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Novartis R&D Investor Event

London, November 28, 2023

NOVARTIS | Reimagining Medicine

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Novartis R&D Investor Event 2023

November 28, 2023 (GMT times)

13.30 – 14.50	**Opening** **Novartis Strategy and Growth Update** **Novartis Research & Development Overview** **Q&A panel**
14.50 – 15.15	Break (25’)
15.15 – 16.35	**Cardiovascular-Renal-Metabolic** **Immunology** **Neuroscience**
16.35 – 17.00	Break (25’)
17.00 – 18.00	**Oncology** **Closing**

Speakers

Vas Narasimhan
Chief Executive Officer

Harry Kirsch
Chief Financial Officer

Fiona Marshall
President, Biomedical Research

Shreeram Aradhye
President, Development and Chief Medical Officer

Angelika Jahreis
Development Head Immunology

David Soergel
Development Head Cardio-Renal-Metabolic

Jeff Legos
Development Head Oncology

Norman Putzki
Development Head Neuroscience and Gene Therapy

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Novartis Strategy & Growth Update

Vas Narasimhan, CEO

NOVARTIS | Reimagining Medicine

Novartis differentiated profile offers an attractive short-, mid- and long-term shareholder value creation opportunity

Focused strategy 1

"Pure-play" innovative medicines

4 core therapeutic areas

2+3 technology platforms

Attractive growth prospects 2

Mid-term sales guidance **upgrade to +5% CAGR**, with core margin of ~40%+

Mid-single digit long-term sales growth driven by strong portfolio and pipeline

Strong returns 3

Substantial cash generation at **32.4%**[1] of sales, and robust balance sheet

Delivering **7%** sales CAGR from 2018-2022 with core operating income at **14%** CAGR[2]

ESG leader 4

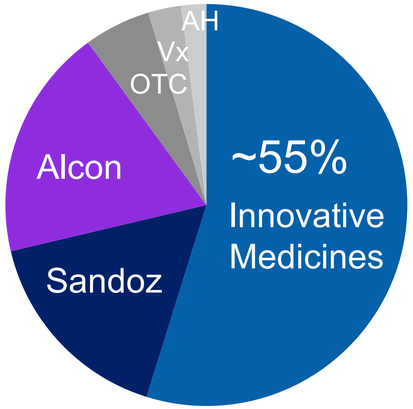
Focus on material factors to **create value**: Innovation, access to medicines and human capital

#1 in Sustainalytics[3]; leaders in ATMI (Reaching >250m patients); AA in CDP climate and water

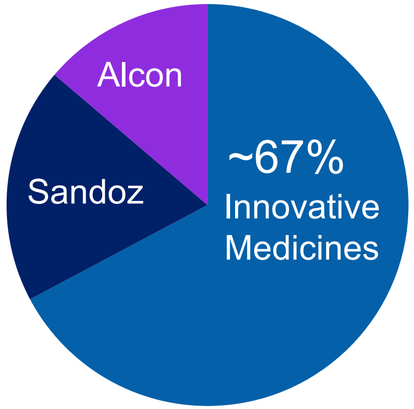
1. 9M 2023 Continuing operations. 2. Continuing operations growth in constant currencies. 3. Pharmaceuticals subindustry group. ATMI – Access to Medicines Index.

Novartis transformation into a pure-play innovative medicines company...

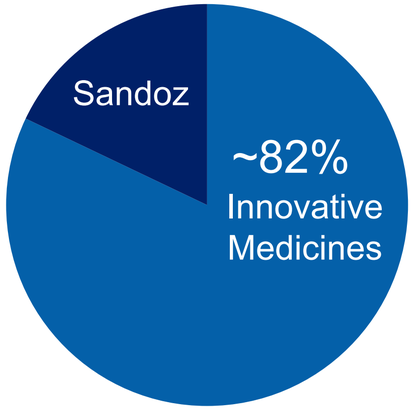
2014
Pre-portfolio transformation



2018
Pre-Alcon spin-off

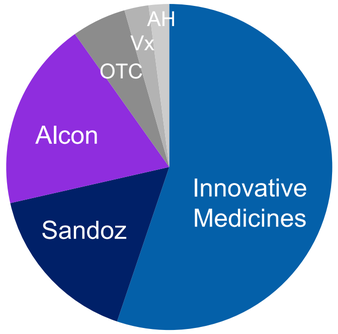


2022
Pre-Sandoz spin-off



2023
Focused company

... has delivered substantial increases in core margin and FCF...



	9M 2014 Pre-portfolio transformation	9M 2023 Focused company
Group core margin	26.0%	36.9%
Group FCF (USD)	6.8bn Q1-Q3 2014	11.0bn Q1-Q3 2023
as % of sales	15.6%	32.4%

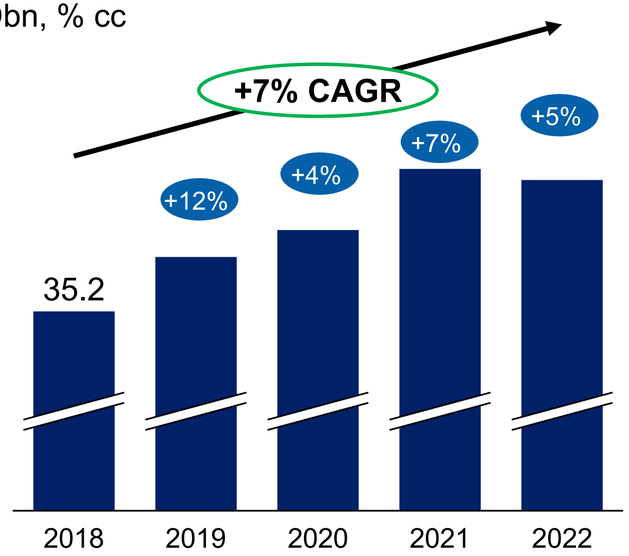
9M 2014 figures reflecting revised free cash flow definition, 2023 figures reflect Continuing Operations.

... whilst continuing to deliver strong operational performance within the single Innovative Medicines division (continuing operations)

Continuing operations performance, numbers restated post-Sandoz spin-off

Net sales

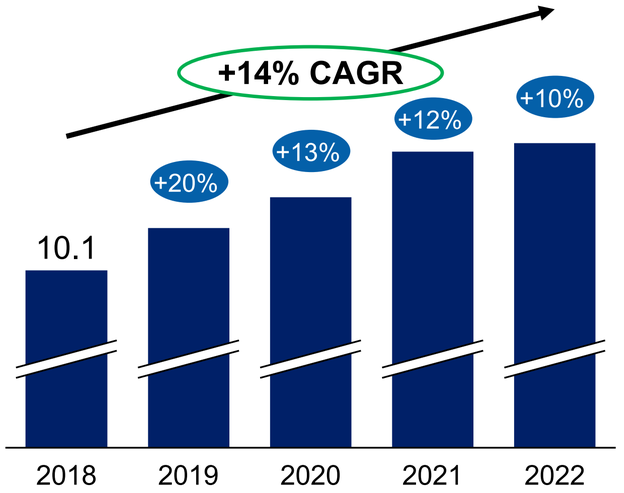
USDbn, % cc



	2018	2019	2020	2021	2022
USDbn	35.2	38.1	39.5	42.8	42.2

Core OpInc

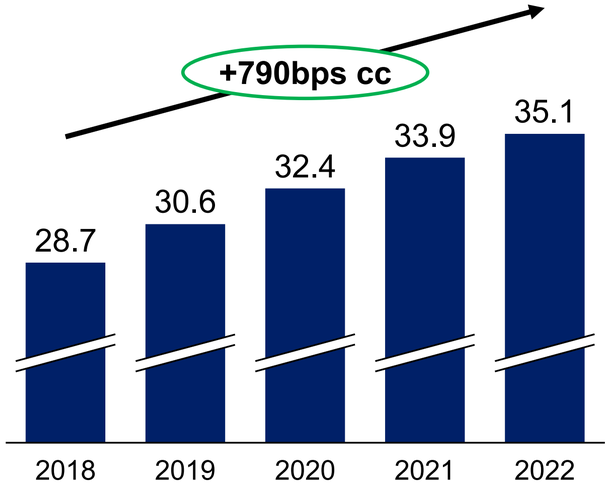
USDbn, % cc



	2018	2019	2020	2021	2022
	10.1	11.7	12.8	14.5	14.8

Core margin

%



We remain committed to executing our focused strategy...

Deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches

Focus

4 core Therapeutic areas
Cardiovascular-Renal-Metabolic, Immunology, Neuroscience, Oncology

2 + 3 technology platforms
Chemistry, Biotherapeutics
xRNA, Radioligand, Gene & Cell Therapy

4 priority geographies
US, China, Germany, Japan

Priorities

Accelerate growth and deliver returns

Deliver **high-value medicines** (including launch excellence)

Strengthen foundations

Unleash the power of **our people**

Scale **data science and technology**

Build trust with **society**

Execution

Delivering through operational excellence

Driving efficiencies and agile resource allocation

Improving R&D productivity

... and continuing to create significant shareholder value

Investing in the business

Investments in organic business
R&D >USD 45bn, CAPEX >USD 5bn 2018-YTD 2023[1]

Value-creating bolt-ons
>USD 33bn 2018-YTD 2023

Substantial cash generation

Returning capital to shareholders

Consistently growing annual dividend[2]
>USD 42bn of dividends 2018-YTD 2023
No rebasing post Alcon and Sandoz spin-off

Share buybacks
>USD 30bn 2018-YTD 2023
New USD 15bn SBB commenced in Jul 2023

Whilst also creating shareholder value via numerous strategic actions

Jun 2018	Apr 2019	Nov 2021	Oct 2023
Divested consumer health JV	**Spun Alcon**	**Exited Roche stake**	**Spun Sandoz**

1. Core R&D and CAPEX actuals. 2. In CHF. YTD: Jan 1, 2023 – Sep 30, 2023.

Focused on deals aligned with our core therapeutic areas and technology platforms

Select recent examples

Cardiovascular, Renal and Metabolic

CHINOOK THERAPEUTICS

IONIS — xRNA

Chong Kun Dang Pharm. Seoul, Korea

Neuroscience

voyager therapeutics — Gene therapy

AVROBIO — Gene therapy

DTX PHARMA — xRNA

Oncology

CLOVIS ONCOLOGY — RLT

bicycle therapeutics — RLT

LEGEND BIOTECH — Cell therapy

We are raising our mid-term sales guidance to +5% CAGR and core margin of ~40%+ by 2027...

Barring unforeseen events

Novartis (Continuing operations)

Net sales expected to grow
+5% cc CAGR 2022-2027

Raised from expected to grow +4% cc CAGR 2022-2027

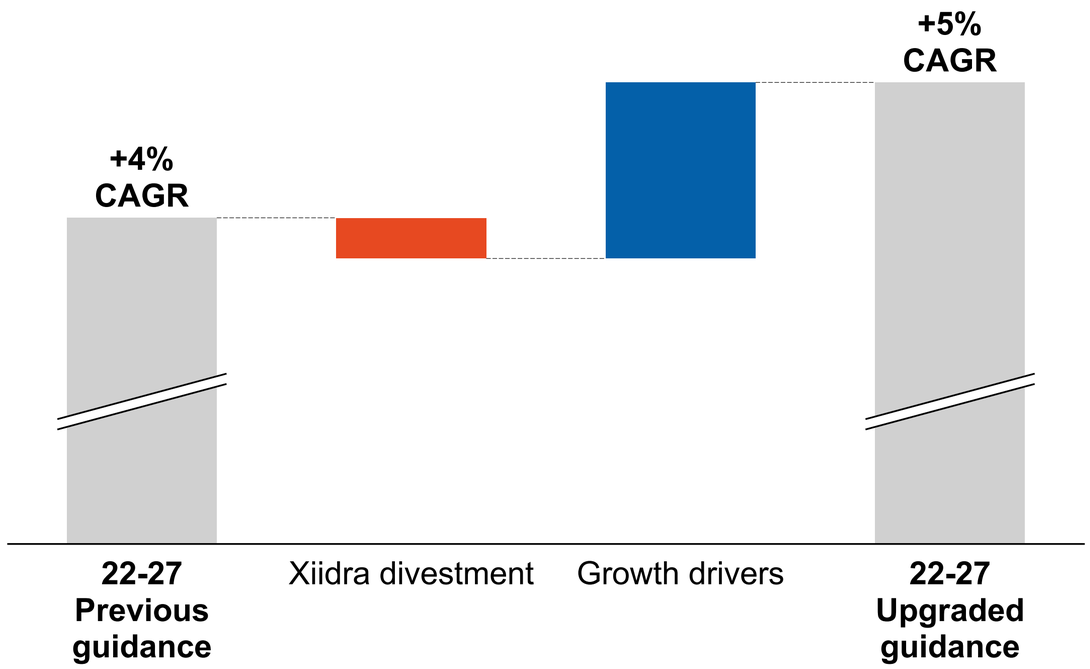
Core operating income margin
~40%+ by 2027

Absorbing corporate costs & low margin contract manufacturing sales to Sandoz

... driven by continued strong momentum of key growth drivers...

Illustrative Novartis net sales

CC

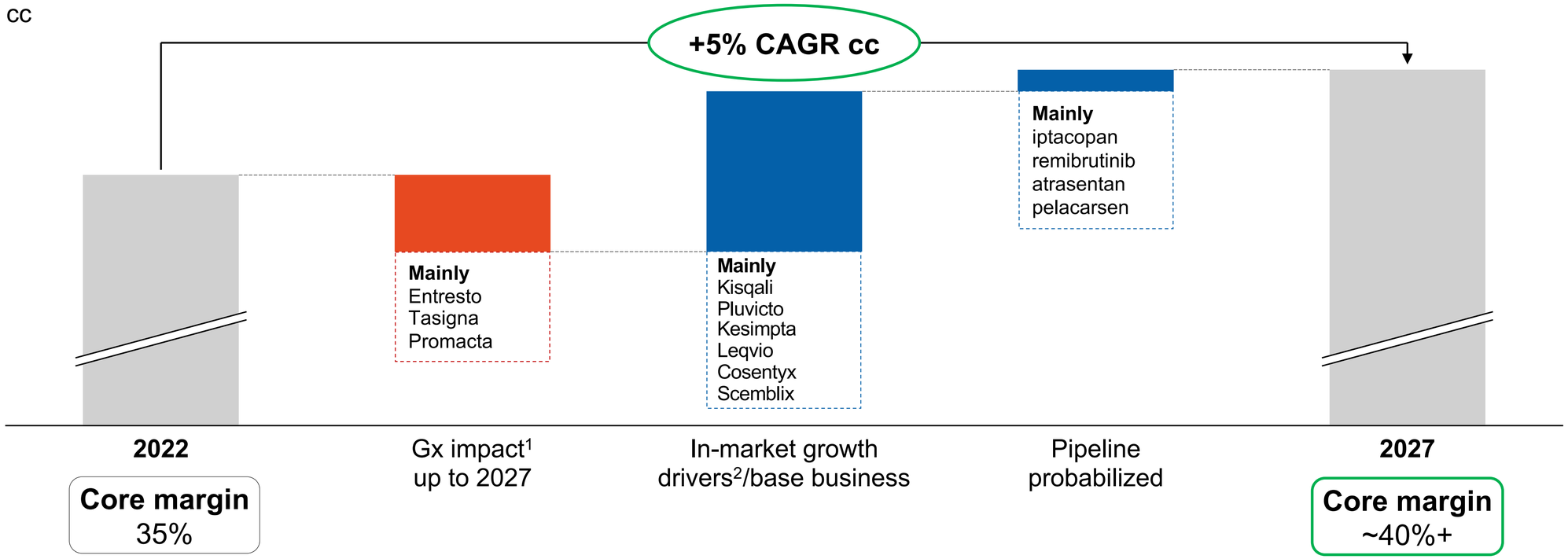


Key drivers

- **Kisqali®** continued momentum in metastatic setting and potential in adjuvant setting
- **Pluvicto®** driving uptake in existing indication and potential in earlier lines
- **Kesimpta®** strong launch trajectory
- **Xiidra** divestment to Bausch + Lomb

... majority of which are de-risked existing brands...

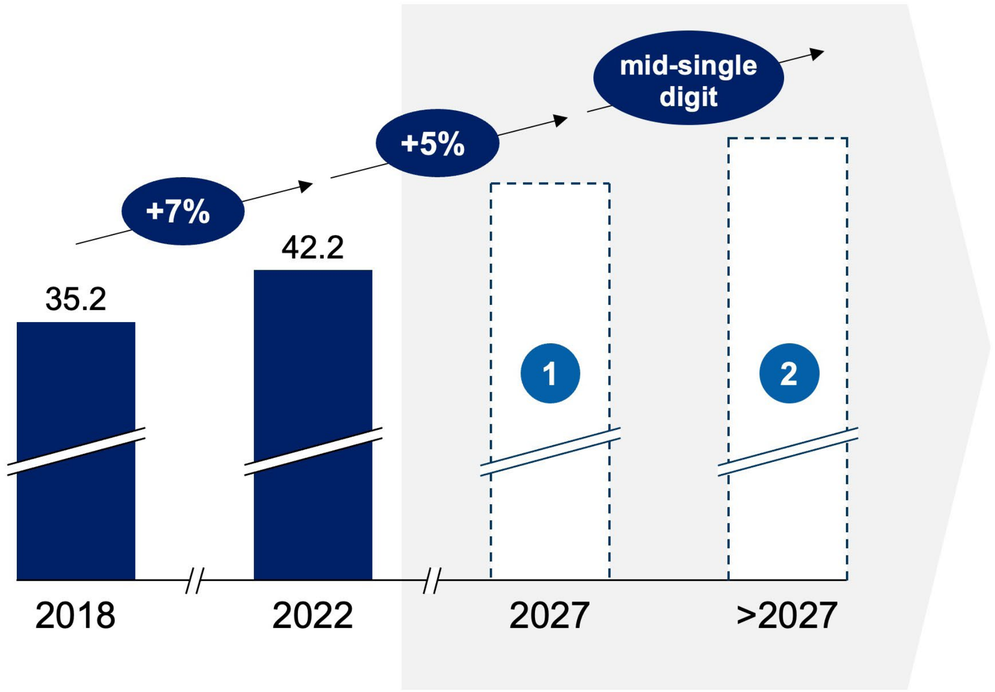
Illustrative Novartis net sales



1. For forecasting purposes, we assume Entresto US LoE in 2025. 2. Including indication expansion. Leqvio – licensed from Alnylam Pharmaceuticals, Inc. Pelacarsen – licensed from Ionis Pharmaceuticals, Inc.

... and these will also be the foundation for mid-single-digit growth beyond 2027

Net sales
Illustrative, USD billion, % CAGR cc



	1 2022-2027 +5% CAGR	2 >2027 mid single digit
De-risked in-market brands	KISQALI®, Kesimpta®, Cosentyx®, SCEMBLIX®, PLUVICTO®, LEQVIO®, zolgensma®	KISQALI®, Kesimpta®, zolgensma®, SCEMBLIX®, PLUVICTO®, LEQVIO®
Pipeline assets	iptacopan, remibrutinib, atrasentan, pelacarsen, ianalumab	iptacopan, remibrutinib, atrasentan, pelacarsen, ianalumab, zigakibart, XXB750, YTB323, JDQ443, AAA614 (FAPi)

6+ currently marketed brands with multi-billion USD potential...

Q3 2023 sales annualized (selected brands)

USDbn, Q3 growth in cc

	Entresto®	Cosentyx®	Kesimpta®	KISQALI®	PLUVICTO®	LEQVIO®
Q3 sales annualized Q3 Growth	**5.9bn** +31%	**5.3bn** +4%	**2.6bn** +124%[1]	**2.2bn** +76%	**1.0bn** +217%	**0.4bn** +165%
Peak sales (approx.) Existing indications	**7bn** assuming US LoE in 2025	**7bn**	**4bn**	**4bn** currently approved indications (mBC)	**multi-bn**	**multi-bn**

1. Without a one-time revenue deduction adjustment recorded in Q3, sales growth +86% cc.

... with additional upside from indication expansion

With expected exclusivity to 2030 and beyond

	Entresto®	Cosentyx®	Kesimpta®	KISQALI®	PLUVICTO®	LEQVIO®
Q3 sales annualized Q3 Growth	5.9bn +31%	5.3bn +4%	2.6bn +124%[1]	2.2bn +76%	1.0bn +217%	0.4bn +165%
Peak sales (approx.) Existing indications	7bn assuming US LoE in 2025	7bn	4bn	4bn currently approved indications (mBC)	multi-bn	multi-bn
Additional sales (approx.) Further indications/LCM		As per above	N/A	multi-bn[2]	multi-bn[3]	multi-bn[4]

1. Without a one-time revenue deduction adjustment recorded in Q3, sales growth +86% cc. 2. Adjuvant, early HR+/HER2- breast cancer. 3. Pre-taxane metastatic castration-resistant prostate cancer, metastatic hormone-sensitive prostate cancer, Oligometastatic prostate cancer. 4. CVRR-LDLC, secondary & primary prevention.

We have a strong presence and expertise in the therapeutic and disease areas we focus on

Select examples	Cardiovascular, Renal and Metabolic	Immunology	Neuroscience	Oncology
Disease areas (selected)	• Heart failure & hypertension • Atherosclerosis • Rare renal, acute kidney injury	• Psoriasis, Psoriatic arthritis • Spondylitis/Spondylarthritis • HS, CSU, CINDU • Sjögren's, SLE, LN • Food Allergy	• Multiple sclerosis • Neurodegeneration (Alzheimer's, Parkinson's) • Neuromuscular (building on Spinal Muscular Atrophy, including ALS)	• Breast cancer • Prostate cancer • Lung cancer • CML, NHL, MM, AML, MDS • PNH, ITP, wAIHA

Supported by anchor brands within each therapeutic area...

Select examples	Cardiovascular, Renal and Metabolic	Immunology	Neuroscience	Oncology
Disease areas (selected)	• Heart failure & hypertension • Atherosclerosis • Rare renal, acute kidney injury	• Psoriasis, Psoriatic arthritis • Spondylitis/Spondylarthritis • HS, CSU, CINDU • Sjögren's, SLE, LN • Food Allergy	• Multiple sclerosis • Neurodegeneration (Alzheimer's, Parkinson's) • Neuromuscular (building on Spinal Muscular Atrophy, including ALS)	• Breast cancer • Prostate cancer • Lung cancer • CML, NHL, MM, AML, MDS • PNH, ITP, wAIHA
Anchor brands	Entresto® LEQVIO®	Cosentyx®	Kesimpta® zolgensma®	KISQALI® LUTATHERA® PLUVICTO® SCEMBLIX®

... and a robust pipeline with submissions by 2027...

Select examples	Cardiovascular, Renal and Metabolic	Immunology	Neuroscience	Oncology
Disease areas (selected)	• Heart failure & hypertension • Atherosclerosis • Rare renal, acute kidney injury	• Psoriasis, Psoriatic arthritis • Spondylitis/Spondylarthritis • HS, CSU, CINDU • Sjögren's, SLE, LN • Food Allergy	• Multiple sclerosis • Neurodegeneration (Alzheimer's, Parkinson's) • Neuromuscular (building on Spinal Muscular Atrophy, including ALS)	• Breast cancer • Prostate cancer • Lung cancer • CML, NHL, MM, AML, MDS • PNH, ITP, wAIHA
Anchor brands	Entresto® LEQVIO®	Cosentyx®	Kesimpta® zolgensma®	KISQALI® LUTATHERA® PLUVICTO® SCEMBLIX®
Assets with planned submission by 2027 (selected)	**iptacopan, atrasentan, zigakibart** IgAN **iptacaopan** C3G **pelacarsen** CVRR-Lp(a) **Leqvio®** Ped Hyperlipidemia, CVRR-LDLC	**Cosentyx®** Multiple indications **remibrutinib** CSU, CINDU **ianalumab** Sjögren's	**Zolgensma®** SMA IT **remibrutinib** Multiple sclerosis	**Kisqali®** HR+/HER2-BC (adjuvant) **Pluvicto®** mCRPC pre-taxane, mHSPC **Scemblix®** CML 1L **iptacopan** PNH

... which have significant sales potential

Select examples

Kisqali®
●●●
Adjuvant breast cancer filed in EMA in **Q3 2023.** FDA regulatory submission expected in **Q4 2023**

Pluvicto®
●●
mCRPC (post-ARDT, pre-taxane), FDA regulatory submission expected in **2024**

mHSPC readout expected in **2025**

Iptacopan
●●●
PNH filed with FDA and EMA in **Q2 2023**

IgAN submission expected in **2024**[1]

C3G readout expected in **Q4 2023**

Atrasentan
●
IgAN submission expected in **2024**[1]

Remibrutinib
●●●
CSU submission expected in **2024**

Multiple sclerosis and CINDU readouts expected in **2026**

Lutathera®
●
GEP-NET 1L G3 EU submission expected in **2024**

Scemblix®
●●
1L CML-CP readout expected in **2024**

OAV-101
●●
SMA IT readout expected in **2024**

Pelacarsen
●●●
CVRR readout expected in **2025**

Ianalumab
●●●
1L and 2L ITP readouts expected in **2025**

Sjögren's readout expected in **2026**

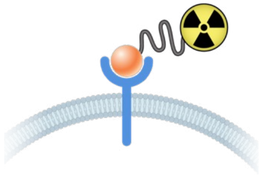
Zigakibart
●
IgAN readout expected in **2026**

1. US submission for accelerated approval.

Unprobabilized estimated peak sales of all asset indications in late-stage development: ● > USD 1bn ●● > USD 2bn ●●● > USD 3bn

Three breakthrough technology opportunities could potentially unlock substantial mid-to-long-term growth for Novartis

Radioligand therapies in solid tumors

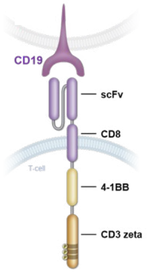


RLT therapies achieving **better efficacy** with **lower side effects** e.g. prostate, neuroendocrine

Promising platform due to more **effective patient selection** (imaging) and **precision targeting** tumor cells

Significant market opportunity with **potential in other solid tumors**: e.g. lung, breast, GI

CAR-T in immunology



Promising early data for **CD19 CAR-T in SLE**[1]

Potential cures in a range of refractory **B-cell driven autoimmune diseases**

Potential in SLE, Sjögren's, severe rheumatoid arthritis, and other neurological diseases

siRNA in neuroscience and cardiovascular

Improving **adherence** whilst **maintaining efficacy** in cardiovascular

Technologies delivering **nucleic assets to the brain** have shown promising early data

Major market **opportunities** in **neurodegenerative**, **neuromuscular** and **cardiovascular** diseases

1. Hernandez, JC, Barba, P, Alberich, ML, et al. (2023) An Open-Label, Multicenter, Ph1/2 Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323 (rapcabtagene autoleucel), a Rapidly Manufactured CAR-T Therapy Targeting CD19 on B Cells, for Severe Refractory Systemic Lupus Erythematosus: Preliminary Results; [abstract]. Arthritis Rheumatol. 75 (suppl 9).

Streamlined industry leading manufacturing network and have become a partner of choice

Transformed manufacturing network to support growth

From ~70[1] sites to ~30

	Sites	Capacity[2]
Small molecules	16	Streamlined
Large molecules	8	Scaled up
Cell & gene therapies	3	Built
Radioligand therapy	6	Built

Scaled operations in advanced technology platforms

- **Optimized network**, and building **new capabilities**
- **Deep technical expertise** supporting pipeline development
- **Have become a partner of choice with multiple contract manufacturing agreements**

Strong quality, compliance and customer service levels

- **100%** YTD[3] health authority inspections with at least acceptable outcomes
- **99.8%** YTD[3] customer service levels
- Meeting **sustainability** targets

1. In 2016 (including Alcon and Sandoz sites). 2. Change of capacity vs. 2016. 3. YTD: Jan 1, 2023 – Sep 30, 2023.

Building trust with society requires a focus on material ESG factors which drive value whilst mitigating risks

Value creation

Innovation and access to medicines

Future-proof pipeline addressing unmet medical and societal needs

Broad access to our medicines, including underserved populations

Dedicated Global Health unit

Human Capital

Diversity, Equity & Inclusion

Culture

Talent

Risk mitigation

Environmental Sustainability

Climate

Water

Waste

Ethical Standards

Ethics

Compliance

Human rights

Enablers

Governance, transparency, Non-financial reporting

Management systems & tools

Right thing to do

Reaching more patients with innovative medicines

Creating sustainable social and economic impact

Building trust with society

Novartis differentiated profile offers an attractive short-, mid- and long-term shareholder value creation opportunity

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"Pure-play" innovative medicines

4 core therapeutic areas

2+3 technology platforms

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Content

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Novartis Research & Development Overview

Fiona Marshall
President, Biomedical Research

Shreeram Aradhye
President, Development and Chief Medical Officer

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Novartis R&D built around our core therapeutic areas and technology platforms; committed to operational excellence

Focus

4 core Therapeutic areas
Cardiovascular-Renal-Metabolic, Immunology, Neuroscience, Oncology

2 + 3 technology platforms
Chemistry, Biotherapeutics
xRNA, Radioligand, Gene & Cell Therapy

4 priority geographies
US, China, Germany, Japan

Priorities

Accelerate growth and deliver returns

Deliver **high-value medicines** (including launch excellence)

Strengthen foundations

Unleash the power of **our people**

Scale **data science and technology**

Build trust with **society**

Execution

Delivering through operational excellence

Improving R&D productivity

Novartis R&D in numbers: An industry leading pipeline and capabilities committed to delivering value for patients

Pipeline and capabilities

4
Therapeutic areas

5
Technology platforms
2 - Established, 3 - Advanced

46
NMEs

>17 000
Associates dedicated to R&D; strong human capabilities

103
Clinical projects[1]

>45bn
R&D spend (USD), last 5 years
c.USD 8bn IM annually

Value commitments

#1
NME US FDA approvals[2] (With 18 approvals (2017-22) 5 major Ph3 readouts YTD 2023)

83
Pipeline projects target areas with high unmet need[3]

>15
Key submissions planned 2024-27

1. Ph1 to approval, excl. Global Health. 2. Source: Evaluate Pharma, US NME FDA Approvals 2017 -2022. 3. Confirmatory development projects.

