, Grade 3+: 0%[2])
- Ph III (SKYGLO) Columvi + Polivy-R-CHP in 1L DLBCL has the potential to further enhance cure rates with minimal safety concerns; FPI achieved in 2023, recruitment on track

[1] Topp M et al, ASH 2023; [2]Data on file. DLBCL=diffuse large B cell lymphoma; ORR=overall response rate; CMR=complete metabolic response; R-CHOP=Rituxan + cyclophosphamide + doxorubicin + vincristine + prednisone; Pola-R-CHP=Polivy + Rituxan + cyclophosphamide + hydroxydaunorubicin + prednisone; PFS=progression free survival; SoC=standard of care; NOS=not otherwise specified; HGBCL=high grade B-cell lymphoma; IPI=International prognostic index; ECOG=Eastern Cooperative Oncology Group; IRC=independent review committee; FU= follow-up; yr=year

Allogeneic CAR-Ts for hematologic malignancies

Partnership with Poseida Therapeutics

Proprietary technologies set Poseida apart



piggyBac

Non-viral, transposon-based system

- Can stably integrate DNA into the genome
- High efficiency transposase carries large DNA cargo
- Preferential insertion into T_{SCM}
- Single-step multi-gene insertion
- Efficient and cost effective

Cas-CLOVER

Gene editing system

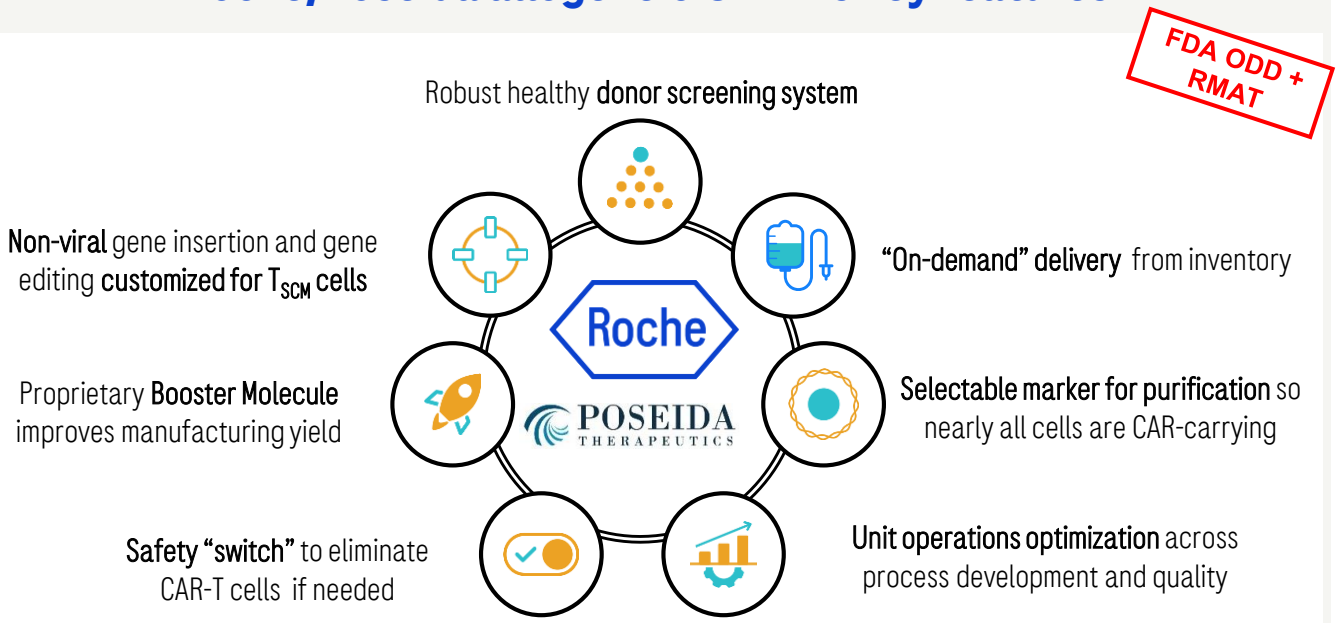
- High-fidelity, gene editing with low to no off-target activity
- Preserves T_{SCM} cell type
- Ease of design in cell therapy, lower cost
- 25x greater fidelity vs. CRISPR-Cas9

Figure adapted from Dholaria et al. Presented at IMS 2024

COG=cost of goods; Tscm=stem memory T cells; CAR-Ts=chimeric antigen receptor T-cells; MHC=Major histocompatibility complex; TCR=T-cell receptor B2M=beta-2-microglobulin

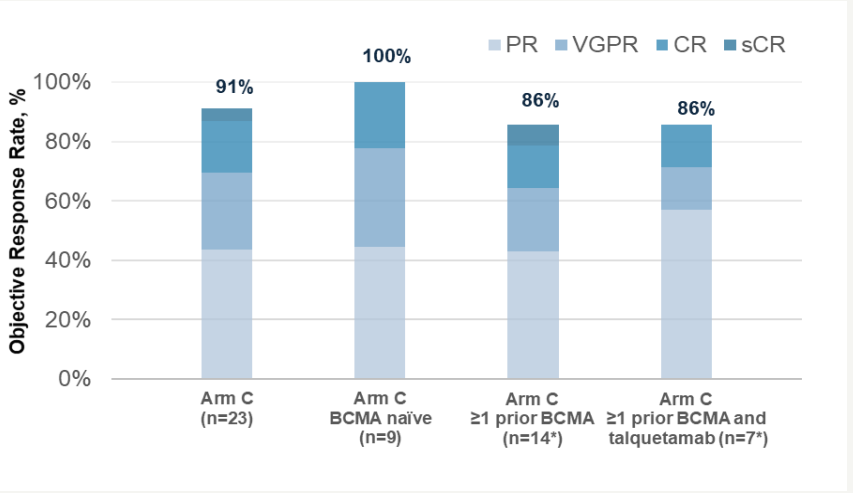
CAR-Ts are complementary to Roche's pipeline

Roche/Poseida allogeneic CAR-Ts key features



- Technology features set Poseida ALLO-CARTs apart as potentially best-in-class
- Exclusive license to P-BCMA-ALLO1 and P-CD19CD20-ALLO1 currently in Ph I
- FDA awarded P-BCMA-ALLO1 orphan drug designation (ODD) for treatment of MM, and Regenerative Medicine Advanced Therapy Designation (RMAT) for R/R MM

High rate of deep responses in R/R MM[1]



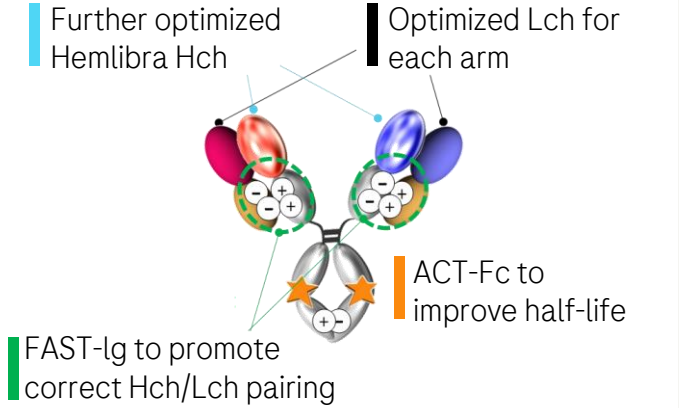
- Full ITT population received lymphodepletion and P-BCMA-ALLO1; several pts received treatment in outpatient setting
- Well tolerated, with no GvHD and low rates of CRS
- Strong clinical activity in heavily pretreated population, including in BCMA-exposed patients
- Activity comparable to auto BCMA CAR-Ts

Poseida company website; [1]Dholaria et al. Presented at IMS 2024
CAR-T=chimeric antigen receptor T-cell; ADC=antibody-drug conjugate; MM=multiple myeloma ODD=orphan drug designation; RMAT=regenerative medicine advanced therapy designation, RR=relapsed refractory; BCMA=B-cell maturation antigen; LD=lymphodepletion; ITT=Intention to treat

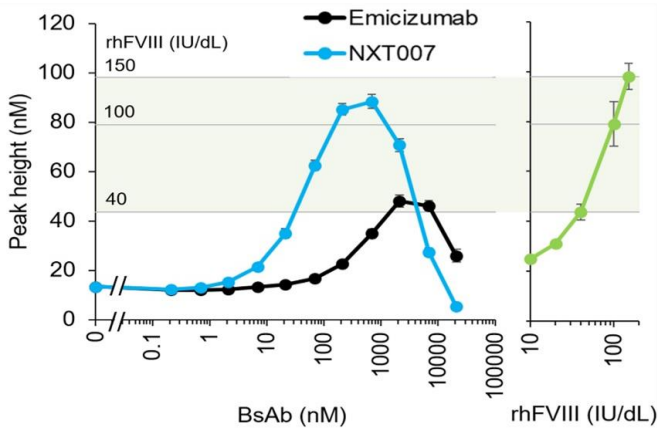
NXT007: A next-generation Factor VIIIa mimetic bispecific mAb

Brings together FIXa and FX to normalise the hemostatic potential of the clotting cascade

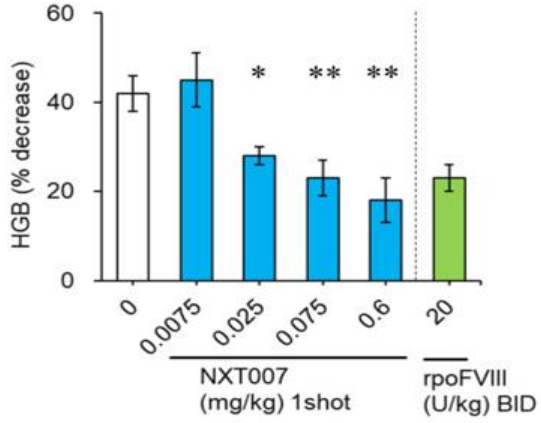
Optimized structure and function based on Hemlibra[1]



NXT007 promotes thrombin generation within non-hemophilic ranges[2]



Dose dependent protection from bleeding in NHP hemophilia model[2]



- NXT007 has the potential to allow people with Hem A to achieve zero treated bleeds with no need for additional factor treatment, by normalising the hemostatic potential at steady state (bleed control equivalent to people without Hem A)
- Engineered based on Hemlibra, to enhance binding affinities, extend half-life, and allow for low volume, infrequent subcutaneous injections
- NXT007 is ~30-fold more potent than Hemlibra and *in vitro* assay indicates that thrombin generation is within the range of people without Hem A[2]
- Using a relatively small injection volume via a device, NXT007 could be a next generation prophylaxis treatment to people with Hemophilia A offering reduced treatment burden with a favorable safety profile
- Ph II data expected in 2025

[1]Koga et al. MABS 2023, 15 (1), 2222441; [2]Teranishi-Ikawa et al. Journal of Thrombosis and Haemostasis 2024.22 (2):430-440; NXT007 developed in collaboration with Chugai; mAb=monoclonal antibody; FIXa=factor 9a; FX=factor 10; FVIIIa=factor 8a; Lch=light chain; Hch=heavy chain; BsAb=bispecific antibody; HGB=hemoglobin; SoC=standard of care

Neurology

Azad Bonni
SVP and Global Head of Neuroscience & Rare Diseases,
Roche Pharma Research & Early Development

Neurology R&D focus areas

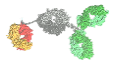
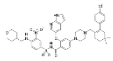
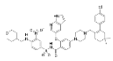
Preserving what makes people who they are

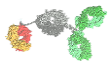
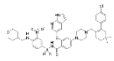
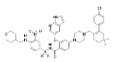
Multiple sclerosis	Neuromuscular disorders	Neurodegenerative diseases
Stop, reverse and prevent MS and preserve quality of life	***Create a future of strength and independence in NMD***	***Slow progression of Parkinson's and Alzheimer's disease***
Recent examples		
Ocrevus (IV/SC/HD) *First-in-class anti-CD20 approved for RMS and the only anti-CD20 for PPMS*	***Elevidys*** *First FDA approved DMD gene therapy*	***Prasinezumab*** *mAb for PD that selectively binds aggregated α-synuclein*
Fenebrutinib *Oral, highly selective and only reversible non-covalent BTK inhibitor in Ph III in RMS and PPMS*	***GYM 329*** *Anti-latent myostatin mAb with monthly subcutaneous administration*	***Trontinemab*** *First Aβ-targeting mAb Brainshuttle™ for AD Ph Ib/II currently ongoing*

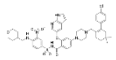
PD=Parkinson's Disease; AD=Alzheimer's Disease; NMD=neuromuscular disease; DMD=Duchenne muscular dystrophy; SMA=spinal muscular atrophy; FSHD=facioscapulohumeral muscular dystrophy; IV=intravenous; SC=subcutaneous; HD=high dose; RMS=relapsing multiple sclerosis; PPMS=primary progressive multiple sclerosis; MS=multiple sclerosis, mAb=monoclonal antibody; BTK=Bruton tyrosine kinase

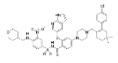
Neurology pipeline

Industry leading portfolio differentiated on targets and platform technologies

Ph I		
	RG6035	**Brainshuttle™ CD20** Multiple Sclerosis
	RG6182	**MAGLi** Multiple Sclerosis
	RG6418	**selnoflast** Parkinson's

Ph II		
	RG7935	**prasinezumab** Parkinson's
	RG6102	**trontinemab** Alzheimer's
	RG6289	**Gamma-secretase modulator** Alzheimer's
	RG6100	**bepranemab**[1] Alzheimer's
	RG6042	**tominersen** Huntington's
	RG6237 + RG7916	**GYM 329 + Evrysdi** SMA RD
	RG6237	**GYM 329** FSHD RD
	RG6356	**Elevidys**[2] DMD (0-<4 y.o.) RD
	RG7816	**alogabat** Angelman Syndrome

Ph III		
	RG6168	**Enspryng** MOG-AD RD
	RG6168	**Enspryng** AIE RD
	RG7845	**fenebrutinib** Multiple Sclerosis
	RG1594	**Ocrevus high dose** Multiple Sclerosis
	RG6356	**Elevidys**[2] DMD (>8 y.o.*) RD

Registration		
	RG7916	**Evrysdi 5mg tablets** SMA RD

 Small molecule

 Antibody

 Gene therapy

 Brainshuttle™

 Locked nucleic acid/antisense

- Neuroimmunologic disorders
- Neurodegenerative diseases
- Neurodevelopmental disorders
- Neuromuscular disorders
- RD = Rare disease

[1]bepranemab in partnership with UCB, studies are currently run by UCB; [2]Elevidys in partnership with Sarepta Therapeutics; *ambulatory, 8-<18 yrs; non-ambulatory, all ages)
NMOSD=neuromyelitis optica spectrum disorders; DMD=Duchenne muscular dystrophy; SMA=spinal muscular atrophy; FSHD=facioscapulohumeral muscular dystrophy; MOG-AD=myelin oligodendrocyte glycoprotein antibody-associated disease; AIE=autoimmune encephalitis; MAGL=monoacylglycerol lipase; y.o.=year old

Fenebrutinib is a highly selective, non-covalent, brain-penetrant BTKi

Fenebrutinib with best-in-class potential, highly differentiated vs. covalent BTKis

Development program

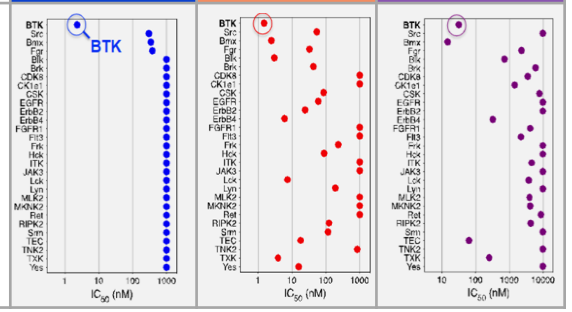
Ind.	Vs.	Ph I > Ph II > Ph III
RMS	placebo	*FENopta* ✔
RMS	teriflunomide	*FENhance 1*
RMS	teriflunomide	*FENhance 2*
PPMS	Ocrevus	*FENtrepid*

- All Ph III studies in RMS and PPMS to read out in 2025
- Ph III (FENtrepid) in PPMS is the only H2H study vs Ocrevus

Fenebrutinib PK profile vs other BTKis [1]

Fenebrutinib	Tolebrutinib	Evobrutinib	Remibrutinib
Non-covalent Reversible	Covalent Irreversible	Covalent Irreversible	Covalent Irreversible
WB B cell IC_{50}: 8 nM	10 nM	84 nM	18 nM
WB Myeloid cell IC_{50}: 31 nM	166 nM	1660 nM	67 nM
Selectivity High	Low	Low	High
RMS, PPMS (vs Ocrevus)	RMS, SPMS, PPMS (vs placebo)	RMS	RMS

Fenebrutinib selectivity vs. other BTKis[3]

	Fenebrutinib	Tolebrutinib	Evobrutinib
Inhibition of BTK and off-target kinases			

- Fenebrutinib binds reversibly to BTK with kinetics that may positively influence efficacy and safety
- Fenebrutinib is the most potent BTKi in the inhibition of FcR and BCR signalling[2]
- In an *in vitro* kinase activity assay, fenebrutinib only inhibited three off-target kinases[3]

Fenebrutinib could disrupt the oral market segment, currently comprising >40% of the global MS market

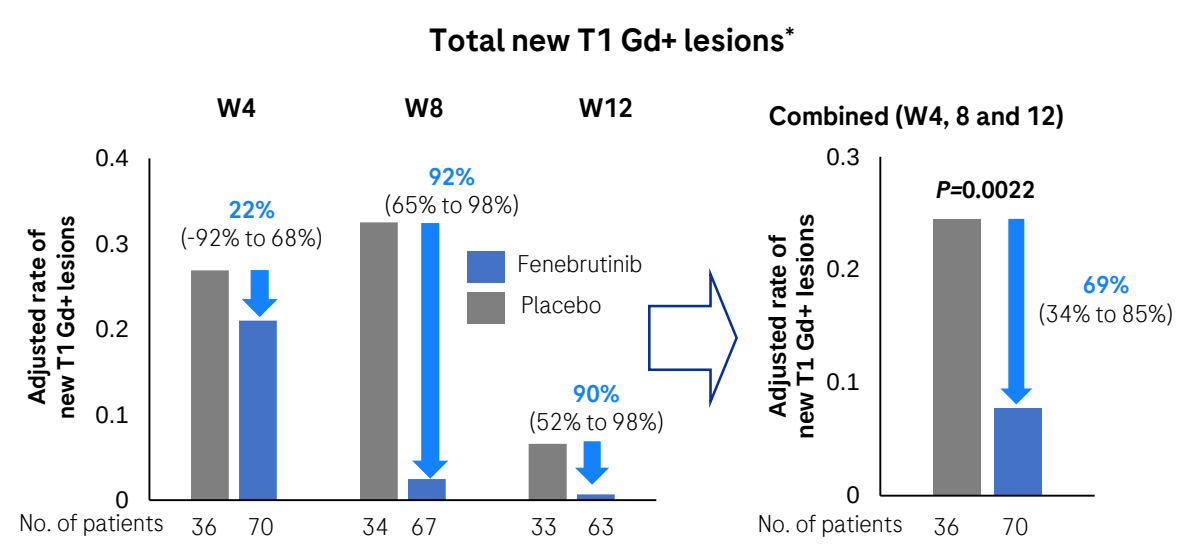
[1]Kramer, et al. (2023) Nat Rev Neurol. 2023;19(5):289-304 ;Crawford et al.(2018) J Med Chem 61, 2227-2245; Francesco et al., ACTRIMS-ECTRIMS (2017) 200644. Haselmayer et al. (2019) J Immunol 202, 2888-2906; Angst et al. (2020) J Med Chem 63, 5102-5118; [2]Weber MS, et al. AAN 2021 (Oral presentation P15.091); [3]Johnson et al. Presented at MSVirtual 2020 (Presentation number P0338) H2H=head-to-head; MS=Multiple sclerosis; RMS=relapsing multiple sclerosis; PPMS=primary progressive multiple sclerosis; SPMS=Secondary progressive multiple sclerosis; BTK=Bruton's tyrosine kinase; nM=nanomolar; WB=whole blood; *As of Sept 2024: including non-MS Ph I/II studies

Ph II (FENopta) with compelling RMS data at weeks 12 and 48

Rapid and sustained suppression of disease activity

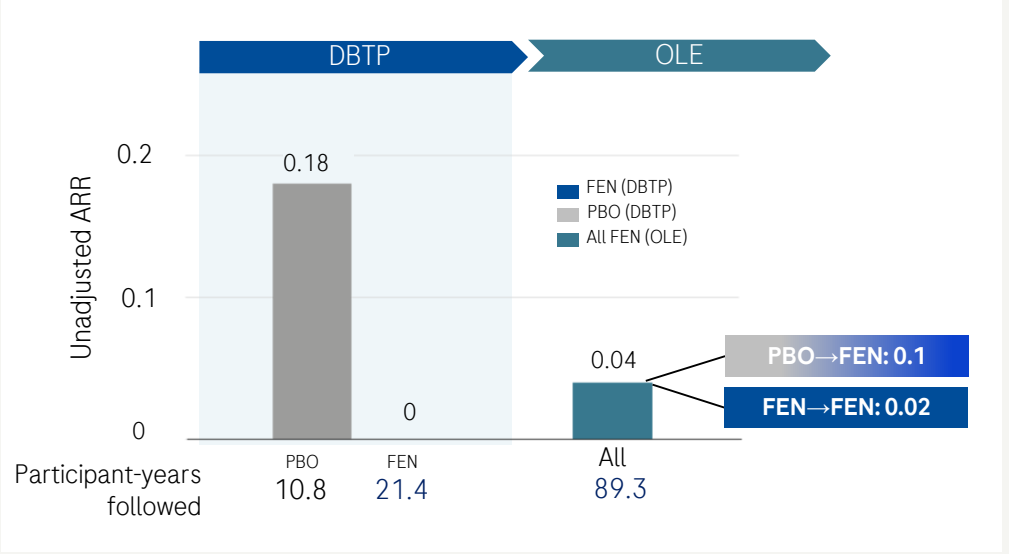
ECTRIMS 2024

Ph II (FENopta) double-blind period at weeks 4, 8, 12[1]



- Rapid onset of T1 Gd+ lesion reduction from W4 onwards with relative reductions of 92%/90% in W8/W12
- CSF concentration sufficient to reduce B-cell & microglia activity *in vitro*
- Safety profile consistent with previous studies in non MS indications[3]

Ph II (FENopta) open label extension at week 48[2]



- 97% of patients remained in the OLE until week 48
- 96% of patients were relapse free with an ARR of 0.04
- 99% of patients were free from new T1 Gd+ lesions
- The median change from baseline in EDSS for each arm was zero