Novartis R&D built around our core therapeutic areas and technology platforms; committed to operational excellence

Focus

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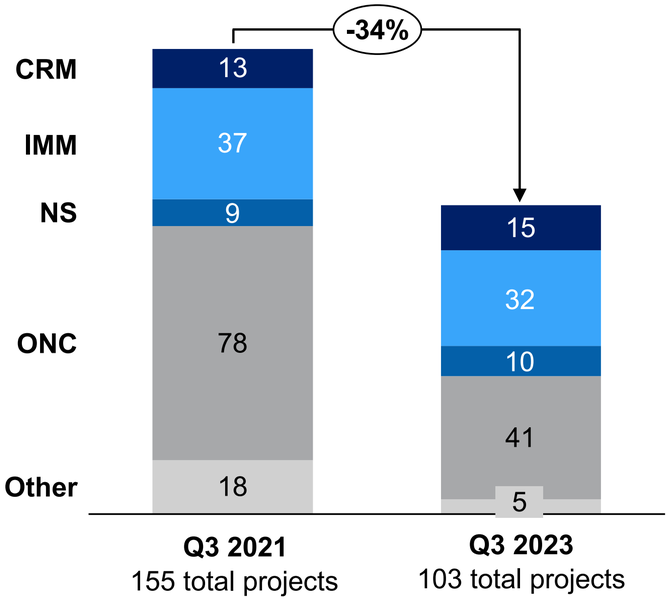
Improving R&D productivity

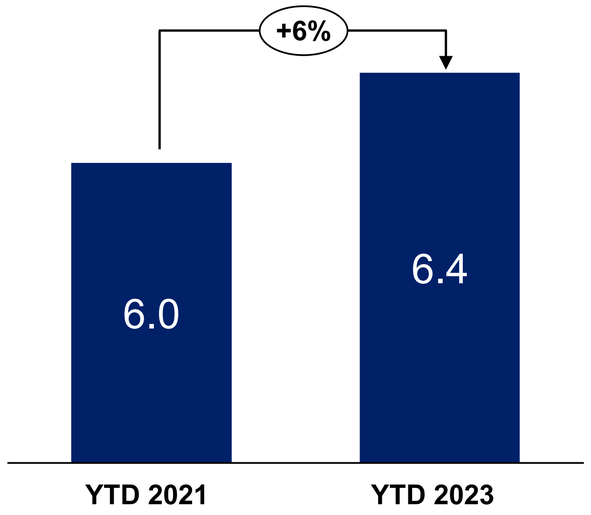
... in which resources are being further focused and capabilities enhanced

Streamlined portfolio and increased TA focus[1]



With increased total IM R&D spend[2]

USD bn, @period rates



Driving focus and enhanced competencies

- **Deep disease expertise** and strong relationship with external stakeholders
- **Functional capability build up**
- **Enhanced operational excellence** in trial design and execution
- **Focused resources** per project

1. Ph1 to approval, excl. Global Health. 2. YTD 2021 and YTD 2023 (Jan 01 – Sep 30 in the respective year).

Delivering on our R&D strategy in CRM

Disease areas (selected)	• Heart failure & hypertension • Atherosclerosis • Rare renal, acute kidney injury
Anchor brands	Entresto® LEQVIO®
Assets with planned submission by 2027 (selected)	**iptacopan, atrasentan, zigakibart** IgAN **iptacopan** C3G **pelacarsen** CVRR-Lp(a) **Leqvio®** Ped Hyperlipidemia, CVRR-LDLC

Strategic approach

1. Focus on new modalities addressing adherence in cardiovascular
2. Fundamentally improve heart failure outcomes
3. Build renal as a key strategic pillar
4. Opportunistic exploration of additional opportunities e.g. metabolism, atrial fibrillation

Delivering on our R&D strategy in **Immunology**

Disease areas (selected)

- Psoriasis, Psoriatic arthritis
- Spondylitis/Spondylarthritis
- HS, CSU, CINDU
- Sjögren's, SLE, LN
- Food Allergy

Anchor brands

Cosentyx®

Assets with planned submission by 2027 (selected)

Cosentyx®
Multiple indications

remibrutinib
CSU, CINDU

ianalumab
Sjögren's

Strategic approach

1. Prioritize Cosentyx LCM indications
2. Address high unmet need for diseases with limited treatment options in Rheumatology and Dermatology
3. Aim for leadership in severe refractory autoimmune diseases with CAR-T therapies and other modalities
4. Opportunistic exploration of additional opportunities e.g. food allergy, osteoarthritis

Delivering on our R&D strategy in **Neuroscience**

Disease areas (selected)

- Multiple sclerosis
- Neurodegeneration (Alzheimer's, Parkinson's)
- Neuromuscular (building on Spinal Muscular Atrophy, including ALS)

Anchor brands

Kesimpta®

zolgensma®

Assets with planned submission by 2027 (selected)

Zolgensma®
SMA IT

remibrutinib
Multiple sclerosis

Strategic approach

1. Maintain leadership in multiple sclerosis by preventing disease progression
2. Target genetically defined core drivers and innate inflammation to significantly slow progression in neurodegenerative diseases
3. Build on success in Zolgensma to deliver transformational genomic medicines for patients with neuromuscular and genetic diseases

Delivering on our R&D strategy in **Oncology**

Disease areas (selected)

- Breast cancer
- Prostate cancer
- Lung cancer
- CML, NHL, MM, AML, MDS
- PNH, ITP, wAIHA

Anchor brands

KISQALI® LUTATHERA® PLUVICTO® SCEMBLIX®

Assets with planned submission by 2027 (selected)

Kisqali®
HR+/HER2-BC (adjuvant)

Pluvicto®
mCRPC pre-taxane, mHSPC

Scemblix®
CML 1L

iptacopan
PNH

Strategic approach

1. Target earlier stages of disease across prioritized solid tumor and hematology indications, ultimately aiming for treatment free remission or cure
2. Build long-term portfolio in breast, prostate, and lung cancer
3. Develop RLT platform across novel surface targets for solid tumors with high unmet medical need
4. Opportunistic exploration of additional opportunities leveraging our platforms and capabilities e.g. PDAC

Novartis R&D built around our core therapeutic areas and **technology platforms;** committed to operational excellence

Focus

4 core Therapeutic areas
Cardiovascular-Renal-Metabolic, Immunology, Neuroscience, Oncology

2 + 3 technology platforms
Chemistry, Biotherapeutics
xRNA, Radioligand, Gene & Cell Therapy

4 priority geographies
US, China, Germany, Japan

Priorities

Accelerate growth and deliver returns

Deliver **high-value medicines** (including launch excellence)

Strengthen foundations

Unleash the power of **our people**

Scale **data science and technology**

Build trust with **society**

Execution

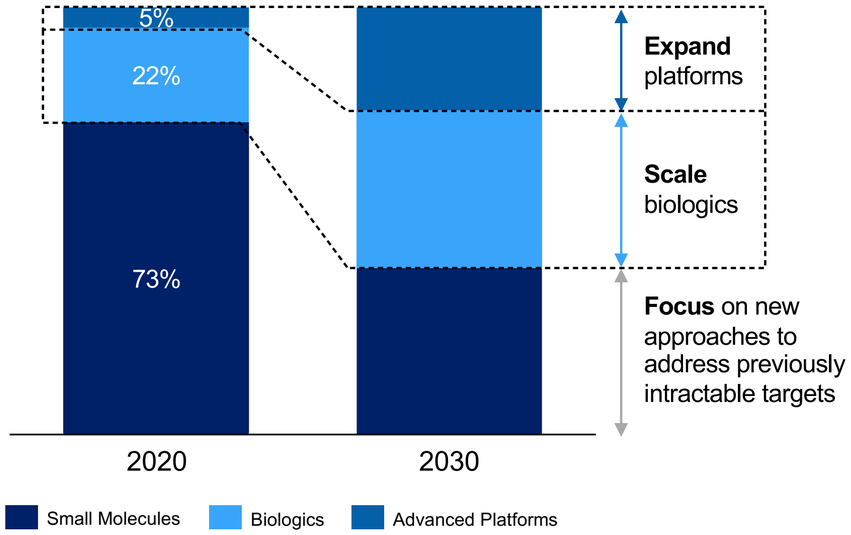
Delivering through operational excellence

Improving R&D productivity

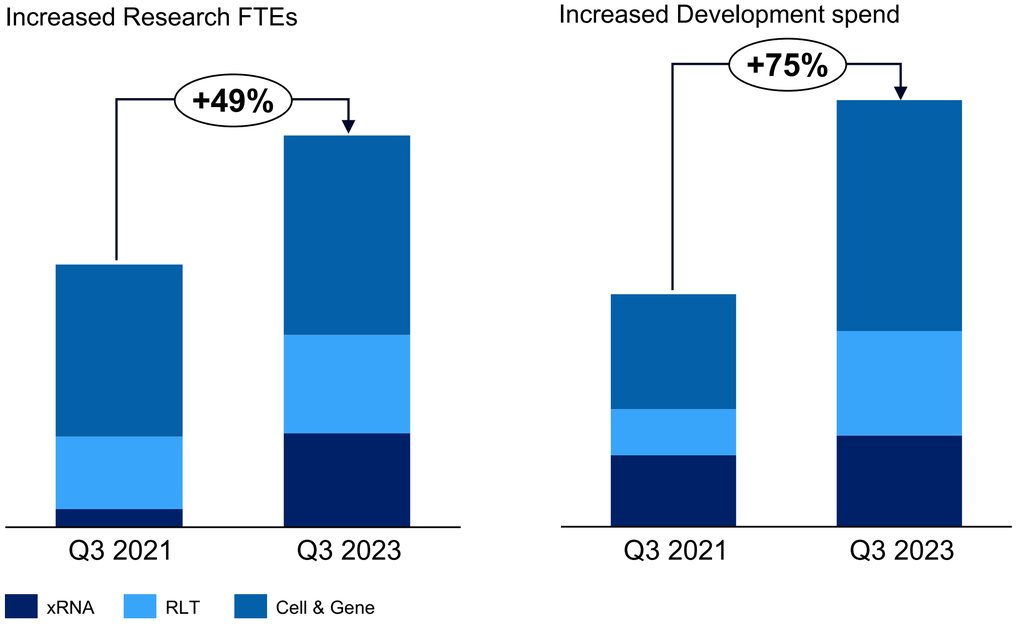
Strategically investing in biologics and advanced technology platforms to build our growing pipeline

Anticipated pipeline shift towards advanced technology platforms...

Proportion % of IM sales by platform
Outlook illustrative



...already increasing resourcing and capabilities[1]



1. Internal NVS data, monthly average FTEs and total external spend logged to pipeline and enabling projects in 3 strategic platforms. Increased development spend comparing Q1-Q3 2021 vs. Q1–Q3 2023.

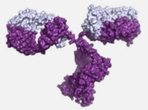
Advancing our biologics capabilities to realize new therapeutic opportunities

Selected technologies, not a comprehensive list

Marketed portfolio

Capturing value from validated technology

Marketed monoclonal antibodies



Established and proven approach, binds single target

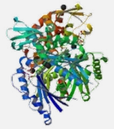
Potential indication and formulation expansion

Cosentyx® (secukinumab)

Clinically tested modalities

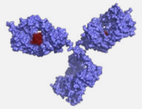
Scaling new therapeutic approaches to the clinic

Protein therapeutics



Natural or engineered proteins as therapeutics

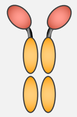
Antibody drug conjugates



ADC payload

Deliver payload to the antibody target

Antibody formats (VHH, scFv)



Formats with different properties (PK/PD, etc.)

Multi-specifics Abs

Chimeric biomolecules to modulate complex biology (e.g. tolerance, anergy)

Discovery strategy

Innovating emerging technology

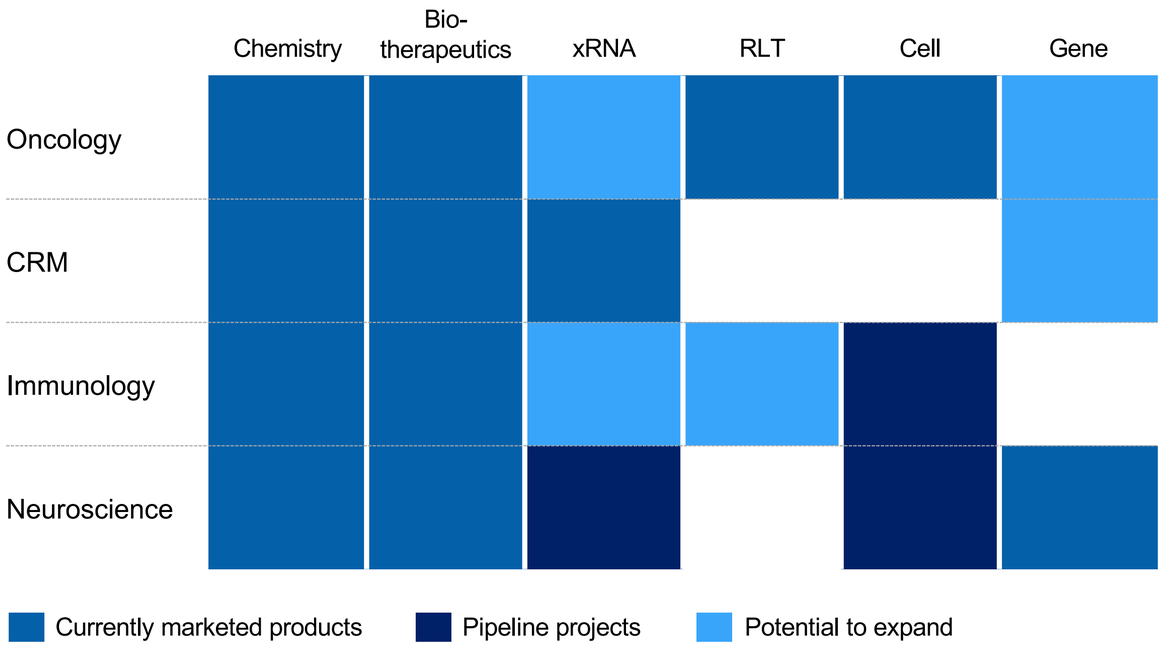
- Building next wave of advanced biologics: immune-cell engagers and next-gen ADCs
- Using AI/ ML approaches for *in silico* discovery and optimization
- Designing for pharmacological control (e.g. duration, environment dependent activation)
- Early cell line engineering and incorporating new technologies to reduce cycle times

Expanding the use of our technology platforms across core therapeutic areas

Approach to technology platforms

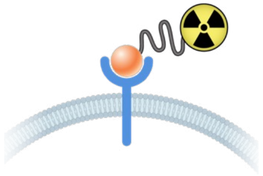
- ✓ **Broad applicability across TAs**
- ✓ **Sustained competitive advantage**
- ✓ **Scalability to build pipeline**
- ✓ **Advances disease area strategy**
- ✓ **Integration of diverse expertise**

Current applications across our core TAs



Three breakthrough technology opportunities could potentially unlock substantial mid-to-long-term growth for Novartis

Radioligand therapies in solid tumors

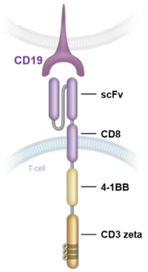


RLT therapies achieving **better efficacy** with **lower side effects** e.g. prostate, neuroendocrine

Promising platform due to more **effective patient selection** (imaging) and **precision targeting** tumor cells

Significant market opportunity with **potential in other solid tumors**: e.g. lung, breast, GI

CAR-T in immunology



Promising early data for **CD19 CAR-T in SLE**[1]

Potential cures in a range of refractory **B-cell driven autoimmune diseases**

Potential in SLE, Sjögren's, severe rheumatoid arthritis, and other neurological diseases

siRNA in neuroscience and cardiovascular

Improving **adherence** whilst **maintaining efficacy** in cardiovascular

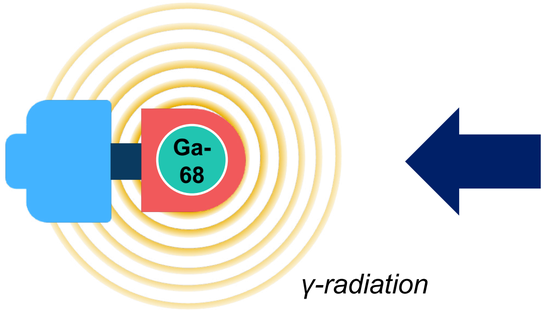
Technologies delivering **nucleic assets to the brain** have shown promising early data

Major market **opportunities** in **neurodegenerative**, **neuromuscular** and **cardiovascular** diseases

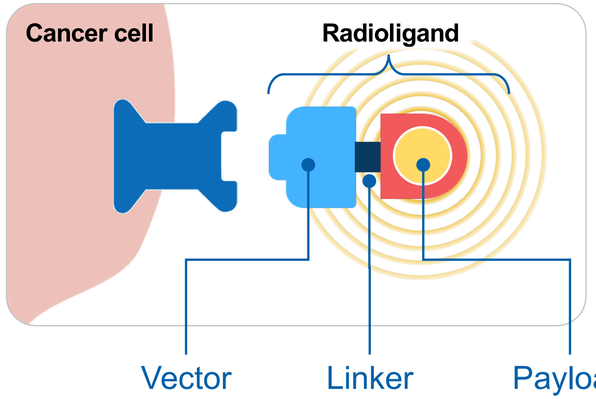
1. Hernandez, JC, Barba, P, Alberich, ML, et al. (2023) An Open-Label, Multicenter, Ph1/2 Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323 (rapcabtagene autoleucel), a Rapidly Manufactured CAR-T Therapy Targeting CD19 on B Cells, for Severe Refractory Systemic Lupus Erythematosus: Preliminary Results; [abstract]. Arthritis Rheumatol. 75 (suppl 9).

Radioligand therapy may offer efficacy and safety benefits over existing treatments

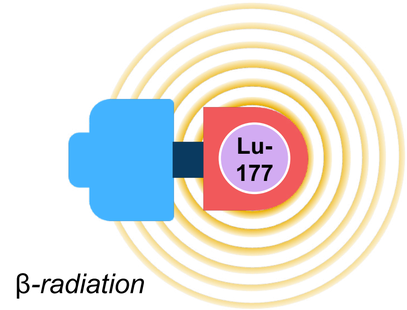
Gallium-68 labelled



One Targeting Molecule



Lutetium-177 labelled



Ga-68 PET Imaging

γ-rays detected for:

- Diagnosis
- Selection for treatment
- Follow-up

If you see it, you can treat it

Lu-177 Radioligand Therapy

β-radiation treats tumors from within:

- DNA breaks
- Disrupted cell replication/cell death

Our strategy is to develop a pipeline leveraging our expertise...

Explore novel surface targets for solid tumors

Pipeline targets FAP, integrin and GRPR have potential broad applicability in multiple solid tumors

Leverage clinical understanding and reverse translation

Advance preclinical models to better understand response and resistance, informing selection of new targets and combinations

Explore rational combinations

Discover and explore complementary mechanisms that enhance the efficacy of RLT

Build on existing platform and extend capabilities

Isotopes, ligand platforms, linker and chelators for improved drug properties

FAP – fibroblast activation protein. GRPR – gastrin-releasing peptide receptor.

... to innovate across each RLT component...

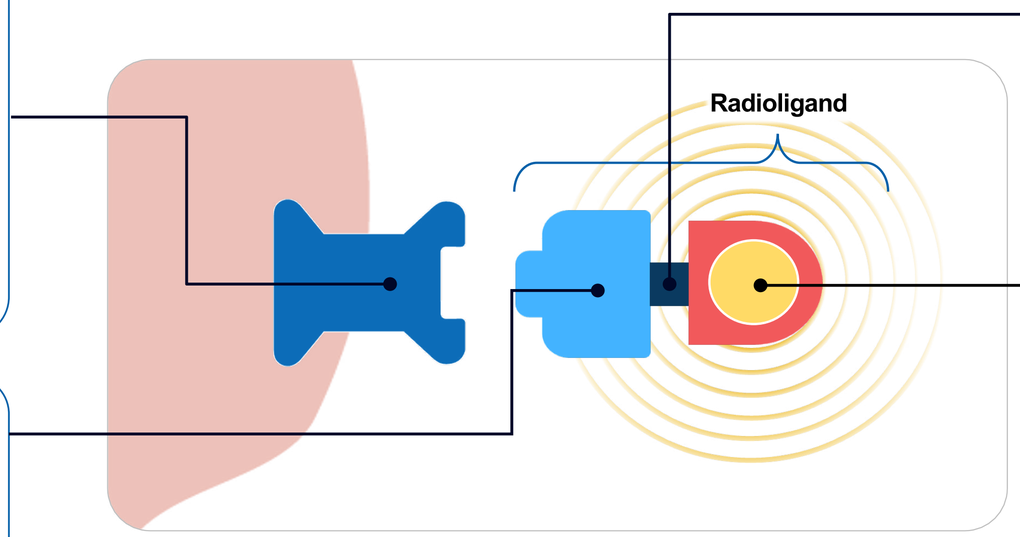
A. Target

Identify novel targets in solid-tumor indications with high unmet needs

- Existing target space
- Data mining
- Innovative target discovery

B. Vector

Deliver innovative vector platforms (biologics, peptides, small molecules)



C. Linkers

Pursue novel solutions to enable novel isotopes and to improve RLT properties

D. Payload (isotope)

Diversify & enhance isotopes

- Short-term: Lutetium-177
- Mid-term: Actinium-225
- Long-term: explore other Isotopes

... whilst building a strong backbone of capabilities

1

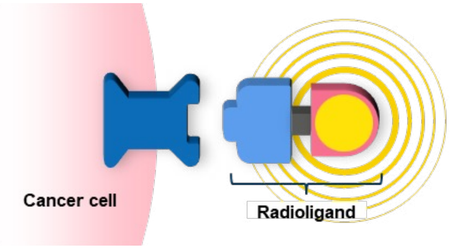
Clinical trial network

Large footprint with 550+ RLT clinical sites by 2025

2

RLT Discovery Engine

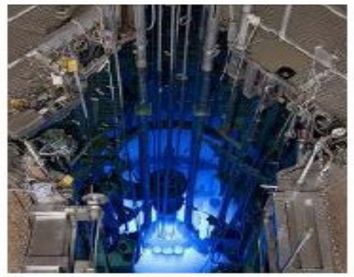
Discovery budget to double 2023-25, with 10+ preclinical assets already in pipeline



3

R&D Manufacturing

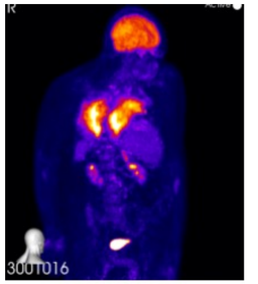
On track to double technical research manufacturing capacity by 2027



4

Clinical Imaging & Analysis

World-class CoE to improve RLT PoS and 7+ imaging agents in development



Strong Human Capabilities

CoE – Center of Excellence.

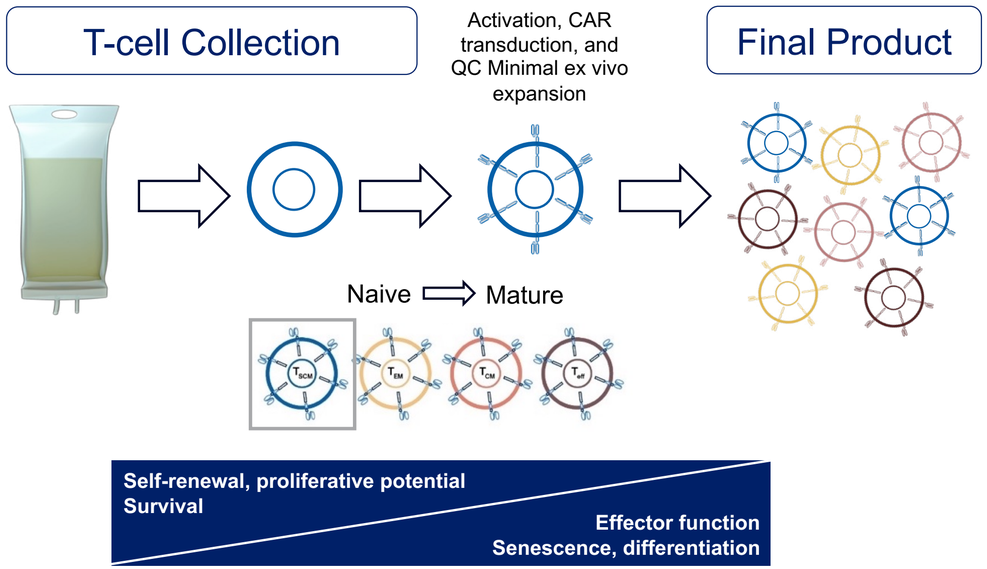
Building a broader RLT pipeline based on validated targets expressed on multiple tumors and additional isotopes

Selected compound	Indication	Phase 1	Phase 2	Phase 3	Marketed
PLUVICTO®	mCRPC post-taxane				
	mCRPC pre-taxane				
	mHSPC				
	Oligometastatic PC				
LUTATHERA®	2L GEP-NET				
	1L GEP-NET				
	Pediatrics + PPGL[1]				
	GBM[2]				
	ES-SCLC[2]				
FAP-2286 (AAA614)	Multi-tumor[2,3]				
ACTINIUM ^{225}Ac-PSMA-617	mCRPC				
ACTINIUM ^{225}Ac-PSMA-R2	mCRPC				
^{177}Lu-NeoB	Multi-tumor				
Integrin (AAA604)	Multi-tumor				
Preclinical projects[4]	Multi-tumor	10			

PDAC – pancreatic ductal adenocarcinoma. CRC – colorectal cancer. BC – breast cancer. NSCLC – non-small cell lung cancer. GEP-NET – gastroenteropancreatic neuroendocrine tumor. ES-SCLC – extensive stage small cell lung cancer. mHSPC – metastatic hormone sensitive prostate cancer. mCRPC – metastatic castration resistant prostate cancer. 1. PPGL, pheochromocytomas and paragangliomas, are an exploratory cohort of NETTER-P. 2. Ph1/2. 3. Being integrated in the NVS pipeline. 4. Including Exploratory, Discovery, Lead Optimization, and Preclinical projects.

Moving to a differentiated second-gen platform in cell therapy...

T-Charge™ second generation rapid manufacturing...



...differentiated from first-gen CAR-T

1. **Younger T-cells preserving stemness**[1,2,3]
   increasing the stem and central memory T cells[3]

2. **Enhances in vivo expansion**[2,3]
   with the potential to improve efficacy and durability of response 25-fold lower CAR-T cell count infused compared to traditional CAR-T

3. **<2 days manufacturing time**[2,3]
   aim of <10 days door-to-door time in the US

1. Engels, B. et al. Blood 138 (Suppl. 1): 2848 (2021). 2. Barba P, et al. Blood (2022) 140 (Supplement 1): 1056–1059. 3. Sperling A, et al. EHA 2022 Congress; June 9-12, 2022; Vienna, Austria. Poster P1446.

... which also expands our footprint beyond hematology, into immunology and potentially neuroscience...

Hematology
Differentiated in proven indications

- **PHE885:** Encouraging Phase 1 Multiple Myeloma data – 100% ORR at active doses, no reports of parkinsonism or delayed neurotoxicity[1]
- **YTB323:** Encouraging Phase 1 3L DLBCL Data – durable responses with 62% CR rate at 6 months, mDOR of 16 months and favorable safety profile[2]
- **Early pipeline:** Pursuing additional targets and tumor types, including solid tumor applications
  - E.g. DLL3 CAR-T for SCLC recently licensed from Legend Biotech

Immunology/Neuroscience
Opportunity to expand platform

- Rapidly moving on emerging data: “B cell reset” and drug-free remission >2 years[3] in academic case series of patients with srSLE/LN
- **YTB323:** Ph1 data in srSLE presented at ACR 2023[4], preliminary data from 3 sentinel patients reveal CAR T cell expansion, sustained B cell depletion and initial efficacy
- Preparations ongoing for srSLE Ph2 and studies in additional B cell driven autoimmune indications, leveraging reverse translation to support expansion
- Neuroscience potential e.g. severe refractory MS

1. Barba P, et al. Blood (2022) 140 (Supplement 1): 1056–1059. 2. Sperling AS et al. ASCO 2023 Abstract 8004; June 3, 2023; Chicago, Illinois. 3. Taubmann et al. EULAR 2023 Congress June 2023 Oral Presentation 0141.
4. Hernandez, JC, Barba, P, Alberich, ML, et al. (2023) An Open-Label, Multicenter, Ph1/2 Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323 (rapcabtagene autoleucel), a Rapidly Manufactured CAR-T Therapy Targeting CD19 on B Cells, for Severe Refractory Systemic Lupus Erythematosus: Preliminary Results; [abstract]. Arthritis Rheumatol. 75 (suppl 9).

... whilst leveraging our strong foundational capabilities and experience across the value chain

1

CAR-T Pioneer

Our C&G platform builds on the successes & leverages key learnings gained from Kymriah to deliver better and more diverse options for patients

2

Extensive CAR-T Network

470+ certified sites globally to deliver CAR-T therapies with established relationships and extensive knowledge across the value-chain

3

State of the Art, Rapid Manufacturing Platform

Manufacturing facilities & capabilities secure the delivery of multiple CAR-T therapies (across MoAs) globally with high quality and reliability

4

End-to-End Global Operational Capabilities

Presence in 35+ countries with innovative access solutions enabled by efficient & scalable customer operations platform

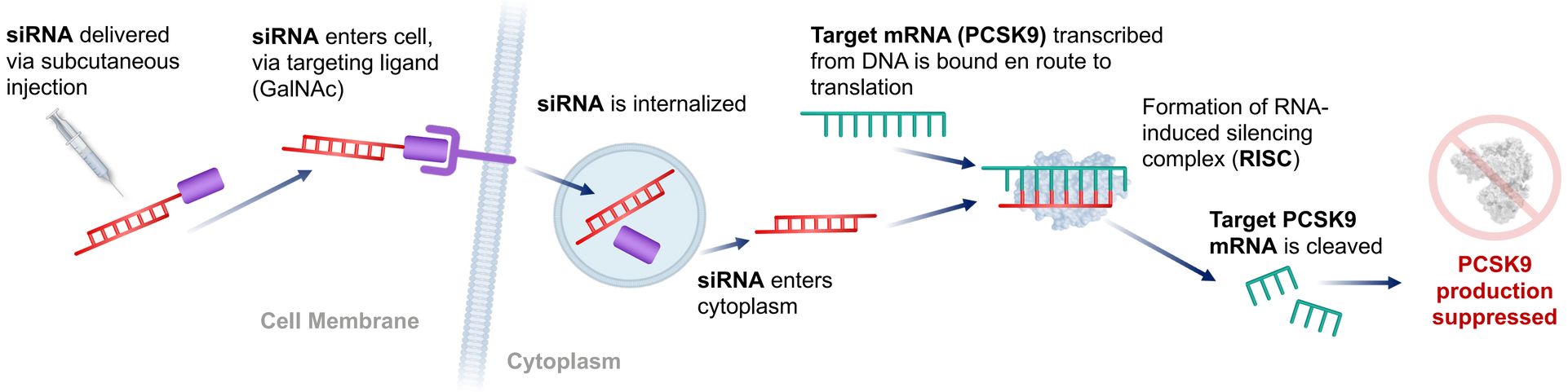
Strong Human Capabilities

Cell therapy pipeline expanding into additional indications across therapeutic areas based on platform experience in hematology

Selected compound	Indication	Phase 1	Phase 2	Phase 3	Marketed
KYMRIAH	Pediatric ALL				
	3L DLBCL				
	r/r FL				
PHE885	4L MM				
YTB323 (Hematology)	1L HR LBCL				
	3L DLBCL				
	Adult ALL				
YTB323 (Autoimmune)	srSLE/LN				
	Additional AIDs	*(in planning)*			
DLL3 CAR-T	SCLC	LEGEND BIOTECH			
Additional preclinical projects[1]	Various	5			

DLBCL: Diffuse large B-cell lymphoma. HR LBCL: High-risk large B-cell lymphomas. mDOR: median Duration of Response. ORR: Overall Response Rate. AID: Autoimmune disease. srSLE/LN: severe refractory Systemic Lupus Erythematosus/Lupus Nephritis. SCLC: Small Cell Lung Cancer. 1. Including Exploratory, Discovery, Lead Optimization, and Preclinical projects.

xRNA platform provides durable downregulation of target protein expression...



Design parameters:

Sequence (e.g. specificity, length)

Chemistry modifications (enhance stability, tune potency, minimize immunogenicity)

Delivery vehicle (e.g. cell-directed ligands)

Platform features:

- ✓ **Broad target potential**
- ✓ **Durable effect:** Biannual dosing proven, potential to extend
- ✓ **Tissue specific delivery:** Tissue-specific delivery once established (e.g. GalNAc -> liver)

... which we are leveraging across organs and disease areas in our core therapeutic areas

Deliver outcomes on key CRM programs

- Cardiovascular risk reduction trials for siRNA targeting PCSK9 (Leqvio) and antisense oligonucleotide targeting Lp(a) (pelacarsen)

Enable improved durability & combinations, toward a xRNA portfolio for population health CRM targets

- Advance next generation program targeting Lp(a) for cardiovascular disease with IONIS
- Pursue combinations of siRNA to enhance efficacy and address multiple CV risk-factors

Expand tissue targeting and TA via biologics, peptides, and small molecules

- Leverage proprietary FALCON siRNA platform from DTx Pharma to develop drugs for neuroscience
- Extra-hepatic targeting through novel ligands will open up further CRM tissues targets (myocardium, kidney, adipocytes), as well as therapeutics areas (e.g. CNS)

Earlier stages of harnessing in-house expertise for broad application across different diseases and delivery beyond the liver

Selected compound	Indication	Phase 1	Phase 2	Phase 3	Marketed
LEQVIO®	Hypercholesterolemia				
	CVRR, primary prevention				
	CVRR, secondary prevention				
	Hyperlipidemia, pediatrics				
Pelacarsen	CVRR-Lp(a)				
NIO752	Progressive supranuclear palsy				
	Alzheimer's disease				
EDK060	Charcot-Marie-Tooth disease	DTx PHARMA			
Additional preclinical projects[1]	CRM	10	*Toward a broad xRNA portfolio for population health CRM targets*		
	Neuroscience	3	*Severe neurodegenerative and neuromuscular applications, unlocked by tissue-targeting improvements*		
	Additional Opportunities	2	*Targets outside of our core TAs uniquely suited to our xRNA platform*		

1. Including Exploratory, Discovery, Lead Optimization, and Preclinical projects.

Novartis R&D built around our core therapeutic areas and technology platforms; **committed to operational excellence**

Focus

4 core Therapeutic areas
Cardiovascular-Renal-Metabolic, Immunology, Neuroscience, Oncology

2 + 3 technology platforms
Chemistry, Biotherapeutics
xRNA, Radioligand, Gene & Cell Therapy

4 priority geographies
US, China, Germany, Japan

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Accelerate growth and deliver returns

Deliver **high-value medicines** (including launch excellence)

Strengthen foundations

Unleash the power of **our people**

Scale **data science and technology**

Build trust with **society**

Execution

Delivering through operational excellence

Improving R&D productivity

We have focused on improving R&D productivity through operational excellence...

1 Optimized Pipeline

Focus on core TAs with active prioritization to build depth and expertise

CHINOOK™ THERAPEUTICS
A Novartis Company

Chinook acquisition, building on increased focus and expertise in renal disease

2 Speed

Reduce cycle time through operational discipline in clinical design planning and trial execution supported by AI solutions

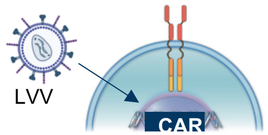
6+ months
Enrollment ahead of target

>90%
Sites initiated within a year

Ianalumab rapid scale up in Sjögren's, with enrollment 6+ months ahead of target

3 Success

Improve success rate through asset-centric planning, end-to-end governance and integrated decision-making



YTB323 in srAIDs, acceleration by seamless R&D and building on existing data and learnings

4 Value

Increase asset value through emphasis on US, strategic LCM and early commercial insights

5
Expected submission-enabling readouts over 5 years (2022-2026)

Iptacopan indication expansion to enable rapid sequential submission

... and scaling the power of data science and AI as an enabler

Clear approach to AI and data science

Strategic investments on AI across the company, with a strong **focus on R&D**

Continuing to build data42 as a critical enabler to harness **full potential of AI in R&D**

Palantir

Focused AI project portfolio in R&D:

- Target identification
- Generative chemistry
- Predictive safety
- Clinical trial transformation

Leveraging long-standing partnership with Microsoft to develop custom Generative AI use cases and deploy fundamental enablers across the company

Microsoft

Microsoft 365 Copilot

OpenAI Chat GPT-4

We are committed to maintaining leading pipeline and capabilities to deliver high-value medicines for patients

Focus on core **Therapeutic Areas**

CRM
Immunology
Neuroscience
Oncology

Enabled by differentiated **Technology Platforms**

Chemistry
Biotherapeutics
RLT
C&G
xRNA

Built on strong human capabilities

Delivers

1. Leading pipeline
2. Improving R&D productivity
3. Clear focus on high-value medicines addressing unmet need
4. Mid-single-digit growth to 2027 and beyond

Therapeutic Area Overview: Cardiovascular-Renal-Metabolic

David Soergel
Development Unit Head, CRM

Shreeram Aradhye
President, Development and Chief Medical Officer

NOVARTIS | Reimagining Medicine

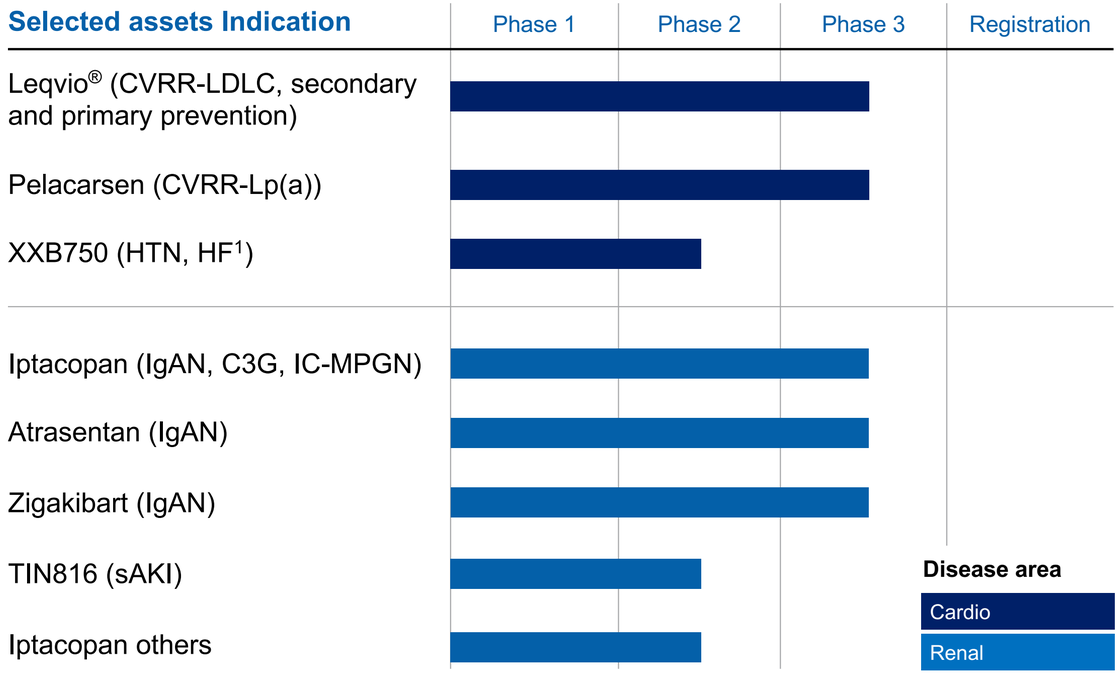
Our cardiovascular-renal-metabolic therapeutic area focuses on areas of high unmet need; strong mid and late-stage pipeline

Cardio-renal-metabolic strategy

- Focus on new modalities (ASO and siRNA) addressing treatment adherence in cardiovascular
- Fundamentally improve HF outcomes by building on Entresto® legacy and first-in-class leading NPR1
- Continue to build renal as a key strategic pillar
- Exploration of additional opportunities e.g., metabolism, atrial fibrillation

Assets highlighted today:
Leqvio®, **pelacarsen**, **XXB750**

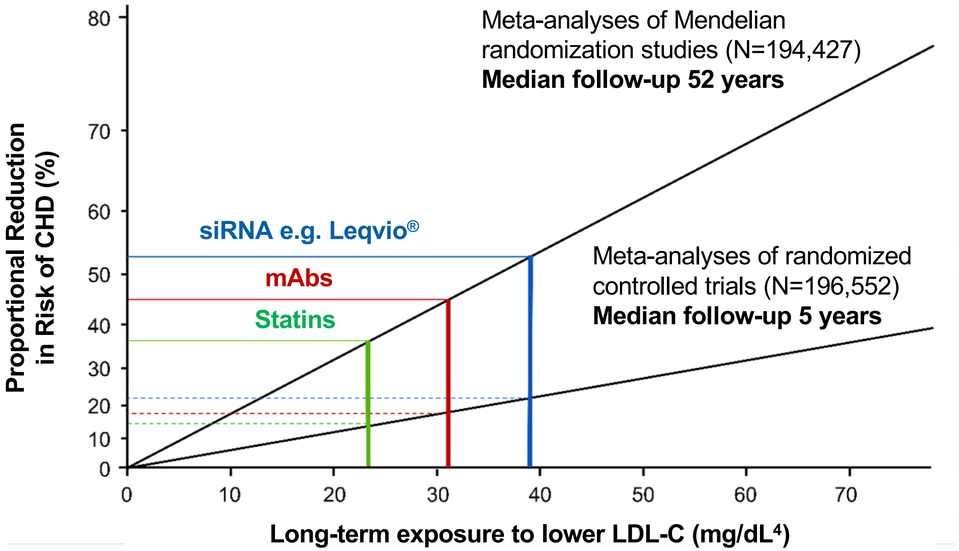
Deep dives: **Iptacopan**, **atrasentan**



ASO – Antisense oligonucleotide NPR1 – Natriuretic peptide receptor 1. C3G – C3 glomerulopathy CVRR-Lp(a) – Secondary prevention of CV events in patients with elevated levels of lipoprotein (a). CVRR-LDLC – Secondary prevention of CV events in patients with elevated levels of LDLC. HF – Heart failure. HTN – Hypertension. IC-MPGN – Immune complex membranoproliferative glomerulonephritis. IgAN – IgA nephropathy. sAKI - Sepsis-associated acute kidney injury. 1. FPFV start H1 2024

Relationship between LDL-C and CV outcomes well established; Leqvio® outcomes trials for secondary and primary prevention ongoing

Log-linear association per unit change in LDL-C and the risk of cardiovascular disease[3]



- **Relationship between LDL-C and CV outcomes is well established and supported by clinical trials involving ~500k patients**[1,2]
- **Each mmol/L (~39mg/dL) reduction in LDL-C** reduces the relative risk of ASCVD events **by 20% after 3 years** and **1.5% in each subsequent year**[1]
- Inclisiran's CVOTs have been designed to cover both magnitude of LDL-C reduction and **show benefits of cumulative exposure**
- **CV outcomes trials ongoing for secondary and primary prevention**: **ORION-4**, **V2P** and **V1P** with data expected in 2026, 2027, and 2029, respectively

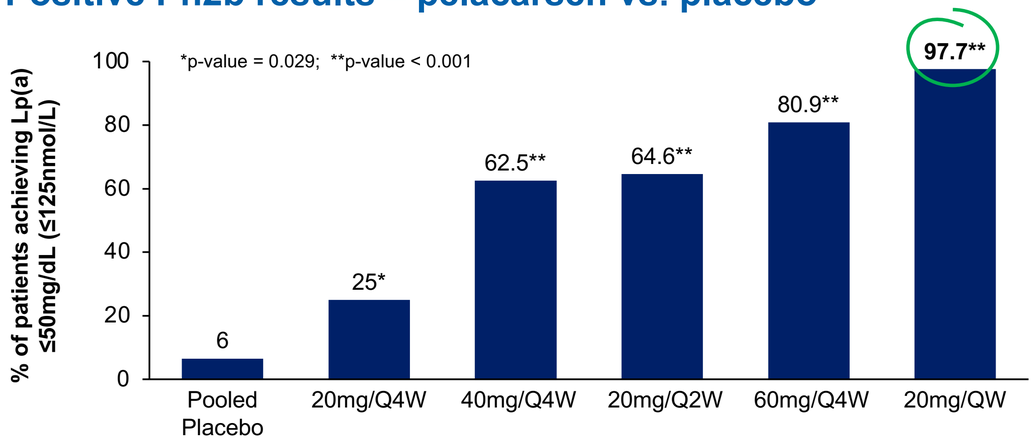
LDL-C – Low Density Lipoprotein Cholesterol. ASCVD – Atherosclerotic Cardiovascular Disease. CV – Cardiovascular. CVOTs – Cardiovascular outcomes trials. V2P – VICTORION-2-PREVENT. V1P – VICTORION-1-PREVENT.
1. Cholesterol Treatment Trialists' (CTT) Collaboration, et al. Lancet. 2010;376(9753):1670-1681. 2. Wang N, et al. Lancet Diabetes Endocrinol. 2020;8:36-49. 3. Figure adapted from Brandts J, et al. Circulation. 2020;141(11):873-876; Cholesterol Treatment Trialists(CTT) Collaboration European Heart Journal (2018) 39, 2540–2545 -doi:10.1093/eurheartj/ehx450. 4. mg/dL= 0.026 × mmol/L.

Pelacarsen: Transformational precision medicine reducing production of Lp(a) in patients with established CVD

- Elevated Lp(a) contributes as an independent, inherited and causal risk-enhancing factor leading to cardiovascular events
- **1 in 5** or 1.4 billion people worldwide have **elevated Lp(a)**[1], increasing their ASCVD **risk ~2-fold**[2,3]
- No therapies available to lower Lp(a)
- Pelacarsen, a GalNAc3 conjugated ASO, binds to apo(a) mRNA in the liver to inhibit protein synthesis and reduce Lp(a) levels
- **HORIZON**, our ongoing Ph3 trial, could be first to establish Lp(a) as an important target for ASCVD

Recruitment completed, primary readout in 2025

Positive Ph2b results – pelacarsen vs. placebo[4]



Ph2b study demonstrated

- **98%** of CVD patients achieved Lp(a) levels ≤50mg/dL (guideline threshold for CVD) with pelacarsen 20mg once a week
- Dose-dependent Lp(a) reductions up to 80%
- Good tolerability and safety profile

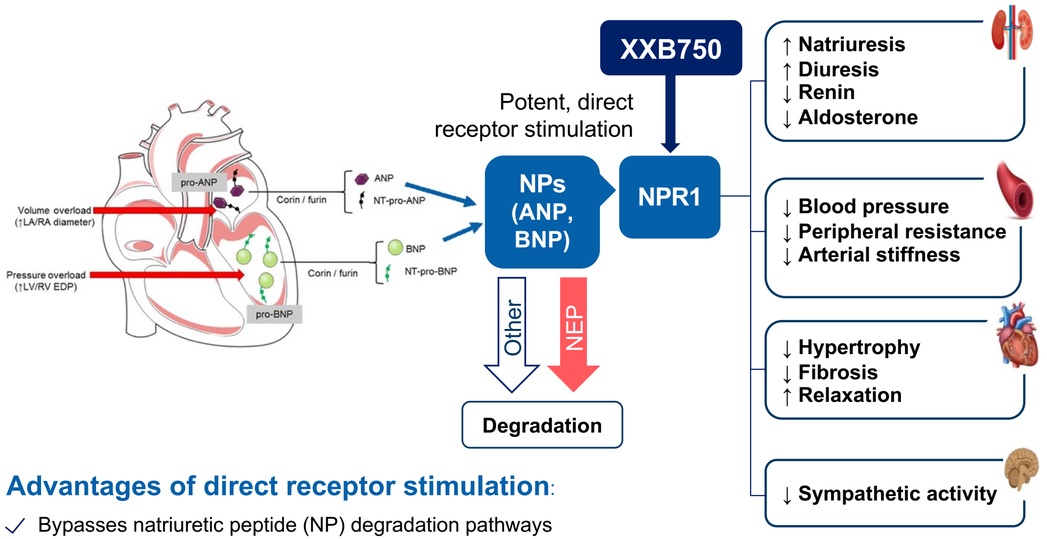
LP(a) – lipoprotein a. CVD – Cardiovascular disease. ASCVD – atherosclerotic cardiovascular disease. ASO – antisense oligonucleotide. 1. Lp(a) >50mg/dL. 2. Tsimikas S et al. J Am Coll Cardiol. 2018;71(2):177–192. 3. Tsimikas S, Stroes ESG. Atherosclerosis 2020;300:1–9. 4. NEJM Tsimikas, et al. 2020.

XXB750: Innovating in natriuretic peptide (NP) biology for refractory HFrEF and resistant hypertension

- Building on our strengths in heart failure research, development and commercialization of Entresto with XXB750
- XXB750 is a fully human monoclonal antibody, activates NPR1 directly via a novel ANP-noncompetitive mechanism
- NPR1 is expressed in multiple organ systems and plays a central role in hypertension and heart failure
- Pre-clinical and early clinical data support potential benefit of XXB750 due to stimulation of the NPR1 receptor

Ph2 in rHTN ongoing; Ph2 HF FPFV H1 2024

XXB750 fully leverages the benefits of the NP system by direct receptor stimulation



Advantages of direct receptor stimulation:

- ✓ Bypasses natriuretic peptide (NP) degradation pathways
- ✓ Overcomes inactive BNP isoforms issue
- ✓ Evidence suggesting ANP as main mediator of cGMP increase by Entresto

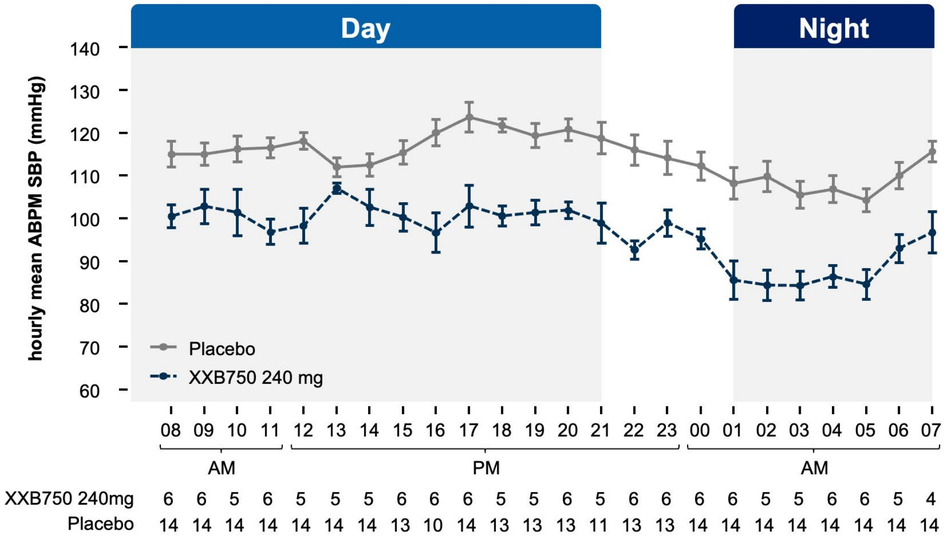
HFrEF – heart failure with reduced ejection fraction. (r)HTN – (resistant) hypertension. NPR1 – natriuretic peptide receptor 1. ANP – atrial natriuretic peptide. FPFV – first patient first visit.

XXB750 has demonstrated sustained systolic blood pressure (SBP) lowering

Ph1, healthy volunteer data 24-hr ABPM SBP at day 2

Placebo vs. XXB750 240mg

Day 2 after XXB750 240mg single dose



- Approximately 10% of hypertensive patients are not well-controlled despite concurrent use of ≥ 3 classes of antihypertensive agents[1]

XXB750

- ✓ Novel mechanism of action orthogonal to RAS inhibition
- ✓ Highly efficacious in healthy volunteers: mean SBP lowering of ~18mmHg
- ✓ Sustained BP lowering over 24 hours
- ✓ Improvement in night time dipping
- ✓ Progressing in Ph2b study in resistant hypertension

SBP – systolic blood pressure (BP). ABPM – ambulatory blood pressure monitoring. RAS – renin-angiotensin system. 1. Sheppard JP, Martin U, McManus RJ, Diagnosis and management of resistant hypertension, Heart 2017;103:1295-1302.

Iptacopan

NOVARTIS | Reimagining Medicine

Iptacopan

Oral factor B inhibitor targeting the alternative complement pathway

Market potential

●●● > USD 3bn

Unprobabilized peak sales of all asset indications in late-stage development

US/EU: Patent on compound (2034/2034)[1]

Potential to be the preferred treatment in several rare diseases - multiple high unmet need indications being pursued across nephrology and hematology

Potential to **change practice** in **paroxysmal nocturnal hemoglobinuria (PNH)**:

- First oral monotherapy to significantly **reduce the need for blood transfusions and improve quality of life** (**e.g. fatigue**) **vs. standard of care**
- Regulatory review underway in US and EU

APPLAUSE-**IgAN** Ph3 demonstrated **clinically meaningful** and highly statistically significant **proteinuria reduction** at 9 months

- US submission for accelerated approval planned in H1 2024; trial continues to confirm modification of disease progression (eGFR)

APPEAR-**C3G** Ph3 readout of primary endpoint expected in December 2023

- Positive Ph2 showed 57% proteinuria reduction at 1 year
- No treatment currently approved

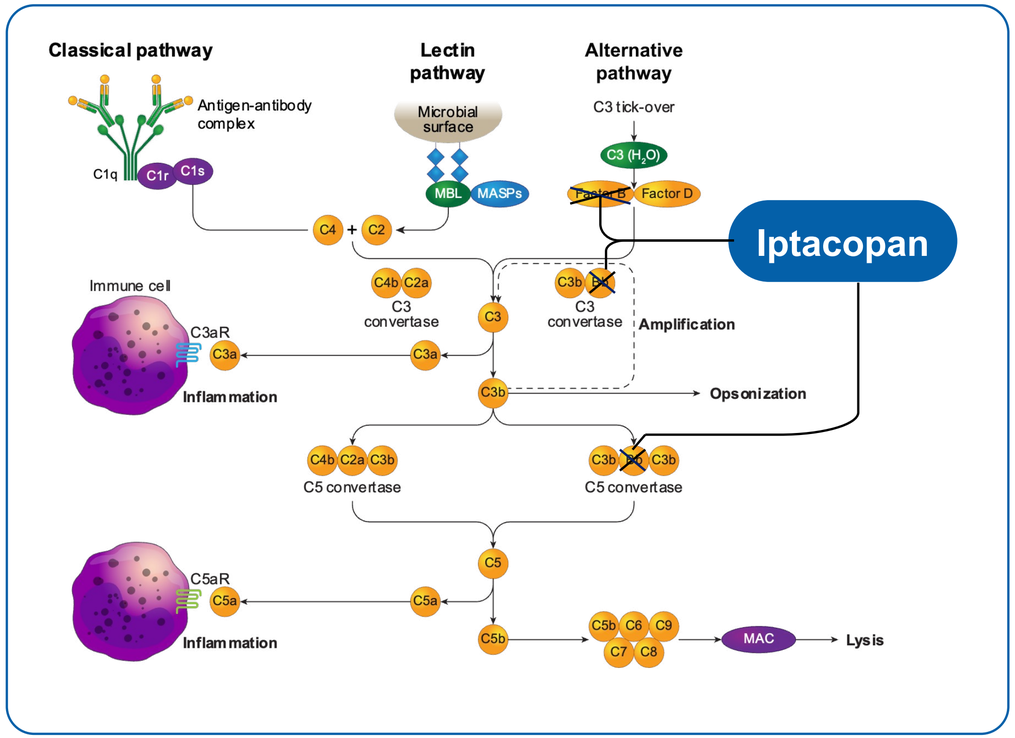
Additional indications are being explored in Ph2 and Ph3 trials: **IC-MPGN**, **aHUS**, **LN**

IgAN – IgA nephropathy. eGFR - estimated glomerular filtration rate. C3G – C3 glomerulopathy. IC-MPGN – immune complex membranoproliferative glomerulonephritis. aHUS – atypical hemolytic uremic syndrome. LN – lupus nephritis. 1. Patent term extensions and regulatory-based exclusivities may be possible.

Iptacopan, a first-in-class, oral, selective factor B inhibitor targeting the alternative pathway and underlying pathophysiology of complement diseases

Dysregulation of the complement pathway is associated with a range of rare diseases

Iptacopan is a proximal complement inhibitor that targets factor B to selectively inhibit the AP while leaving the direct signaling from the lectin and classical pathways intact[1-3]



1. Schubart A et al. Prot Natl Acad Sci USA. 2019;116:7926–31. 2. Risitano AM et al. Lancet Haematol. 2021;8:e344–e54. 3. Merle NS et al. Front Immunol. 2015;6:262. Scheme adapted from Trouw et al, Nature Rev Immunol 2017.

Iptacopan has the potential to become the preferred treatment option and redefine care across multiple complement-driven diseases

	Phase 3					Phase 2
	PNH	**IgAN**	**C3G**	**aHUS**	**IC-MPGN**	**LN**
	Up to 82% of patients remain anemic despite anti-C5 therapy	~30% patients with ≥1g/day of proteinuria progress to kidney failure within 10y	~50% patients progress to kidney failure within 10y High recurrence rate post kidney transplant	Untreated, ~50% of patients progress to kidney failure within 1y of diagnosis	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Remission achieved in only 30-50% of patients 10-20% of patients develop kidney failure within 10y
US prevalence:	**~6k**	**~185k**	**~10k**	**<5k**	**~11k**	**~111k**

PNH – paroxysmal nocturnal hemoglobinuria. C3G – C3 glomerulopathy. IgAN – IgA nephropathy. aHUS – atypical hemolytic uremic syndrome. IC-MPGN – immune-complex membranoproliferative glomerulonephritis. LN – lupus nephritis.