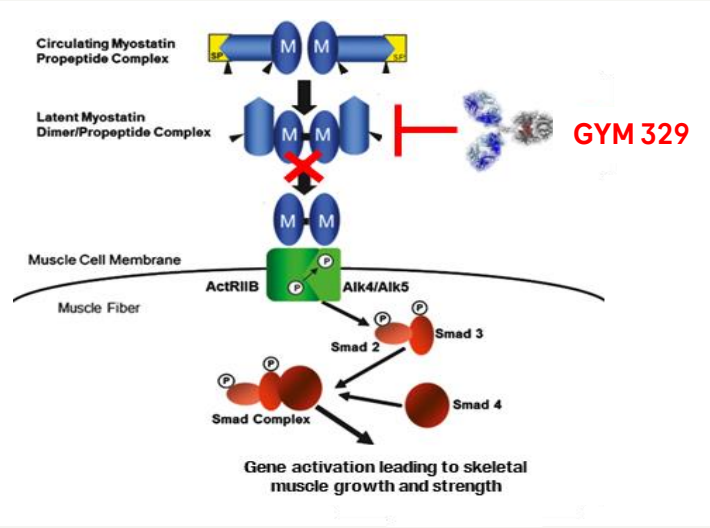
[1]Hua et al. 2023 European Journal of Neurology, 30 (Suppl. 1), 431–542: EPO688; [2]Bar-Or et al. Presented at ECTRIMS 2024; [3]Oh et al. MSJ 2024;30(IS):18-270; Abstract P094

*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; CSF=cerebrospinal fluid; RMS=relapsing multiple sclerosis; Gd+=gadolinium-enhancing; DBTP=double blind treatment period; OLE=open label extension; W=week; EDSS=expanded disability status scale; PBO=placebo; FEN=fenebrutinib; ARR=annualized relapse rate

GYM 329 (anti-latent myostatin mAb) to promote muscle growth in SMA

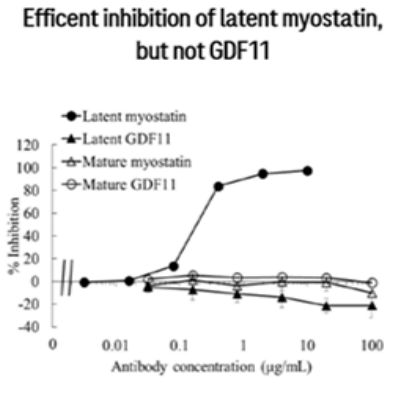
Ph II (MANATEE) Part 1 results expected in 2025

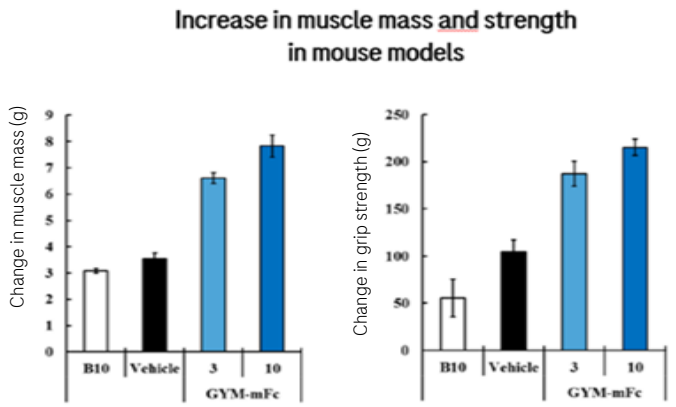
GYM 329 (Anti-latent myostatin mAb)



- GYM 329 inhibits latent myostatin, a key negative regulator of skeletal muscle growth and strength
- Unique sweeping[1] and recycling technology allows Q4W SC dosing and highly specific myostatin inhibition, but not GDF11, the related muscle hormone[2]

Pre-clinical data in a mouse models of muscle disease[2]





Combination rationale

Evrysdi treats the underlying disease, SMA, throughout the CNS and in peripheral tissues

GYM 329 targets skeletal muscles to increase their size and strength

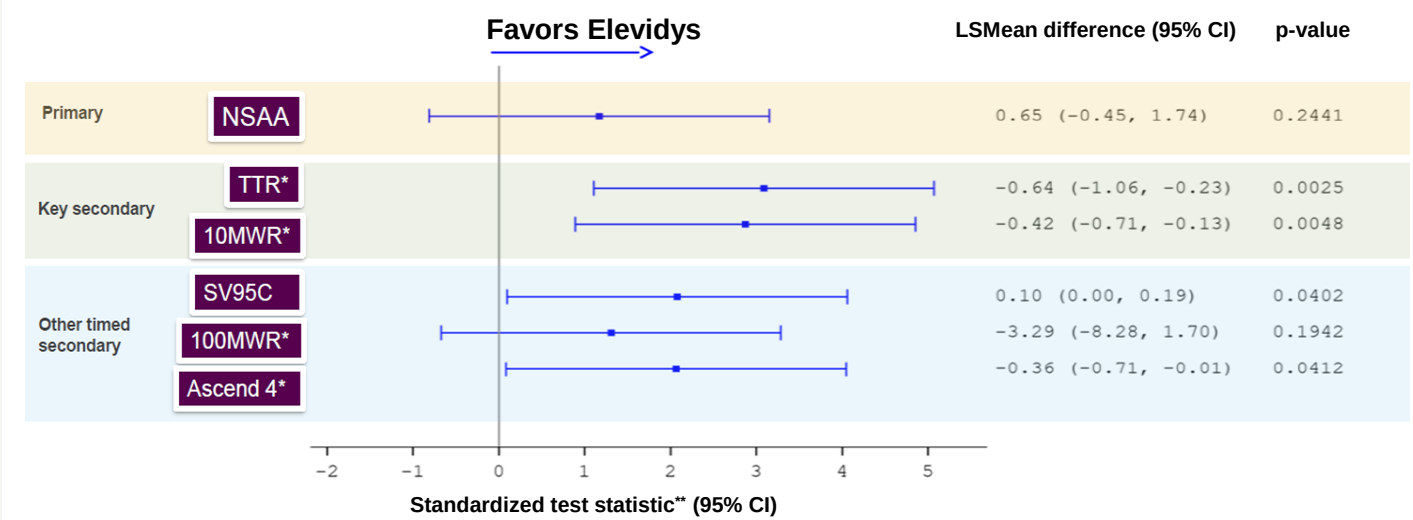
- Preclinical studies show that GYM 329 has superior muscle strength-improvement effects in mice vs other anti-myostatin therapies[2]
- The combination of myostatin inhibition and SMN2 splice modification ameliorates muscle atrophy in an animal model of SMA[3]
- Ph II/III (MANATEE) GYM 329 + Evrysdi in SMA ongoing; Part 1 (n=36) to select the optimal dose; Part 2 (n=144) assesses the efficacy and safety of the selected optimal dose

[1]Igawa et al. Immunol. Rev. 2016;270:132–151; [2]Muramatsu H. et al., Nature Scientific Reports 2021. [3]Feng et al. Human Molecular Genetic. 2016: 25(5: 964–975; SC=subcutaneous; mAb=monoclonal antibody; SMA=spinal muscular atrophy; BL=baseline; PD=pharmacodynamics; PK=pharmacokinetics; RHS=Revised Hammersmith Scale; FSHD=facioscapulohumeral muscular dystrophy; GYM 329 in collaboration with Chugai

Elevidys providing clinically meaningful benefits in DMD

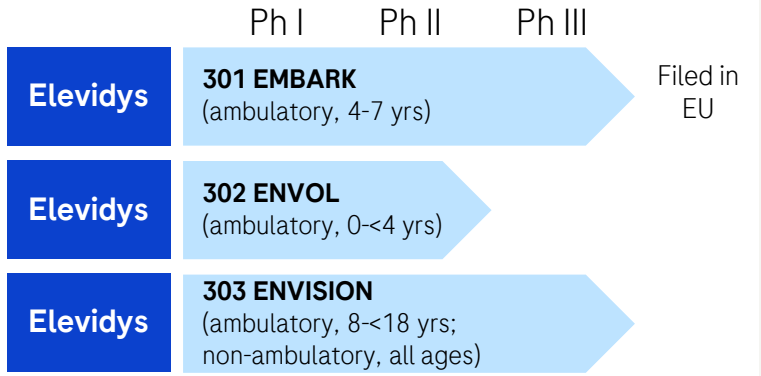
EU filing completed in DMD patients aged 3-7 years; final decision expected in H2 2025

Ph III (EMBARK) results in DMD



- Ph III (EMBARK) in DMD favors Elevidys treatment for all key secondary endpoints
- The positive benefit-risk profile is supported by the totality of the efficacy data and its consistent, monitorable, and manageable safety profile[1]
- First and only GT approved for ambulatory & non-ambulatory DMD pts 4 yrs and older
- Positive experience with first ex-US patients[2] across 5 countries with over 400 patients treated globally across clinical and commercial settings

Key development projects



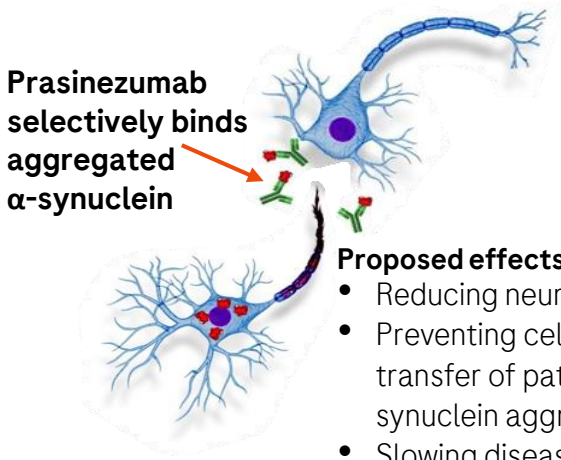
- Largest clinical program to support broader DMD populations across various ages and ambulatory status
- EMBARK Part 2 will provide 2-year follow-up data from Part 1 patients

[1]Mendell et al. 2024 Pediatric Neurology;153:11-18. [2]US approval by partner Sarepta, Roche approval 6 countries ex-US; *Timed function tests sign reversed to align favorable directions among effect endpoints; **Blue lines plot standardized t test statistic (+/- 1.96) after dividing LSMean (95% CI) by standard error; DMD=Duchenne muscular dystrophy; NSAA=North Star Ambulatory Assessment; TTR=time to rise; GT=gene therapy; 10MWR/100MWR=10/100-m walk/run velocity; SV95C=stride velocity 95th centile; Ascend 4=time to ascend 4 steps; LSM=least-squares mean; CI=confidence interval; Elevidys in collaboration with Sarepta

Prasinezumab is a mAb selectively binding aggregated α-synuclein

Current symptomatic treatments only address motor symptoms, but do not affect PD progression

Prasinezumab: First potential disease modifying therapy in PD[1, 2]

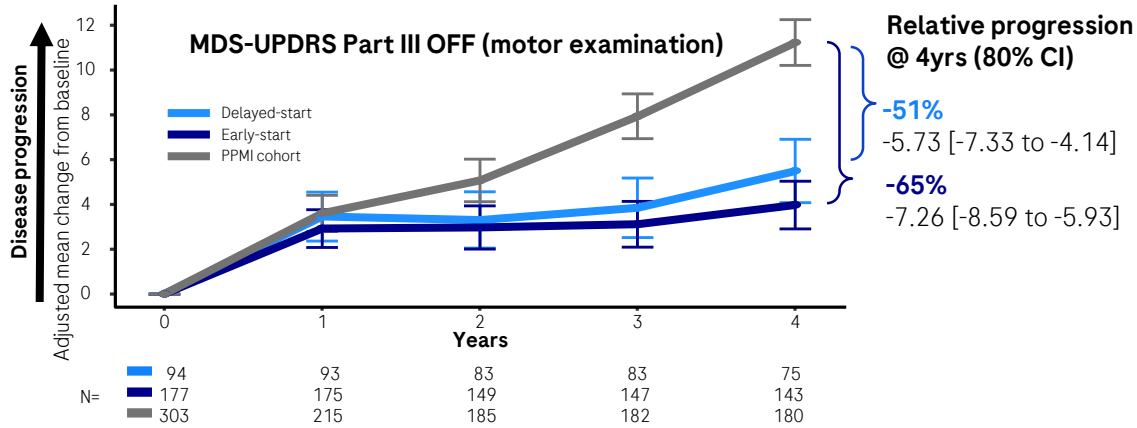


Proposed effects:

- Reducing neuronal toxicity
- Preventing cell-to-cell transfer of pathogenic α-synuclein aggregates
- Slowing disease progression

- Parkinson's disease is one of the fastest growing neurological disorders with high unmet need, economic and societal burden

Ph II (PASADENA): Prasinezumab-treated individuals progress less than PPMI propensity-matched population[3]



- Comparison of Ph II (PASADENA) and PPMI data suggests potential benefit in slowing motor progression in favor of prasinezumab on multiple endpoints
- Slowing of progression on clinician-rated motor examination (MDS-UPDRS Part III) OFF and ON symptomatic medication state, was consistent with previous data analyses
- Slowing of progression on patient-reported motor experiences of daily living (MDS-UPDRS Part II) emerges after the effect on Part III

[1]Pagano et al. Front Neurol. 2021; 12: 705407 [2]Pagano et al N Engl J Med 2022 Aug 4;387(5):421-432; [3]Pagano et al. Presented at ADPD 2024; PASADENA Phase II clinical trial. Available at: https://clinicaltrials.gov/ct2/show/NCT03100149 (last accessed Sept 2024); MDS-UPDRS=Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; OFF=practically defined OFF state; PD=Parkinson's disease; PPMI=Parkinson progression marker initiative; In collaboration with Prothena

Ph II (PADOVA) is based on Ph II (PASADENA) learnings to evaluate prasinezumab in patients on symptomatic therapy

Ph II (PASADENA) subpopulation analysis[1]

Category	Subgroup	Total *n*	Adj. mean difference	80% CI	Relative difference
MAO-B inhibitor	Yes	115	−2.66	(−4.87, −0.45)	−39.0%
	No	201	−0.87	(−2.69, 0.94)	−17.3%
Hoehn and Yahr stage	2	238	−2.55	(−4.19, −0.90)	−40.2%
	1	78	3.14	(0.32, 5.95)	144.7%
RBDSQ	≥5	85	−2.76	(−5.78, 0.25)	−35.6%
	<5	230	−1.03	(−2.63, 0.57)	−20.7%
Data-driven subphenotype	Diffuse malignant	59	−7.86	(−12.90, −2.82)	−64.0%
	Nondiffuse malignant	257	−0.77	(−2.20, 0.66)	−16.2%

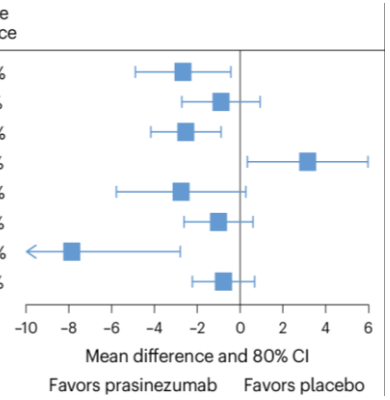
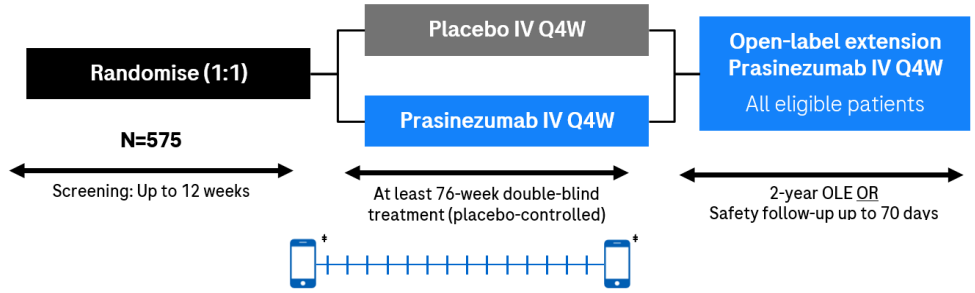


Figure adapted from Pagano et al. *Nat Med* 30, 1096–1103 (2024)

- Prasinezumab may reduce motor progression to a greater extent in more rapidly progressing Parkinson's disease
- Longer studies could further distinguish the effect of prasinezumab on progression of patient reported motor symptoms, functional activity or progression of non-motor symptoms
- PADOVA will follow up on slowing of motor progression observed in PASADENA, in patients on stable background symptomatic therapy

Ph IIb (PADOVA) results expected in Q4 2024[2]



Primary endpoint:
Time to confirmed motor progression event defined as ≥5 points on MDS-UPDRS Part III in OFF medication state at 18 months

- Time-to-event design used to measure the impact of prasinezumab on meaningful motor progression and to mitigate the impact of symptomatic medication
- PADOVA enrolled 586 pts with early-stage PD, of whom 74.4% were on stable L-DOPA and 25.6% on MAO-Bi at baseline
- PADOVA readout in Q4 2024

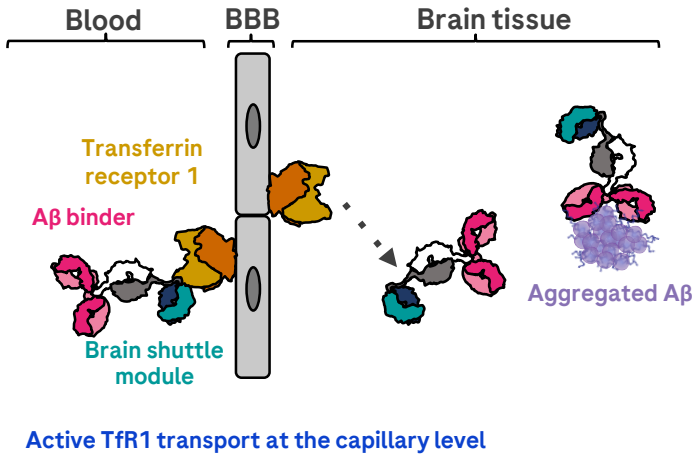
[1]Pagano et al. Nat Med,. 2024. 30, 1096–1103; 2. ClinicalTrials.gov. NCT04777331. PADOVA Phase II clinical trial. Available at: https://clinicaltrials.gov/ct2/show/NCT04777331 (last accessed Sept 2024).; ‡Digital biomarkers (smartphone and wrist-worn wearable assessments); IV=intravenous; Q4W=every 4 week; OLE=open label extension; L-DOPA=levodopa; MAO-Bi=monoamine oxidase type B inhibitor; MDS-UPDRS=movement disorder society-sponsored revision of the unified Parkinson's disease rating scale; OFF=practically defined OFF state, i.e. 12 hours after last dose; PD=Parkinson's disease; In collaboration with Prothena

Trontinemab in AD clears Aβ more rapidly than conventional mAbs

Brainshuttle™ technology efficiently transports anti-Aβ mAb across the blood-brain-barrier (BBB)

IR call at CTAD 31 Oct

Trontinemab (Brainshuttle™ anti-Aβ mAb)

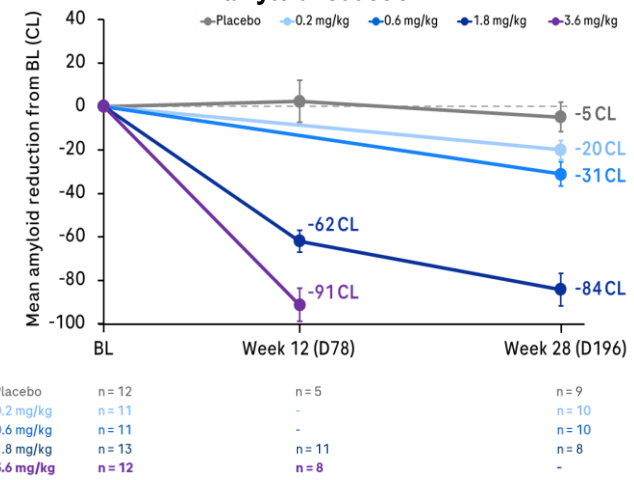


Active TfR1 transport at the capillary level

- Trontinemab uses Roche's proprietary Brainshuttle™ technology, combining an Aβ binding mAb with a transferrin receptor shuttle module
- Designed for efficient transport across the BBB to remove amyloid plaques in the brain

Trontinemab reduces plaques rapidly and robustly with low ARIA rates

Ph Ib/IIa trontinemab: Dose-dependent amyloid reduction



Ph Ib/IIa trontinemab AEs: ARIA and anemia

Total # with event [events/pt], (%)	C1 0.2 mg/kg or Pbo (n = 14)	C2 0.6 mg/kg or Pbo (n = 13)	C3 1.8 mg/kg or Pbo (n = 15)	C4 3.6 mg/kg or Pbo (n = 14)
ARIA-E	0	0	1 [2] (6.7%)	**0**
ARIA-H Microhemorrhage	0	0	0	**0**
Leptomeningeal hemosiderosis (LH)	0	0	1 [2] (6.7%)	**0**
ARIA-E with concurrent ARIA-H	0	0	0	**0**
Macrohemorrhage	0	0	0	**0**
Anemia Total # of pts with at least one AE , (%)	2 (14.3%)	0	5 (31.2%)	**1 (6.7%)**

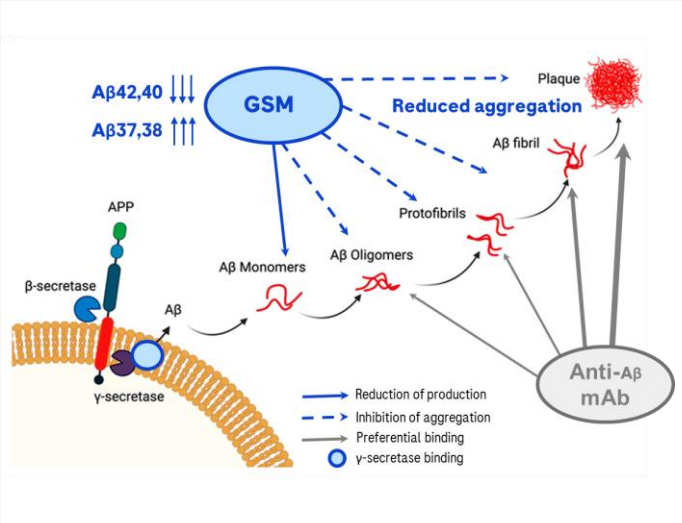
- Trontinemab demonstrated rapid and robust amyloid plaque reduction at relatively low doses (1.8 mg/kg Q4W; 3.6 mg/kg Q4W), compared with placebo
- Sustained low incidence of ARIA
- Updated Ph Ib/IIa data to be presented at upcoming conference (CTAD 2024)

[1]Kulic L et al., ADPD 2024; AD=Alzheimer's disease; CL=centiloid unit; mAb=monoclonal antibody; Aβ=amyloid β; q4w=every 4 weeks; ARIA=amyloid-related imaging abnormalities; BBB=blood-brain barrier; C=cohort; Pt=patient; Pbo=placebo; AE=adverse event; ARIA=amyloid related imaging abnormalities

RG6289, a FIC oral γ-secretase modulator in Alzheimer's disease

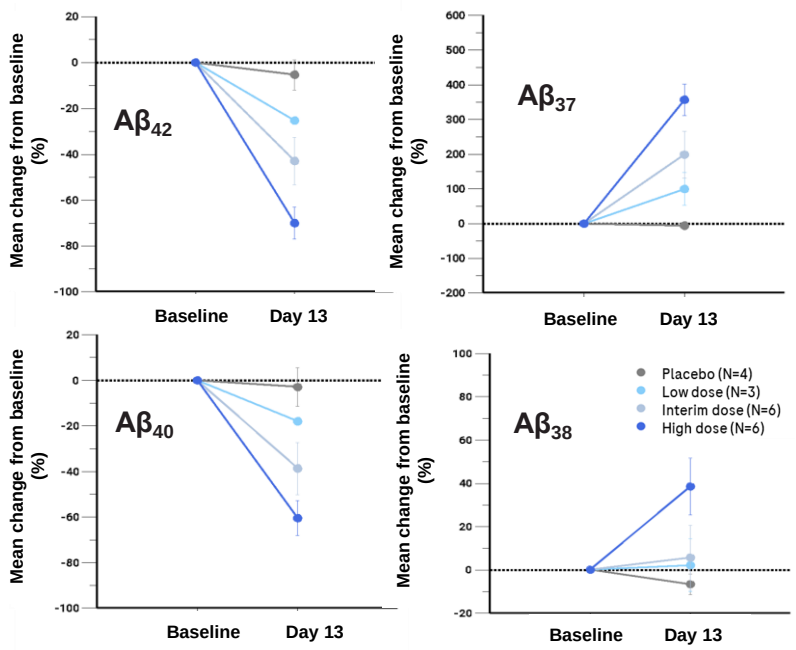
Targeting amyloid precursor protein processing to prevent Aβ-aggregation

GSMs reduce Aβ aggregation[1]



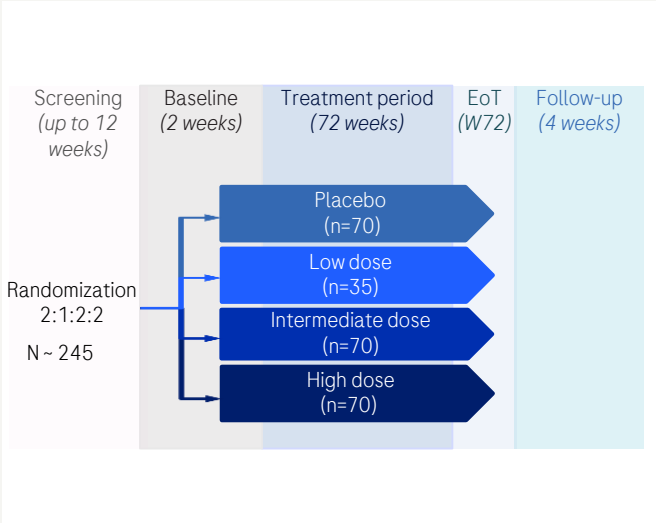
- RG6289 a potentially first-in-class oral GSM with high potency and selectivity
- GSMs alter APP processing: Reduction of Aβ42/40 and elevation of Aβ38/37
- Selective for APP with no effect on Notch
- GSMs prevent amyloid accumulation and halt plaque formation in animal model

Ph I dose escalation results for RG6289[2]



- Daily administrations of RG6289 decreased Aβ42/40 and increased Aβ37/38 concentrations in CSF of healthy volunteers in a dose dependent manner

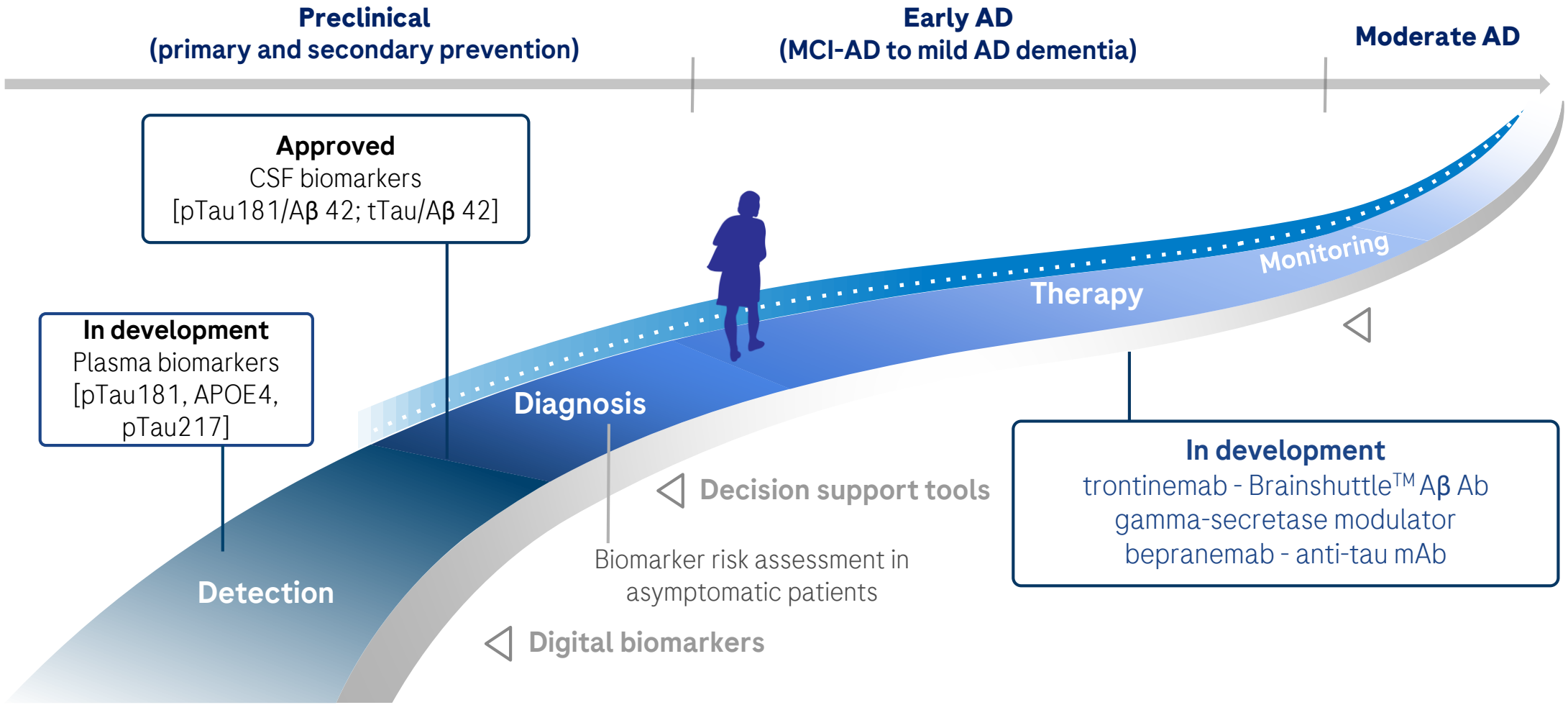
Ph II (GABriella) study design[3]



- Ph IIa (GABriella) investigates RG6289 in individuals at risk for or at prodromal stage of AD exploring safety, tolerability and effects on AD-related biomarkers
- Interim data expected in 2026

[1]Figure adapted from Vogt et al., Int. J. Mol. Sci. 2023; [2]Sturm et al; presented at CTAD 2023; [3]Tortelli et al. presented at ADPD 2024; FIC=first-in-class; GSM=gamma-secretase modulator; AD=Alzheimer's disease APP=amyloid precursor protein; Aβ=amyloid β; mAb=monoclonal antibody; HV=healthy volunteers

Roche is committed to transforming the AD journey by developing solutions across the breadth of AD



AD=Alzheimer's disease; MCI=mild cognitive impairment; CSF=cerebrospinal fluid; Aβ=amyloid β; mAb=aonoclonal antibody; Ab=antibody

Immunology

Larry Tsai
SVP and Global Head of Product Development
Immunology

Drivers of innovation in Immunology

Roche is well positioned to capture future innovation

Optimize pathways	Combinations	Endotypes	Cure
Improve known pathways/targets for transformational benefit	***Target multiple pathways to achieve improved efficacy and deeper remission***	***Identify patients subsets to improve efficacy and guide therapy***	***Aim for curative treatment to achieve long-term remission***

Recent examples

Optimize pathways	Combinations	Endotypes	Cure
Gazyva (LN) *Next-generation aCD20 with enhanced B-cell depletion*	***Undisclosed (IBD)*** *Combining orthogonal, validated pathways to raise efficacy*	***Astegolimab (COPD)*** *Potential to address difficult to treat low-eosinophil patients*	***CD19xCD3 (SLE)*** *T cell-engaging bispecific mAb targeting CD19 on B-cells & CD3 on T-cells*
Lunsumio (SLE) *Bispecific targeting CD20 on B-cells and CD3 on T-cells*	***Undisclosed (COPD)*** *Combining orthogonal, validated pathways to raise efficacy*	***Anti-TL1A (IBD)*** *Exploring biomarker which may predict better response to treatment*	
Selnoflast (asthma) *NLPR3i potential to be first new oral asthma therapy in 25 years*			

LN=Lupus nephritis; SLE=systemic lupus erythematosus; mAb=monoclonal antibody; IBD=inflammatory bowel disease; COPD=chronic obstructive pulmonary disease

Immunology pipeline

Phase I

RG6341	**undisclosed** Asthma
RG6287	**undisclosed** immunology
RG6382	**CD19 x CD3** SLE
RG7828	**Lunsumio** SLE
RG6418	**selnoflast** Asthma
RG6421	**TMEM16A potentiator** Muco-obstructive respiratory disease
RG6315	**undisclosed** Systemic sclerosis
RG6377	**undisclosed** IBD
CHU	**Anti-HLA-DQ2.5 x gluten peptides** Celiac disease
CHU	**RAY121 (anti-C1s recycling Ab)** Immunology

Phase II

RG6341	**undisclosed** Chronic cough
RG6536	**vixarelimab** IPF/SSc-ILD
RG6536	**vixarelimab** IBD

Phase III

RG7159	**Gazyva** Lupus nephritis	✓
RG7159	**Gazyva** Membranous nephropathy	
RG7159	**Gazyva** SLE	
RG7159	**Gazyva** Childhood onset INS	
RG6149	**astegolimab** COPD	
RG6299	**ASO Factor B** IgAN	
RG6631	**Anti-TL1A** Ulcerative colitis	
RG6631	**Anti-TL1A** Crohn's disease	

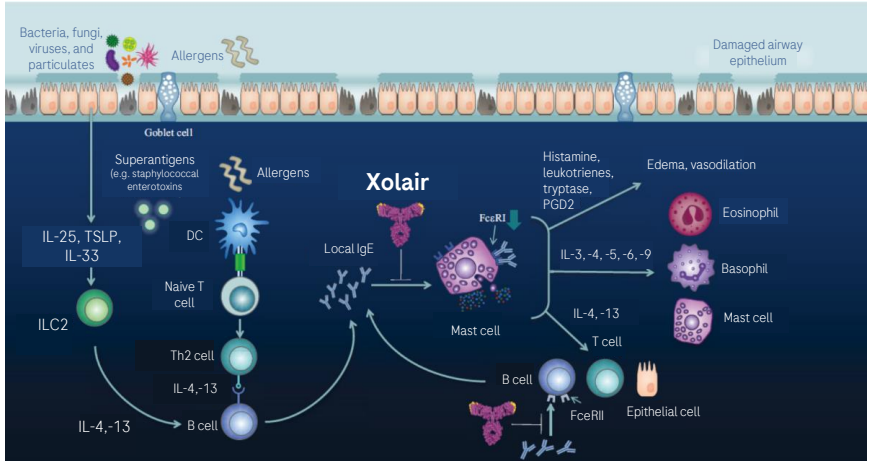
- Immunological kidney diseases
- Respiratory & allergy
- Gastroenterology
- Others/undisclosed

- Small molecule
- Antibody
- Locked nucleic acid / antisense
- Bispecifics
- ✓ Primary endpoint met

SLE=systemic lupus erythematosus; IBD=inflammatory bowel disease; IPF=idiopathic pulmonary fibrosis; SSC-ILD=systemic sclerosis-interstitial lung disease; INS=idiopathic nephrotic syndrome; COPD=chronic obstructive pulmonary disease; IgAN=IgA Nephropathy

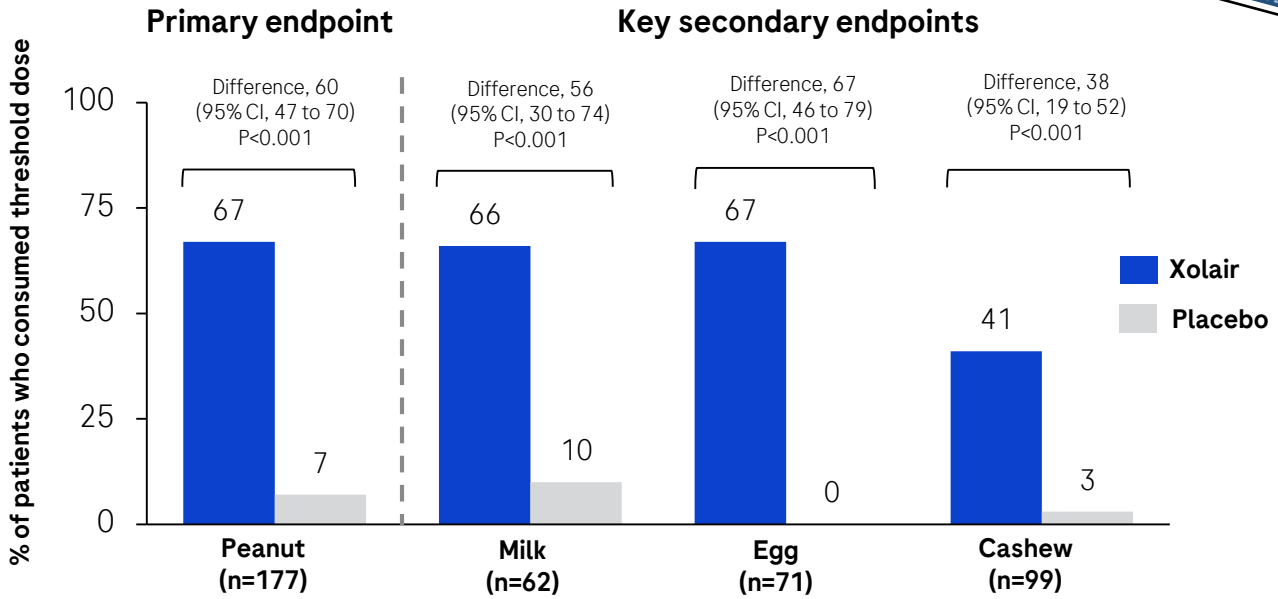
Xolair in food allergy is the first and only FDA-approved medicine to reduce allergic reactions to multiple foods

Xolair (anti-IgE mAb)



- Inhibits binding of IgE to high affinity IgE receptor on the surface of mast cells, basophils, and dendritic cells
- Approved for asthma, chronic spontaneous urticaria, nasal polyps, and food allergy

Ph III (OUtMATCH) in food allergy[1,*]



- >15k patients on treatment in first four months post-launch
- >40% of children and >50% of adults with food allergies have experienced a severe reaction at least once[2,3]

1 Wood et al., 2024 NEJM; 2 Gupta et al., 2019 JAMA Netw Open; 3 Gupta et al., 2018 Pediatrics; *The phase III OUtMATCH study is being sponsored and funded by the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, and conducted by the NIAID-funded Consortium for Food Allergy Research (CoFAR) across 10 clinical sites throughout the U.S. The study is also supported by Genentech, a member of the Roche Group, and Novartis Pharmaceuticals Corporation; mAb=monoclonal antibody; CI=confidence interval

Well positioned for a strong future in immunological kidney diseases

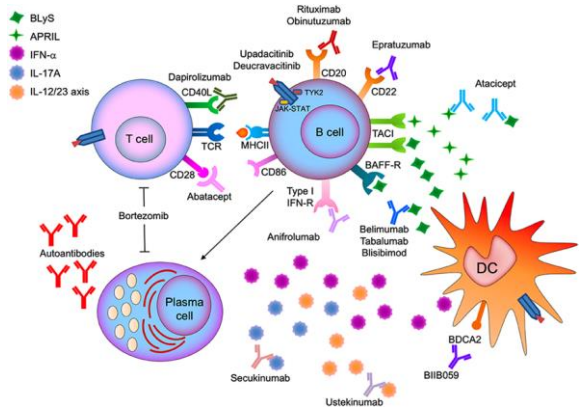
Development programs

Molecule	Indication	Ph1	Ph2	Ph3	
Gazyva	LN	REGENCY			✓
	SLE	ALLEGORY			
	MN	MAJESTY			
	INS	INShore			
PiaSky	aHUS	COMMUTE-a			
		COMMUTE-p			
ASO Factor B	IgAN	IMAGINATION			
Lunsumio	SLE				
CD19xCD3	SLE				

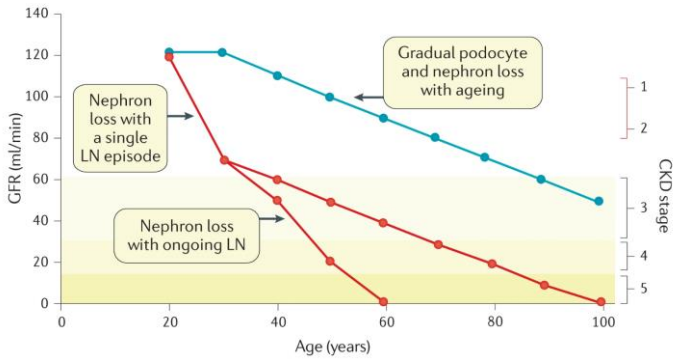
✓ Primary endpoint met

Lupus nephritis (LN)

B cells are central to LN pathogenesis



Risk of ESKD in patients with LN over lifetime



- LN is a severe manifestation of systemic lupus erythematosus (SLE); around 50% of SLE patients will develop LN within 5 years of SLE diagnosis
- Up to 25% of these patients develop end stage kidney disease (ESKD) despite treatment with current available therapies (dialysis or transplant)
- LN is associated with 6x increased risk of mortality vs the general population
- There is currently no cure for LN

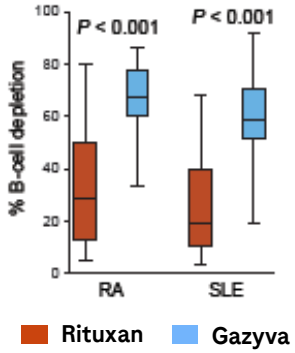
LN=lupus nephritis; SLE=systemic lupus erythematosus; MN=membranous nephropathy; INS=Idiopathic nephrotic syndrome (Childhood onset INS also known as PNS=Pediatric nephrotic syndrome); aHUS=atypical hemolytic uremic syndrome; IgAN=IgA nephropathy; ESKD=end stage kidney disease; CKD=chronic kidney disease; GFR=glomerular filtration rate

Gazyva Ph III (REGENCY) in lupus nephritis met primary endpoint

Gazyva shows superiority in CRR over SoC with clinically meaningful treatment benefits

Gazyva (anti-CD20 mAb)

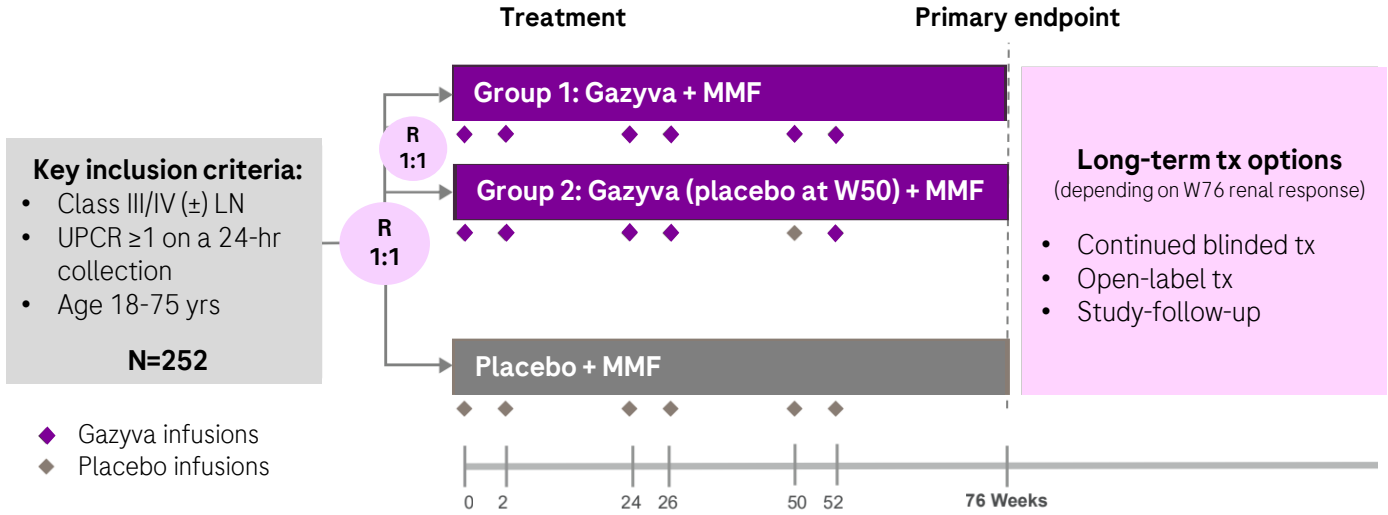
B cell depletion vs Rituxan



- Type II anti-CD20 region with increased direct cell death, decreased CDC and reduced internalization
- Glycoengineered Fc region with higher FcγR affinity and increased ADCC/ADCP
- Greater potency than Rituxan in depleting peripheral and tissue B-cells

Ph III (REGENCY) in LN trial design

FDA BTD



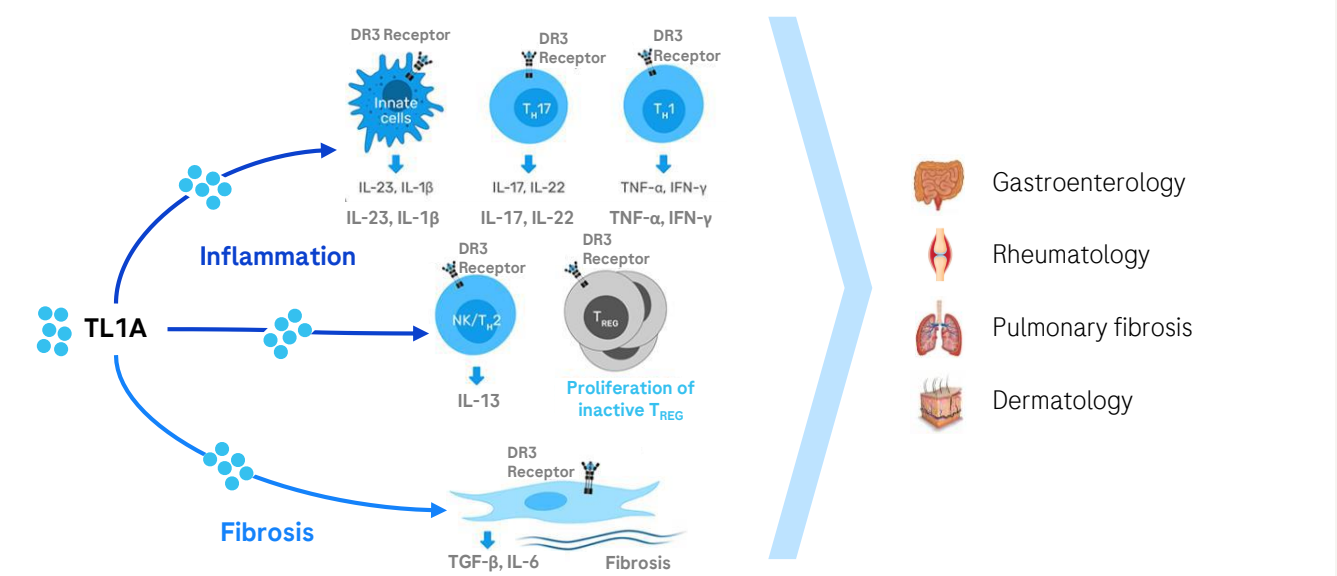
- Study results show a higher proportion of people treated with Gazyva plus standard therapy (mycophenolate mofetil and glucocorticoids) achieved a CRR at 76 weeks compared to those treated with standard therapy alone
- Safety was in line with well-characterised profile of Gazyva, no new safety signals identified
- Data will be filed with global health authorities and presented at upcoming medical meeting

mAb=monoclonal antibody; LN=lupus nephritis; MMF=mycophenolate mofetil; CDC=complement-dependent cytotoxicity; ADCC=antibody-dependent cell-mediated cytotoxicity; ADCP=antibody-dependent cellular phagocytosis; CRR=complete renal response; SoC=standard of care; tx=treatment; UPCR=urine protein creatinine ratio; W=week