Significant unmet need in PNH despite current SoC anti-C5 therapy

PNH prevalence 10-20 cases/million = ~6k patients in the US[1]

Delays in diagnosis and treatment...

- Up to 3 years to diagnose
- Median age at disease onset 36 years[7]
- Common symptoms with multiple causes
- "Watch & Wait" for disease progression before treatment is initiated
- Patients experience symptoms and may be receiving transfusions

… once treated with C5i, results are sub-optimal

Up to **82%** of patients **do not achieve normal hemoglobin** levels[2]

Up to **39%** of patients remain **transfusion dependent** due to **persistent anemia**[3,4]

75-89% of patients experience **fatigue**; often recognized as the **most disabling PNH symptom**[5,6]

1. Cançado RD, 2021 and Jalbert JJ, 2019, Mon Pere N, 2018. 2. Fishman J et al. Hematol Rep 2023;15:266–82. 3. Debureaux et al. Bone Marrow Transplant 2021;56:2600–2. 4. Schrezenmeier H et al. Ther Adv Hematol 2020;111:1–14.
5. Young NS et al. Semin Hematol 2009;46:S1–16. 6. Dingli D et al. Ann Hematol 2022;101:251–63. 7. Schrezenmeier H et al. Ann Hematol. 2020;99(7):1505-1514. Source: Patient journey market research 2022.

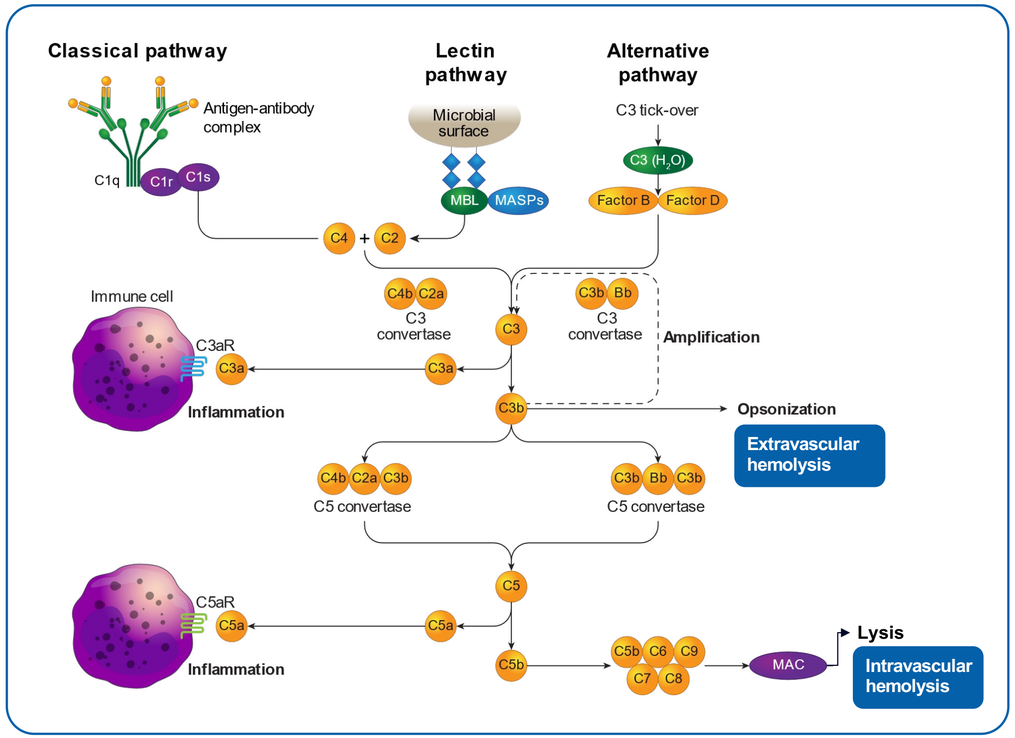
PNH treatment paradigm: Targeting the pathway upstream may prevent amplification downstream and help shut down hemolysis

Hemolysis is the destruction of RBCs.

In PNH:

- **Intravascular hemolysis** is the main mechanism of hemolysis in untreated PNH
- **Extravascular hemolysis** occurs in the liver and spleen and emerges when the terminal pathway is inhibited[1,2]

Addressing ongoing hemolysis may play a significant role in reducing PNH disease activity[3]



Scheme adapted from Trouw et al, Nature Rev Immunol 2017. 1. Brodsky RA. Blood. 2014;124(18):2804-2811. 2. Risitano AM. Immunobiology. 2012;217(11):1080-1087. 3. Risitano AM, et al. Front Immunol. 2019;10:1157.

Ph3 results confirm the practice-changing potential of iptacopan in treating PNH

	APPOINT Adult PNH patients **naive** to complement inhibitor therapy	**APPLY** Adult PNH patients with residual anemia (Hb<10g/dL) **despite treatment with anti-C5s**
Improved hemoglobin levels	92.2% Hb ≥2g/dl increase from baseline 62.8% Hb level ≥12g/dl	82.3% Hb ≥2g/dl increase from baseline vs. 2% with C5i 68.8% Hb level ≥12g/dl vs. 1.8% with C5i
Lower need for transfusions	97.6% RBC transfusion avoidance	96.4% RBC transfusion avoidance vs. 26.1% with C5i
Improved QoL and safety	Reduced patient-reported fatigue | Demonstrated safety with no serious breakthrough hemolysis[1]	

"...a potentially groundbreaking benefit for those living with this chronic disorder."

Prof. Peffaut de Latour
Hematology and Bone Marrow Transplant Department of the Saint-Louis Hospital, Paris

The data "underscore the potential of iptacopan to be a practice-changing oral medicine for this devastating disease."

Prof. Risitano
Director of Hematology and Hematopoietic Stem Cell Transplantation; AORN San Giuseppe Moscati

1. During the 24-week core treatment period.

Opportunity to redefine PNH treatment paradigm and establish iptacopan as the new standard of care

~6k
Prevalent[2] PNH patients in US

Treated with complement inhibitor[3]
30%
Displace Anti-C5

Untreated
70%
Potentially increase treatment rate

400
Incident[1] PNH patients/year in US
Start appropriate patients on iptacopan

In Ph3 studies to date:

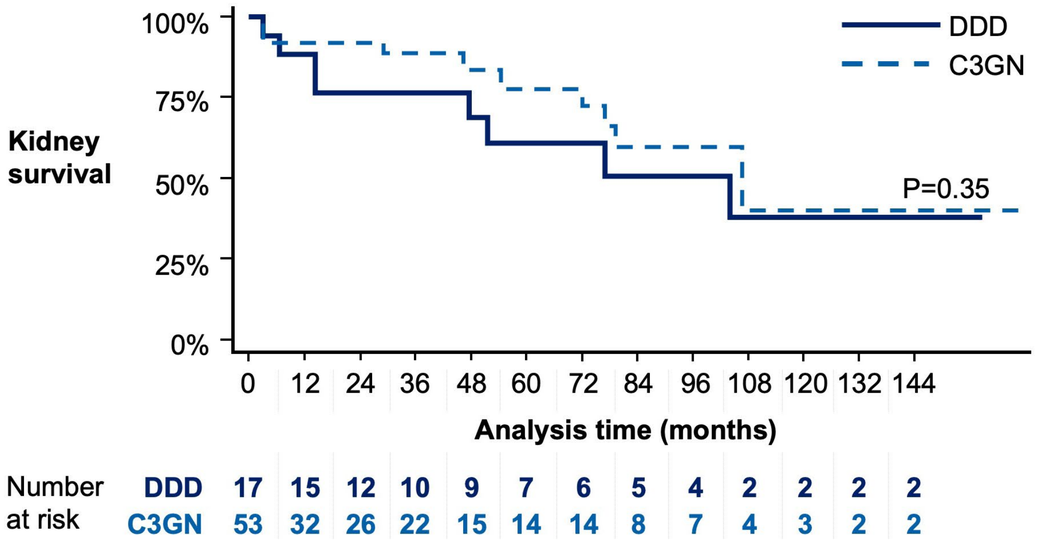
- ✓ Enables near-normal hemoglobin (≥ 12g/dL)
- ✓ Provides comprehensive hemolysis control (both intravascular and extravascular hemolysis)
- ✓ Enables transfusion independence
- ✓ Significant improvement in patient-reported fatigue
- ✓ Oral convenience

Next steps > On track for **FDA decision in December**

1. Incidence: 1.0-1.5 per million individuals (Hill A, 2017). 2. Prevalence: 12-18 per million individuals in the US (Jalbert JJ, 2019, Mon Pere N, 2018). 3. Treated with anti-C5 or anti-C3.

C3G is an ultra-rare, severe form of primary glomerulonephritis commonly diagnosed in adolescents/young adults...

K-M analysis of kidney survival[1] by C3G subtype[2]



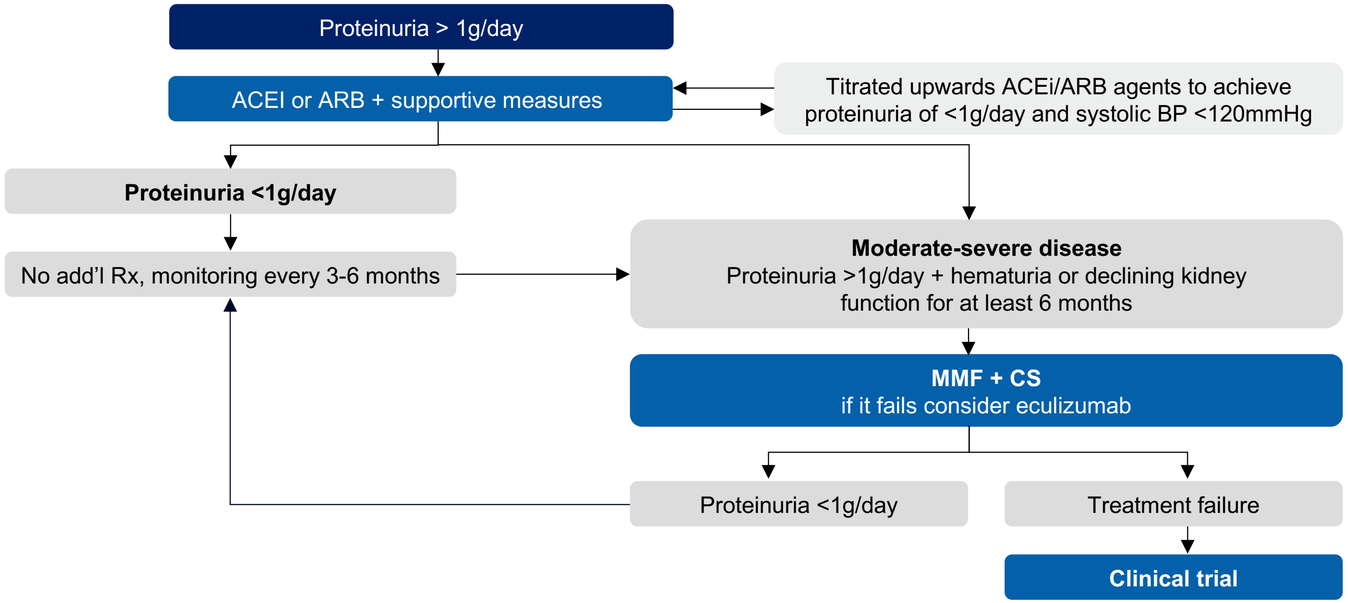
- Characterized by complement dysregulation and complement C3 deposition in the kidney
- Incidence: 1–2 per million
- Prevalence: ~20 per million (US: ~10k; EU5: ~10.5k; China: ~23.5k; Japan: ~3k)
- **~50% of patients develop kidney failure requiring dialysis or transplant within 10 years of diagnosis[3,4]**
- Treatment goals: Preserve kidney function
- Post-transplantation recurrence and allograft loss is common (50% in DDD, 75% in C3G)

DDD – dense deposit disease. C3G – C3 glomerulonephritis. 1. End-stage kidney disease (ESKD) free renal survival. 2. Medjeral-Thomas et al. Clin J Am Soc Nephrol. 2014;9(1):46-53. 3. Smith RJH, et al. Nat Rev Nephrol 2019;15:129–143. 4. Martin B, Smith RJH. In: Adam MP, Ardinger HH, Pagon RA, et al. GeneReviews® [Internet]. Updated 2018. University of Washington, Seattle; 1993–2022.

... without approved treatments, managed with supportive care and immunosuppression

Treatment algorithm for patients at risk[1]:

- There is a lack of trial-based evidence for C3G treatments: KDIGO recommendations are based on expert opinion
- An optimal treatment strategy for C3G using currently available therapeutics has not been established



ACEi – angiotensin-converting enzyme inhibitor. ARB – angiotensin II receptor blocker. BP – blood pressure. C3G – complement 3 glomerulopathy. IS – immunosuppression. KDIGO – Kidney Disease: Improving Global Outcomes. MMF – mycophenolate mofetil. CS – corticosteroid. SoC – standard of care. 1. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. Kidney Int. 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.

Data from Ph2 and roll-over extension study confirm iptacopan potential to become the treatment of choice for C3G

Sustained effects observed from 12 weeks to 1 year

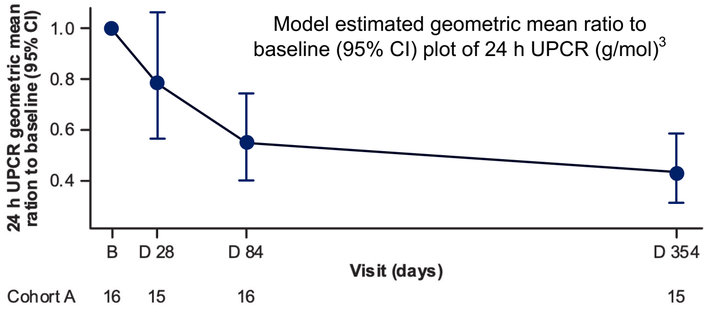
Native kidney

- **Decrease in proteinuria** (primary endpoint) -45% at 12 weeks, -57% at 1 year (RoE)
- **Stabilization of kidney function** at 12 weeks, +6.83 ml/min/m^2 at 1 year (RoE)
- **Normalization of serum C3 levels** at 12 weeks and 1 year[2]
- **Renal composite endpoint met by >50% patients**[1]: **53%** of patients met all three components of composite endpoint at 1 year (RoE)

Transplanted kidney

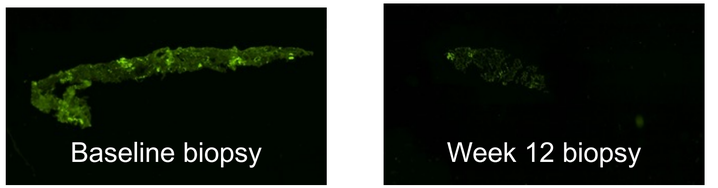
- **Decrease in C3 deposits** (primary endpoint) at 12 weeks
- **Stabilization of kidney function** at 12 weeks and 1 year
- **Normalization of serum C3 levels** at 12 weeks and 1 year[2,3]

Primary endpoint native kidney



Primary endpoint transplanted kidney[4]

Kidney biopsy baseline → Week 12 C3 Deposit Score



RoE – Roll-over extension. UPCR – urine protein creatinine ratio. CI – confidence interval. 1. Renal endpoint criteria of stable eGFR, ≥50% decrease in proteinuria and ≥50% increase in serum C3 levels. 2. C3 was normalized at 1 year in 8/16 patients in native kidney (C3 levels increased by more than 250% vs baseline) and 7/9 patients in transplanted cohort C3 levels increased by 96% vs baseline). 3. ASN 2022 poster. 4. Wong EK, et al. ePoster ASN 2021.

Ph3 APPEAR-C3G ongoing with readout imminent

Trial overview

1:1 placebo randomization

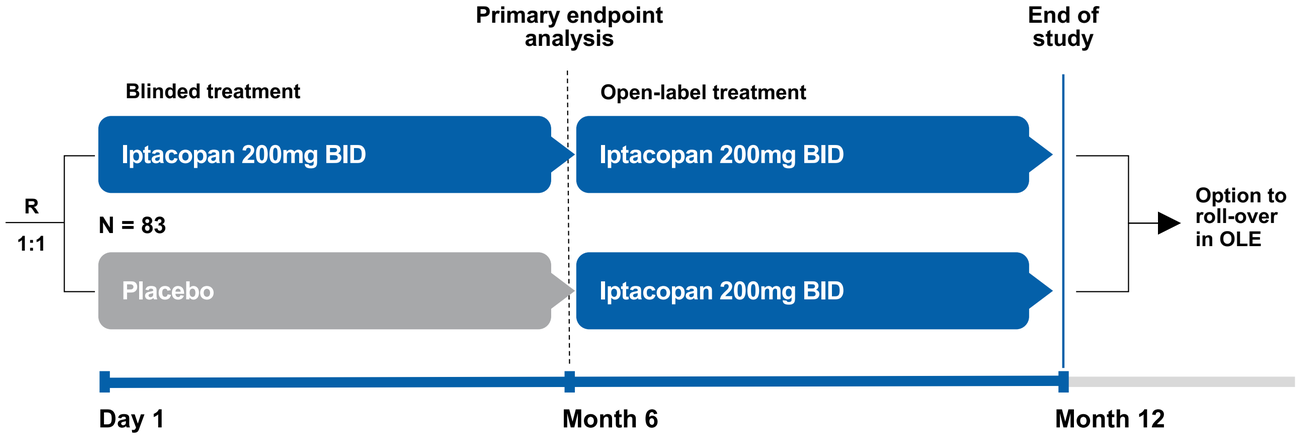
Biopsy-confirmed and native kidney

Proteinuria ≥ 1g/g (24h UPCR)

Primary endpoint (EP): 6m proteinuria

Secondary EPs: eGFR, proportion achieving a composite renal endpoint, reduction in glomerular inflammation, safety and tolerability

Study design



Next steps > Primary endpoint **readout expected December 2023**

eGFR – estimated glomerular filtration rate. OLE – open label extension study. UPCR – urinary protein to creatinine ratio. BID – twice a day.

Next steps for C3G

APPEAR-C3G expected to readout in Dec 2023, US filing 2024

Ph3 study has proteinuria reduction as primary endpoint and at submission will also include secondary endpoint assessments such as eGFR

Started enrolling adolescent patients

APPARENT-IC-MPGN started Q4 2023, expected to read out in 2026

Second Ph3 study in IC-MPGN patients (closely related to C3G) to ensure the broadest possible patient population will benefit from iptacopan/potential label expansion

We pursue multiple opportunities in parallel to accelerate delivery of innovation to patients

Phase 3

Phase 2

PNH	IgAN	C3G	aHUS	IC-MPGN	LN
Up to 82% of patients remain anemic despite anti-C5 therapy	~30% patients with ≥1g/day of proteinuria progress to kidney failure within 10y	~50% patients progress to kidney failure within 10y High recurrence rate post kidney transplant	Untreated, ~50% of patients progress to kidney failure within 1y of diagnosis	~50% patients progress to kidney failure within 10y High recurrence post kidney transplant	Remission achieved in only 30-50% of patients 10-20% of patients develop kidney failure within 10y
Decision expected US Dec 2023 EU Jul 2024	**Submission for accelerated approval expected H1 2024**	**Submission-enabling readout Dec 2023**	**Submission-enabling readout expected 2025**	**Submission-enabling readout expected 2026**	**Readout expected 2025**

PNH – paroxysmal nocturnal hemoglobinuria. C3G – C3 glomerulopathy. IgAN – IgA nephropathy. aHUS – atypical hemolytic uremic syndrome. IC-MPGN – immune-complex membranoproliferative glomerulonephritis. LN – lupus nephritis.

IgAN (iptacopan, atrasentan, zigakibart)

NOVARTIS | Reimagining Medicine

IgAN: Unmet need for targeted treatments and improved safety

Disease background

- About 25 adults per million are affected each year worldwide[1]
- Slowly progressive auto-immune kidney disease
- Young age at diagnosis (teens to 30's)
- ~30% of high-risk patients[2] progress to kidney failure in ~10 years
- Nephrologists' top treatment goals are reduction of proteinuria and preservation of kidney function
- Preventing dialysis saves ~USD 200k per patient per year (US)

Unmet need

Novel, efficacious drugs with better safety profiles

- Current treatments only help manage "worsening of the disease"
- Novel treatments that target the pathogenic mechanisms in IgAN are needed to prevent irreversible renal damage
- 75%[3] of the nephrologists want to minimize steroid use

Annual incidence (per million) by country/region[4–15]

US[4,5]	7-21
Europe[3,6-11]	4.9-26
China[12,13]	~30
Japan[14]	24-40

1. Lai KN et al. Nat Rev Dis Primers. 2016;2:16001; 2. Patients with uncontrolled proteinuria (>1g/day). 2. Reich HN, Troyanov SAA, Scholey JW, Cattran DC. Remission of Proteinuria Improves Prognosis in IgA Nephropathy. J Am Soc Nephrol. 2007;18(12):3177-3183. doi:10.1681/ASN.2007050526. 3. Spherix Global Insights, REALWORLD DYNAMIX, IgA nephropathy (US) 2023. 4. Sim JJ et al. Am J Kidney Dis. 2016;68(4):533-544. 5. Swaminathan S et al. Clin J Am Soc Nephrol. 2006;1(3):483-487. 6. Hanko JB et al. Nephrol Dial Transplant. 2009;24(10):3050-3054. 7. McQuarrie EP et al. Kidney Int. 2014;85(1):198-203. 8. Rivera F et al. Nephrol Dial Transplant. 2002;17(9):1594-1602. 9. Simon P et al. Kidney Int. 2004;66(3):905-908. 10. Zaza G et al. Nephrol Dial Transplant. 2013;28(2):367-372. 11. Zink CM et al. Clin Kidney J. 2019;12(6):795-800. 12. Clarivate. Accessed February 2, 2022. https://clarivate.com/products/research-reports/report/epidne0002-biopharma-iga-nephropathy-epidemiology-mature-markets. 13. Data on file. [Name of doc]. Novartis Pharmaceuticals Corp; [date]. 14. Local data from J-RBR and national guideline data. 15. Magistroni R, et al. Kidney Int 2015;88:974–989.

Evidence supports that overactivation of the alternate pathway markedly contributes to kidney inflammation and glomerular injury in IgAN (Hit 4)[1-4]

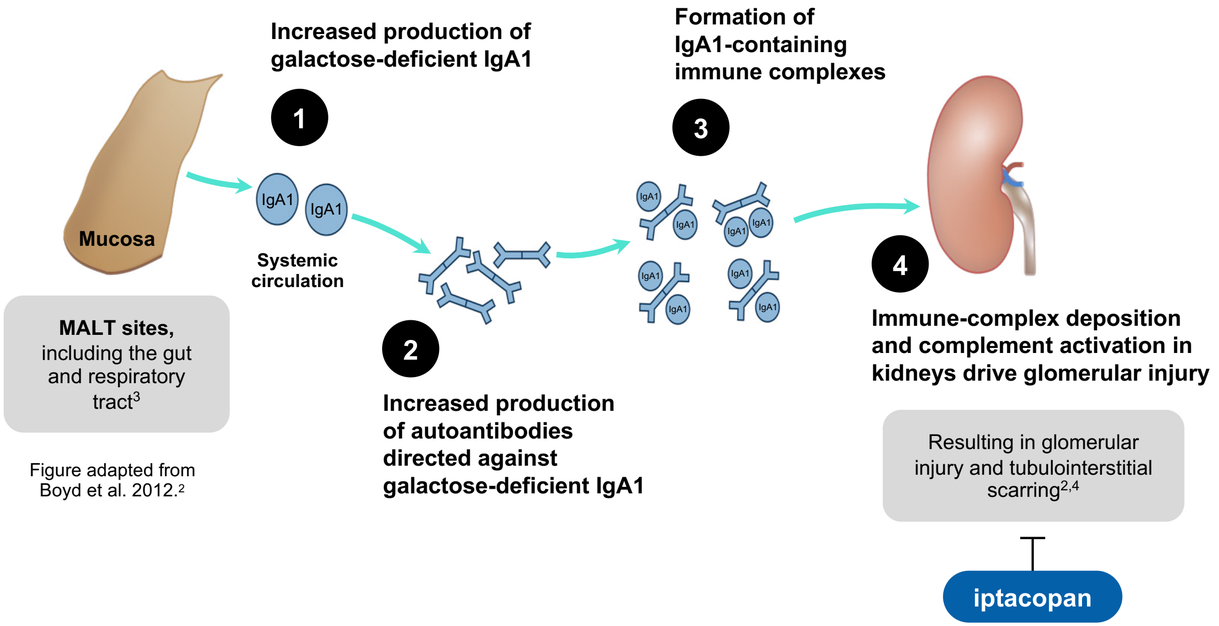


Figure adapted from Boyd et al. 2012.[2]

IgAN pathophysiology is represented by a 'multi-hit model'[1,2]

- Iptacopan is a **proximal complement inhibitor** that targets factor B to **selectively inhibit the AP** while leaving the direct signaling from the lectin and classical pathways intact.[5-7]
- Inhibition of factor B **prevents the activity of AP-related C3 convertase** and the **subsequent formation of C5 convertase.**[5]

IgA – immunoglobulin. IgAN – immunoglobulin A nephropathy. MALT – mucosa-associated lymphoid tissue. 1. Rizk DV et al. Front Immunol. 2019;10:504. 2. Boyd JK et al. Kidney Int. 2012;81(9):833-843. 3. Gesualdo L et al. Semin Immunopathol. 2021;43(5):657-668. 4. Tecklenborg J et al. Clin Exp Immunol. 2018;192(2):142-150. 5. Suzuki 2021 Sem Immunol. 6. Kohan 2014 KI. 7. Raina 2020 Kidney Dis.

IgAN is a heterogenous disease; Novartis has the potential to offer a trio of highly differentiated therapies, each with its own unique MoA

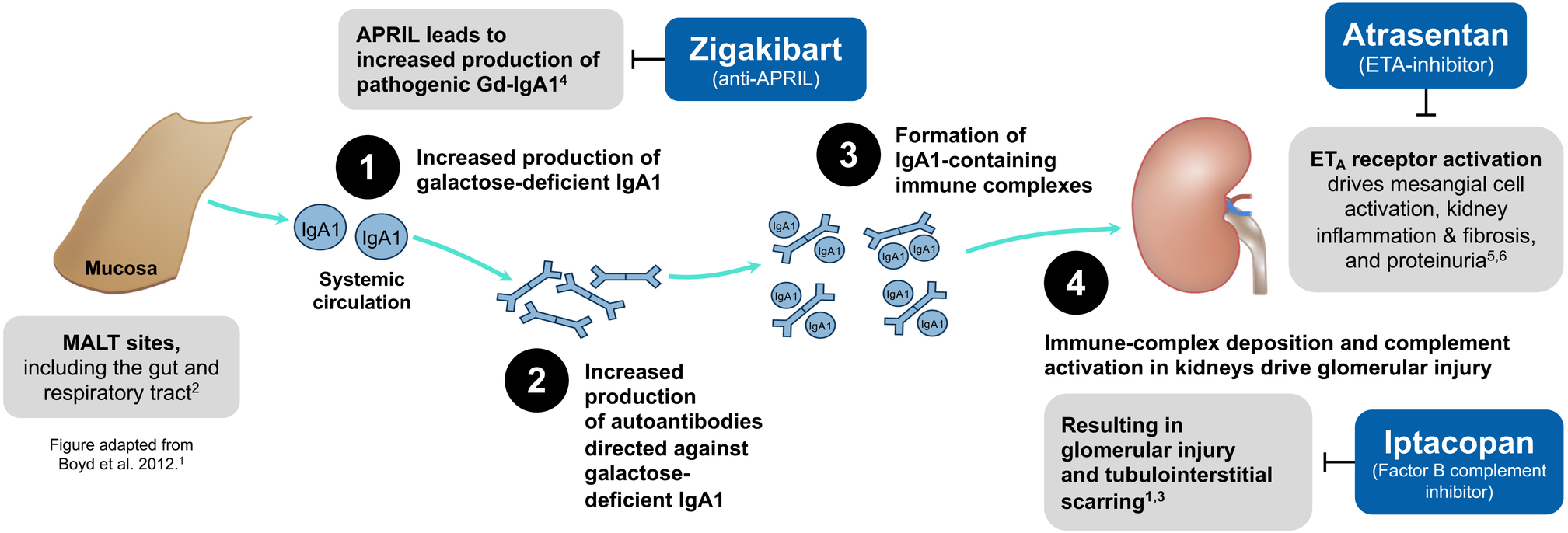


Figure adapted from Boyd et al. 2012.[1]

IgAN – immunoglobulin A nephropathy. MALT – mucosa-associated lymphoid tissue. 1. Boyd JK et al. Kidney Int. 2012;81(9):833-843. 2. Gesualdo L et al. Semin Immunopathol. 2021;43(5):657-668. 3. Tecklenborg J et al. Clin Exp Immunol. 2018;192(2):142-150. 4. Suzuki 2021 Sem Immunol. 5. Kohan 2014 Kl. 6. Raina 2020 Kidney Dis.