TL1A is implicated in multiple immunological diseases

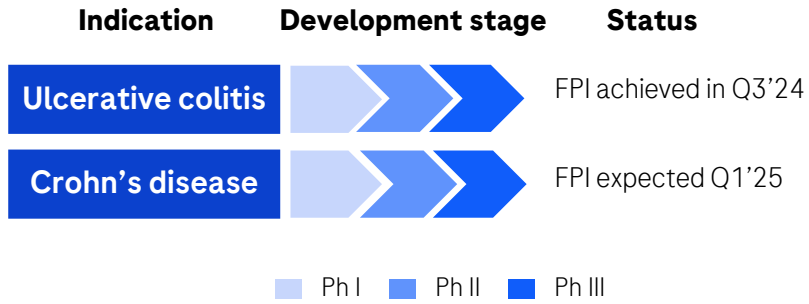
Continuing to explore additional indications

TL1A implicated in inflammatory and fibrotic processes[1,2]



- TL1A binds and activates the DR3 receptor, stimulating downstream inflammation and fibrosis processes
- TL1A is dysregulated in patients with immune-mediated diseases, with clinical and translational links to IBD, rheumatoid arthritis amongst others
- Non-clinical and translational studies demonstrated its involvement in pathogenesis of fibrotic conditions

RG6631 (anti-TL1A) development program



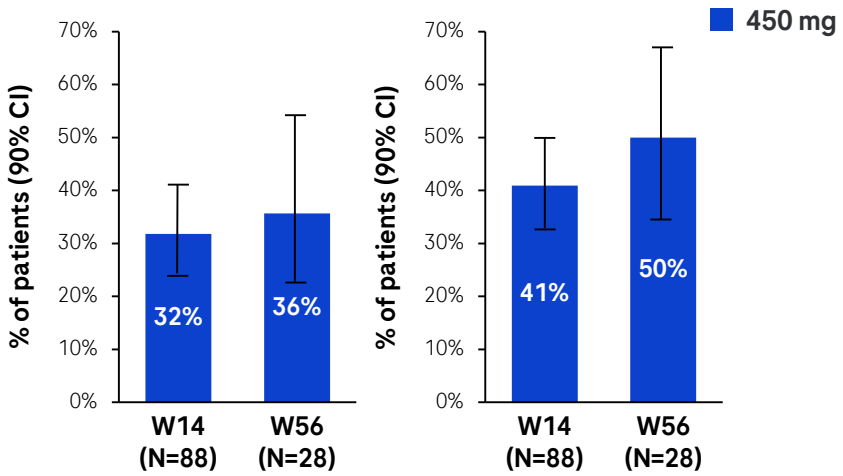
- Ph III study in UC achieved FPI
- Initiating Ph III study in CD with FPI expected Q1'25
- Continuing to explore additional indications with update to be communicated in H1 2025

1 Xu WD, Li R, Huang AF. Role of TL1A in Inflammatory Autoimmune Diseases: A Comprehensive Review. Front Immunol. 2022 Jul 14;13:891328. doi: 10.3389/fimmu.2022.891328. PMID: 35911746; 2 Herro R, et al. TL1A Promotes Lung Tissue Fibrosis and Airway Remodeling. J Immunol. 2020 Nov 1;205(9):2414-2422. doi: 10.4049/jimmunol.2000665. Epub 2020 Sep 21. PMID: 32958689; PMCID: PMC7577982.; PMCID: PMC9329929; TL1A=tumor necrosis factor-like cytokine 1A; DR3=dopamine 3; IBD=inflammatory bowel disease; UC=ulcerative colitis; CD=Crohn's disease

Anti-TL1A in ulcerative colitis

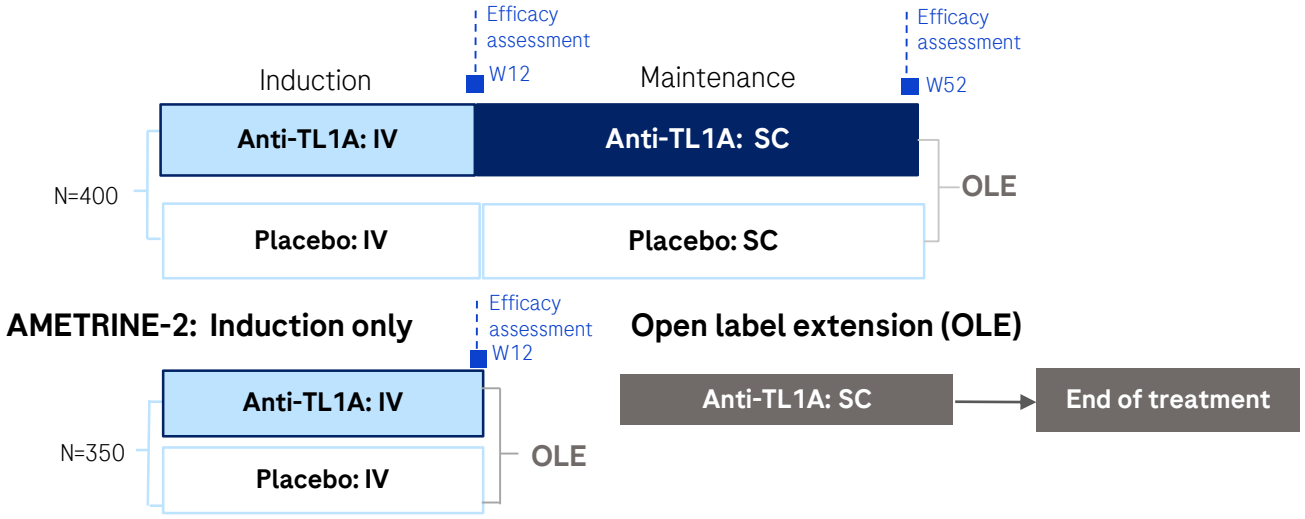
Ph III (AMETRINE-1&2) trials in UC initiated; Ph III (AMETRINE-1) achieved FPI

Ph IIb (TUSCANY-2) in UC[1]



- Ph IIb (TUSCANY-2) in UC demonstrated strong efficacy and safety in a large group of pts (n=245)
- Sustained clinical remission and endoscopic improvement from induction to chronic phase
- Roche to present updated analysis at UEG 2024

Ph III (AMETRINE-1&2) in UC study design



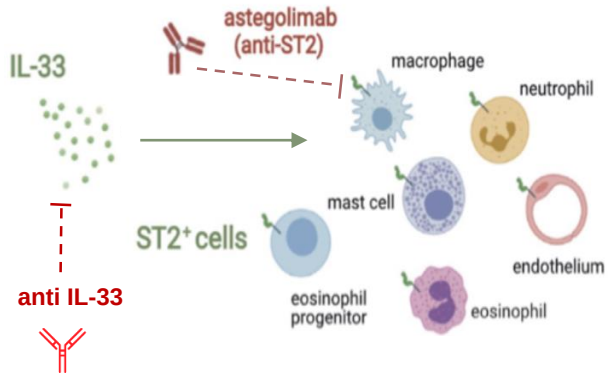
- Treat-through study design with no re-randomization after induction phase
- Inclusion of participants who have not responded to more than three previous advanced therapies
- Exploring biomarker test which may predict better response to treatment

*biomarker not yet disclosed; 1 Danese S. et al. UEG 2024 abstract; †Defined per FDA definition with an mMS 0–2 (endoscopic subscore=0 or 1, ≥1 point decrease from baseline to achieve a stool frequency subscore=0 or 1, and rectal bleeding subscore=0). ‡Defined as endoscopic subscore=0 or 1; mMS=modified Mayo score; CI=confidence interval; UC=ulcerative colitis; FPI=first-patient-in; aTL1A=anti-tumor necrosis factor-like cytokine 1A; IV=intravenous; SC=subcutaneous; W=week; OLE=open label extension; UEG=United European Gastroenterology

Astegolimab a first-in-class anti-ST2 mAb in COPD

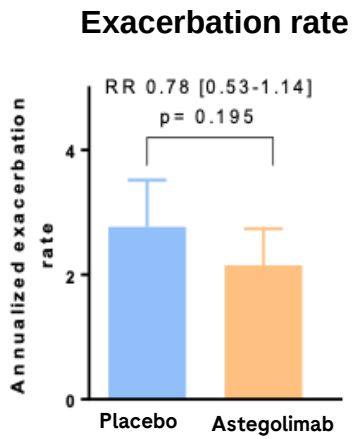
Early results show benefit in key endpoints throughout broad patient populations

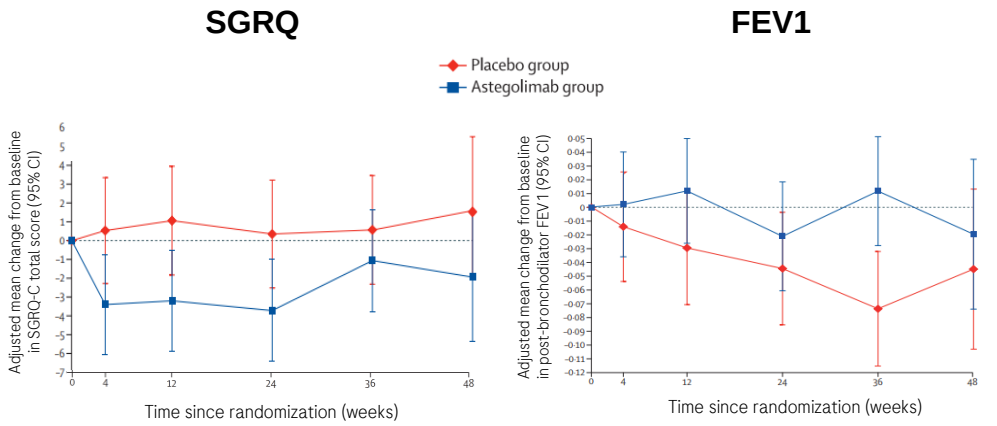
Anti-ST2 mAb



- Astegolimab binds both soluble ST2 and membrane bound ST2 (IL-33) receptor
- IL-33/ST2 blockade may impact airway remodeling in COPD patients

Ph IIa (COPD-ST2OP) results at 48 weeks[1]





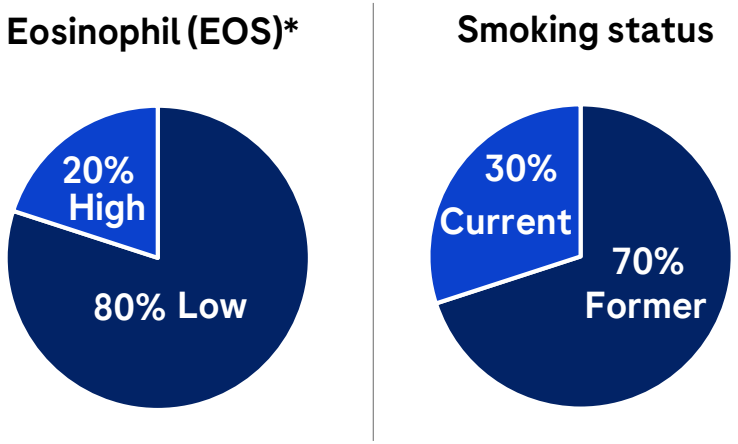
- AER reduction of -22% in ITT population and -37% in EOS low* patients
- Significant improvement in symptoms (reduction in SGRQ of -3.3) and expiratory volume (increased FEV_1 by +40 ml)
- No safety concerns were identified

1 Yousuf et al. Lancet Respir. Med. 2022;10 (5):469-77; 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; FEV1=forced expiratory value

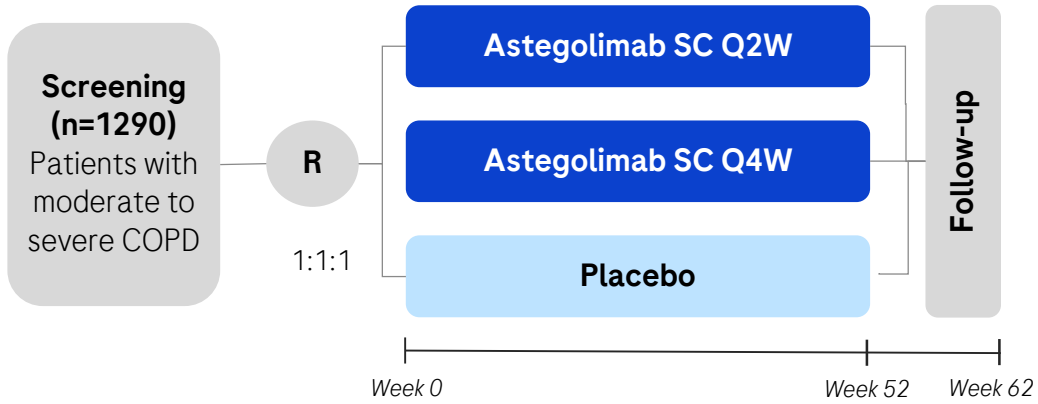
Ph IIb/III results for astegolimab in COPD expected 2025

Aiming to address all COPD patients

COPD patient population[1]



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



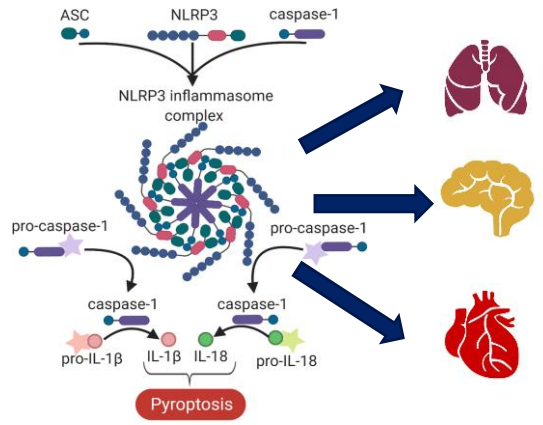
- Near-term biologics in COPD are focused on EOS high or former smokers only
- Astegolimab pivotal trials enrolled broad patient population including former and current smokers, and EOS low to high
- Astegolimab has the potential to address neutrophilic inflammation as well as eosinophilic inflammation that could be key to reducing exacerbations across a broader population of patients
- Ph IIb (ALIENTO) and Ph III (ARNASA) pivotal results expected 2025

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; Q2/4W=every 2/4 weeks; EOS=eosinophils

Selnoflast (NLRP3i) is a potent inhibitor of the NLRP3 inflammasome

Potential to be the first new oral asthma therapy in 25 years where high unmet need remains

Selnoflast (NLRP3 inflammasome inhibitor)



- Selnoflast is an orally active, potent, selective and reversible NLRP3 inhibitor
- NLRP3 is a cytosolic multi-protein complex implicated in multiple disorders across different therapeutic areas; its activation triggers inflammatory response leading to pyroptotic cell death

Development program

	Indication	Ph I	Ph II	Ph III	Status
Immunology	Asthma				FPI achieved Q2'24
Neurology	Parkinson's disease				Recruitment completed
CVRM	Coronary artery disease				Recruitment completed

- Ph Ib study in moderate-severe asthma: NLRP3 inhibition reduced airway inflammation and hyper-responsiveness in models of steroid-resistant asthma
- Ph Ib study in Parkinson's disease: NLRP3 inhibition may reduce local brain inflammation and mircoglia activation, potentially resulting in slowing down the progression of PD
- Ph Ic study in coronary artery disease: NLRP3 inhibition can drive pro-inflammatory cell signaling down, therefore reduce inflammatory activities in heart that cause MACE

Figure adapted from O'Brien et al (2020). Journal of Neuroinflammation. 17. 10.1186/s12974-020-01778-5; MACE=major adverse cardiovascular events; CVRM=cardiovascular, renal and metabolism; NLPR3=NOD-, LRR- and pyrin domain-containing protein 3

Our contribution to Global Health Security

Delivering curative therapies in areas of high unmet need

Influenza

1bn cases of influenza annually, including

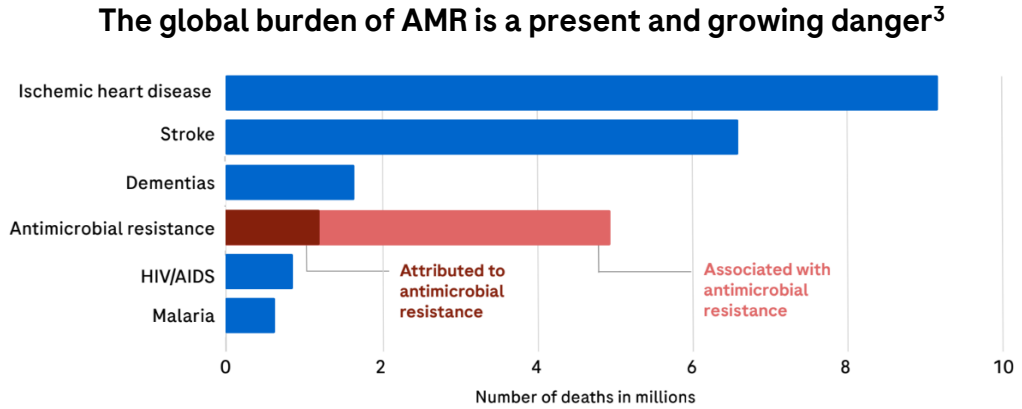
3-5mn cases of severe illness and up to

650,000 respiratory deaths [1]

Risk of infection in a household contact can be up to **40%**[2]

- Influenza represents a serious threat to public health and is a significant burden on economies and healthcare systems
- Ph III (CENTERSTONE) result shows Xofluza reduces transmission of influenza from an infected person to household members which has the combined benefits of alleviating illness in the infected person and reducing spread within communities

Antimicrobial resistance (AMR)



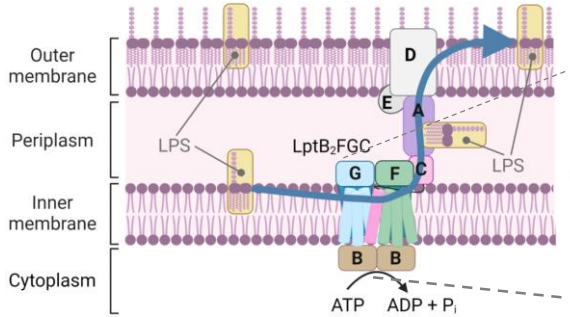
- AMR is a 'silent pandemic' expected to claim more lives over the next 30 years than cancer today
- Despite the need for antibiotics and the rise of antibiotic resistance, no novel class of antibiotics effective against gram-negative bacteria has been discovered since 1968

1 WHO Influenza (Seasonal). Accessed May 2024; 2 Tsang TK, et al. Trends Microbiol. 2016; 24:123–133; 3.Lancet 2022; 399: 629–55; AMR=antimicrobial resistance

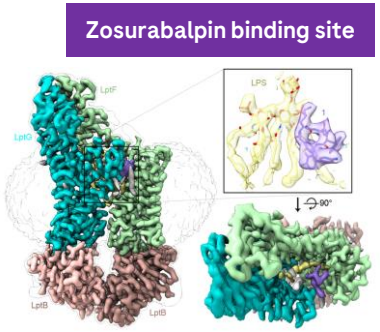
Zosurabalpin and RG6436 (LepBi) represent the first new classes of antibiotics against gram negative bacteria in 50 years

Zosurabalpin (Abx macrocyclic peptide)

Localization of the LPS transport system in gram-negative cell envelope[1]

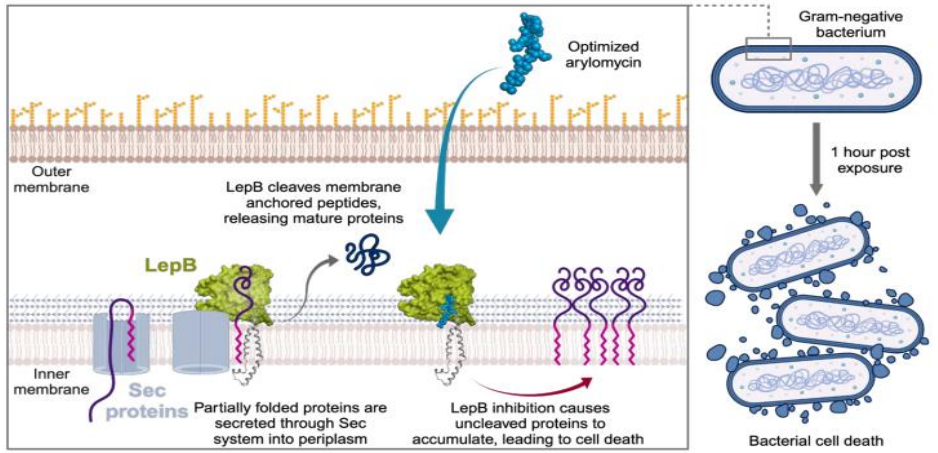


Cryo-EM structure of zosurabalpin bound to the $LptB_2FBG$ transporter and LPS[2]



- Zosurabalpin blocks transport of lipopolysaccharide (LPS) by inhibition of LptB2FG complex
- This novel MoA prevents *carbapenem-resistant A. baumannii* (the highest threat pathogen according to WHO and CDC) from properly constructing its protective membrane
- Currently in Ph I development

LepB inhibitor (macrocyclic lipopeptides)



- RG6436 inhibits LepB bacterial type I signal peptidase, an essential membrane-bound protease that cleaves pre-proteins following translocation across the cytoplasmic membrane
- *In vitro* potency against *carbapenem*-resistant Enterobacterales and *Pseudomonas aeruginosa*
- Currently in Ph I development