Iptacopan demonstrated clinically meaningful and highly statistically significant proteinuria reduction in Ph3 APPLAUSE-IgAN

Trial overview

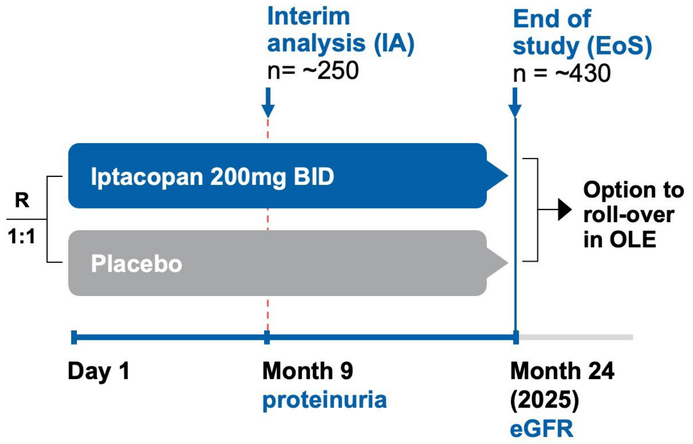
1:1 placebo randomization
SGLT2is permitted (no stratification)

Biopsy-proven IgAN despite stable background therapy[1]

Proteinuria ≥1g/g (24h UPCR) and eGFR ≥30ml/min/1.73m^2

Primary endpoints:
At IA: proteinuria reduction at 9 months
At EoS: annualized total slope of eGFR decline over 24 months

Study design



Top-line results at pre-specified IA

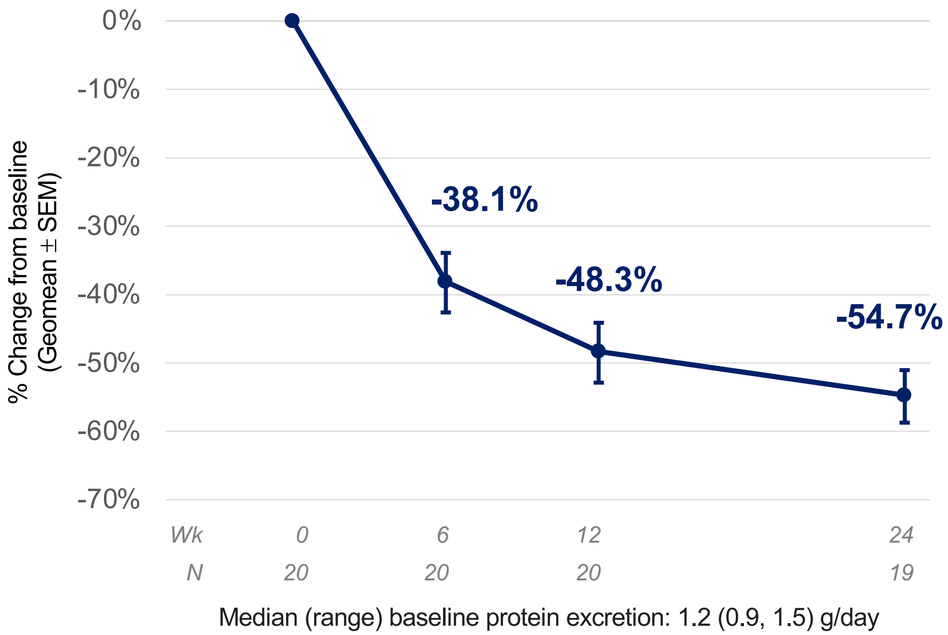
- ✓ **Superiority vs. placebo** in proteinuria reduction on top of optimized supportive care
- ✓ **Clinically meaningful and highly statistically significant** proteinuria reduction
- ✓ Safety profile consistent with previously reported data
- ✓ **Oral**

Next steps 〉 US submission for **accelerated approval** planned H1 2024
Study continues to assess superiority in slowing disease progression (eGFR slope) for full approval

IgAN – IgA nephropathy. eGFR – estimated glomerular filtration rate. OLE – open label extension. BID – twice daily. SGLT2i - SGLT2 inhibitor. UPCR – urine protein creatinine ratio. 1. Including at least maximally tolerated dose of ACEi/ARB for at least 90 days.

Atrasentan, a potent and selective ETA receptor inhibitor, reduces proteinuria with potential to preserve kidney function

% Reduction in UPCR, Ph2 AFFINITY



Median (range) baseline protein excretion: 1.2 (0.9, 1.5) g/day

Reasons to believe

- ✓ Ongoing Ph2 AFFINITY IgAN cohort interim results demonstrated a mean **54.7% reduction in proteinuria** at week 24[1]
- ✓ Ph3 ALIGN study met its primary endpoint, demonstrating superiority of atrasentan vs. placebo in proteinuria reduction
- ✓ Highly potent and very specific ETA receptor inhibitor[2]
- ✓ Well-characterized safety profile (SONAR dataset of >5k patients with diabetic kidney disease)[3,4]
- ✓ Atrasentan lacks sulfonamide associated with liver risk in other ERAs
- ✓ ETA receptor inhibitor that permits independent RASi optimization dose
- ✓ SGLT2i combo could drive adoption in earlier lines of therapy

Graph: Kidney International Reports. Vol 8 Issue 11 pages 2198-2210 (November 2023). ETA – endothelin A. ERA – endothelin A receptor inhibitor. RASi – Renin-angiotensin system inhibitor. 1. Kim et al., ASN 2022. 2. Wessale et al, 2002, Clin Sci. 3. de Zeeuw et al, 2014, JASN. 4. Heerspink et al, 2019, WCN.

Atrasentan demonstrated clinically meaningful and highly statistically significant proteinuria reduction in Ph3 ALIGN

Trial overview

1:1 placebo randomization

Biopsy-proven IgAN

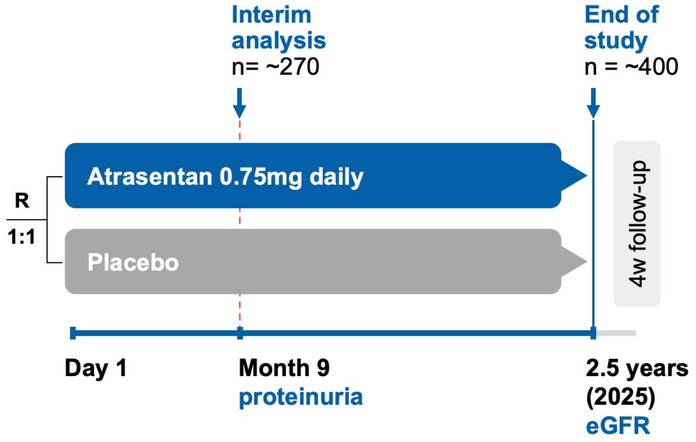
Maximally-tolerated RASi, or RASi intolerant, SGLT2i stratum

Proteinuria >1g/day and eGFR >30ml/min/1.73m^2

Primary endpoint: proteinuria reduction at 9 months

Secondary endpoint: 2.5 year eGFR

Study design



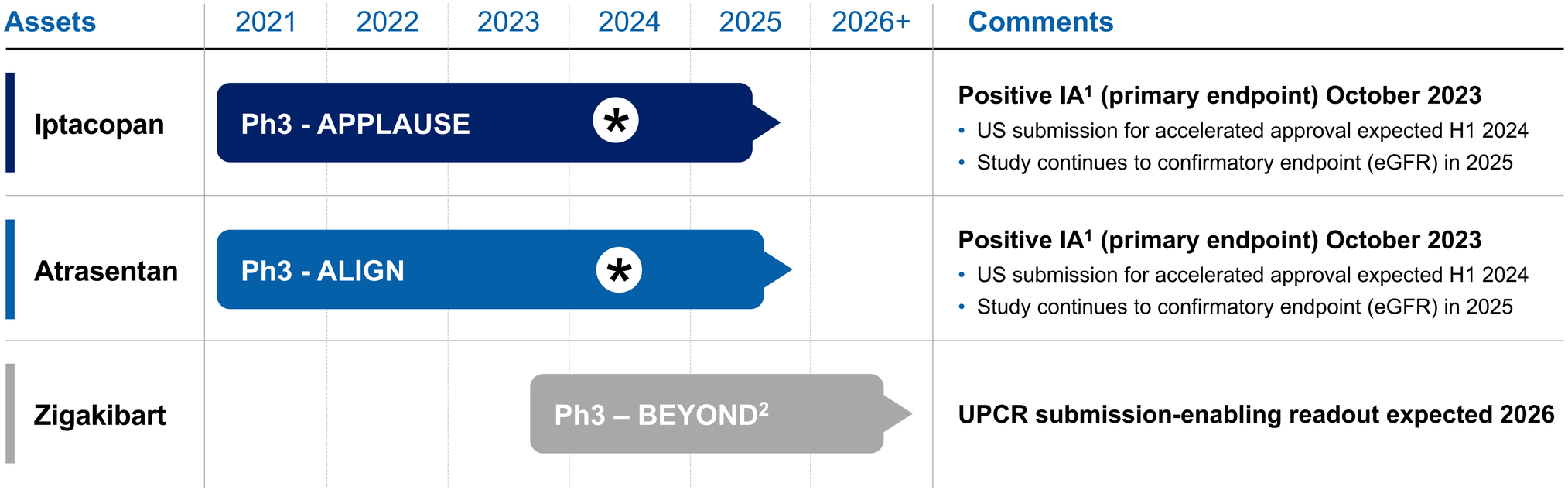
Top-line results at pre-specified IA

- ✓ **Superiority vs. placebo** in proteinuria reduction on top of optimized supportive care
- ✓ **Clinically meaningful and highly statistically significant** proteinuria reduction
- ✓ Safety profile consistent with previously reported data
- ✓ **Oral**

Next steps 〉 US submission for **accelerated approval** planned H1 2024
Study continues to assess superiority in slowing disease progression (eGFR slope) for full approval

SGLT2i – SGLT2 inhibitor. IgAN – IgA nephropathy. IA – Interim analysis. RASi – RAS inhibition. eGFR – estimated glomerular filtration rate. OLE – open label extension. BID – twice daily.

Advancing development of promising treatments for the benefit of patients with IgAN



(*) US submission for accelerated approval

UPCR – urine protein creatinine ratio. 1. 9 months readout may support US submission for accelerated approval. 2. Global, randomized, multicenter, double-blind, placebo-controlled Ph3 comparing safety and efficacy of zigakibart (600mg Q2W) vs. placebo in patients (N~272) with IgAN at risk of progressive loss of kidney function.

Therapeutic Area Overview: Immunology

Angelika Jahreis
Development Unit Head, Immunology

Shreeram Aradhye
President, Development and Chief Medical Officer

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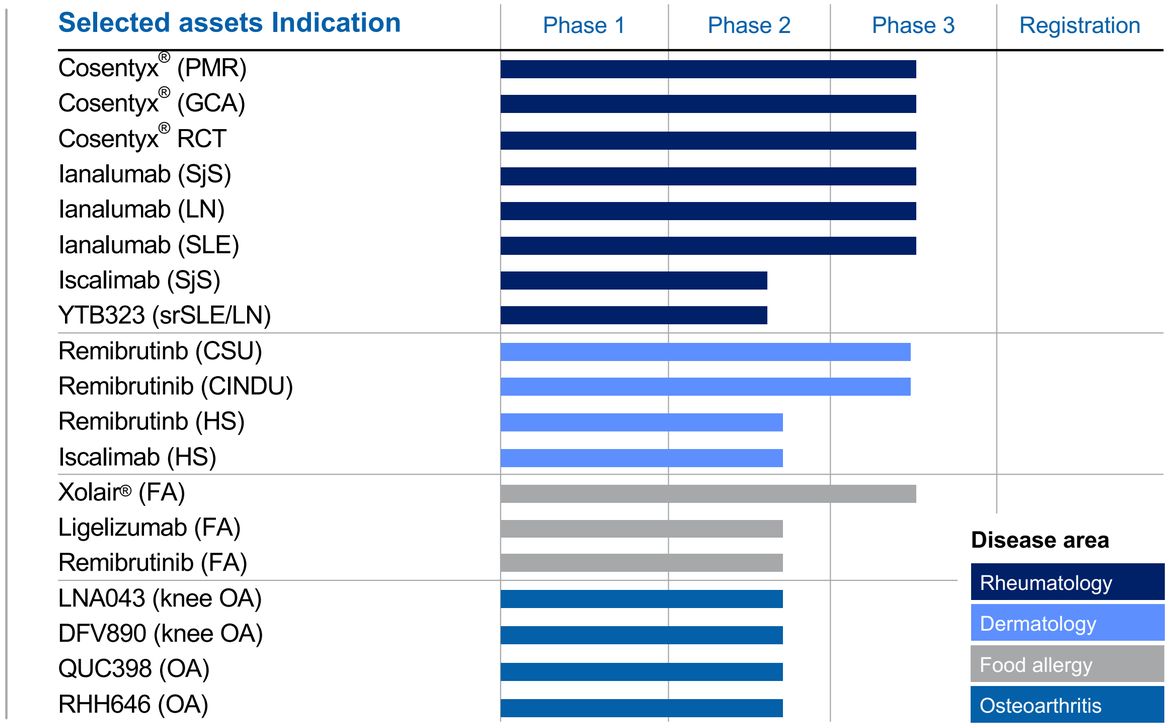
Immunology therapeutic area focuses on areas of highest unmet need with a differentiated pipeline

Immunology strategy

- Prioritize **Cosentyx® LCM** indications (PMR, GCA and RCT)
- Address high unmet need for diseases with limited treatment options in **Rheumatology** and **Dermatology**
- Aim for leadership in severe refractory autoimmune diseases with **CAR-T therapies and other modalities**
- Explore additional opportunities, e.g. food allergy, osteoarthritis

Assets highlighted today: **Cosentyx®**, **ianalumab**, **YTB323**

Deep dives: **Remibrutinib**



PMR – Polymyalgia rheumatica. GCA – Giant cell arteritis. RCT – Rotator cuff tendinopathy. LN – Lupus nephritis. SLE – Systemic lupus erythematosus. SjS – Sjögren's syndrome. CSU – Chronic spontaneous urticaria. CINDU – chronic inducible urticaria. FA – Food allergy. OA – Osteoarthritis.

Cosentyx® now approved for HS. Pivotal Ph3 data showed durable efficacy sustained up to 1 year

Hidradenitis suppurativa (HS) unmet need

Lesions and **abscesses** in sensitive areas of the body

~97% patients suffer from pain[1]

~95% eligible patients not on biologic[2]

~50% biologic treated patients can lose response[3]

Cosentyx opportunity

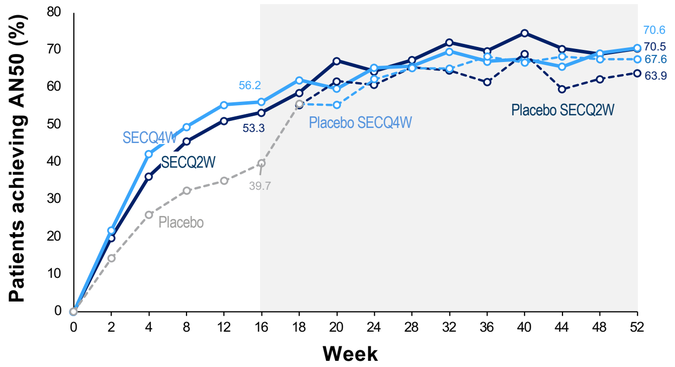
~400k addressable patients in US and EU[4]

Other assets in development for HS

Iscalimab (Ph2), remibrutinib (Ph2)

Cosentyx pivotal Ph3 data (SUNRISE, SUNSHINE)

Durable efficacy sustained to 1 year, **fast onset** of action



>70% with at least a 50% reduction in total abscess and inflammatory nodule count[5]

≥70% flare free[5]

>65% with pain relief[6]

Fast and lasting QoL improvement[5]

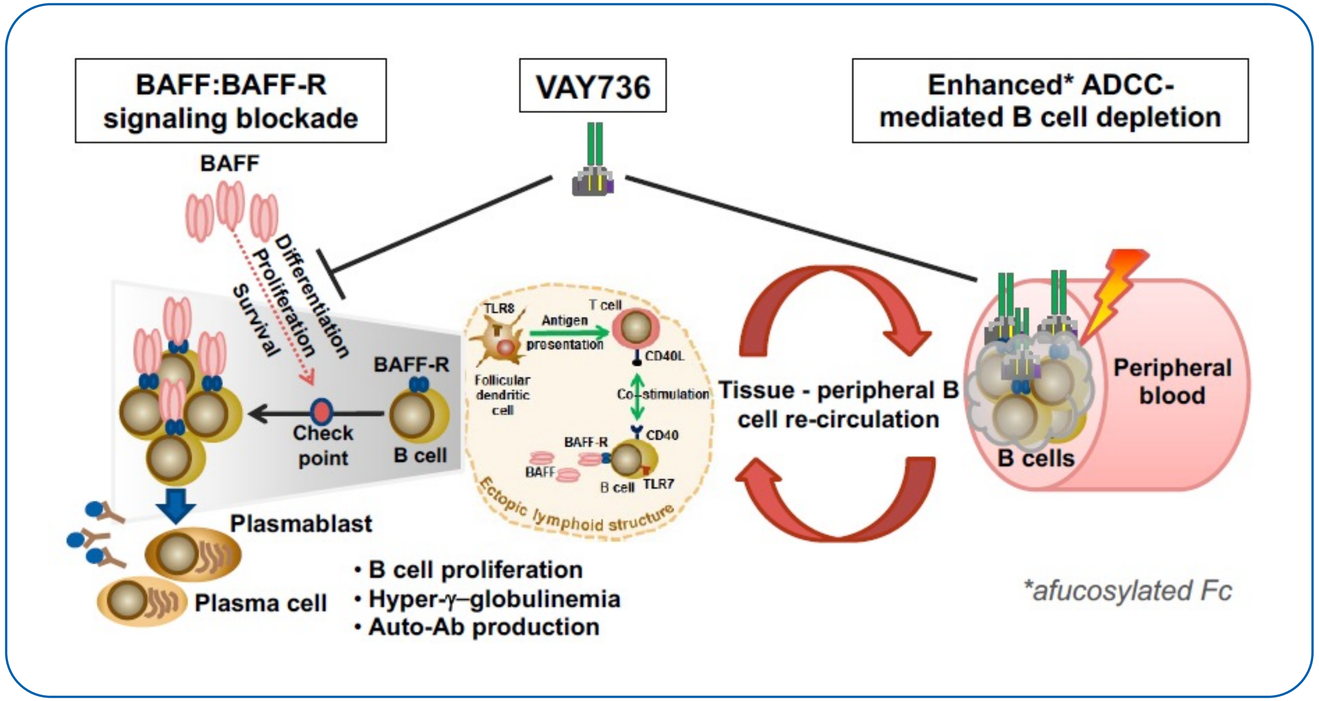
Safety consistent with well-established[9] profile[7,5] in its approved indications

Well tolerated	Infrequent SAEs	Candidiasis uncommon[8]	Low immunogenicity

HS – hidradenitis suppurativa. QoL – quality of life. SAE – serious adverse event. 1. Matusiak Ł. Br J Dermatol. 2020;183(6):e171-e177. 2. G6 market estimations based on IQVIA PADDS 2021. 3. Kimball A, et al. N Engl J Med. 2016;375:422–434. 4. Data on file. IQVIA PADSS. Novartis Pharmaceuticals Corp; March 2023. 5. Kimball A, et al. Lancet. 2023;401(10378):747-761. 6. Post hoc analysis: patients with moderate to severe pain at baseline who improved to mild or no pain at Week 52. 7. Novartis data on file. SUNNY Clinical Study Program pooled data tables and post hoc analyses. 8. Between 1 in 100 and 1 in 1,000 exposed patients. 9. Refers to approved indications.

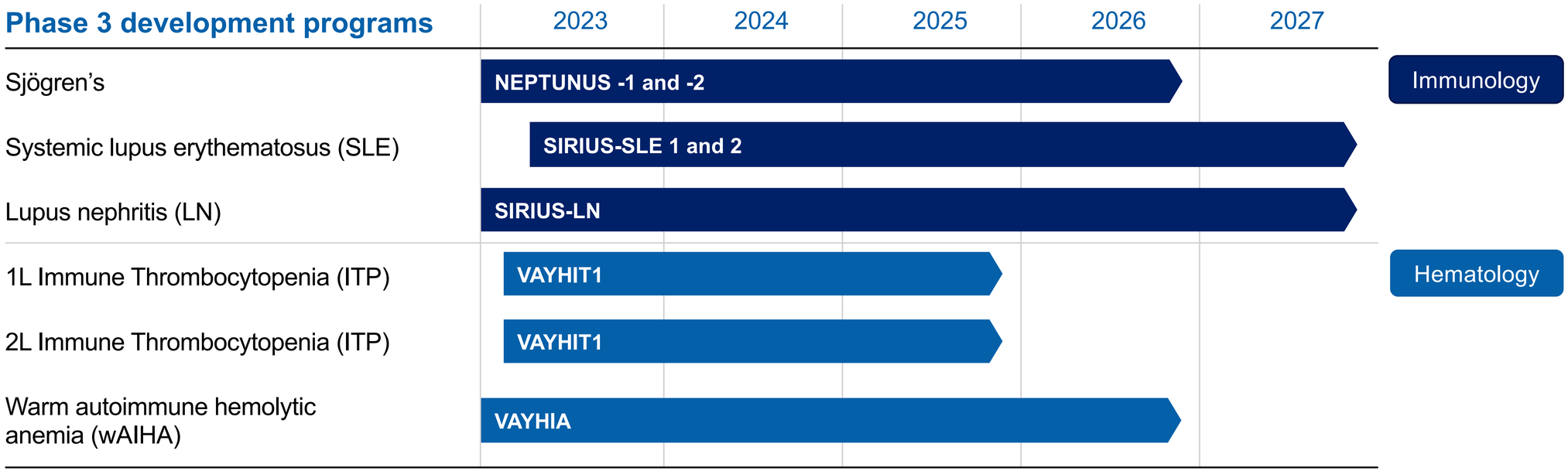
Ianalumab (VAY736): Potential to induce remission in B-cell driven autoimmune diseases by blocking BAFF-R...

- **Unique dual MoA** of **BAFF-R antagonism** coupled with **enhanced-ADCC B cell depletion**
- Expected to deliver deeper, longer term disease remissions vs. other B-cell depleting agents



ADCC – Antibody-dependent cellular cytotoxicity. Picture previously shared at EULAR 2023.

... being developed in multiple indications with high unmet need across both immunology and hematology



Phase 2 development program(s): Autoimmune hepatitis (AIH)

Ianalumab (VAY736): Positive Ph2 data in Sjögren's suggest potential to become first disease-modifying therapy

Rationale for ianalumab in Sjögren's

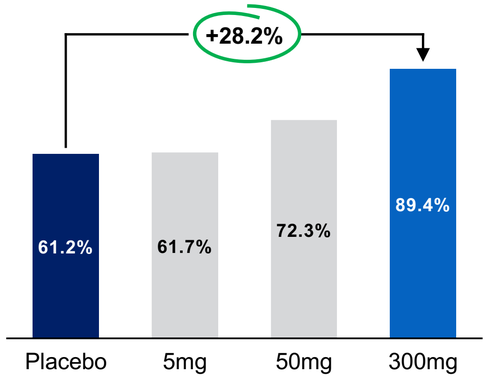
- Hallmark diagnostic features:
  - B-cell hyperreactivity and autoantibodies
  - Autoimmune inflammatory infiltrate including BAFF-R+ B cells in exocrine glands (salivary and tear glands show ectopic lymphoid structures)
- Depleting B-cells and blocking BAFF-R targets underlying disease mechanism

Ianalumab is expected to provide both **rapid** and **efficient depletion** as well functional inhibition of any remaining pathogenic tissue and circulating B cells

Next steps 〉 **NEPTUNUS-1 and -2 readouts expected in 2026**

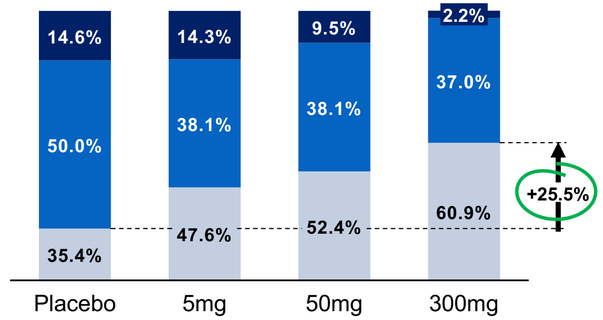
Ianalumab Sjögren's study showed dose dependent efficacy and good tolerability[1-2]

ESSDAI responders w24



28% more responders vs. placebo with 300mg ianalumab

Disease activity w24



26% more patients improved to **low disease activity**

Only 2% remained at high disease activity with 300mg

1. S. Bowman et al, ACR Annual Congress 2019. 2. T. Dörner, EULAR Annual Congress 2020. ESSDAI assesses 12 organ-specific domains (cutaneous, respiratory, renal, articular, muscular, peripheral nervous system, central nervous system, haematological, glandular, constitutional, lymphadenopathic, biological).

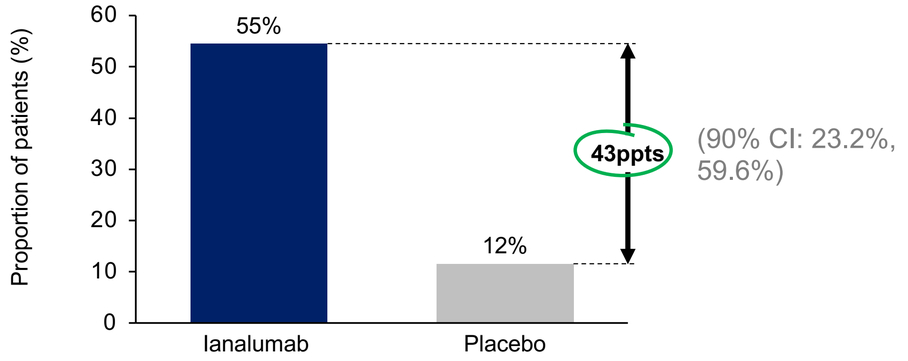
Ianalumab: Positive Ph2 data in SLE indicative of transformative efficacy

- ✓ Primary composite objective met: Proportion of patients with SRI-4 response at week 28 also achieving sustained glucocortoid taper requirements
- ✓ Treatment effects seen across secondary, exploratory outcomes:
  - Decreased incidence of moderate or severe flares
  - Increased number of patients achieving Lupus Low Disease Activity State
  - Potent B cell depletion, reduced anti-dsDNA antibodies, germinal center marker CXCL13
- ✓ Monthly s.c. dose ianalumab well-tolerated

Next steps 〉 **Ph3** studies in **SLE and LN** ongoing, **readouts in 2027**

Ph2 SLE results – ianalumab vs. placebo

Composite primary endpoint week 28 SRI-4 response with sustained steroid reduction (Lupus & KRC 2023)



Flare severity[1]		n (%)		n (%)
Moderate	**VAY736** (*N=22*)	9 (40.9)	**Placebo** (*N=26*)	19 (73.1)
Severe		4 (18.2)		8 (30.8)

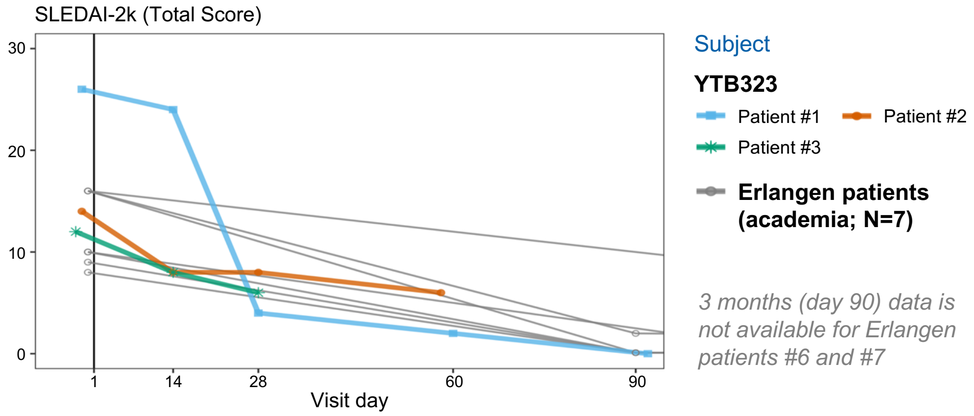
SLE – Systemic lupus erythematosus. LN – Lupus nephritis. CI – Confidence interval. 1. Flare definition severe flare: ≥1 BILAG-2004 'A' score; moderate flare: ≥2 BILAG-2004 'B' score.

YTB323, rapidly manufactured autologous CAR-T, has potential to reset immunity in severe refractory autoimmune diseases

- YTB323 a novel, rapidly manufactured, autologous CAR-T cell therapy, has shown preserved T cell stemness and enhanced CAR-T cell efficacy in hematological malignancies
- CD19 CAR-T validation in several severe refractory autoimmune diseases (srAIDs) by academia (G. Schett, Erlangen)
- Open-label, single-arm Ph1/2 study ongoing in patients with severe refractory SLE. Preliminary data from 3 sentinel patients suggest:
  - CAR T cell expansion and sustained B cel depletion
  - Substantial decreases in SLE Disease Activity Index (SLEDAI), in line with improvements in relevant disease biomarkers such as dsDNA
  - No serious adverse events or deaths

Early efficacy data from YTB323 in line with data from academia

(ACR 2023)[1,2]



3 months (day 90) data is not available for Erlangen patients #6 and #7

Next steps Preparation for **srSLE/LN Ph2b/3 study** ongoing
Preparations for **other B cell driven indications** ongoing

SLE – Systemic lupus erythematosus. SRI-4 – Systemic lupus erythematosus responder index). 1. Study G12101 Listing 16.2.6-5.8, Mackensen A, Müller F, Mougiakakos D, et al. (2022) Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nat Med; 28(10):2124-32. 2. Hernandez, JC, Barba, P, Alberich, ML, et al. (2023) An Open-Label, Multicenter, Ph1/2 Study to Assess Safety, Efficacy and Cellular Kinetics of YTB323 (Rapcabtagene Autoleucel), a Rapidly Manufactured CAR-T Therapy Targeting CD19 on B Cells, for Severe Refractory Systemic Lupus Erythematosus: Preliminary Results; [abstract]. Arthritis Rheumatol. 75 (suppl 9).

Remibrutinib

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Remibrutinib

Oral BTK inhibitor

Market potential

● ● ● > USD 3bn

Unprobabilized peak sales of all asset indications in late-stage development.

US/EU: Patent on compound (2034/2034)[3]

Highly selective, potent and covalent BTK inhibitor with **best-in-class potential; Ph3 in multiple indications** including CSU, CINDU and MS

- In US, **~400k CSU patients[1] not controlled or refractory to antihistamines[2]**
- Single therapeutic option with low (< 20%) penetration for these patients[1]

First BTKi with robust and consistent efficacy and favorable safety from CSU Ph3[4]

- Statistically significant efficacy in patients with inadequate response to antihistamines
- Onset of action as early as week 2
- Sustained response up to week 12
- Safety in general comparable to placebo

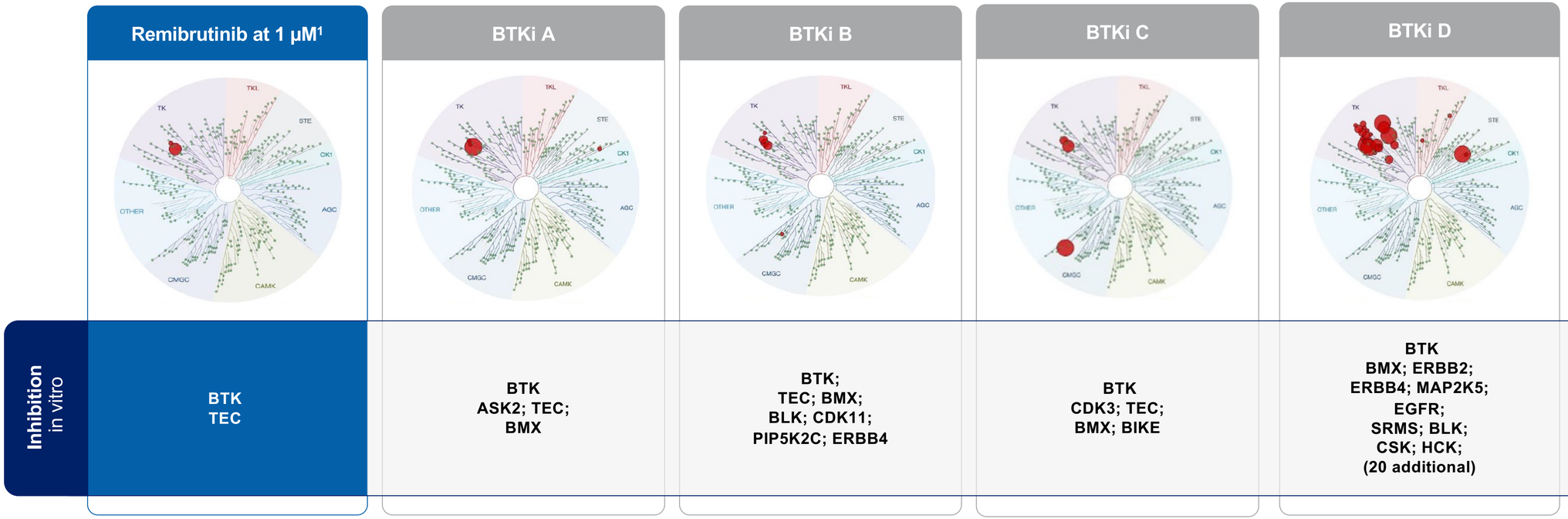
Significant opportunity as potential **first option post H1-antihistamines with oral convenience**

On track for global CSU submissions in 2024 (based on 52-weeks data)

CSU – Chronic spontaneous urticaria. CINDU – Chronic inducible urticaria. MS – Multiple sclerosis. 1. US only Novartis internal analysis. 2. H1-antihistamines at approved and increased doses. 3. Patent term extensions and regulatory-based exclusivities are possible. 4. S. Saini et al.. ACAAI meeting 11 2023.

CSU

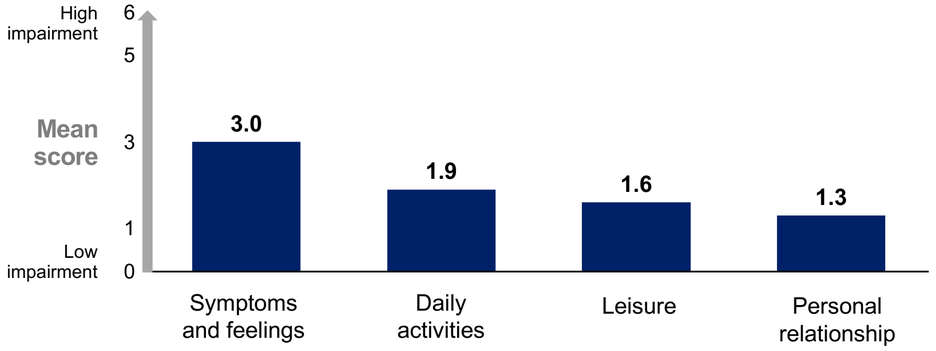
Remibrutinib is a highly selective BTKi



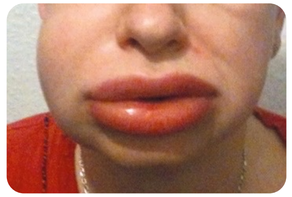
ASK - apoptosis signal-regulating kinase. BLK – B lymphocyte kinase. BMX - bone marrow tyrosine kinase. BTKi – BTK inhibitor. CDK – cyclin-dependent kinase. CSK – c-terminal src kinase. EGFR – epidermal growth factor receptor. ERBB – ERB-B2 receptor tyrosine kinase. HCK – hematopoietic cell kinase. MAPK – mitogen-activated protein kinase. PIP5K2 – phosphatidylinositol 5-phosphate 4-kinase type-2. SRMS – src-related tyrosine kinase. TEC – tyrosine-protein kinase. 1. KINOMEscan green dots indicate kinases tested for inhibition and red dots indicate inhibited kinases (large dots indicate strong inhibition). Data are internally generated using Eurofins DiscoverX.
Pulz R et al. poster presented at: the 38th congress of the ECTRIMS 2022; October 26-28, 2022. EPO0896.

"CSU does not kill you, but it also does not let you live"[4]

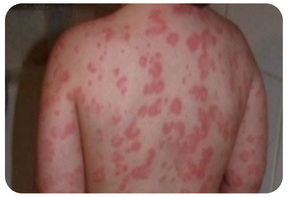
CSU has a negative impact on all aspects of HRQoL[2,3]



Angioedema



Hives



- Systemic **debilitating** mast cell-driven autoimmune (autoallergic) disease[1]
- 60% CSU patients experience **mental health disorders**, mainly **depression** and **anxiety**[1]
- **Quality of life impairment** comparable to PsO and AD: Patients report sleep as one of the most affected aspects of their life[2]
- **Economic burden**: About 1 in 5 patients report having to take time away from work due to their CSU[2]

Achieving symptom control as quickly as possible to improve patient QoL is an important treatment goal for CSU[3]

CSU – Chronic spontaneous urticaria. PsO – Psoriasis. AD – Atopic dermatitis. 1. P Kolkhir et al. Urticaria Nature Reviews Disease Primer (2022) 8:61. 2. Maurer M et al. Allergy. 2017. 3. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA2LEN task force report. Allergy. 2011;66:317-330. 4. Patient testimony.

CSU treatment goal is disease control with absence of hives and itch, maintaining a normal HRQoL

Antihistamines

~600k[2] adult US patients responsive to SoC[3]

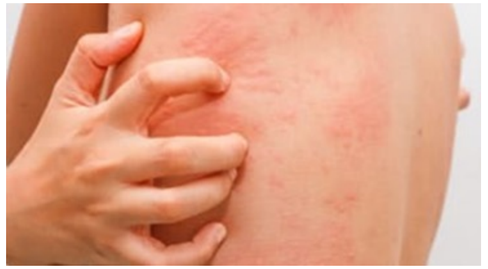
H1-antihistamines used at higher than approved doses could provoke somnolence, dizziness, dry mouth or fatigue[1]

Disease control remains unmet need

CSU treatment gap

~400k[2] adult US patients not controlled with SoC[3]

High unmet need remains

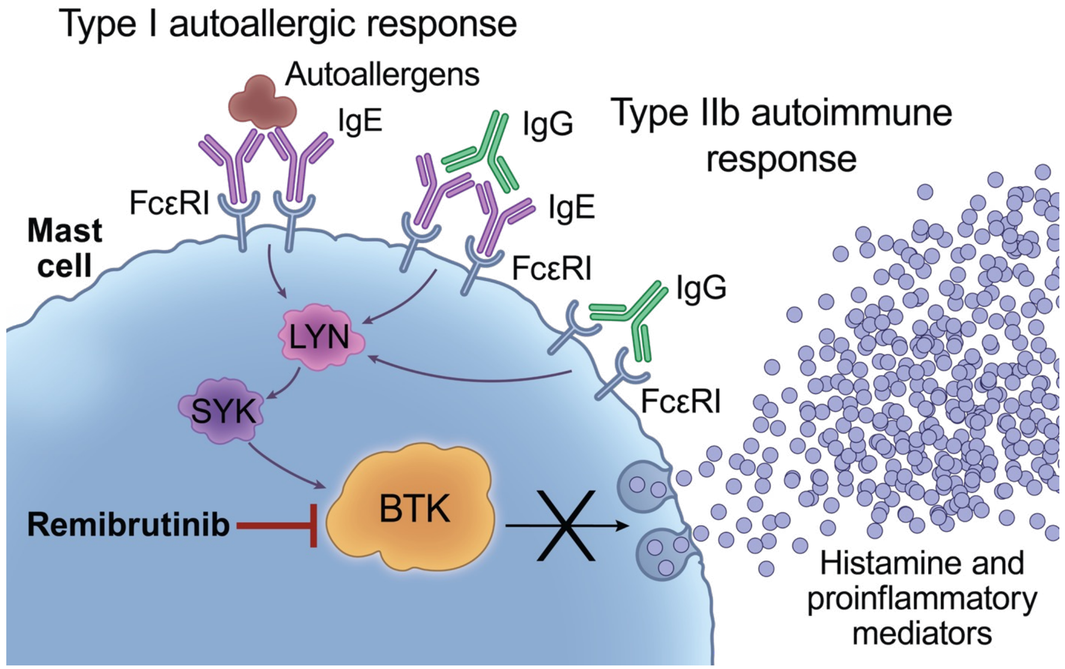


Biologics

~80k[2] adult US patients treated with biologics

CSU – Chronic spontaneous urticaria SoC – Standard of care. HRQoL – Health related quality of life. 1. P Kolkhir et al. Urticaria Nature Reviews Disease Primer (2022) 8:61. 2. US only Novartis internal analysis. 3. H1-antihistamines at approved and increased doses.

Remibrutinib inhibits a central node in the pathogenesis of CSU; a systemic debilitating mast cell-driven auto-immune disease



- CSU autoallergic and autoimmune mechanisms drive pathogenesis[1-3]
- FcεRI cross-linking activates BTK, leading to degranulation of mast cells and basophils, with release of histamine and other proinflammatory mediators[1-3]

Remibrutinib

Putative dual inhibitory mechanism:

- Mast cell degranulation (FcεR)
  - Blocks mast cell activation and prevents release of histamine and other proinflammatory mediators[4-6]
- B cell proliferation and autoantibody production (BCR)[4-6]

Figure originally presented at ACAAI annual meeting 2023. 1. Dispenza MC, et al. Expert Rev Clin Immunol. 2017;13:921-923. 2. Kolkhir P, et al. J Allergy Clin Immunol. 2017;139:1772-1781. 3. Mendes-Bastos P, et al. Allergy. 2022;00(1):1. 4. Maurer M, et al. J Allergy Clin Immunol. 2022: S0091-6749(22)01181-2. 5. Angst D, et al. J Med Chem. 2020;63:5102-5118. 6. Kaul M, et al. Clin Transl Sci. 2021;14:1756-1768.

REMIX Ph3 evaluated efficacy and safety of remibrutinib in CSU

Primary endpoint (week 12)

Change from baseline in UAS7

Change from baseline in ISS7 and HSS7

Key secondary endpoints

Proportion of participants achieving **well-controlled disease** (UAS7≤6) at **week 12**

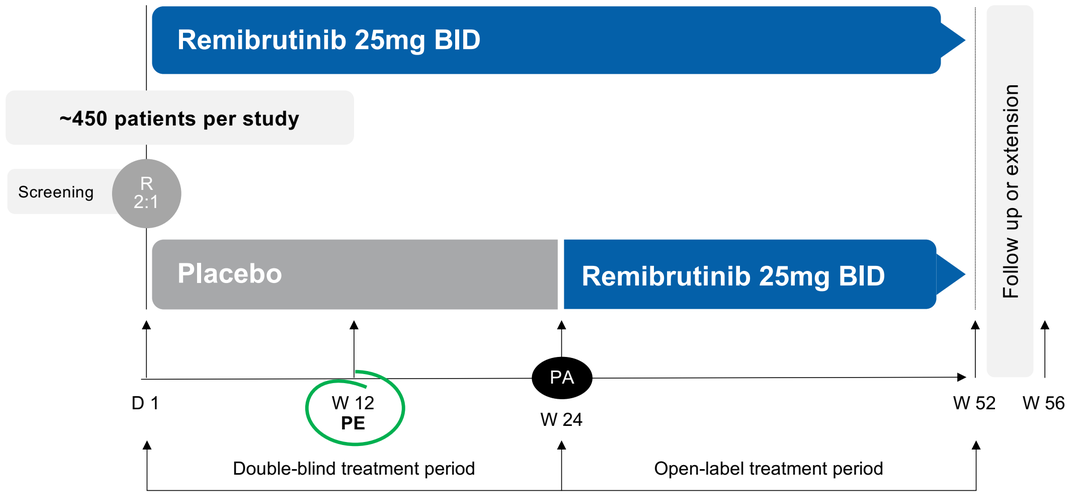
Proportion of participants achieving **complete response** (UAS7=0) at **week 12**

Early onset of disease activity control, defined as achievement of UAS7≤6 at **week 2**

Occurrence of treatment-emergent AEs and serious AEs during the study

Next steps 〉 **52-week data** for regulatory **submission in 2024**

Ph3 REMIX 1 and 2 studies



All participants on a stable, locally label approved dose of a second generation H_1-AH (“background therapy”) throughout the entire study

CSU – chronic spontaneous urticaria. AE – adverse event. PE – primary endpoint. PA – primary analysis. AH – antihistamines. BID – twice daily. HSS7 – weekly Hives Severity Score. ISS7 – weekly Itch Severity Score. UAS7 – weekly Urticaria Activity Score.

Study patients had moderate to severe CSU, many of them with angioedema

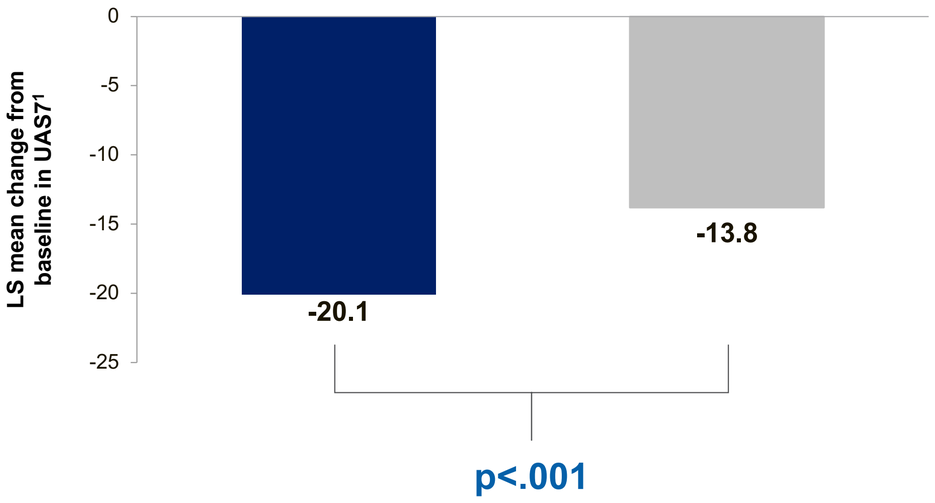
Selected baseline characteristics	REMIX-1			REMIX-2		
	Remibrutinib 25mg BID (N=313)	Placebo (N=157)	Total (N=470)	Remibrutinib 25mg BID (N=300)	Placebo (N=155)	Total (N=455)
Age (years), mean	44.6	45.9	45.0	41.9	41.2	41.7
Gender (female), %	67.7	69.4	68.3	65.7	64.5	65.3
UAS7 (urticaria), mean	30.7	29.7	30.4	30.2	29.5	30.0
HSS7 (hives), mean	15.9	15.3	15.7	15.9	15.7	15.8
ISS7 (itch), mean	14.8	14.3	14.6	14.3	13.9	14.2
Previous experience of angioedema, %	55.3	44.6	51.7	48.0	45.2	47.0
Previous exposure to anti-IgE biologics, %	31.3	33.1	31.9	30.0	32.3	30.8

All randomized patients

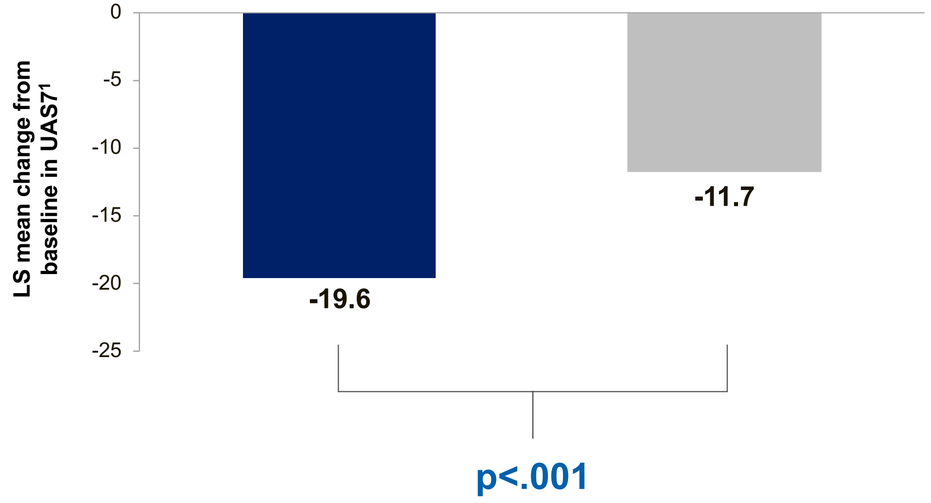
Originally presented at ACAAI annual meeting 2023. BID – twice daily. HSS7 – weekly Hives Severity Score. ISS7 – weekly Itch Severity Score. IgE – immunoglobulin E. UAS7 – weekly Urticaria Activity Score.

Remibrutinib significantly reduced urticaria activity and severity across both global Ph3 studies...

REMIX-1



REMIX-2

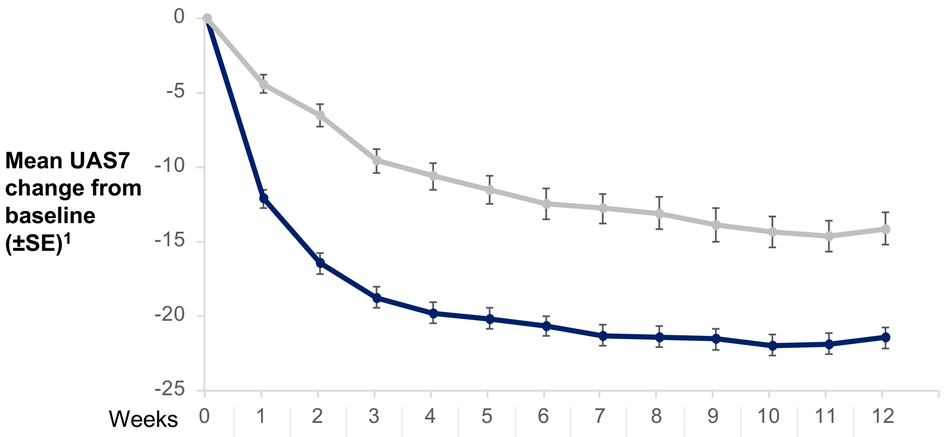


Remibrutinib 25mg BID Placebo

Originally presented at ACAAI annual meeting 2023. BID – twice daily. LS – least square mean. SE – standard error. UAS7 – weekly Urticaria Activity Score. 1. Full analysis set; imputed data. Superiority defined as statistically significant difference in change from baseline with remibrutinib vs. placebo at week 12 using a linear mixed model with repeated measures.

... impacting symptoms as early as week 2 and sustained up to week 12...

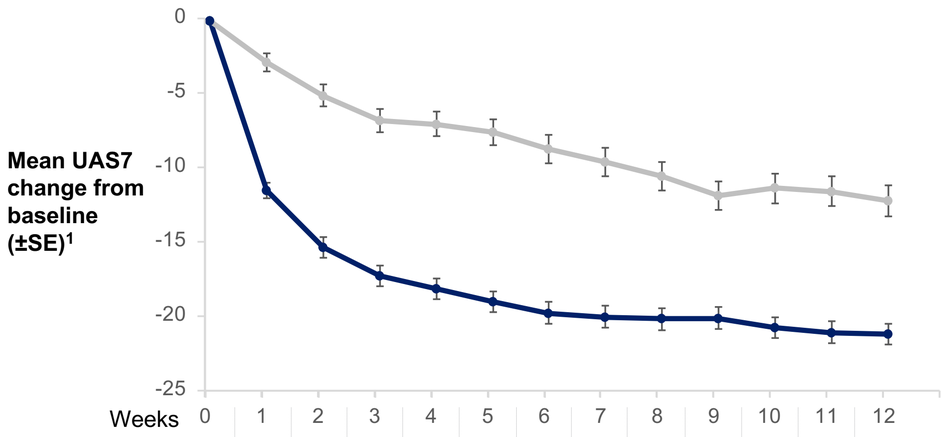
REMIX-1



Number of evaluable patients at each visit

Remibrutinib 25mg BID	309	308	305	301	295	293	294	288	285	290	289	287	284
Placebo	153	150	150	146	144	141	143	142	138	138	139	135	139

REMIX-2



Number of evaluable patients at each visit

Remibrutinib 25mg BID	297	296	295	293	287	278	276	273	274	269	268	263	264
Placebo	153	153	150	149	146	142	142	138	135	139	142	137	134

Remibrutinib 25mg BID Placebo

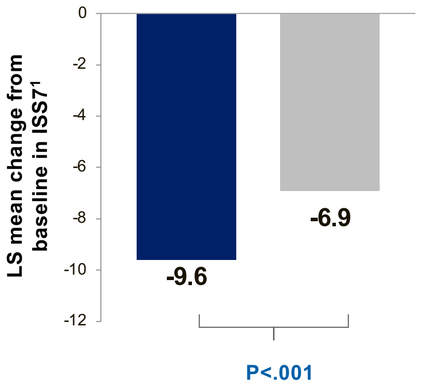
Originally presented at ACAAI annual meeting 2023. UAS7 – weekly Urticaria Activity Score. 1. Full analysis set; observed data.

CSU

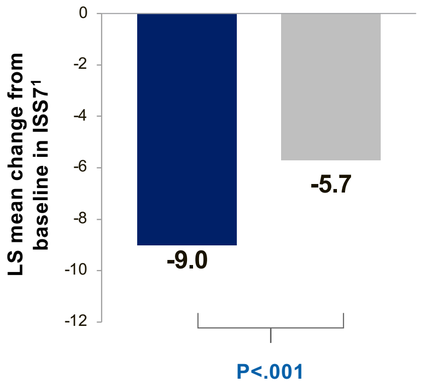
... leading to consistent and substantial reduction of both itch and hives

ISS7 (itch)

REMIX-1

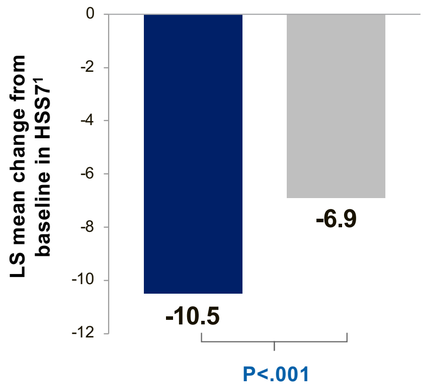


REMIX-2

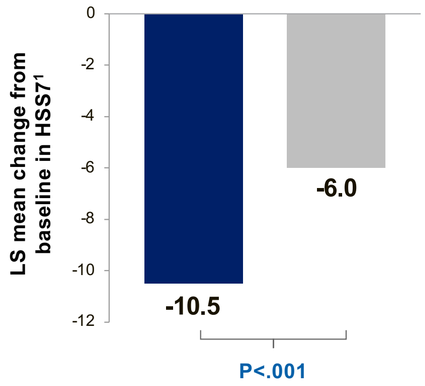


HSS7 (hives)

REMIX-1



REMIX-2

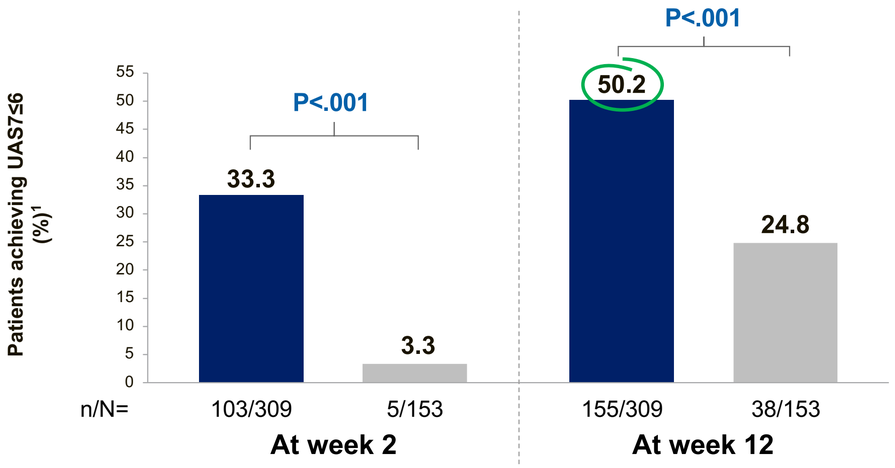


Remibrutinib 25mg BID Placebo

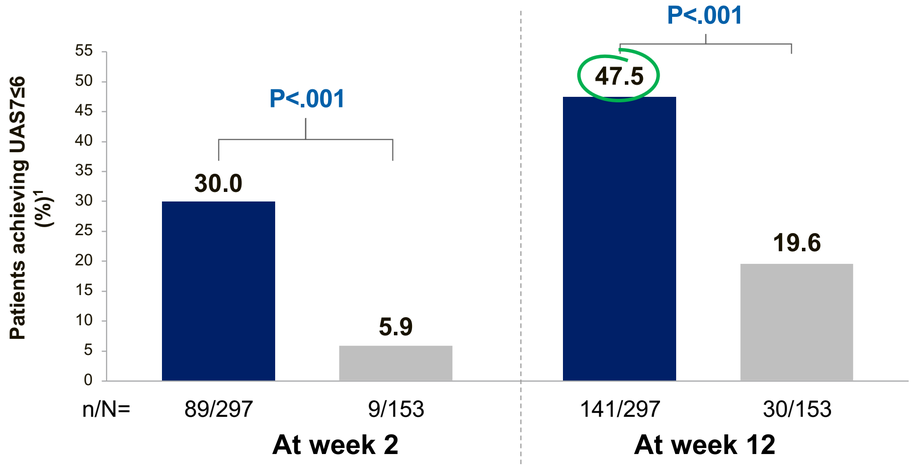
Originally presented at ACAAI annual meeting 2023. BID – twice daily. BL – baseline. HSS7 – weekly Hives Severity Score. ISS7 – weekly Itch Severity Score. LS – least squares. SE – standard error. 1. Full analysis set; imputed data. Superiority defined as statistically significant difference in change from baseline with remibrutinib vs. placebo at week 12 using a linear mixed model with repeated measures.