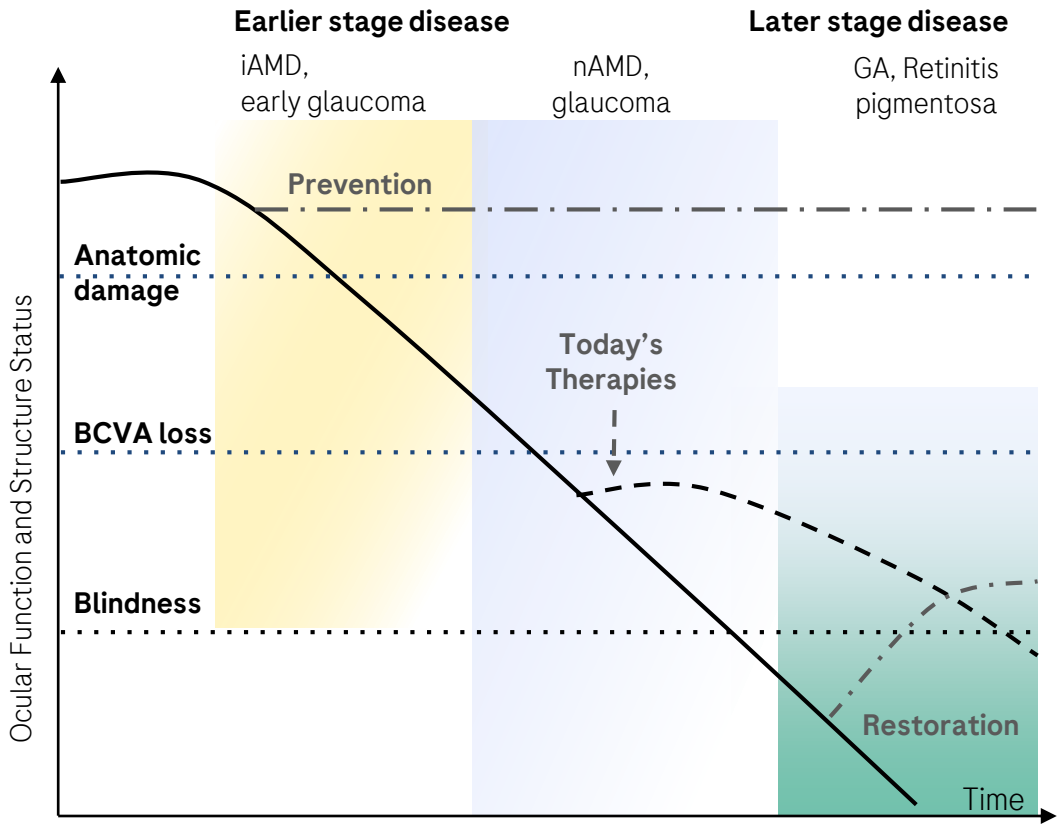
1 Picture created with BioRender.com. Adapted from Owens et al., Nature 2019, 567, 550; 2 Cryo-EM structure derived from Roche pRED / Dan Kahne Laboratory, Harvard University, collaboration; MoA=mechanism of action; LPS=lipopolysaccharide; WHO=World Health Organization; CDC=Centers for Disease Control and Prevention

Ophthalmology

Christopher Brittain
SVP and Global Head of Product Development
Ophthalmology

Ophthalmology pipeline

Aiming to alter the trajectory of vision loss as experienced today



Improve outcome across all stages of ocular diseases

Earlier stage disease: Vision preservation

- Supplement current target approaches: Inhibit inflammation & neo-angiogenesis
- Explore clinically useful biomarkers predicting rapid vision loss
- Protect key retinal lineages

Later stage disease: Vision restoration

- Replace photosensitive cells once vision is lost
- Continue investment in new therapeutic modalities e.g. cell therapy and gene therapy/optogenetics

iAMD=intermediate age-related macular degeneration; nAMD=neovascular age-related macular degeneration; GA=geographic atrophy; BCVA=best-corrected visual acuity

Ophthalmology R&D focus areas

Improving patient outcomes and reducing treatment burden

Extended durability & future technologies

Long acting delivery
- *Port delivery platform*
- *DutaFabs (i.e. zifibancimig)*

Cell therapy
OpRegen in GA: Potential for vision restoration

LINEAGE CELL THERAPEUTICS

Gene therapy
Development of AAV capsids for intravitreal targets

avista TX

Novel MoAs and new indications, addressing multiple disease pathways

Novel MoAs
- *Vabysmo first dual pathway inhibitor (VEGF/Ang-2)*
- *IL-6 addresses retinal inflammation*
- *Semaphorin-3A*
- *Wnt pathway*

SEMA

ANTLERA

New indications
UME, GA, DR, Glaucoma

Disease pathways
Inflammation, atrophy, ischaemia, vascular stability

Digital Capabilities

Biomarker and data analytics
- *Integration of omics, clinical & imaging data*
- *Real world data and natural history*
- *Improved disease understanding*

Remote vision monitoring tools
Accessible, effective and low cost tracking of disease activity

myVisionTrack®

AI supports clinical decision
e.g. automatic image segmentation and treatment response prediction algorithms for personalized management of disease

DutaFab=dual targeting fragment antigen-binding; GA=geographic atrophy; AAV=adeno-associated virus; MoA=mode of action; VEGF=vascular endothelial growth factor; Ang-2=angiopoietin-2; IL-6=inter-leukin 6; UME=uveitic macular edema; DR=diabetic retinopathy; AI=artificial intelligence

Ophthalmology pipeline gaining momentum

Further improving the standard of care and expanding in new indications

Phase I		Phase II		Phase III		Registration	
RG6351	NME Retinal disease	RG6179	vamikibart DME	RG6179	vamikibart UME	RG6321	Susvimo DME
RG6209	NME Retinal disease	RG6501	OpRegen[1] GA	RG6168	Enspryng TED	RG6321	Susvimo DR
RG7921	NME RVO			RG7716	Vabysmo CNV		
RG6120	zifibancimig nAMD			RG6321	Susvimo nAMD (36-week)		

nAMD
DME/UME
GA
DR
RVO
TED
CNV
Retinal disease

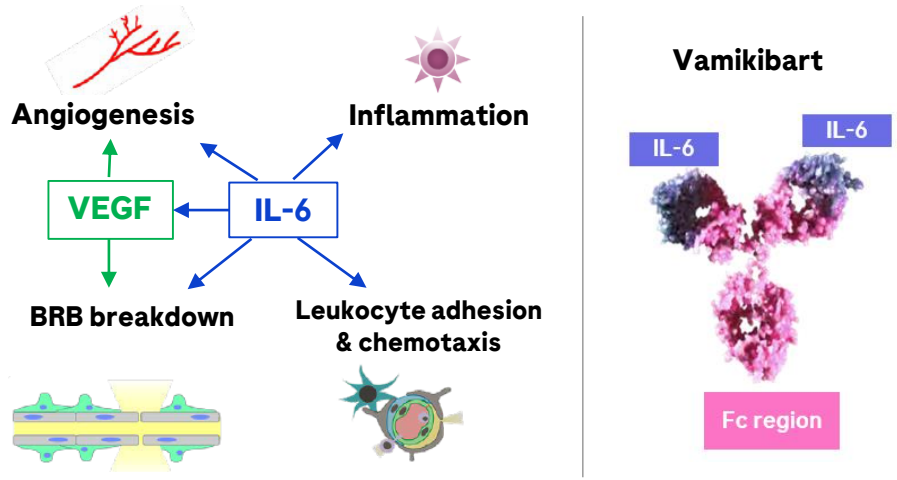
Antibody
DutaFab
Port Delivery Platform
Stem cell therapy

1. In collaboration with Lineage Cell Therapeutics (LCTX); NME=new molecular entity; RVO=retinal vein occlusion; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; GA=geographic atrophy; UME=uveitic macular edema; TED=thyroid eye disease; CNV=myopic chorodial neovascularization; DR=diabetic retinopathy; DutaFab=dual targeting fragment antigen-binding

Vamikibart in UME and DME

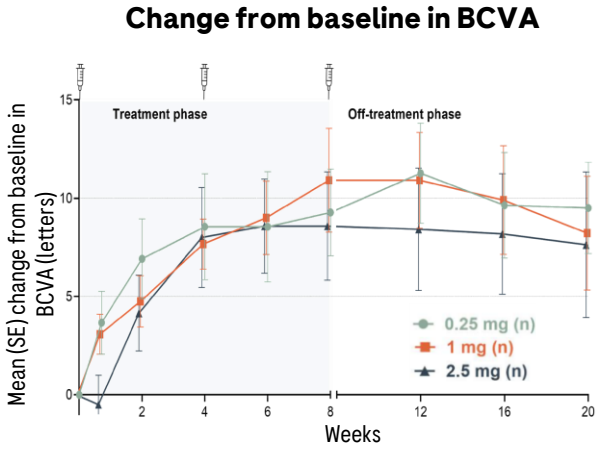
Addressing the inflammatory component (IL-6) in macular edema

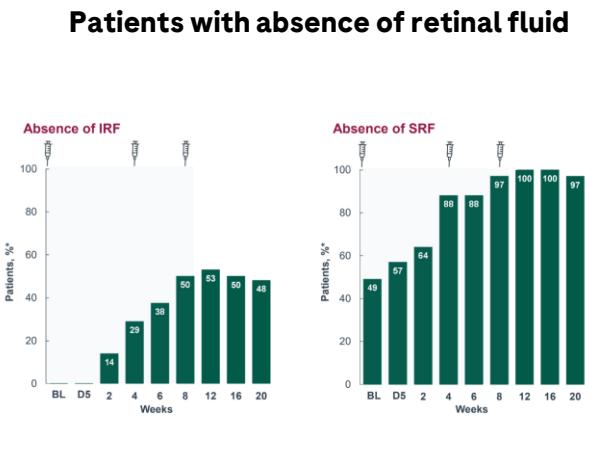
IL-6 is involved in many pathways, including inflammation



- Inflammation is a currently sub-optimally treated pathway in a number of ocular diseases
- IL-6 is upregulated in retinal diseases
- Vamikibart inhibits all known forms of IL-6 signaling; specifically designed for intraocular use and optimized for a rapid systemic clearance

Ph I (DOVETAIL) data in UME: Improved vision and retinal thickness in all dosing cohort [1]





- 25-36% of patients gained 15 letters or more at week 12
- All doses of vamikibart were well tolerated across all patients, with no treatment-related serious AEs, sustained IOP increase, or new cataracts
- Ph III (SANDCAT/MEERKAT) trials in UME ongoing with MEERKAT fully enrolled, data expected 2025
- Ph II (BARDENAS/ALLUVIUM) trials in DME ongoing, data expected 2025

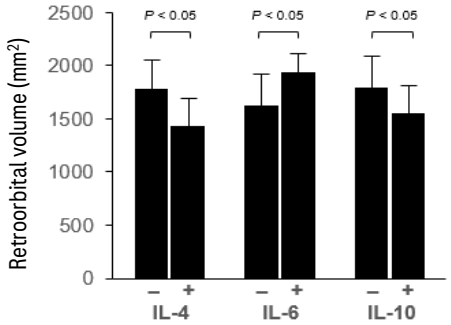
1. Sharma et al. ARVO 2023; UME=uveitic macular edema; DME=diabetic macular edema; BRB=blood-retinal barrier; IOP=intraocular pressure; IL-6=interleukin-6; VEGF=vascular endothelial growth factor; AE=adverse event; BCVA=best-corrected visual acuity; SE=standard error; IRF=intraretinal fluid; SFR=subretinal fluid

Enspryng in thyroid eye disease

Potential to be the first SC therapy in TED with strong efficacy and a well-established safety profile

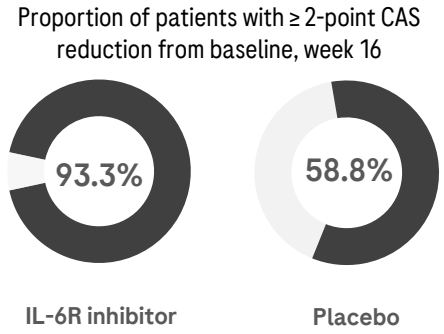
IL-6 and IL-6R play a key role in the pathogenesis of TED[1] and clinical evidence supports IL-6 signaling inhibition in TED

IL-6 expression correlates with orbital tissue expansion[2]



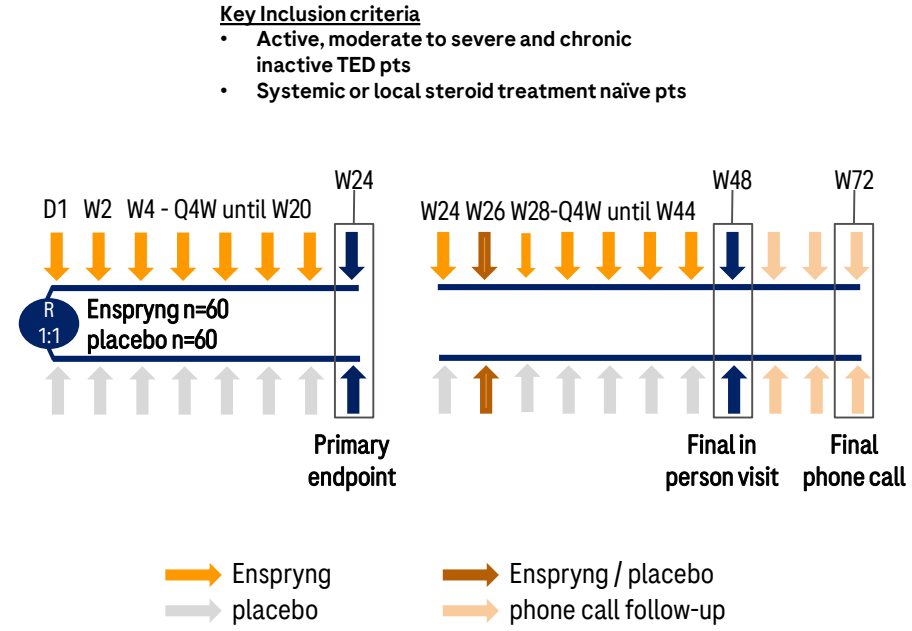
Cytokine gene expression in orbital fat tissue

CAS reduction of ≥ 2 points achieved with IL-6 inhibition



- IL-6 is a key mediator of inflammation and drives fibrosis in TED; blocking IL-6R signaling has the potential to reverse the manifestation of the disease
- In a placebo-controlled randomized trial, CAS reduction of ≥ 2 point and proptosis reduction were achieved with IL-6R inhibition
- Enspryng is designed to enable maximal sustained suppression of IL-6 signaling and allow practical Q4W dosing with an established safety profile

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



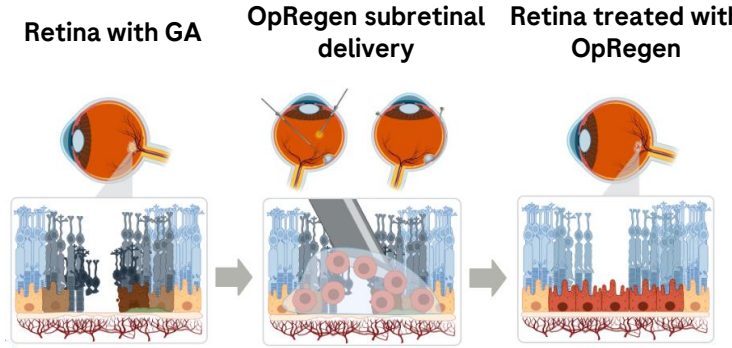
- Ph III (SatraGO-1/SatraGO-2) trials in TED ongoing, data expected 2026

Ezra D et al, ASOPRS 2023;1. Slowik M et al. Endocr Res. 2012;37(2):89–95; 2. Hiromatsu Y et al. J Clin Endocrinol Metab. 2000;85(3): 1194–99; 3. Perez-Moreiras JV et al. AJO. 2018;195:181–90; TED=thyroid eye disease; IL-6=interleukin-6; IL6R-interlukin-6 receptor; SC=subcutaneous; CAS=clinical activity score

OpRegen in GA: Replenishing the retinal pigment epithelium

FDA RMAT Designation granted based on preliminary clinical evidence

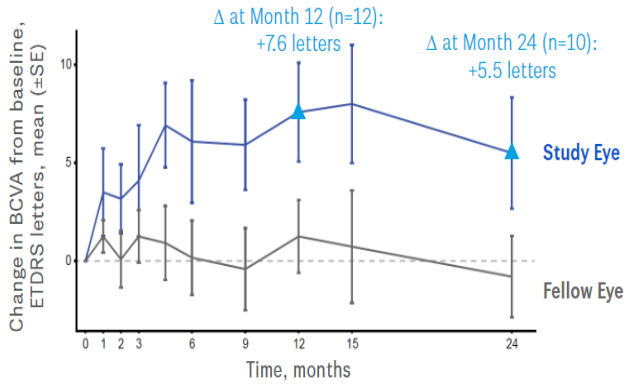
Potential to counteract RPE loss in GA



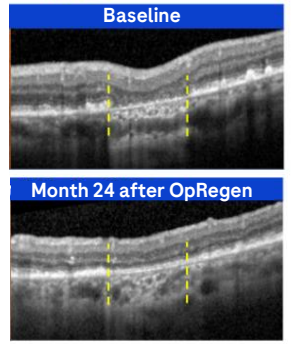
- OpRegen is a suspension of human allogeneic RPE cells delivered as a single injection to the subretinal space in area of GA lesion
- Ph IIa surgical development study currently enrolling; designed to optimize lesion targeting while maintaining safety profile

Ph I/IIa data: Visual function and retinal structure improvements sustained through month 24[1-2]

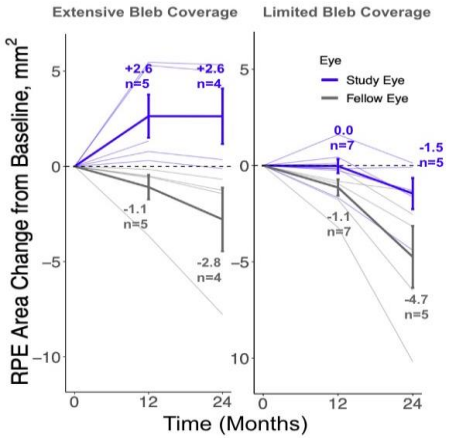
Cohort 4 (n=12) Patients with impaired vision (BCVA≥20/250 and ≤20/64)[1]



Case 14[2]



RPE layer quantification[1]



- BCVA gains in patients in Cohort 4 (impaired vision) measured at month 12 remain evident at month 24, with an average 5.5 letter gain
- Preliminary evidence of maintenance of structural improvement maintained 24 months following OpRegen delivery
- With extended follow-up, OpRegen continues to show an acceptable safety profile

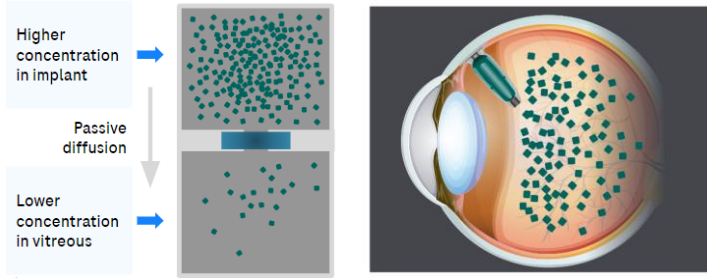
In collaboration with Lineage Cell Therapeutics, Inc. (LCTX); 1. Telander D, et al. Retinal Cell and Gene Therapy Innovation Summit 2024; 2. Banin E, et al. ARVO 2023; RMAT=regenerative medicine advanced therapy; RPE=retinal pigment epithelium; GA=geographic atrophy; BCVA=best-corrected visual acuity; ETDRS=early treatment of diabetic retinopathy study

Continuing to innovate on Port Delivery Platform beyond Susvimo

Zifibancimig in nAMD: Combining the benefits of dual VEGF/Ang-2 inhibition and continuous drug delivery

Port Delivery Platform (PDP)

(Intraocular refillable implant)



- Port Delivery Platform is designed for continuous delivery of customized molecules through passive diffusion
- Assets in development with Port Delivery Platform: 3 DutaFab molecules (including zifibancimig) and 2 preclinical molecules

Zifibancimig

VEGF/ Ang-2 DutaFab

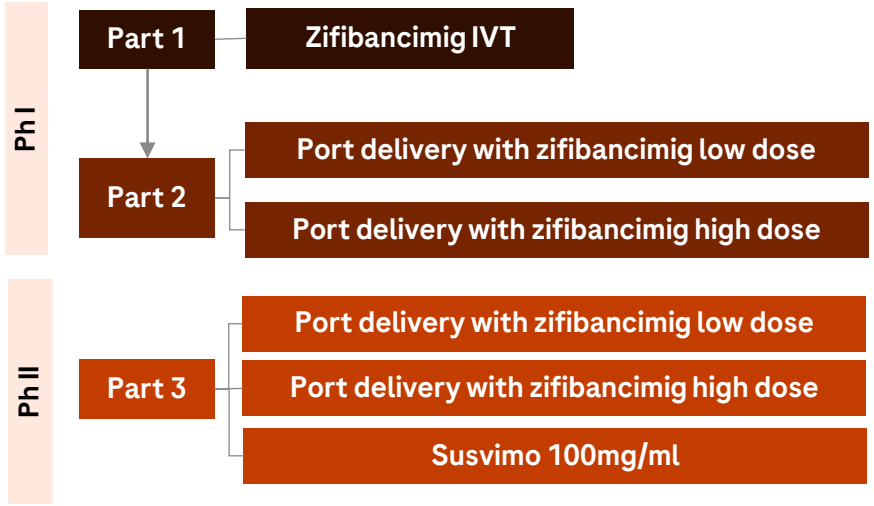
Anti-VEGF-A
Reduces vascular leakage
Inhibits neovascularization

Anti-Ang2
Stabilizes vessels:
Reduces vascular leakage and inflammation

Single antigen-binding fragment binding two targets independently with high potency and selectivity

- Zifibancimig is specifically designed for compatibility with Port Delivery Platform
- Potential for sustained vascular stability and improved visual outcomes with fewer refill-exchanges
- PhI/II (BURGUNDY, Part 2 and Part 3) in nAMD ongoing, data expected 2026

PhI/II (BURGUNDY) trial design

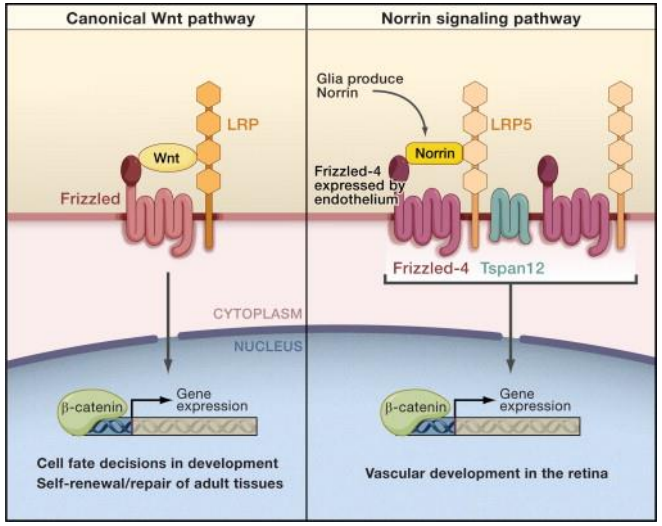


DutaFabs=dual targeting fragment antigen-binding; VEGF=vascular endothelial growth factor; Ang-2=angiopoietin-2; mAb=monoclonal antibody; IVT=Intravitreal; Q6M=every 6 months; nAMD=neovascular age-related macular degeneration