About half of the remibrutinib treated patients achieved well-controlled disease at week 12 with fast reduction of clinical symptoms

REMIX-1



REMIX-2



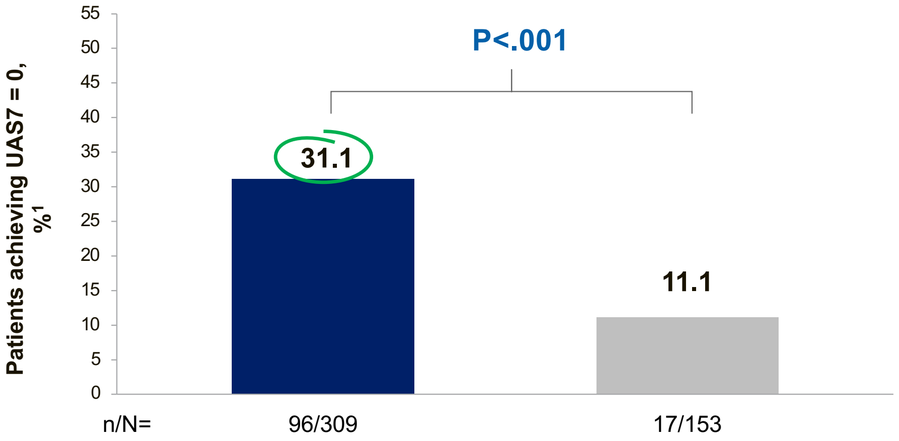
More patients achieved well-controlled disease (UAS7 ≤6) with remibrutinib vs. placebo as early as week 2, which was sustained at week 12

Remibrutinib 25mg BID Placebo

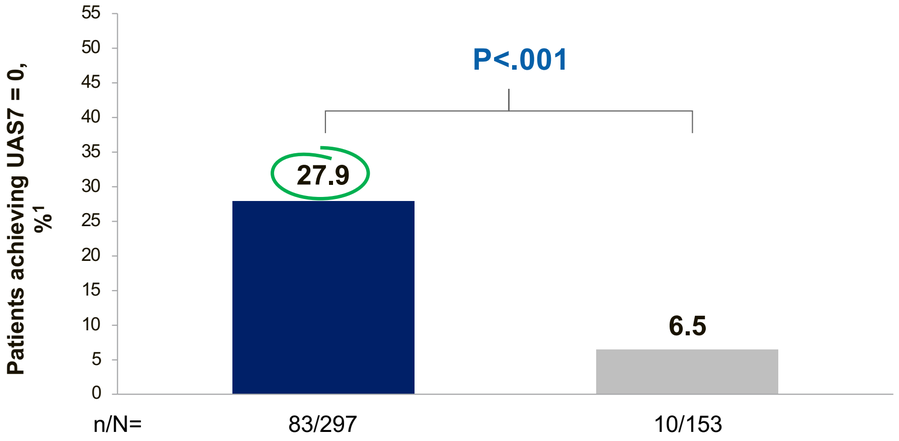
Originally presented at ACAAI annual meeting 2023. UAS7 – weekly Urticaria Activity Score. 1. Full analysis set using a logistic regression model; imputed data.

Remibrutinib in Ph3 achieves CSU treatment goal of complete disease response with absence of hives and itch in almost one third of patients

REMIX-1



REMIX-2



More patients achieved complete response (UAS7=0) with remibrutinib vs. placebo at week 12

Remibrutinib 25mg BID Placebo

Originally presented at ACAAI annual meeting 2023. UAS7 – weekly Urticaria Activity Score. 1. Full analysis set using a logistic regression model; imputed data.

In summary, remibrutinib Ph3 showed consistent improvements across all measures of disease activity...

Robust efficacy	remibrutinib vs. placebo REMIX-1/REMIX-2	
✓ **Statistically significant** improvements in urticaria activity	UAS7[1] (urticaria)	**-6.32/-7.86**
✓ **Statistically significant** improvements in itch	ISS7[1] (itch)	**-2.68/-3.32**
✓ **Statistically significant** improvements in hives	HSS7[1] (hives)	**-3.65/-4.55**
		p<.001

	% of remibrutinib patients REMIX-1/REMIX-2	
✓ **Fast onset** as early as Week 2 and sustained up to Week 12	UAS7≤6[2]	**33.3/30.0**
✓ **~1/2** of patients had well-controlled disease at week 12	UAS7≤6[3]	**50.2/47.5**
✓ **~1/3** of patients were free of itch and hives at week 12	UAS7=0[3]	**31.1/27.9**
		p<.001

Originally presented at ACAAI annual meeting 2023. Full analysis set imputed data. 1. Change from baseline at week 12, treatment difference in least squares mean remibrutinib vs. placebo. 2. Week 2, using a logistic regression model. 3. Week 12, using a logistic regression model.

... with a favorable safety profile

Favorable safety[1]	Remibrutinib (%[2])	Placebo (%[2])
✓ Overall AEs **comparable** to placebo	64.0	64.7
✓ Overall Infection AEs **comparable** to placebo	32.8	34.0
✓ Serious **AEs**	3.3	2.3
✓ Treatment discontinuations due to AEs **balanced**	2.6	2.6
✓ Imbalance in petechiae: all **mild or moderate**	3.8	0.3
✓ ALT/AST >3x ULN **balanced**[3]	1.3	1.3

Studied across immunology and neurology indications; well tolerated in over 2,200 participants

Originally presented at ACAAI annual meeting 2023. 1. During 24-week treatment in safety set. 2. % of patients experiencing ≥1 event. 3. Newly occurring ALT or AST elevations >3x ULN. AE – adverse event. ALT – alanine aminotransferase. AST – aspartate aminotransferase. ULN - upper limit of normal.

Balanced liver function tests across treatment groups

Liver function	Pooled REMIX-1 and REMIX-2	
	Remibrutinib 25mg BID (n=606), n (%)[1,2]	Placebo (n=306), n (%)[1,2]
ALT or AST elevations >3x ULN[3]	8 (1.3)	4 (1.3)

Liver transaminase (ALT or AST) elevations were asymptomatic, transient/reversible, and balanced across treatment groups

Originally presented at ACAAI annual meeting 2023. ALT – alanine aminotransferase. AST – aspartate aminotransferase. BID – twice daily. ULN – upper limit of normal. 1. Safety set. 2. Number of patients experiencing ≥1 event. 3. Newly occurring ALT or AST elevations.

Next steps for CSU

REMIX-1 and-2, week 52 readout in H1 2024

Global submissions in H2 2024

Remibrutinib ongoing programs in chronic inducible urticaria (CINDU), hidradenitis suppurativa (HS) and food allergy (FA)

Remibrutinib

- Highly selective and potent covalent BTK inhibition
- Specifically targets a central node in the pathophysiology of chronic urticaria, a mast cell-driven skin disease

Chronic Inducible Urticaria - Ph3 starting

Unmet need

- Up to 1/3 of chronic urticaria patients have CINDU[3]
- Standard of care is H1-antihistamines with no approved other therapy[2]
- Many patients remain symptomatic despite H1-antihistamines[4]
- Substantial impact on QoL[2,3]
- **Therapeutic goal: control of symptoms even when triggers are present[1]**

Other ongoing immunology indications based on MoA

- **Ph2 HS** data to be presented at upcoming conference in 2024
- **Ph2 FA** recruiting

1. Maurer M, et al. J Allergy Clin Immunol. 2018 Feb;141(2):638-649. 2. Zuberbier et al. Allergy 2022;77:734-766. 3. Maurer et al. Allergy 2011;66: 317-330" Please add that reference. 4. Magerl et al. Allergy 2016.

Remibrutinib program in multiple sclerosis continues with readout expected in 2026

Primary endpoint

Annualized relapse rate (ARR)

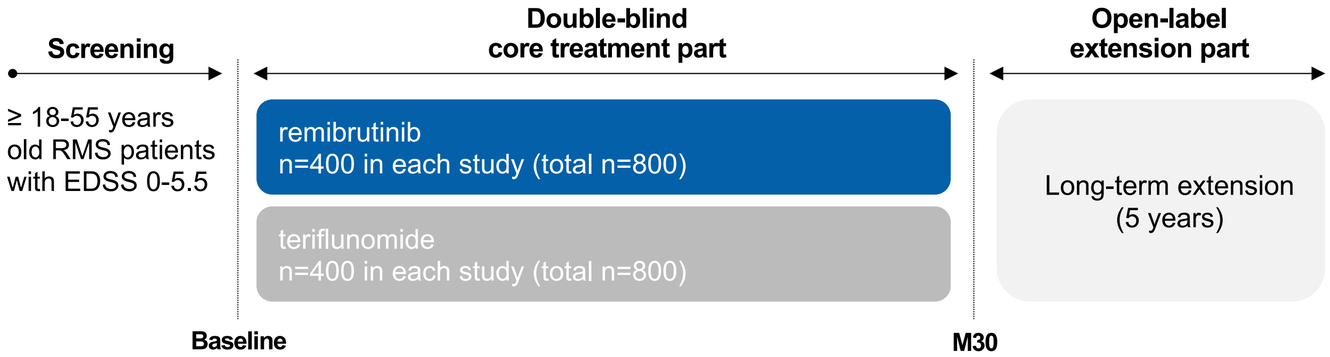
Key secondary endpoints

- 3mCDP
- 6mCDP
- Gd-T1 lesions
- New/enlarging T2 lesions
- Neurofilament (NfL)
- NEDA-3

Next steps 〉 **Readout** expected **in 2026**

REMODEL 1 and 2

Randomized, double-blind, double-dummy, active comparator-controlled, fixed-dose, parallel-group, event-driven multi-center studies



Population

18-55 years (inclusive), EDSS 0-5.5 (inclusive)

Diagnosis of MS according to 2017 McDonald diagnostic criteria; Relapsing MS (RRMS or SPMS)

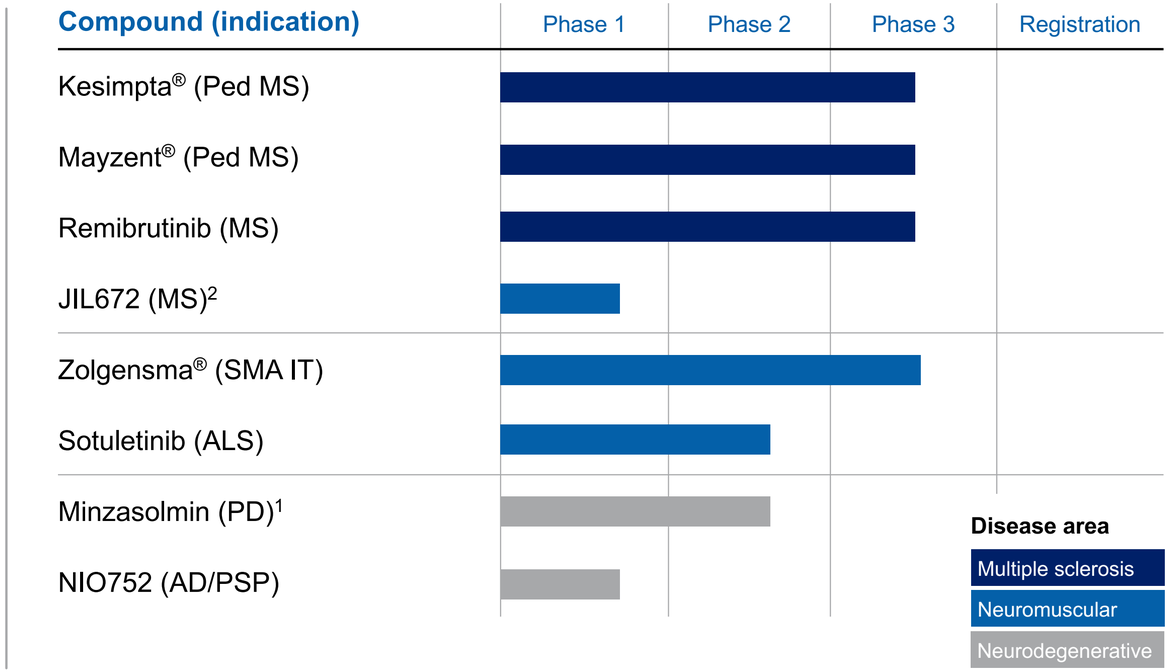
At least: 1 relapse in the previous year, OR 2 relapses in the previous 2 years, OR 1 active Gd-enhancing lesion in 12 months prior to screening

RMS – Relapsing Multiple Sclerosis. EDSS – Expanded Disability Status Score. MS – Multiple Sclerosis. RRMS – Relapsing Remitting Multiple Sclerosis. SPMS – Secondary Progressive Multiple Sclerosis. CDP – Confirmed Disability Progression. NEDA – No Evidence of Disease Activity.

Neuroscience disease area focus is multiple sclerosis, neurodegenerative and neuromuscular diseases

Neuroscience strategy

- Maintain leadership in multiple sclerosis by preventing disease progression independent of relapses and achieving complete disease control
- Target genetically defined core drivers and innate inflammation to significantly slow progression in neurodegenerative diseases
- Build on success in Zolgensma® to deliver transformational genomic medicines for patients with neuromuscular and genetic diseases



1. In partnership with UCB. 2. In partnership with Cellerys.

Therapeutic Area Overview: Oncology

Jeff Legos
Development Unit Head, Oncology

Shreeram Aradhye
President, Development and Chief Medical Officer

NOVARTIS | Reimagining Medicine

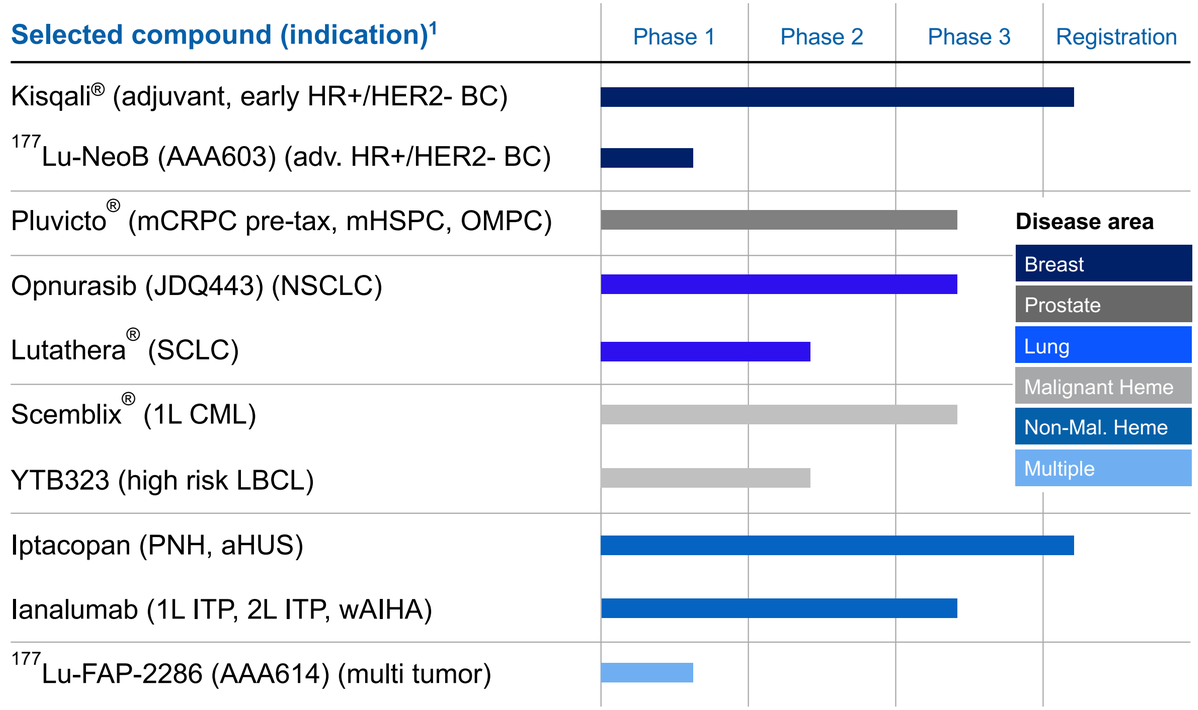
Our Oncology strategy is to discover differentiated, high-value, practice-changing medicines that provide meaningful outcomes for patients

Oncology strategy

- Target earlier stages of disease across prioritized solid tumor and hematology indications, ultimately aiming for treatment free remission or cure
- Build long-term portfolio in breast, prostate, lung cancer
- Develop RLT platform across novel surface targets for solid tumors with high unmet medical need
- Explore additional opportunities leveraging our platforms, e.g., PDAC

Assets highlighted today:
Ianalumab, **Lutathera®**, **JDQ443**

Deep dives: **Kisqali®**, **Pluvicto®**, **Scemblix®**



PDAC – pancreatic ductal adenocarcinoma. BC – breast cancer. mCRPC – metastatic castration-resistant prostate cancer. mHSPC – metastatic hormone-sensitive prostate cancer. OMPC – oligometastatic prostate cancer. NSCLC – non-small-cell lung cancer. SCLC – small-cell lung cancer. CML – chronic myeloid leukemia. LBCL – large B-cell lymphoma. PNH – paroxysmal nocturnal hemoglobinuria. aHUS – atypical hemolytic uremic syndrome. ITP – immune thrombocytopenia. wAIHA – warm autoimmune hemolytic anemia. 1. Table depicts most advanced development stage of Oncology indications listed; iptacopan asset detailed in Cardiovascular-Renal-Metabolic section.

Ianalumab (VAY736): Potential to disrupt early ITP and wAIHA treatment landscape by providing long-term disease control with short-course therapy

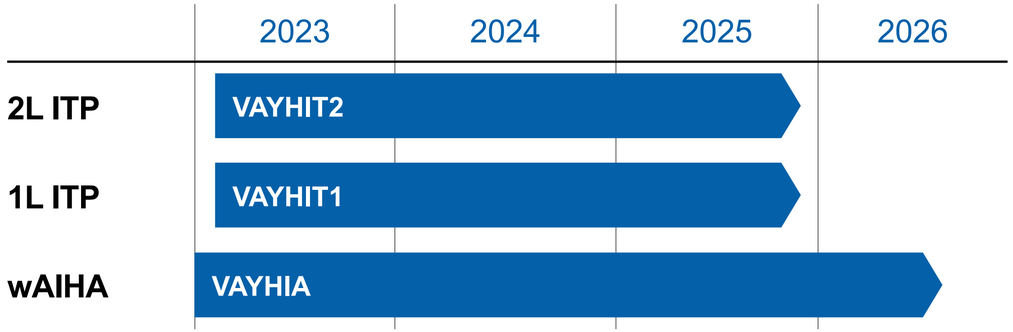
High unmet need

For short-course disease-modifying therapies that:

- **induce and maintain safe platelet counts in ITP**
- **induce durable hemoglobin response in wAIHA**

and are sustained after treatment completion, alleviating the burden/side effects of chronic treatment (e.g., corticosteroids) and improving patient quality of life

Ph3 development programs



Reasons to believe

Unique dual MoA:
- Enhanced ADCC mediated B-cell depletion
- Inhibition of B-cell activation/differentiation/ survival through BAFF-R blockage

- Ianalumab has demonstrated a **favorable safety profile** and **promising efficacy** (SjS and SLE) where other B-cell depleting agents have demonstrated limited activity

- Ianalumab provides superior B-cell depletion compared to CD20 mAbs

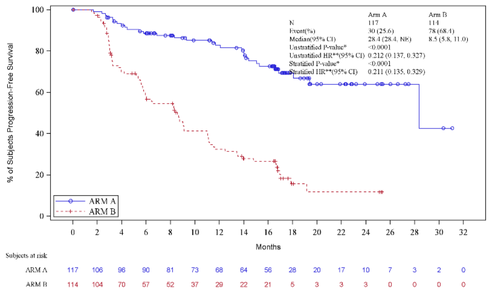
ITP – immune thrombocytopenia. wAIHA – warm autoimmune hemolytic anemia. Source: Bowman et al, 2022, Cortes-Hernandez et al, 2023, Santos de Costa et al, 2023, McWilliams et al, 2019.

Lutathera Ph3 NETTER-2 results highlight the potential for radioligand therapy (RLT) in early GEP NET tumors

Maximize NET

NETTER-1: FDA awarded broad label allowing use in GEP NET independent of line or grade

NETTER-1

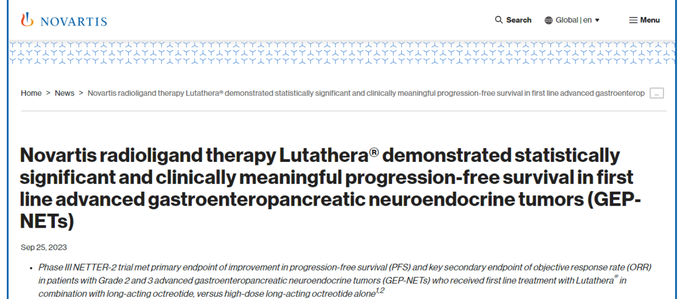


mPFS 28.4 vs 8.5 months; **HR, 0.18**
[95% CI: 0.14, 0.33]; P<0.0001)[1]

Original pivotal data in G1/G2 progressive disease only

NETTER-2: New Ph3 data supplements NETTER-1 with 1L G2/G3 GEP NET randomized data

NETTER-2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Home > News > Novartis radioligand therapy Lutathera® demonstrated statistically significant and clinically meaningful progression-free survival in first line advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs)

Sep 25, 2023

- *Phase III NETTER-2 trial met primary endpoint of improvement in progression-free survival (PFS) and key secondary endpoint of objective response rate (ORR) in patients with Grade 2 and 3 advanced gastroenteropancreatic neuroendocrine tumors (GEP-NETs) who received first line treatment with Lutathera® in combination with long-acting octreotide, versus high-dose long-acting octreotide alone*[1,2]

New data to be presented at upcoming medical congresses in Q1 2024

Go Beyond NET

Potential to improve SoC in high unmet need diseases

SCLC

- Is of neuroendocrine origin, like NET
- Is highly sensitive to radiation

GBM

- In clinic for ndGBM and rGBM
- Potential to establish new SoC in combination with EBRT+ TMZ (induction) followed by combo with TMZ (maintenance)

GBM – glioblastoma. SCLC – small cell lung cancer.

JDQ443 (KRAS inhibitor) clinical data support moving to 1L combinations in NSCLC

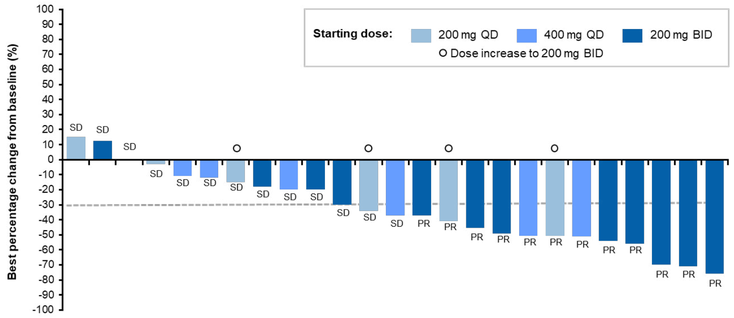
Selective, covalent and orally bioavailable irreversible $KRAS^{G12C}$ inhibitor

- Traps $KRAS^{G12C}$ in the inactive GDP-bound state
- Structurally distinct KRASG12C inhibitor vs. other KRASG12C inhibitors

Encouraging monotherapy safety profile supports role as anchor for anti PD-1 combination (SOC) in front line $KRAS^{G12C}$-mutated NSCLC

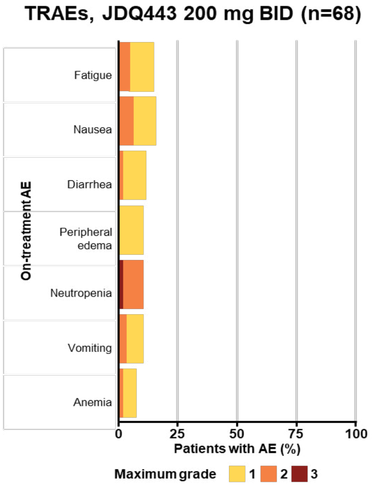
Emerging data for combination
JDQ443 + anti-PD-1 support moving to 1L combinations

Confirmed anti-tumor activity in NSCLC[1]



- Confirmed ORR 57% at recommended dose
- Safety/tolerability profile with low rates of GI toxicity and ALT/AST elevation

Safety profile



1. DeMiguel et al., ASCO 2023. Data cutoff 01-Feb-2023.

Pluvicto®

NOVARTIS | Reimagining Medicine

Pluvicto®

lutetium (177Lu) vipivotide tetraxetan

Radioligand therapy targeting PSMA

Market potential

●●● > USD 3bn

Unprobabilized peak sales of all asset indications in late-stage development

US: Patent on compound (2034)[1]

EU: Patent application on compound pending

Prostate cancer is the **second most common cancer in men**; 35% develop metastases within 2 years of diagnosis. In mCRPC, the **5-year survival** prognosis is **only 30%**

First approved in PSMA-positive mCRPC patients previously treated with ARPi and taxane chemotherapy based on **VISION** study (**38% reduction in risk of death**); Pluvicto® in-market performance has so far surpassed expectations

PSMAfore study shows first PSMA-targeted RLT to **demonstrate clinical benefit** (59% reduction in risk of progression) in pre-taxane patients with mCRPC, offering the potential of practice-changing utility in an earlier line of prostate cancer; filing planned in 2024

VISION and PSMAfore strengthen confidence in moving into even **earlier lines of prostate cancer**, with **PSMAddition** and **PSMA-DC**

Multiple efforts ongoing to further strengthen our RLT leadership overall, building upon our pipeline and infrastructure

PSMA – prostate-specific membrane antigen. mCRPC – metastatic castration-resistant prostate cancer. ARPI – androgen receptor pathway inhibitor. 1. Patent term extensions possible.

High remaining unmet need in prostate cancer requires novel therapies to delay progression, increase QoL, and prolong survival

1.4 million
cases per year WW; 2nd most common cancer in men

>375k
deaths per year WW; 2nd leading cause of cancer death in men

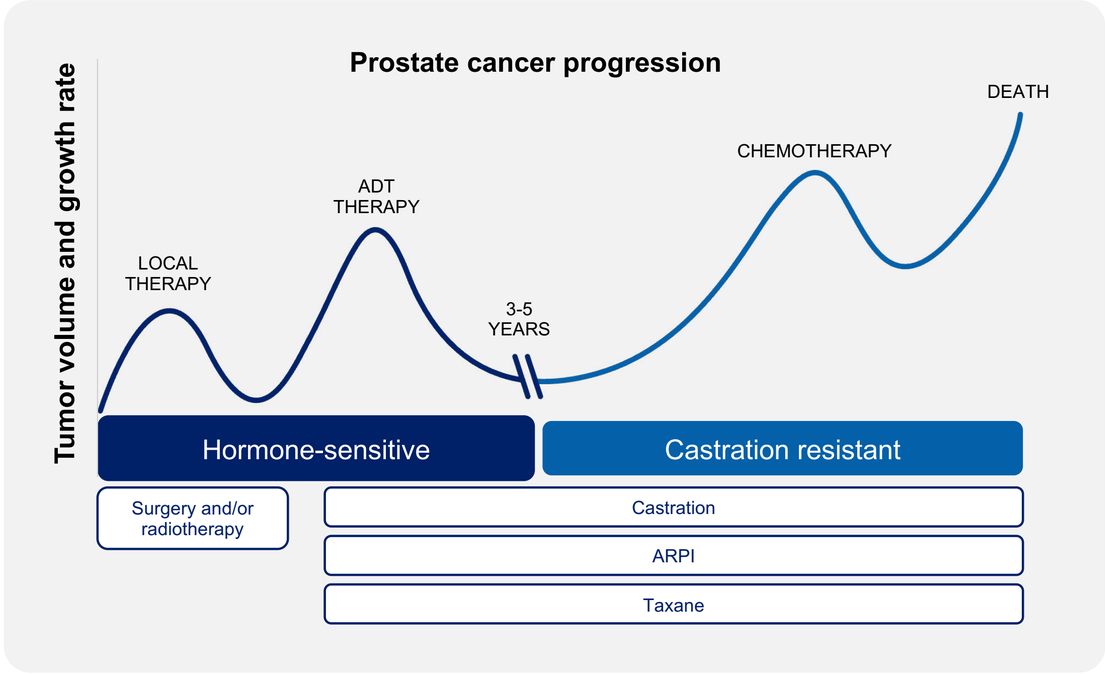
35%
develop metastases within 2 years of diagnosis

30%
5-year survival prognosis for mCRPC patients

~15-20%
of patients harbor BRCA mutations eligible for PARPi therapy (HHR mutations total ~30% of mCRPC pts)

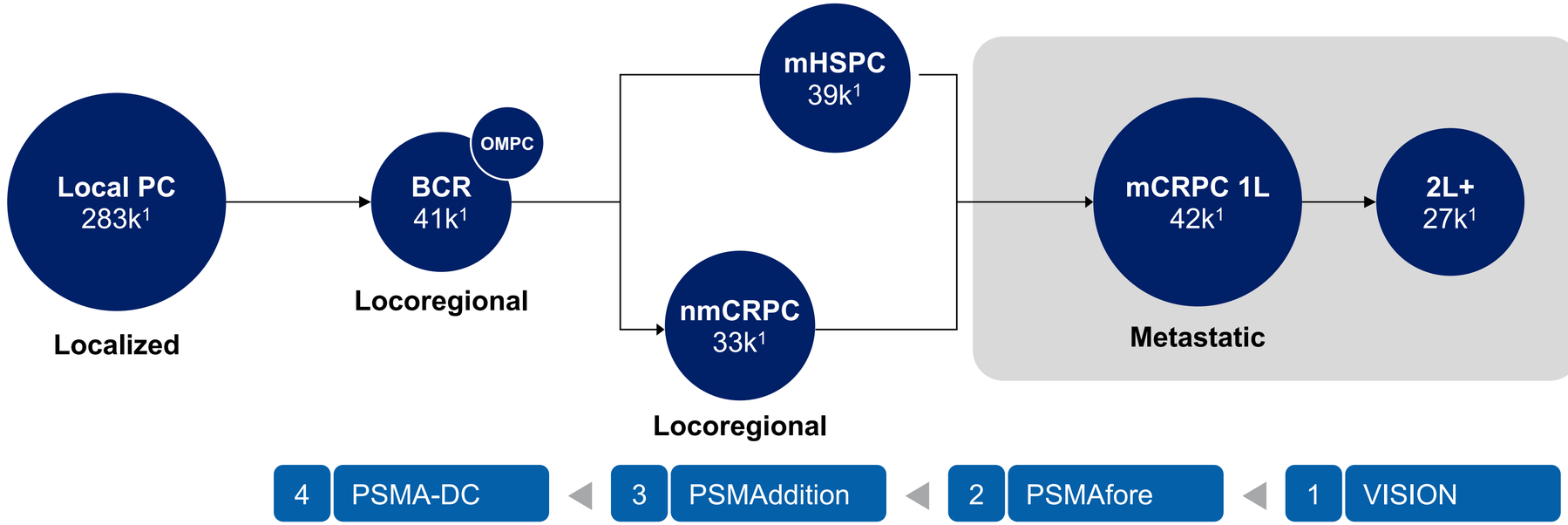
High-burden SoC
mainly unspecific hormonal therapy (castration) and cytotoxic chemotherapy

>90%
of patients overexpress PSMA, targeted with Pluvicto®



Source: Wang L. Et all, Front. Public Health, 16 February 2022 (Frontiers | Prostate Cancer Incidence and Mortality: Global Status and Temporal Trends in 89 Countries From 2000 to 2019 (frontiersin.org)).