Investigating Wnt agonism with ANT-Pharm

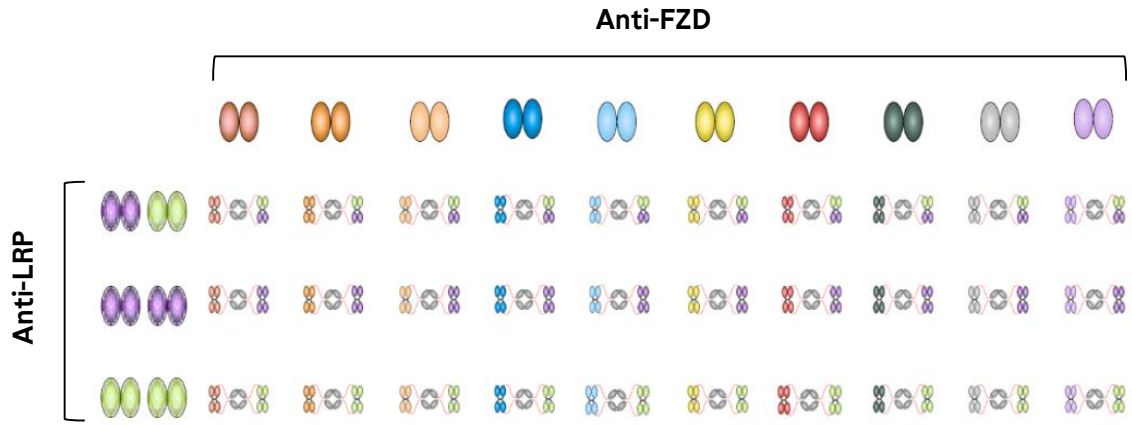
Acquisition of AntlerA, a leader in Wnt signaling, added a library of anti-FZD/LRP drug candidates

Wnt pathway



- Extensive scientific expertise on the Wnt pathway in Roche
- Approaches mimicking the natural ligand Norrin, which agonizes the Wnt pathway, have been shown to be effective in restoring and maintaining a sealed blood retinal barrier in preclinical models
- Clinical proof of concept of agonizing Wnt has been demonstrated in DME

ANT-Pharm: A combinatorial Wnt-mimetic library platform



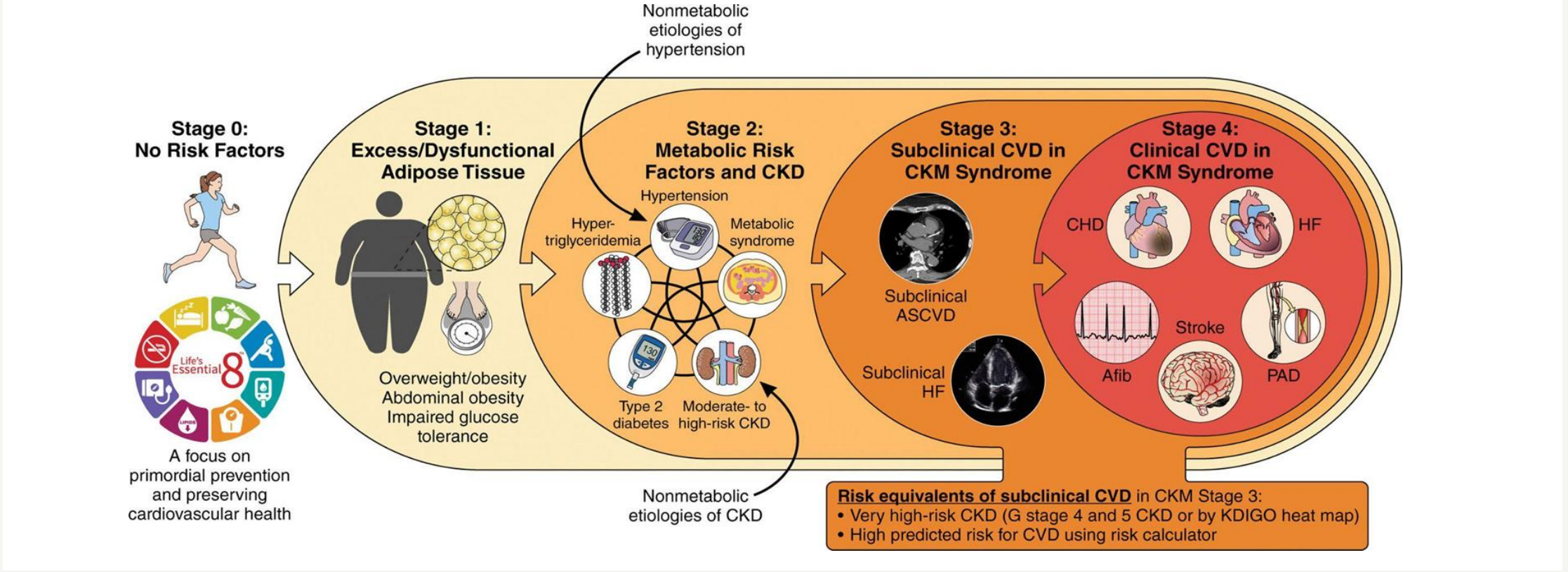
- ANT-Pharm is a library of anti-FZD/LRP molecules capable of activating the Wnt Pathway in various cell types and tissues
- Preclinical lead asset, has the potential to be best-in-class treatment for nAMD and DME
- Potential to expand to indications beyond Ophthalmology where Wnt signaling plays an important role

MoA figure modified from Clevers, H; Cell (2009); nAMD=wet age-related macular degeneration; DME=diabetic macular edema

Cardiovascular, Renal and Metabolism

Manu Chakravarthy M.D. Ph. D.
SVP and Global Head of Cardiovascular, Renal and Metabolism (CVRM) Product Development

Cardiovascular, renal and metabolic diseases are interdependent, and obesity is a key driver



Individuals with a BMI ≥30 kg/m^2 carry more than a 40% elevated risk for overall mortality

Despite numerous approved treatments in cardiometabolic diseases, unmet needs remain

Afib=atrial fibrillation; ASCVD=atherosclerotic cardiovascular disease; BMI=body mass index; CHD=coronary heart disease; CKD=chronic kidney disease; CKM=cardiovascular, kidney, and metabolic; CVD=cardiovascular disease; HF=heart failure; KDIGO=Kidney Disease Improving Global Outcomes; PAD=peripheral artery disease.; Ndumele CE, et al. Circulation 2023;148:1606–1635 (American Heath Association).

Strategic pillars of Cardiovascular, Renal & Metabolism at Roche

Incretins	Comorbidities	Combinations	E2E patient solutions
Incretins to combat obesity as a driver for metabolic diseases	***Roche portfolio set up to address further causal factors of metabolic disease***	***Establish a portfolio of combination therapies on the backbone of incretins***	***Synergies with Roche Diagnostics and Digital Health solutions***
Recent examples			
CT-388/ CT-868 *CT-388 BIC potential obesity ± T2D* *CT-868 BIC/FIC potential in OW/OB pts with T1D*	***Hypertension*** *Zilebesiran BIC and BID potential + SoC in people with established/high risk of CVD*	***GYM 329/ CT-173*** *Other MoAs can be tailored as add-on-therapies to address various comorbidities*	***CGM*** *AccuChek SmartGuide including differentiating predictive algorithm to better control diabetes*
CT-996 *BIC potential in obesity ± T2D*	***Expansion to adjacent indications*** *e.g., HFpEF, CKD, DR*, PD/AD**	***Inflammation*** *Selnoflast (NLRP3i) - ASCVD*	***Detection*** *Next generation solutions for the diagnosis of myocardial infarct (TropC), heart failure (proBNP), CV risk (Lp(a))*

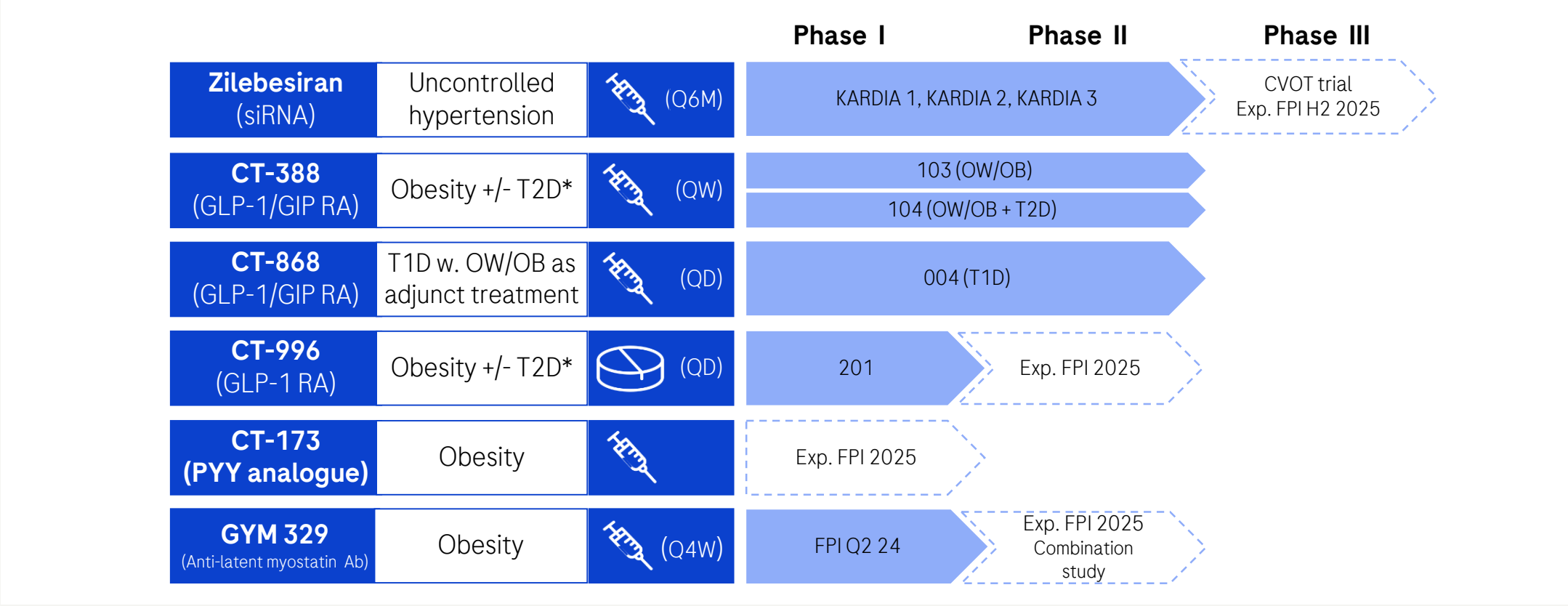
*Assets already exist within the current Roche Ophthalmology and Neurology pipeline to enable potential combinations with incretins

CV=cardiovascular; (AS)CVD=atherosclerotic cardiovascular disease; CKD=chronic kidney disease; HF=heart failure; MoA=mode of action; CGM=continuous glucose monitoring; UC=ulcerative colitis; SBP=systolic blood pressure; SC=subcutaneous; DR=diabetic retinopathy; PD=Parkinson's disease; AD=Alzheimer's disease

Roche Clinical Development in Cardiovascular, Renal & Metabolism

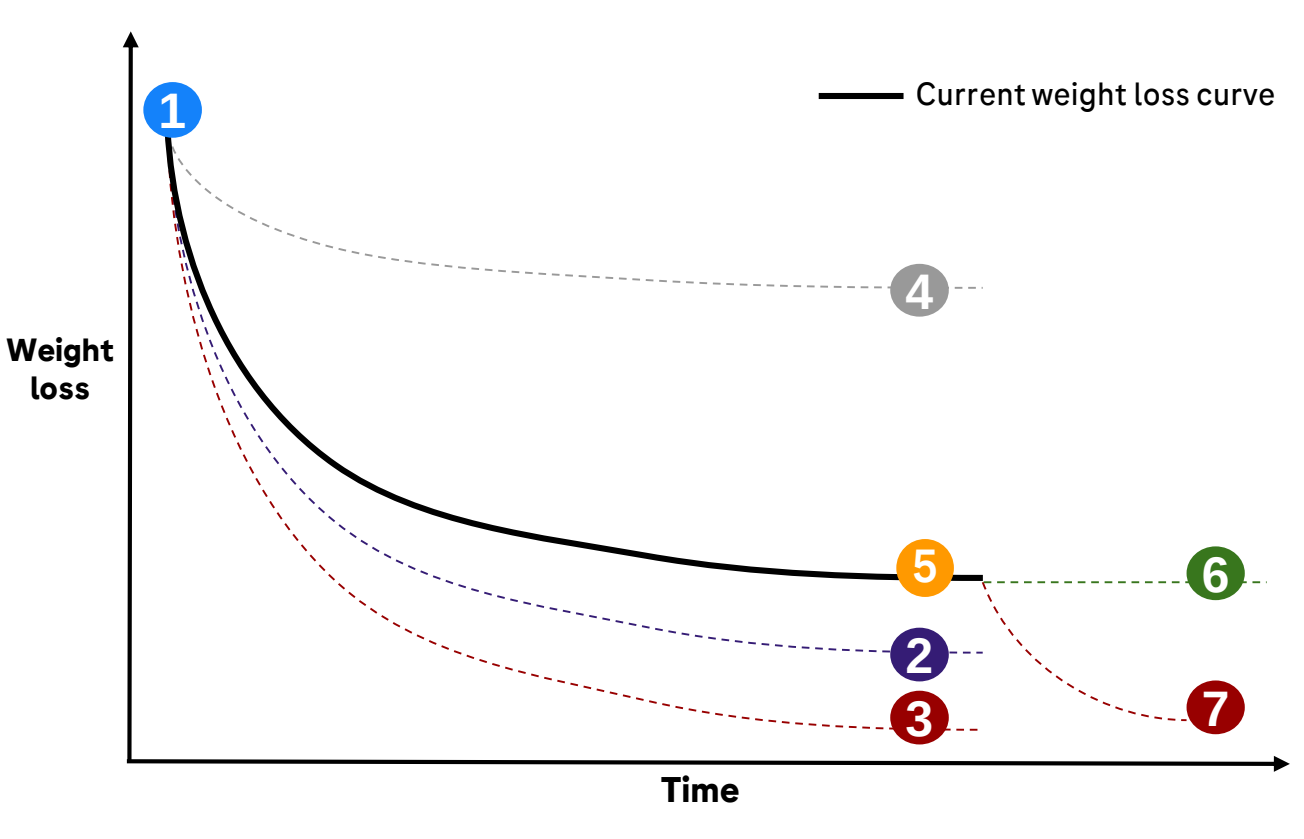
Broad portfolio of differentiated assets

Development program



GLP-1=glucagon-like peptide-1; GIP=glucose-dependent insulinotropic polypeptide; RA=receptor agonist; T2D=type-2 diabetes; T1D=type-1 diabetes; QW=once weekly; QD=once daily; OW=overweight; OB=obese; CVOT=CV outcomes trial; *Patients with obesity or overweight with at least one weight-related comorbidity including type 2 diabetes

Obesity: Addressing remaining unmet needs for weight loss and weight maintenance



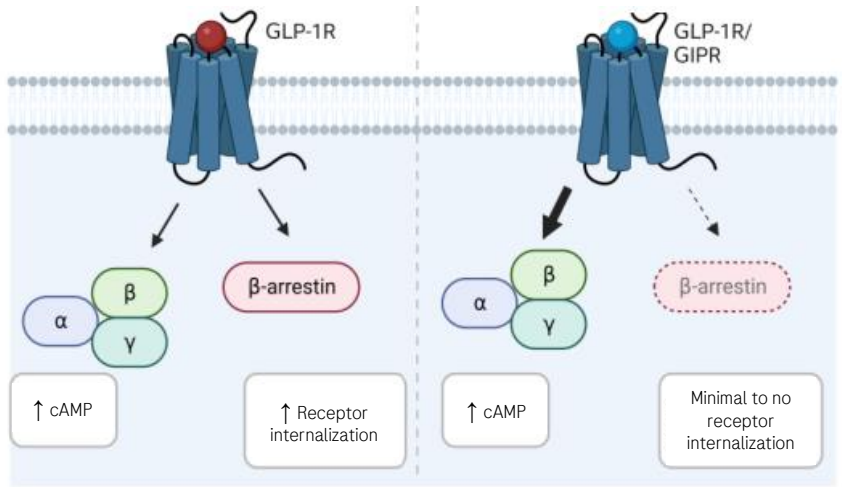
Weight loss unmet needs	Roche portfolio
1 Improved tolerability and/or simple up-titration	CT-388 (low dose)
2 Better quality weight loss (muscle preservation)	GYM 329 + incretin
3 Deeper weight loss (esp. in patients with higher BMI)	CT-388 (high dose)
4 Non/inadequate responders	CT-173 + incretin
5 Improved convenience (orals) (equivalent efficacy to injectables)	CT-996
6 Weight maintenance	CT-996
7 Further weight loss once incretins achieve “plateau”	CT-173 + incretin

BMI=body mass index

CT-388, 868 and 996 are purposefully designed with biased-signaling

Novel incretin agonists with unique signaling have potential to improve weight loss and glycemic control

CT-388, CT-996 and CT-868 are biased agonists



Minimal to no ß-arrestin recruitment results in prolonged glucose lowering and weight loss

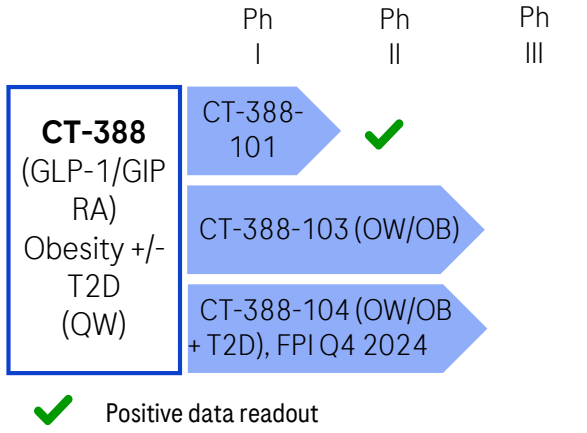
- CT-868, CT-388, and CT-996 are G protein-biased with robust cAMP potency and minimal to no β-arrestin recruitment
  - This biased signaling resulted in greater magnitude with more sustained glucose lowering and weight loss in relevant rodent models[1-3]
- Other preclinical data support biased signaling to increase efficacy with reduced adverse effects[4,5]

1. Rodriguez R et al. Presented at the American Diabetes Association 83rd Scientific Session, 23-26 June 2023; San Diego, CA. 2. Chakravarthy MV et al. Presented at the European Association for the Study of Diabetes, 59th Annual Meeting, 2-6 October 2023; Hamburg, Germany. 3. Luo J et al. Presented at the American Diabetes Association 84th Scientific Sessions; June 21-24, 2024; Orlando, FL.4. Jones B. Br J Pharmacol. 2022 Feb;179(4):492-510. 5.Smith, Lefkowitz, Rajagopal. Nature Reviews Drug Discovery 17, 243- 260 (2018), CA; cAMP=cyclic adenosine monophosphate; GLP-1R=glucagon-like peptide 1 receptor; GIPR=glucose-dependent insulinotropic polypeptide receptor

CT-388 being developed for overweight/obese patients +/- T2D

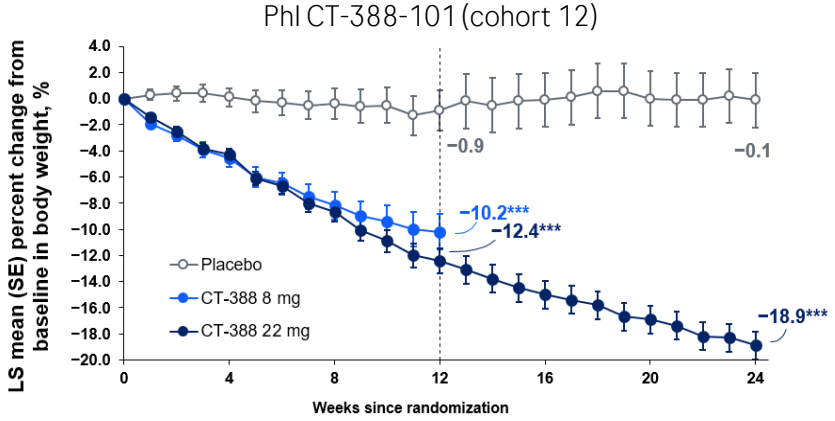
Robust Ph I weight loss results indicate best-in-class potential

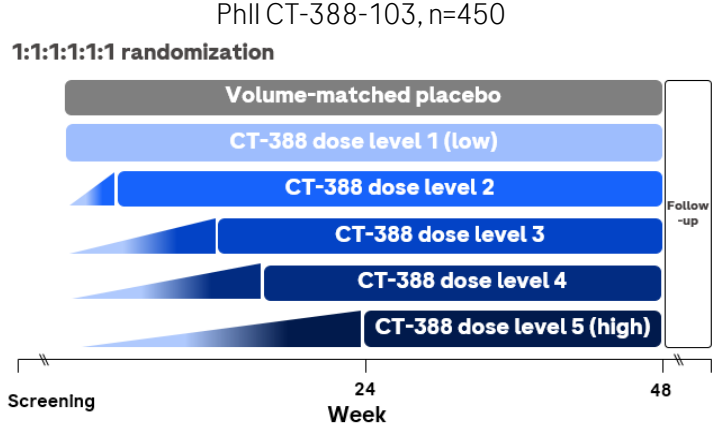
Development program



- Positive Ph Ib data for patients with OW/OB at 12 weeks (cohort 11) and 24 weeks (cohort 12) were presented at EASD
- Data in OW/OB patients with T2D (cohort 13) are expected in Q4 '24

CT-388 led to clinically meaningful weight loss over 12 and 24 weeks of treatment[1], Ph2 study initiated





- 22 mg dose of CT-388 titrated within 8 weeks produced ~12%WL at week 12 and ~19%WL at week 24
- CT-388 tolerability profile generally consistent with other incretin-based therapies at a similar (early) stage of development
- CT-388-103 is a multi-center, randomized, double-blind, placebo-controlled, parallel group dose-finding study to evaluate the efficacy and safety of CT-388 at low, middle, and high doses (levels 1-5); FPI Q3 2024

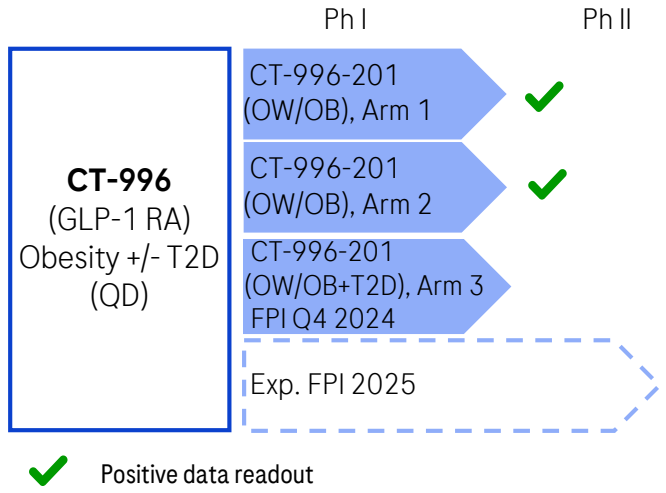
Clinical data support potential to be a best-in-class SC treatment for type 2 diabetes and chronic weight management

1. Chakravarthy et al, EASD 2024; *** P < 0.001 vs placebo. P values are nominal and have not been adjusted for multiplicity; CT-388-103: BMI=body mass index; EOT=end of treatment; QW=once weekly; SC=subcutaneous; GLP-1R=glucagon-like peptide 1; GIPR=glucose-dependent insulinotropic polypeptide receptor; T2D=type-2 diabetes; OW=overweight; OB=obese

CT-996 being developed for overweight/obese patients +/- T2D

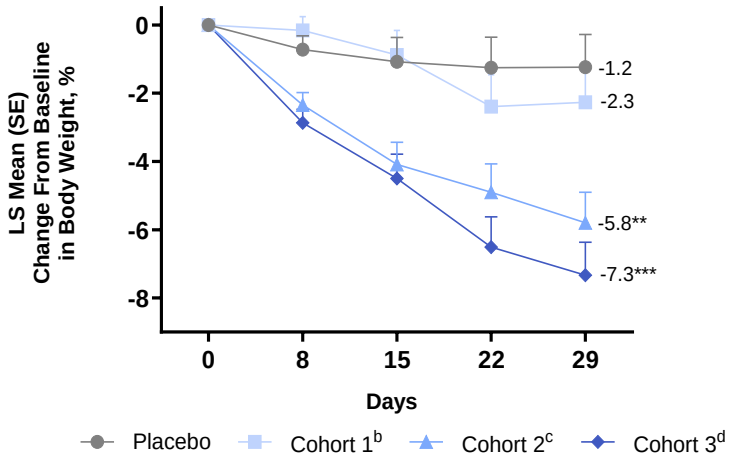
Potentially best-in-class oral small molecule with high bioavailability and no food restrictions

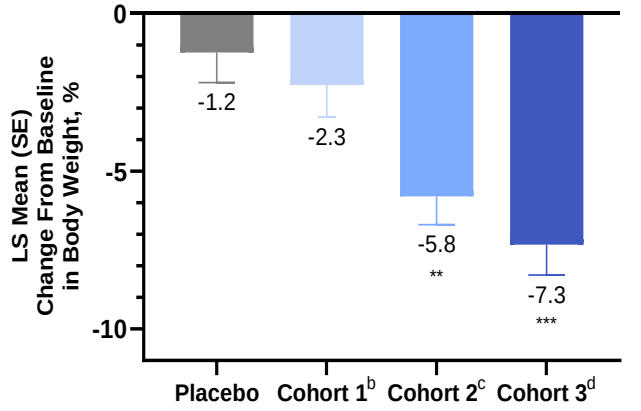
Development program



- Positive Ph I data in patients with OW/OB (arm 2) at 4 weeks were presented at EASD; arm 3 in pts with OW/OB+T2D is expected to have FPI in Q4 2024
- Ph II in OW/OB +/- T2D patients expected to start in 2025

Once-daily oral dosing of CT-996 over 4 wks with weight loss of up to 7.3%





**P < 0.01[a]; ***P < 0.001.[a]

- Percent change in body weight is linear over time with no plateau
- Clinically meaningful placebo-adjusted weight loss up to 6.1% was observed within 4 weeks
- GI-Related TEAEs were mostly mild and none were severe; patterns are generally consistent with other incretin therapies at a similar (early) stage of development
- Plasma half-life (17-22 hrs) supports once-daily dosing

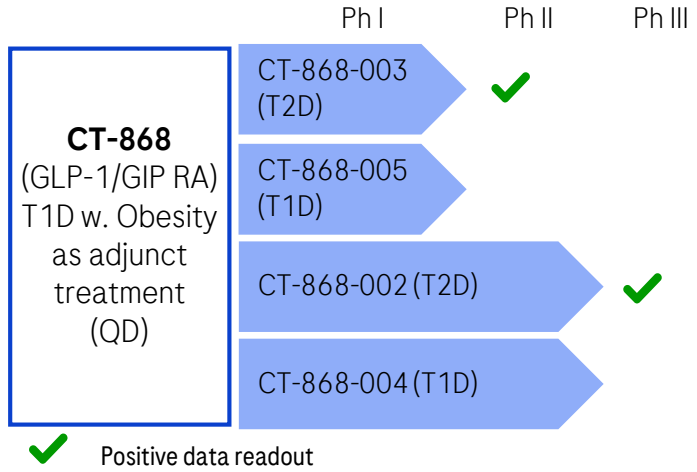
Clinical data support further evaluation for T2D, obesity, and obesity-related comorbidities; able to adequately address at scale

* Patients with obesity or overweight with at least one weight-related comorbidity including type 2 diabetes; GLP-1: Glucagon-like peptide 1; T2D=type-2 diabetes; OW=overweight; OB=obese, d= day; LS= least squares.; aP values are nominal and have not been adjusted for multiplicity.
bCohort 1 (CT-996 10/30/60/90): planned 10/30/60/90 mg: each dose for 7 days (actual: all participants followed planned titration path).
cCohort 2 (CT-996 10/30/60/90/120): planned 10 mg × 3d, 30 mg × 4d, 60 mg × 7d, 90 mg × 7d, 120 mg × 7d (actual: 2 participants needed 3 additional days at 90 mg before escalating to 120 mg; 1 participant remained at 60 mg).
dCohort 3 (CT-996 10/30/50/80/120): planned 10 mg × 3d, 30 mg × 4d, 50 mg × 7d, 80 mg × 7d, 120 mg × 7d (actual: all except 1 participant followed the planned path; 1 participant decreased their dose from 50 mg to 30 mg to 10 mg and completed the study at 10 mg).

CT-868 being developed for overweight/obese patients with T1D

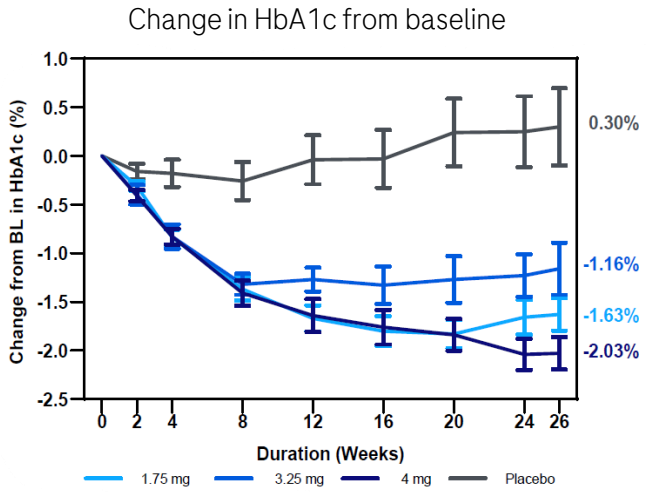
First-in-class and best-in-class potential as adjunctive therapy in patients with type 1 diabetes

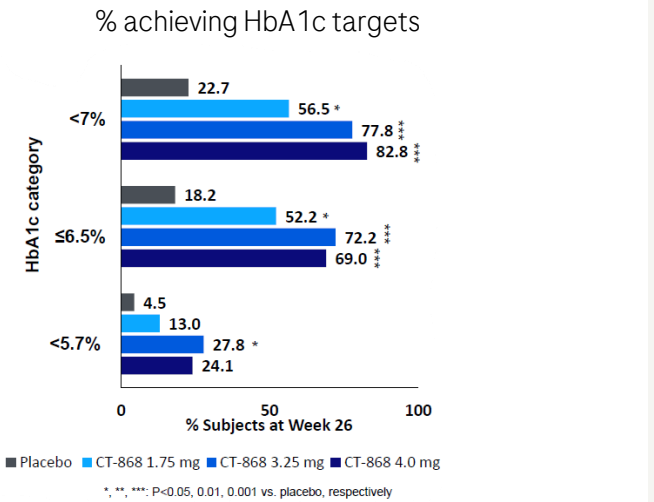
Development program



- A Ph II proof-of-concept trial for glucose control in patients with T1D who are OW/OB (BMI >27) is ongoing
- Data expected in 2025

Clinically meaningful reduction in HbA1c demonstrated in T2D Ph II trial[4]





- Hypoglycemia[1], weight gain[2], CV disease[3] and insulin resistance[2] remain unaddressed challenges for pts with T1D; insulin therapy exacerbates these
- CT-868 could have *insulin-independent* glucose disposal, via GIP activation
- CT-868 demonstrated robust glycemic control (–2.3% HbA1c lowering vs placebo) with ~70% of participants achieving HbA1c ≤6.5% at Week 26, even at low doses
- CT-868 improved CV risk factors (LDL-C, apoB, VLDL, TG, blood pressure) and liver enzymes

Flexible and easy integration into standard insulin regimens for patients with T1D through once-daily dosing

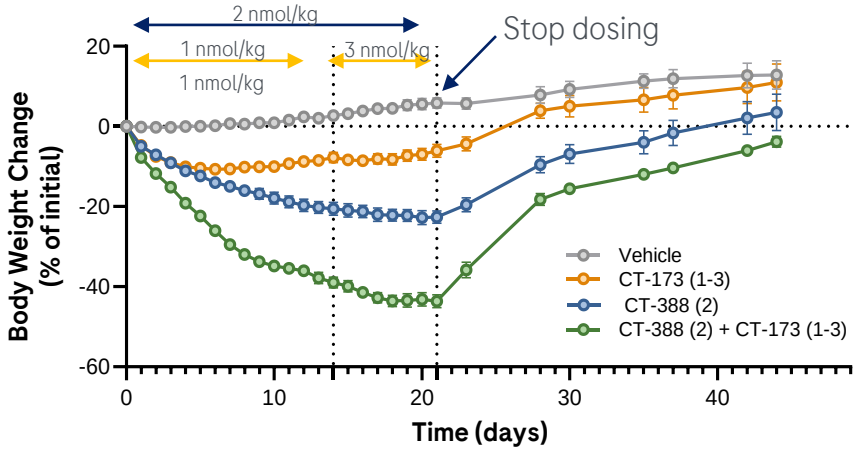
1 Adverse events and their association with treatment regimens in the diabetes control and complications trial. Diabetes Care. 1995 Nov;18(11):1415-27. doi: 10.2337/diacare.18.11.1415. PMID: 8722064. 2. Van der Schueren (2021), Obesity in people living with type 1 diabetes, The Lancet Diabetes & Endocrinology, 9(11), 776-785. ISSN: 2213-8587, 3. Vergès B. Cardiovascular disease in type 1 diabetes: A review of epidemiological data and underlying mechanisms. Diabetes Metab. 2020 Nov;46(6):442-449. doi: 10.1016/j.diabet.2020.09.001. Epub 2020 Sep 28. PMID: 32998054., 4. Chakravarthy MV, et al.Obesity Week 2023; GLP-1=glucagon-like peptide 1; GIPR=glucose-dependent insulinotropic polypeptide receptor; T1D= type-1 diabetes; T2D=type-2 diabetes; OW=overweight; OB=obese

CT-173 + CT-388 further induced weight loss in DIO mice

In vivo data support CT-173+388 combination to overcome weight loss plateau, Ph I expected to start in 2025

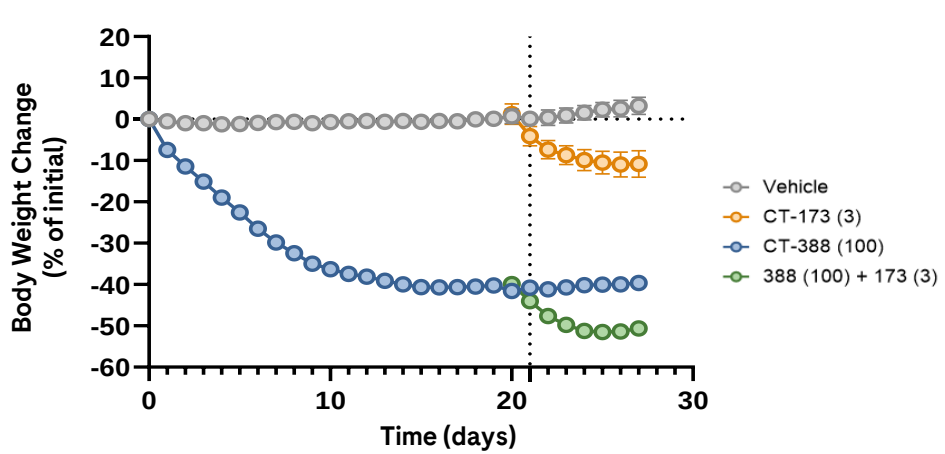
Weight loss in DIO mice by combining CT-173 (PYY analogue) and CT-388 (QD dosing)

CT-173 + CT-388 initiated together



- Low dose CT-173 in combination with low dose CT-388 led to 44% weight loss in DIO mice (21% more vs CT-388 alone)
- Slower weight rebound after treatment stop (~4% weight loss 23 days later) compared with CT-388 or CT-173 alone

CT-173 initiated only after CT-388 plateaus



- Low dose CT-173 synergizes with high dose CT-388 even after CT-388's weight loss has plateaued and led to 52% weight loss
- Suggests orthogonal mechanisms could potentially reset body weight set points

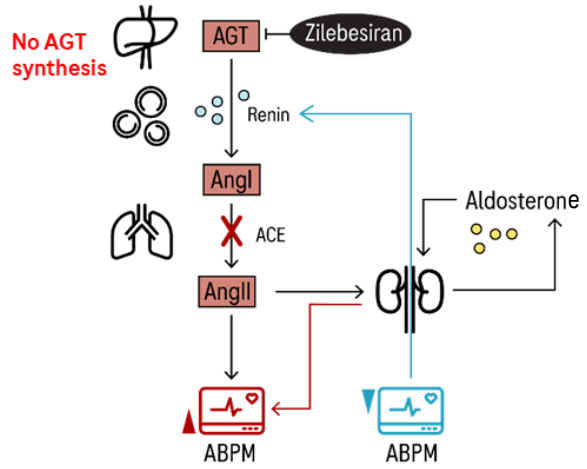
Preclinical data demonstrate improved weight loss effect

DIO=diet induced obese; QD=once daily

Despite available therapies hypertension often remains uncontrolled

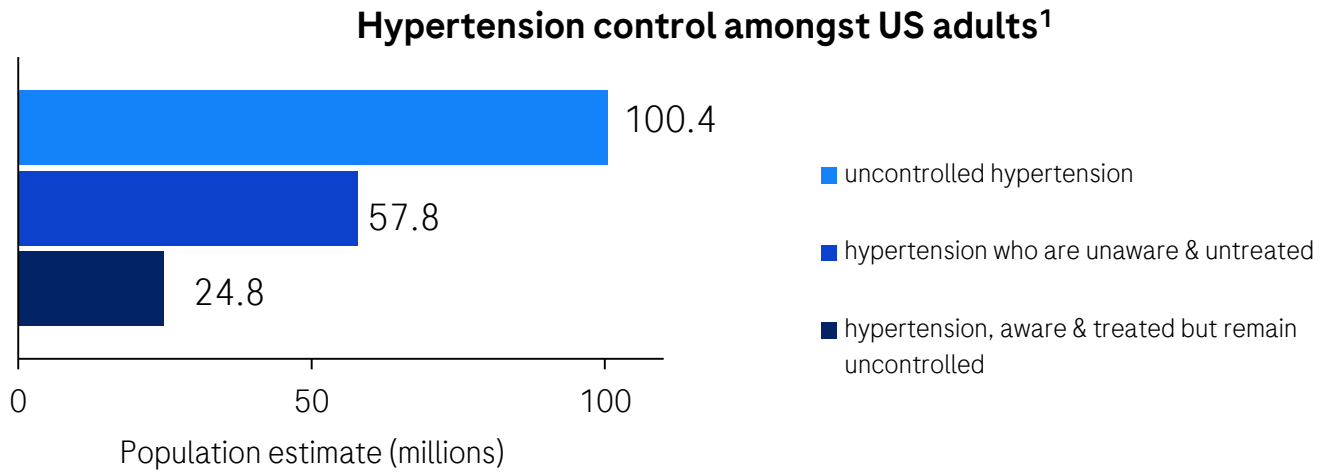
Zilebesiran has an innovative MoA with first-in-class and best-in-disease potential in hypertension

Zilebesiran (siRNA targeting AGT)



- siRNA targeting angiotensinogen, the most upstream precursor of all angiotensin peptides
- Could potentially prevent RAAS escape

Half of adults in US with uncontrolled hypertension unaware of their condition



- 1.6- to 3.0-fold increased risk of mortality (all-cause to stroke-related) in patients with treated but uncontrolled hypertension[2]
- Consistent + durable blood pressure control with improved adherence is therefore critically needed to change this trajectory

Zilebesiran has the potential for twice yearly SC dosing

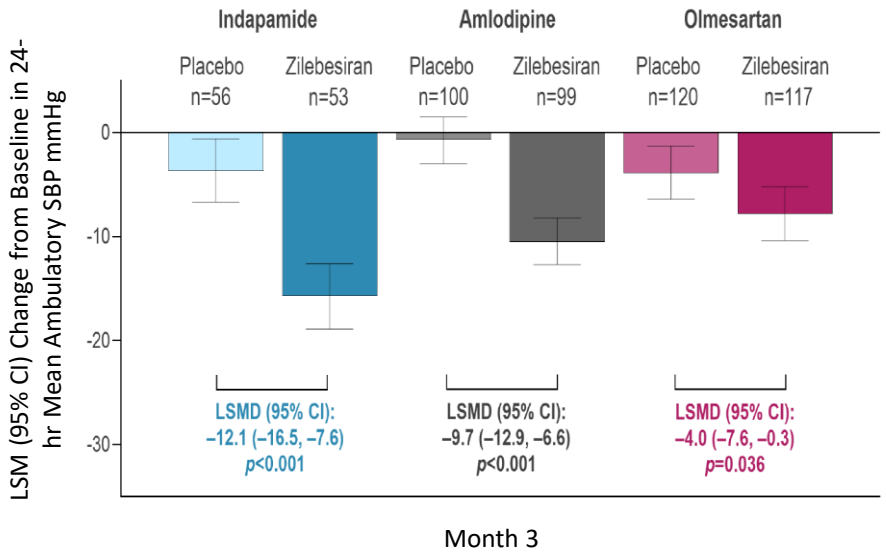
1 Richardson, Vaughan et al, JAMA Netw Open. 2024;7(9); 2. Data is based on a study of 13,947 U.S. adults aged ≥18 years, enrolled in the Third National Health and Nutrition Examination Survey (1988–1994); MoA=mode of action; siRNA=small interfering RNA; SC=subcutaneous; RAAS=renin angiotensin aldosterone system; AGT=angiotensinogen; AngI/II=angiotensin I/II; ACE=angiotensin-converting enzyme; ABPM=ambulatory blood pressure monitoring; SoC=standard of care.

Zilebesiran with best-in-disease potential in hypertension

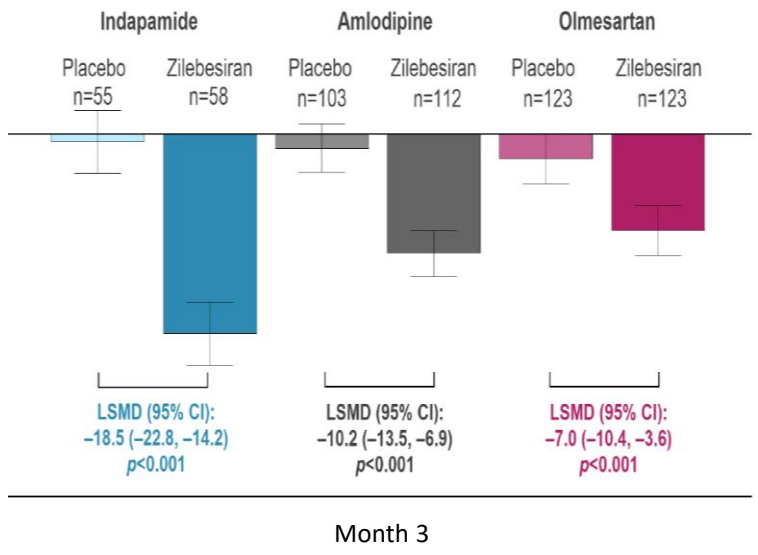
Robust Ph II results with zilebesiran alone and as add-on to SoC

Ph II (KARDIA-2): Zilebesiran add-on to 1 SoC in mild-to-mod HTN

Primary endpoint: Change in baseline to month 3 in 24h mean ambulatory SBP*



Secondary endpoint: Change in baseline to month 3 in 24h Office SBP*



- Single dose reduced 24h mean ambulatory and office SBP at 3-mo when added to a diuretic, calcium channel blocker, or maximum-dose angiotensin receptor blocker
- Placebo-adjusted differences in blood pressure were sustained to month 6 despite add-on antihypertensive therapy
- Results support the potential for twice-yearly dosing

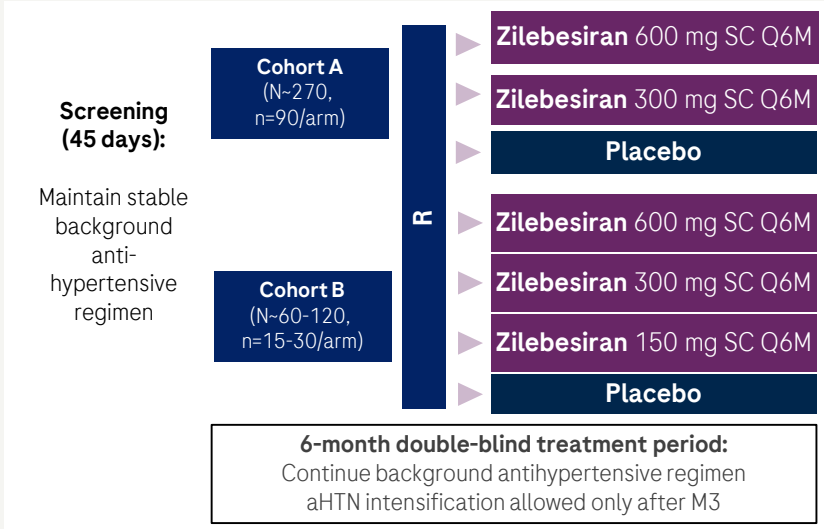
Bakris GL et al. KARDIA-2. Presented at the American College of Cardiology Annual Scientific Session & Expo , April 6 8, 2024, Atlanta, GA, USA

*Ambulatory/office blood pressure assessed while patients were receiving or within 2 weeks of stopping any rescue medication is censored; HTN= hypertension; SoC=standard of care; SBP=systolic blood pressure; CI=confidence interval; LSM=least-squares mean; LSMD=LSM difference; CV=cardiovascular; Q3M = every 3 months; Q6M = every 6 months; zilebesiran in partnership with Alnylam Pharmaceuticals

Zilebesiran: Comprehensive development program ongoing

Ph II (KARDIA-3) with zilebesiran as add-on to 2-4 SoC for uncontrolled hypertension with high CV risk initiated

Ph II (KARDIA-3): Combination Study in High CV Risk[1]



FPI April 24

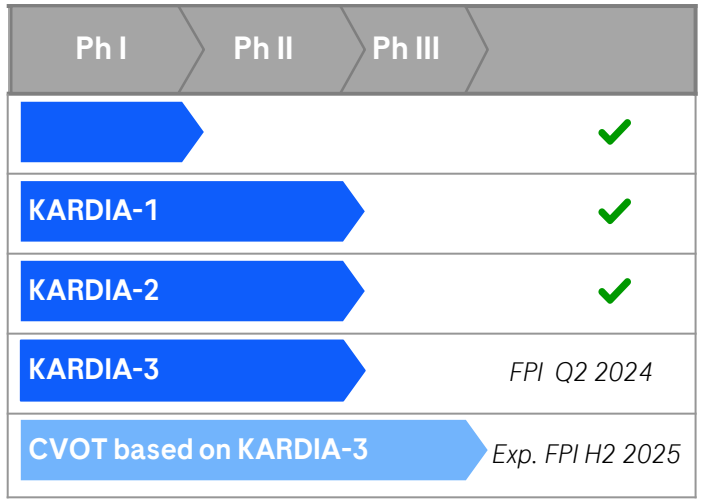
Primary Endpoint:

- Change at Month 3 in seated office SBP

Secondary Endpoints Include:

- Change at Month 3 and Month 6 in 24-hour mean SBP and DBP, assessed by ABPM
- Change at Month 3 in seated office DBP
- Change at Month 6 in seated office SBP and DBP
- Change in serum AGT

Clinical development program

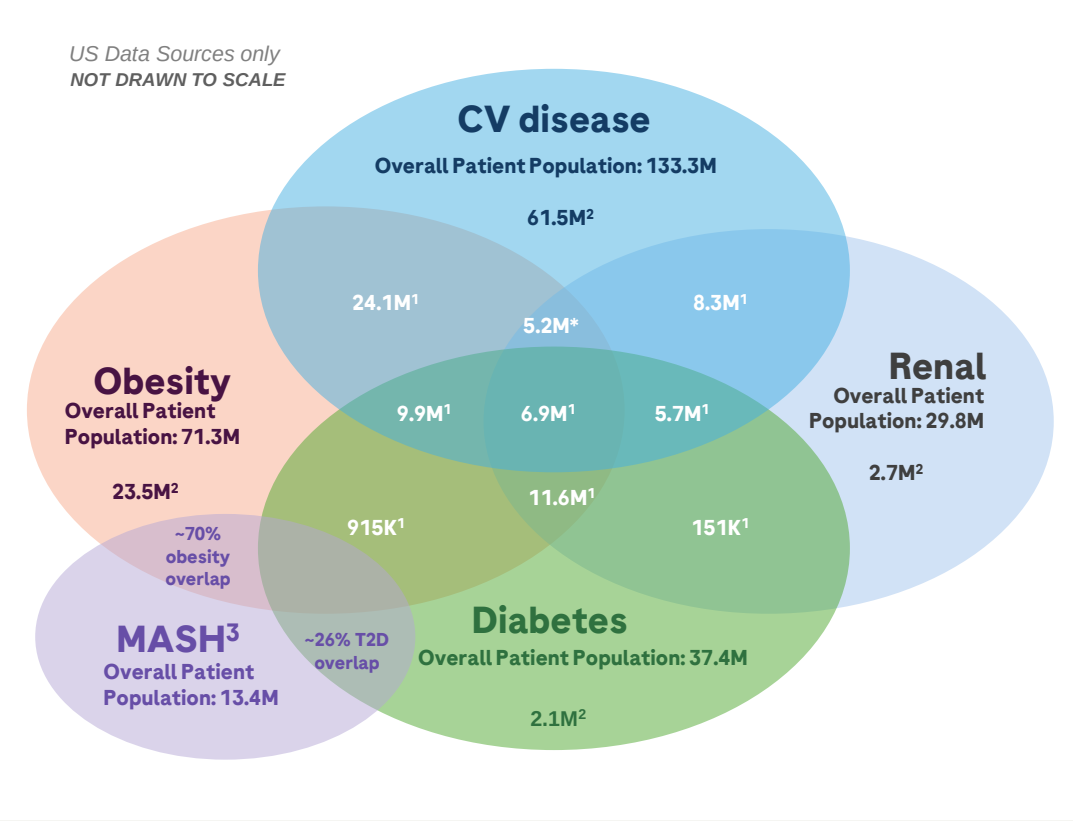


- Ph II (KARDIA-1): Monotherapy in mild/mod hypertension; primary endpoint of reduction of 24-h mean systolic blood pressure at 3 months met
- Ph II (KARDIA-2): Add-on to 1 SoC in uncontrolled hypertension; primary endpoint of systolic blood pressure reductions in all arms at month 3 met
- Ph II (KARDIA-3): FPI 2024; Cohort A fully enrolled (results will inform pivotal Ph III trial design); Cohort B currently enrolling
- Ph III (CVOT): Composite MACE endpoint in uncontrolled hypertension at high CV risk, to deliver robust label and access with CV outcomes benefits at launch; Potential for expansion to other CV indications

1 NCT06272487; aHTN=antihypertensive; 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; zilebesiran in partnership with Alnylam Pharmaceuticals

Roche committed to rapidly expand footprint in CVRM

CVRM diseases continue to be the leading causes of death and have high patient overlap



Roche is well-positioned to tackle one of the most important public health challenges of our modern times

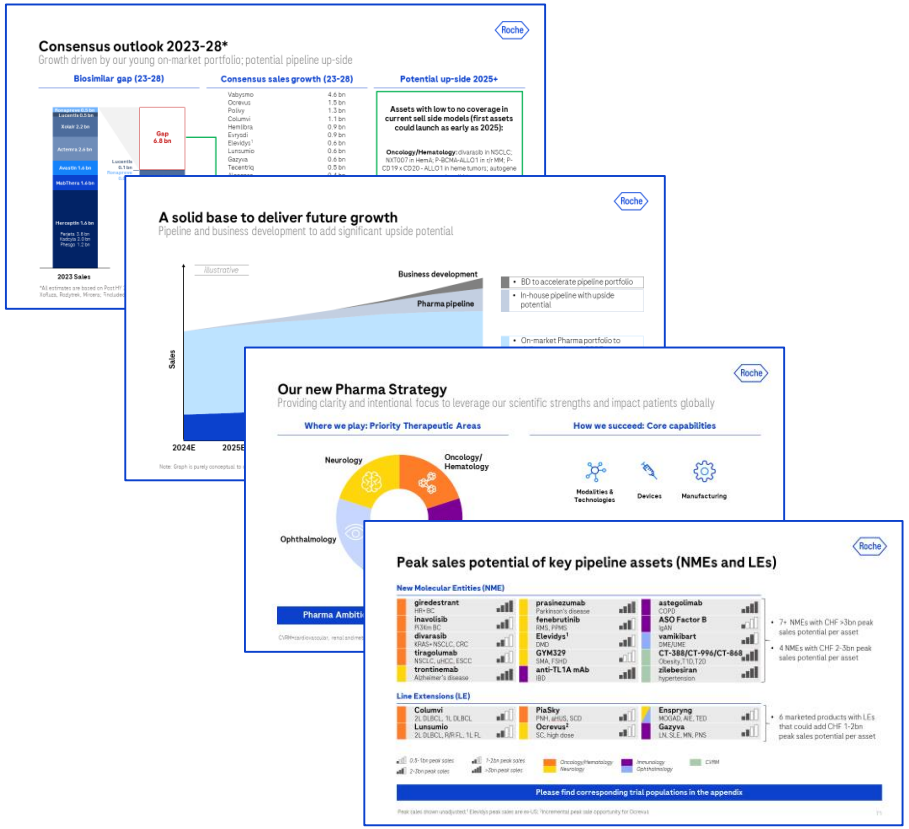
Core foundation of clinically validated MoAs

- Solid portfolio of foundational assets as well as innovative new MoAs to address CVRM diseases (>5 assets across CVRM, Immunology, Neurology, and Ophthalmology)
- Roche to build on successful acquisitions and partnering opportunities, e.g. Carmot and Alnylam

Time frame of analysis is January 2018 to June 2023. Source: IQVIA LAAD; US Market Access Strategy Consulting analysis, Cusi, K. Time to include Non Alcoholic Steatohepatitis in the Management of Patients with Type 2 Diabetes. Diabetes Care, 2020; 1 Represents number of patients in each Venn Diagram overlap; 2 Represents number of patients in a single TA, i.e., have no comorbidity overlap; 3 Overlap for MASH, Diabetes, and Obesity unknown; approximate percentages have been included. Patient population sizes include 2022+ data-active patients, or those with Rx or Dx claims in 2022 or 2023; CV=cardiovascular; CVRM=cardiovascular renal metabolism; MASH=metabolic dysfunction associated steatohepatitis; NME=new molecular entity

Setting up Roche for the next innovation cycle and long-term growth

Significant progress over past 12 months



Our young portfolio, people and scientific capabilities serve as a strong foundation for future growth

We have made significant progress over the last year:

- Strengthening our portfolio and implementing a new portfolio governance
- Implementing R&D Excellence and applying the ‘Bar’ to reach top-quartile R&D productivity
- Accelerating key assets and adding promising external molecules
- Establishing a purposeful balance between scientific exploration and focus on disease areas to continuously deliver transformative medicines
- Launching Pharma Strategy and defining 5 TAs, including CVRM, and core capabilities
- Focusing on synergies between Diagnostics & Pharma to address unmet needs along the entire patient journey

Thank you for your attention and we are happy to answer your questions

Appendix

Changes to the development pipeline

Pharma Day update

New to phase I

2 NMEs:
RG6221 LTBR agonist
RGXXXX* CDK4/2i (RGT-419B) - (HR+) breast cancer

New to phase II

1 NME:
RG6512 FIXa x FX (NXT007) - hemophilia

1 AI:
RG6640 GLP-1/GIP RA (CT-388) - obesity + comorbidities***

New to phase III

1 NME:
RG6631 anti-TL1A - ulcerative colitis

New to registration

Removed from phase I

2 NMEs:
RG6234 forimtamig monotherapy + combos - multiple myeloma
RG6449 HBsAg Mab - chronic hepatitis B

Removed from phase II

4 NMEs:
RG7854/ RG6346/ RG6084**
ruzotolimod/xalnesiran/PDL1 LNA - HBV
RG6139 tobemstomig monotherapy + combos - solid tumors

Removed from phase III

Approvals

1 NME (EU):
RG6107 PiaSky (crovalimab) - PNH

2 AIs (EU):
RG7716 Vabysmo – BRVO
RG7716 Vabysmo – CRVO

2 AIs (US):
RG7446 Tecentriq SC - all approved indications
RG1594 Ocrevus SC - RMS & PPMS

Status as of September 18, 2024

*TBD; **combination platform; ***comorbidities include prediabetes, hypertension, dyslipidemia, obstructive sleep apnea

Roche Group development pipeline

Phase I (46 NMEs + 8 AIs)

RG6026	Columvi monotherapy + combos	heme tumors
RG6058	tiragolumab combos	solid tumors
RG6076	englumafusp alfa combos	heme tumors
RG6114	inavolisib	solid tumors
RG6160	cevostamab	r/r multiple myeloma
RG6171	giredestrant monotherapy + combos	solid tumors
RG6194	runimotamab	breast cancer
RG6221	LTBR agonist	solid tumors
RG6279	eciskafusp alfa ± T	solid tumors
RG6323	efbalropendekin alfa (IL15/IL15Ra-Fc) ± T	heme & solid tumors
RG6330	divarasib monotherapy + combos	solid tumors
RG6344	BRAF inhibitor (3)	solid tumors
RG6411	-	solid tumors
RG6440	anti-latent TGF-β1 (SOF10)	solid tumors
RG6457	WRN covalent inhibitor	solid tumors
RG6468	-	solid tumors
RG6524	DLL3 trispecific	solid tumors
RG6537	AR degrader	mCRPC
RG6538[1]	P-BCMA-ALLO1	heme tumors
RG6540[1]	P-CD19 x CD20 - ALLO1	heme tumors
RG6596[2]	HER2 TKI	HER2+ BC
RG6614	USP1 inhibitor	solid tumors
RG6648[5]	cMET ADC	solid tumors
RG7827	FAP-4-1BBL combos	solid tumors
RG7828	Lunsumio monotherapy + combos	heme tumors
RGXXXX**	CDK4/2i (RGT-419B)	(HR+) breast cancer
CHU	glypican-3 x CD3	solid tumors
CHU	codrituzumab	HCC
CHU	CD137 switch antibody	solid tumors
CHU	RAS inhibitor	solid tumors
CHU	SPYK04	solid tumors
CHU	anti-CLDN6 trispecific	CLDN6+ solid tumors
CHU	ROSE12	solid tumors
RG6287	-	immunology
RG6315	-	fibrosis
RG6382	CD19 x CD3	SLE
RG6377	-	IBD
RG6418*	selnoflast	inflammation
RG6421	TMEM16A potentiator	cystic fibrosis
RG7828	Lunsumio	SLE
CHU	anti-HLA-DQ2.5 x gluten peptides	celiac disease
CHU	Anti-complement C1s recycling antibody	Immunology
RG6006	zosurabalpin	bacterial infections
RG6436	LepB inhibitor	complicated urinary tract infection
RG6237	anti-latent myostatin	obesity
RG6640	GLP-1/GIP RA (CT-388)	obesity +/- T2D
RG6652	GLP-1 RA (CT-996)	obesity +/- T2D
RG6035	Brainshuttle™ CD20	multiple sclerosis
RG6182	MAGL inhibitor	multiple sclerosis
RG6120	zifibancimig	nAMD
RG6209	-	retinal disease
RG6351	-	retinal disease
RG7921	-	RVO
CHU	REVN24	acute diseases

Phase II (16 NMEs + 9 AIs)

RG6058	tiragolumab + T	NSCLC
	tiragolumab + T	1L PD-L1+ mSCCHN
RG6107	PiaSky (crovalimab)	sickle cell disease
RG6171	giredestrant	endometrial cancer
RG6180	autogene cevumeran	solid tumors
RG6357	dirloctocogene samoparvovec A	hemophilia
RG6512	FIXa x FX (NXT007)	hemophilia
RG6341	-	chronic cough
RG6536	vixarelimab	IPF/SSc-ILD
RG6631[3]	anti-TL1A	Crohn's disease
RG6615[4]	zilebesiran	hypertension
RG6641	GLP-1/GIP RA (CT-868)	T1D with BMI ≥ 25
RG6640	GLP-1/GIP RA (CT-388)	obesity + comorbidities***
RG6042	tominersen	Huntington's
RG6102	trontinemab	Alzheimer's
RG6237	anti-latent myostatin + Evrysdi	SMA
	anti-latent myostatin	FSHD
RG6289	gamma-secretase modulator	Alzheimer's
RG6356	Elevidys	0 to <4 year old DMD
RG6416	bepranemab	Alzheimer's
RG7816	alogabat	Angelman syndrome
RG7935	prasinezumab	Parkinson's
RG6179	vamikibart	DME
RG6501	OpRegen	geographic atrophy
CHU	anti-IL-8 recycling antibody	endometriosis

Status as of September 18, 2024

RG-No - Roche/Genentech; CHU - Chugai managed; [1]Poseida Therapeutics managed; [2]Zion Pharma managed; [3]Telavant managed; [4]Alnylam Pharmaceuticals managed; [5]MediLink managed; T=Tecentriq; *also developed in neurology; **TBD;***comorbidities include prediabetes, hypertension, dyslipidemia, obstructive sleep apnea; RA=Receptor agonist

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Cardiovascular, Renal & Metabolism
Neurology
Ophthalmology
Other

Roche Group development pipeline

Phase III (8 NMEs + 34 AIs)

RG3502	Kadcyla + T	HER-2+ eBC high-risk
RG6026	Columvi + chemo	2L+ DLBCL
	Columvi + Polivy + R-CHP	1L DLBCL
	Columvi	r/r MCL
RG6058	tiragolumab + T	1L PD-L1 high NSCLC
	tiragolumab + T + chemo	1L esophageal cancer
	tiragolumab + T	locally advanced esophageal cancer
	tiragolumab + T	stage III unresectable 1L NSCLC
	tiragolumab + T + Avastin	1L HCC
RG6107	PiaSky (crovalimab)	aHUS
RG6114	inavolisib + fulvestrant	post CDKi HR+ PIK3CA-mut. BC
	inavolisib + Phesgo	1L HER2+ PIK3CA-mut. mBC
RG6171	giredestrant + palbociclib	1L ET sensitive ER+/HER2- mBC
	giredestrant	ER+ BC adj
	giredestrant + Phesgo	1L ER+/HER2+ BC
	giredestrant + CDK4/6i	1L ET resistant ER+/HER2- BC
RG6330	divarasib	2L NSCLC
RG7446	Tecentriq + platinum chemo	NSCLC periadj
	Tecentriq + BCG	NMIBC, high-risk
	Tecentriq	ctDNA+ high-risk MIBC
	Tecentriq + lurbinectedin	1L maintenance SCLC
RG7601	Venclexta + azacitidine	1L MDS
RG7828	Lunsumio + lenalidomide	2L+ FL
	Lunsumio + Polivy	2L+ DLBCL
RG6149	astegolimab	COPD
RG6299	ASO factor B	IgA nephropathy
RG66313	anti-TL1A	ulcerative colitis
RG7159	Gazyva	lupus nephritis
	Gazyva	membranous nephropathy
	Gazyva	systemic lupus erythematosus
	Gazyva	childhood onset idiopathic nephrotic syndrome*
RG6152	Xofluza	influenza direct transmission
RG1594	Ocrevus higher dose	RMS & PPMS
RG6168	Enspryng	MOG-AD
	Enspryng	autoimmune encephalitis
RG6356	Elevidys	amb. 8 to <18y & non amb. DMD
RG7845	fenebrutinib	RMS
	fenebrutinib	PPMS
RG6168	Enspryng	TED
RG6179	vamikibart	UME
RG6321	Susvimo	wAMD, 36-week
RG7716	Vabysmo	CNV

Registration US & EU (2 NME + 4 AIs)

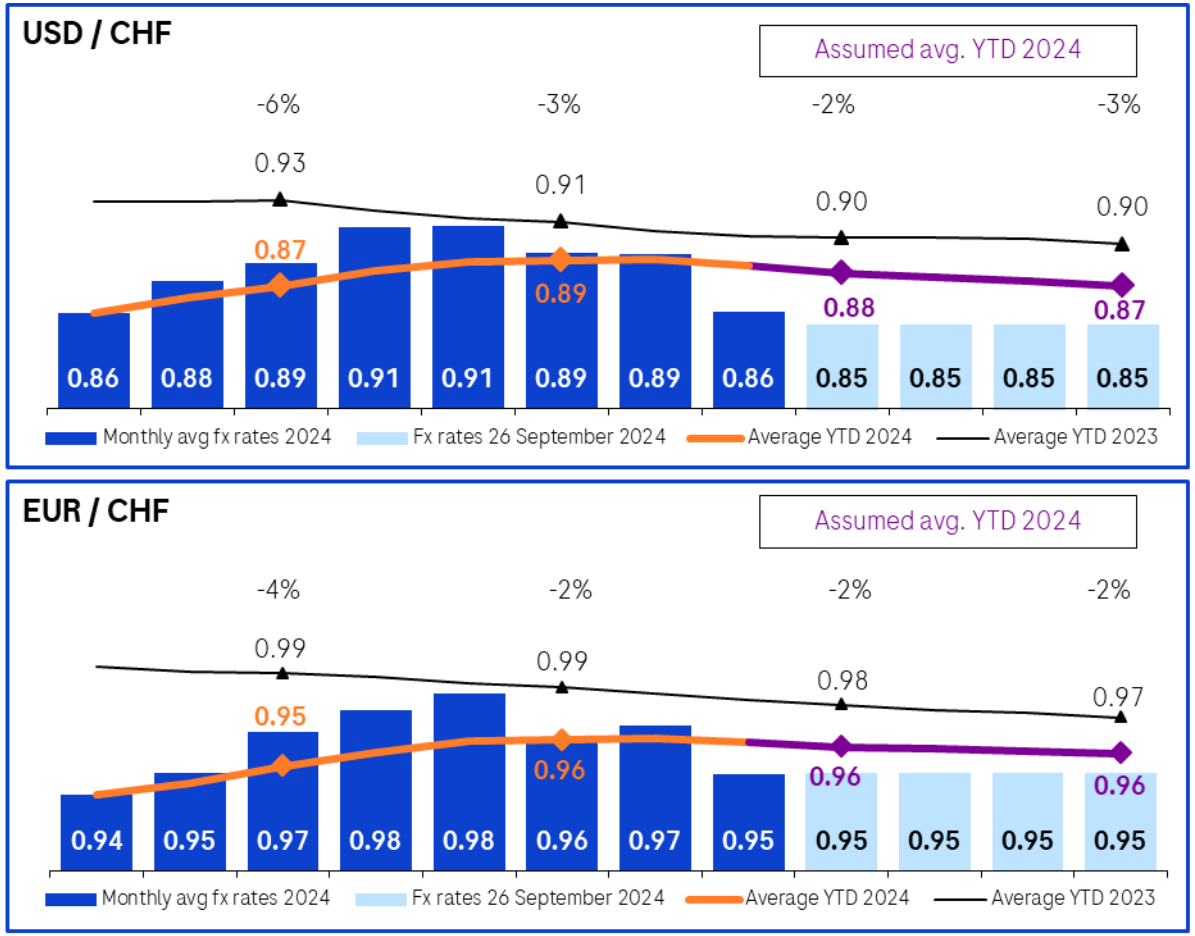
RG6114	inavolisib + palbociclib + fulv.	1L HR+ PIK3CA-mut. mBC
RG6152	Xofluza[3]	influenza, pediatric (0-1 year)
RG6356	Elevidys[2]	DMD
RG3625	TNKase[1]	stroke
RG6321	Susvimo[1]	DME
	Susvimo[1]	DR

[1]Filed in US
[2]Filed in EU, approved in US (Sarepta)
[3] Filed in EU

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Cardiovascular, Renal & Metabolism
Neurology
Ophthalmology
Other

Status as of September 18, 2024

Expected 2024 currency impact



Assuming the 26 September 2024 exchange rates remain stable until end of 2024,
2024 impact[1] is expected to be (%p):

	Q1	Q2	Q3	Q4
Sales	**-8**	**-2**	**-3**	**-4**

	Q1	HY	Sep YTD	FY
Sales	**-8**	**-5**	**-4**	**-4**
Core operating profit		-7		-6
Core EPS		-8		-7

[1]On group growth rates

Doing now what patients need next