Ambition to transform advanced prostate cancer across four main segments with Pluvicto® studies

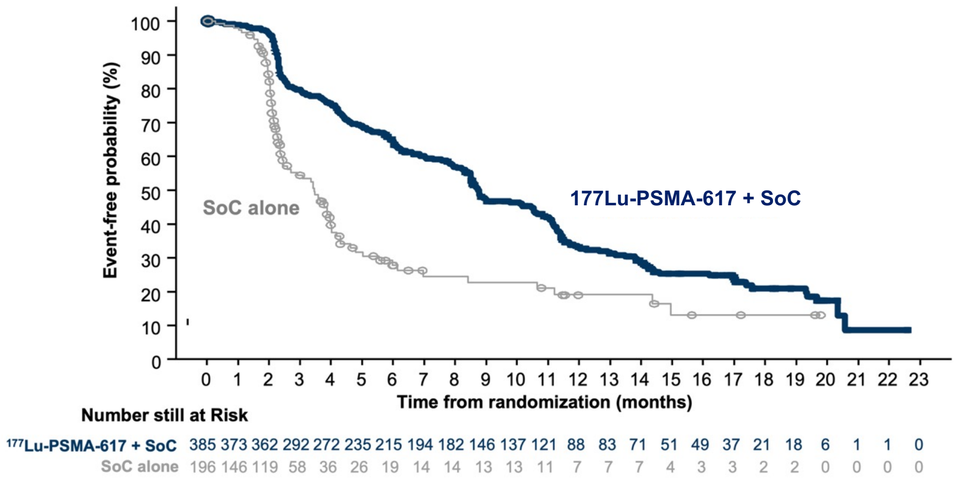


Source: Cerner Enviza 2023 US prostate cancer incidence. PC – prostate cancer BCR – biochemical recurrence. OMPC – oligometastatic prostate cancer. nmCRPC – non-metastatic castration-resistant prostate cancer. mHSPC – metastatic hormone-sensitive prostate cancer. mCRPC – metastatic castration-resistant prostate cancer. 1. Refers to US incidence only.

Ph3 VISION study: Pluvicto® met both primary endpoints of rPFS and OS in the mCRPC post-taxane setting[1]

Reduced risk of progression or death by 60%

rPFS HR: **0.40** (99.2% CI: 0.29, 0.57), p<0.001 (one-sided)
Median rPFS, months: **8.7** vs. **3.4**

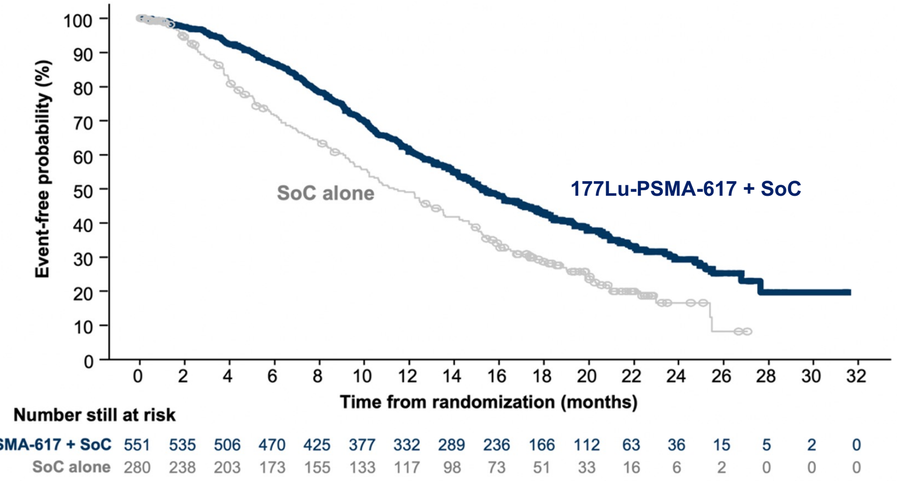


Number still at Risk

^{177}Lu-PSMA-617 + SoC	385	373	362	292	272	235	215	194	182	146	137	121	88	83	71	51	49	37	21	18	6	1	1	0
SoC alone	196	146	119	58	36	26	19	14	14	13	13	11	7	7	7	4	3	3	2	2	0	0	0	0

Reduced risk of death by 38%

OS HR: **0.62** (95% CI: 0.52, 0.74), p<0.001 (one-sided)
Median OS, months: **15.3** vs. **11.3**



Number still at risk

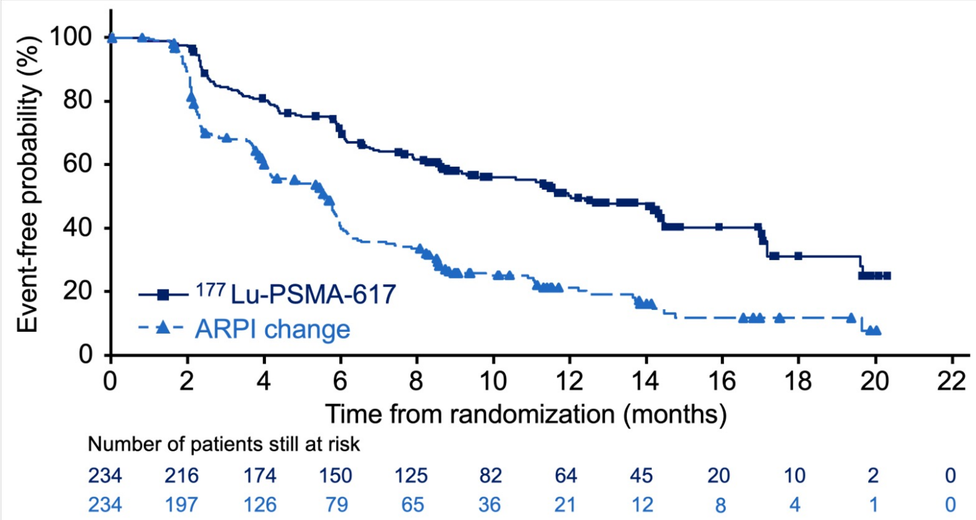
^{177}Lu-PSMA-617 + SoC	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
SoC alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

1. Sartor, N Engl J Med 2021;385:1091-103.

Ph3 PSMAfore study: Pluvicto® showed clinically meaningful rPFS benefit in taxane-naive patients with mCRPC

Primary[1] HR: 0.41 (95% CI: 0.29, 0.56); p < 0.0001

Updated[2] HR: 0.43 (95% CI: 0.33, 0.54); p < 0.0001 (nominal)



	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	115 (49.1%)	168 (71.8%)
Median rPFS (95% CI)	12.0 months (9.3, 14.4)	5.6 months (4.2, 6.0)

Impact to practice

Pluvicto® demonstrated clinically meaningful efficacy and favorable tolerability, offering a new treatment option for patients suitable to delay chemotherapy, and hence avoid high toxicity burden

Relevant comparator

A large proportion of mCRPC patients is ineligible or unwilling to take chemotherapy[3]. Instead, change in ARPI is commonly used in patients progressing on prior APRI and ADT[4]

ARPI – androgen receptor pathway inhibitor. ADT – androgen deprivation therapy. 1. Primary rPFS analysis based on centrally confirmed rPFS events with Oct. 2022 data cutoff. 2. Updated rPFS analysis (at time of 2nd interim OS analysis) based on Jun. 2023 data cutoff. 3. Clinical practice varies by geography. 4. George et al 2020, Shore et al 2021.

Ph3 PSMAfore study: Robust efficacy, complemented by favorable safety and quality of life compared to daily oral ARPI

Robust efficacy	Pluvicto® vs. ARPI arm
✓ rPFS[1]	HR **0.41** (0.29, 0.56)
✓ Median rPFS[2]	**12.0** vs. 5.6 months
✓ PSA50 response	**57.6%** vs. 20.4%
✓ Time to SSE	HR **0.35** (0.22, 0.57)
✓ ORR[3]	**50.7%** vs. 14.9%
✓ Time to worsening (FACT-P[4])	HR **0.59** (0.47, 0.72)
✓ Time to worsening (BPI-SF[5])	HR **0.69** (0.56, 0.85)
Crossover-adjusted OS	HR **0.80** (0.48, 1.33)
Unadjusted OS **(84% crossover)**	HR 1.16 (0.83, 1.64)

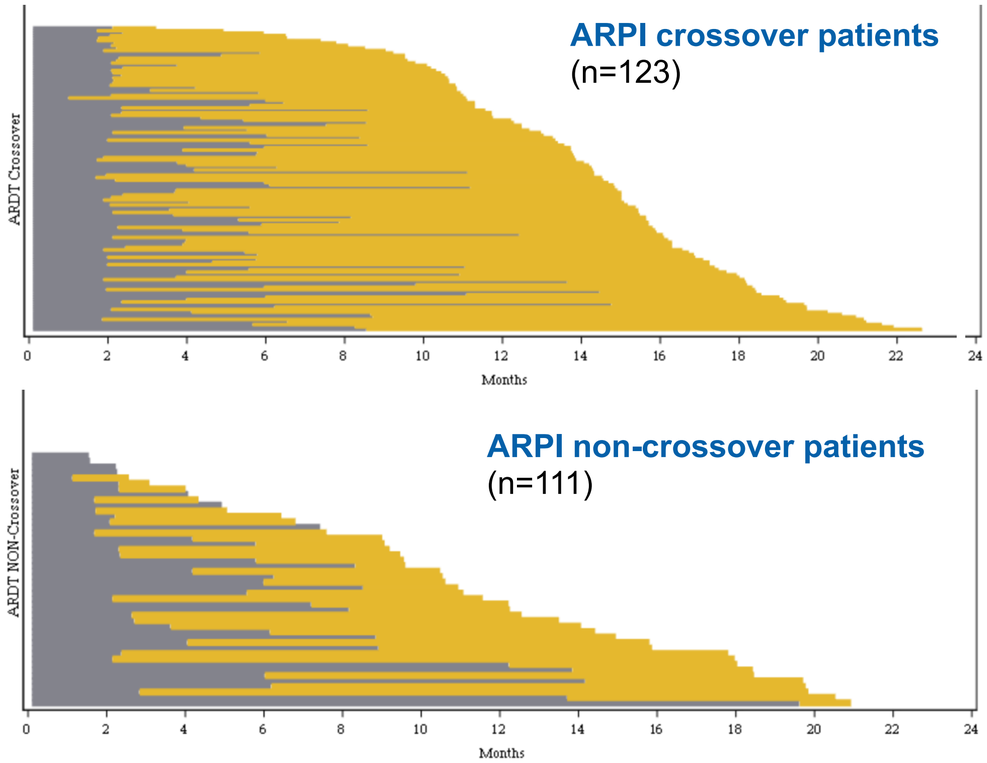
Favorable safety profile

- ✓ Vast majority of AEs low-grade
- ✓ Grade 3-4 AEs: 33.9% Pluvicto® vs. 43.1% ARPI
- ✓ SAEs: 20.3% Pluvicto® vs. 28.0% ARPI
- ✓ AEs leading to discontinuation[6]: 5.7% vs. 5.2%
- ✓ AEs leading to dose adjustment[6]: 3.5% vs. 15.1%
- ✓ Renal toxicity SAEs[6]:
  Acute kidney injury: 0.9% vs. 1.3%
  Hematuria: 0% vs. 1.3%

Overall exposure to Pluvicto® ~2,000 patient-years
(incl. VISION, PSMAfore and post-marketing experience)

ARPI – androgen receptor pathway inhibitor. 1. Primary rPFS analysis based on 166 rPFS events per BICR assessment (or centrally confirmed rPFS events); 1-sided p-value: <0.0001. Updated analysis of rPFS (at time of 2nd interim OS analysis) was consistent, with HR 0.43 (0.33, 0.54). All other data points from updated analysis with more mature data. 2. (95% CI): 12.0 (9.3, 14.4) vs. 5.6 (4.2, 5.95). 3. ORR in soft tissue per RECIST 1.1 for pts with measurable disease at baseline; (95% CI): 50.7% (38.6, 62.8) vs. 14.9% (7.7, 25.0). 4. FACT-P: prostate cancer-specific quality of life. 5. BPI-SF: severity of pain and impact of pain on daily functions. 6. Comparisons for Pluvicto® vs. ARPI arm.

ARPI patients who crossed over to Pluvicto® had a survival benefit over ARPI patients who did not cross over



Estimated OS probability at 12 months

92.1% for patients randomized to ARPI arm who crossed over

68.6% for patients randomized to ARPI arm who did not cross over

rPFS time

OS time from rPD

ARPI – androgen receptor pathway inhibitor. rPFS – radiographic progression-free survival. OS – overall survival. rPD – radiographic progressive disease.

Ph3 PSMAfore study: Next steps for OS data and submission

PSMAfore continues to 3rd interim analysis for OS after ~75% of target events

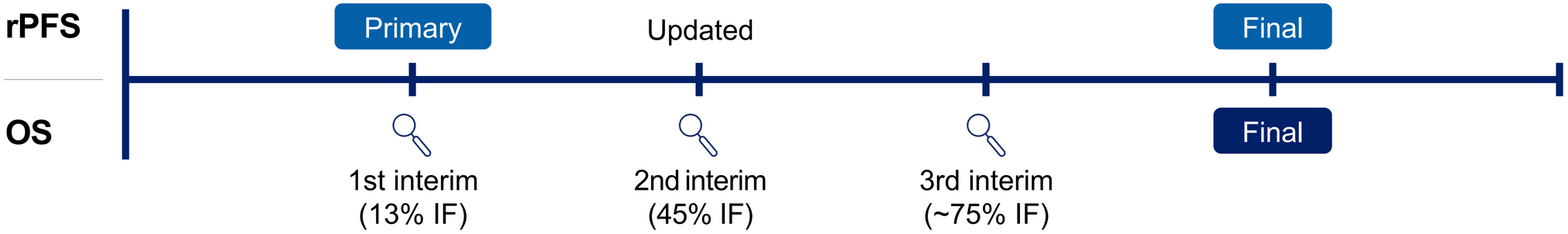
Submission to health authorities to follow in 2024

PRIMARY ENDPOINT

rPFS
BICR per PCWG3/ RECIST v1.1

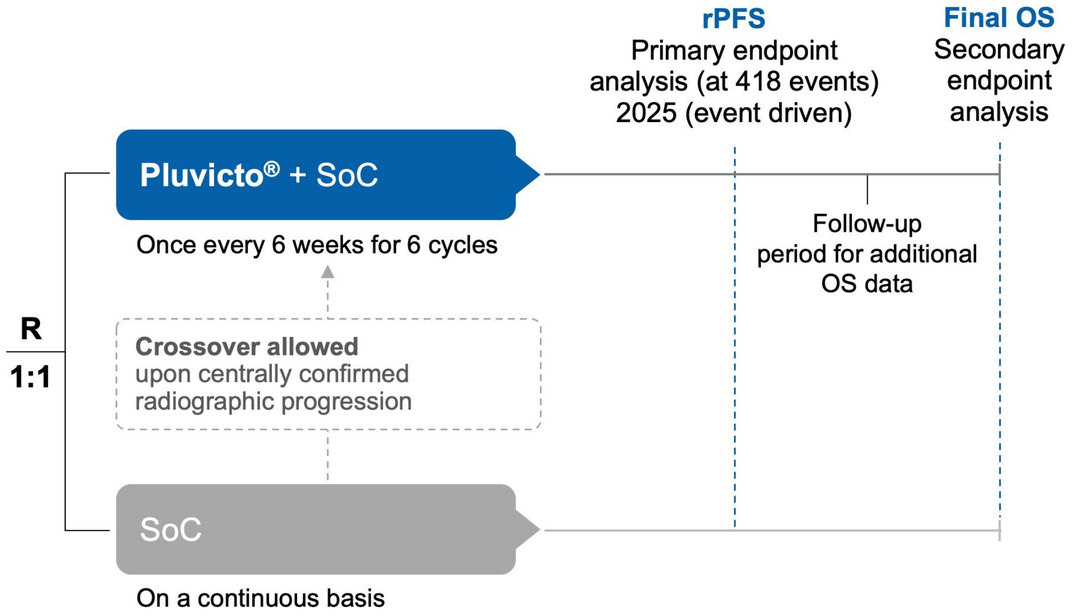
KEY SECONDARY ENDPOINT

OS
Pre-specified for RPSFT crossover-adjusted analysis



Ph3 PSMAddition: Evaluating efficacy and safety of Pluvicto® in patients with hormone-sensitive metastatic prostate cancer (mHSPC)

Population: Patients with untreated or minimally treated metastatic HSPC (high and low volume) | N=1144



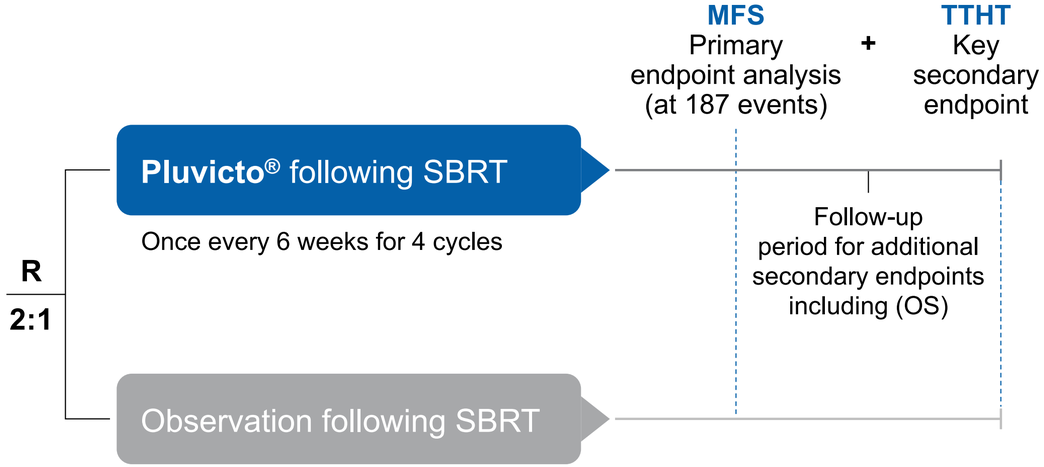
Study status

- Study fully enrolled ahead of schedule, despite prior enrollment hold due to previous Pluvicto® drug supply challenges
- Event driven trial; latest projections show primary analysis (rPFS) by 2025, submission to follow (including sufficient OS data)
- Pluvicto® has demonstrated a strong tolerability profile in mCRPC, including combination with ARPI and ADT as part of standard of care in VISION, therefore we anticipate the combination to be well tolerated in an earlier line setting
- The study allows for cross-over based on confirmed progression by BIRC (patients progressing to mCRPC), with close monitoring of OS events to ensure strong data package at submission

rPFS – radiographic progression free survival. OS – overall survival. mHSPC – mCRPC – metastatic castration-resistant prostate cancer.

Ph3 PSMA-DC study: Evaluating efficacy and safety of Pluvicto® to delay castration in patients with oligometastatic prostate cancer

Population: Patients with recurrent oligometastatic prostate cancer by PSMA-PET only, after stereotactic body radiation (SBRT) | N=450



Study status

- FPFV upcoming in 2024
- **Primary endpoint**: Metastasis-free survival (MFS) by conventional imaging
- **Key secondary endpoint**: Time to initiation of hormonal therapy for castration (TTHT) Other secondary endpoints: QoL/PRO, OS
- **No cross-over allowed**
- Study will enroll high risk patients from the BCR population with up to 5 lesions per PSMA-PET scan, but no lesion (yet) per conventional imaging
- Expanding collaboration with urologists and radiation oncologists, including community practices

PSMA-targeted RLT as a precision medicine has the potential to be indicated across all prostate cancer stages, offering new MoA for treatment, delaying resistance mechanisms and reserving current treatment options for later line of disease

rPFS – radiographic progression free survival. OS – overall survival. mHSPC – mCRPC – metastatic castration-resistant prostate cancer. QoL – Quality of life. PRO – Patient Reported Outcome.

Next steps for Pluvicto®

PSMAfore
mCRPC pre-taxane

PSMAfore continues to next interim analysis for OS after ~75% of target events

Submission to health authorities to follow in 2024

PSMAddition
mHSPC

Fully recruited; event-driven: rPFS readout expected 2025

PSMA-DC
OMPC

Study start-up

Scemblix®

NOVARTIS | Reimagining Medicine

Scemblix®

(asciminib)

BCR-ABL inhibitor that works by Specifically Targeting the ABL Myristoyl Pocket (STAMP)

Market potential

> USD 2bn

Unprobabilized peak sales of all asset indications in late-stage development

US/EU: Patent on compound (2033/2033)[2]

Despite advances in chronic myeloid leukemia (CML) care, many patients do not achieve efficacy treatment goals, suffer from treatment-related adverse events/TKI intolerance or develop treatment resistance.

By **S**pecifically **T**argeting the **A**BL **M**yristoyl **P**ocket (**STAMP**), Scemblix® inhibits the growth of BCR-ABL1-dependent cancer cells and is designed to overcome resistance and minimize off-target activity.

In **3L+** CML, **Scemblix®** is now **approved**[1] in **>60 countries** and **achieved market leadership** in total patient share in key markets with continued growth momentum.

Ph3 ASCEMBL study with now >2-year follow-up confirmed superior efficacy and tolerability of Scemblix vs. 2nd generation TKI bosutinib.

Ph3 ASC4FIRST 1L CML study o**n track for readout in H1 2024**, with filings planned globally.

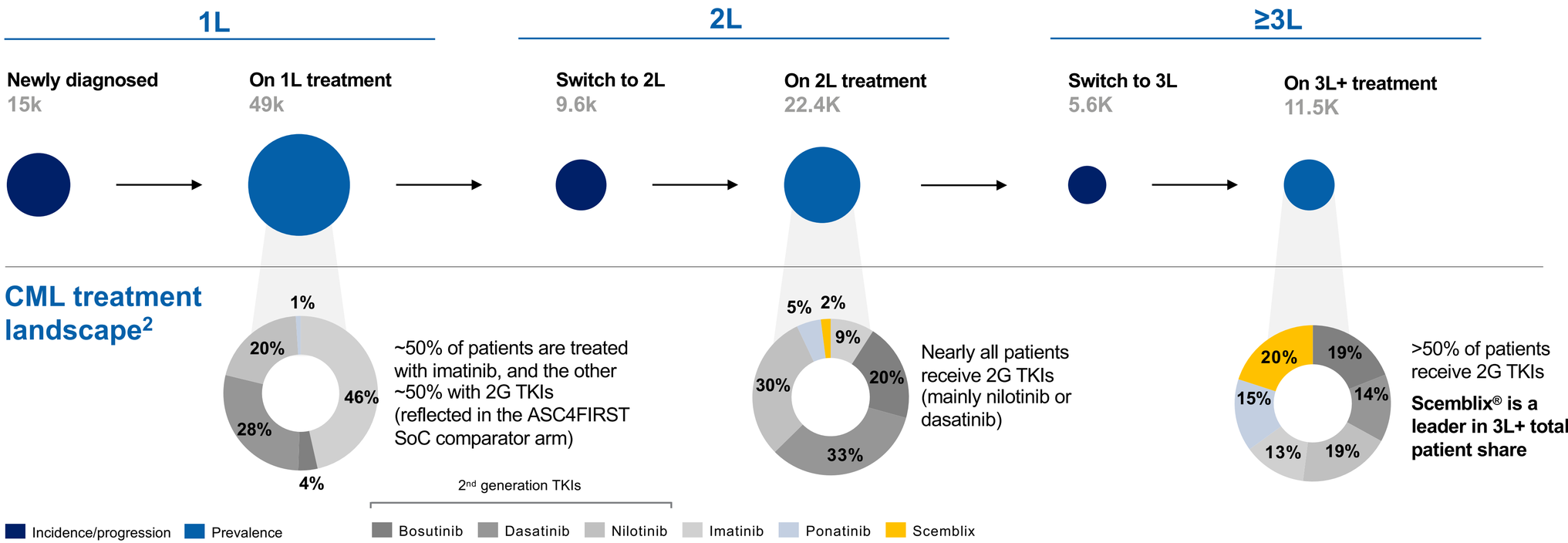
ASC4FIRST aims to show that Scemblix® is providing **superior efficacy**, more rapid and deeper responses, and **improved tolerability vs. current standard of care.**

Additional medical affairs studies ongoing including in 2L setting.

TKI - tyrosine kinase inhibitor 1. Scemblix is approved in adult patients with Philadelphia chromosome positive (Ph+) CML in Chronic Phase (CP), previously treated with two or more TKIs; in US and certain countries, also for the treatment of adult patients with Ph+ CML in CP with T315I mutation. 2. Patent term extensions and regulatory-based exclusivities are possible.

Opportunity for nearly four times more patients that could benefit from Scemblix® in 1L CML[1]

CML patient population[2,3,4]



CML treatment landscape[2]

~50% of patients are treated with imatinib, and the other ~50% with 2G TKIs (reflected in the ASC4FIRST SoC comparator arm)

Nearly all patients receive 2G TKIs (mainly nilotinib or dasatinib)

>50% of patients receive 2G TKIs

Scemblix® is a leader in 3L+ total patient share

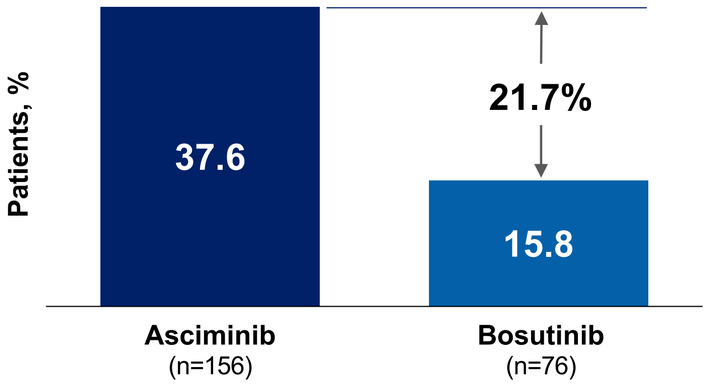
1. If approved. 2. Newly diagnosed: Kantar health CML incidence in G7, patients in 2022. 2. 2L-, 3L switch: Based on average rate resistance/intolerance of all previous line TKIs. 3. CML prevalence in G7, 2022: Kantar health. 4. IQVIA Market Sizing, IPSOS & IQVIA Oncology Dynamics (G7, MAT Jun 2023).

Two-year follow-up confirms Scemblix' superior and sustained efficacy and improved tolerability vs. bosutinib in 3L+ CML

Efficacy

Scemblix® is the **1st agent** to show **superiority vs. 2G TKI** (bosutinib): more than **doubles the MMR rate**

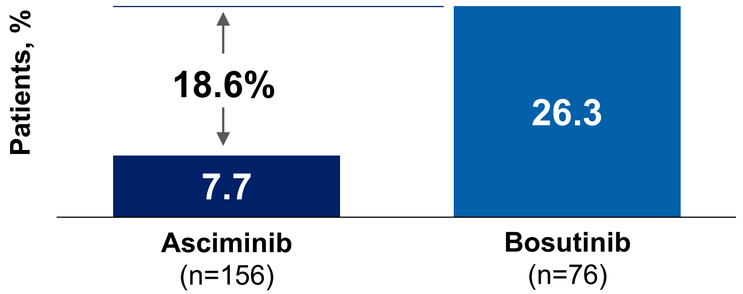
Major Molecular Response (MMR) Rates at week 96



Safety and tolerability

AEs leading to treatment discontinuation **were nearly 4x lower**

Adverse events leading to discontinuation at week 96, all grades

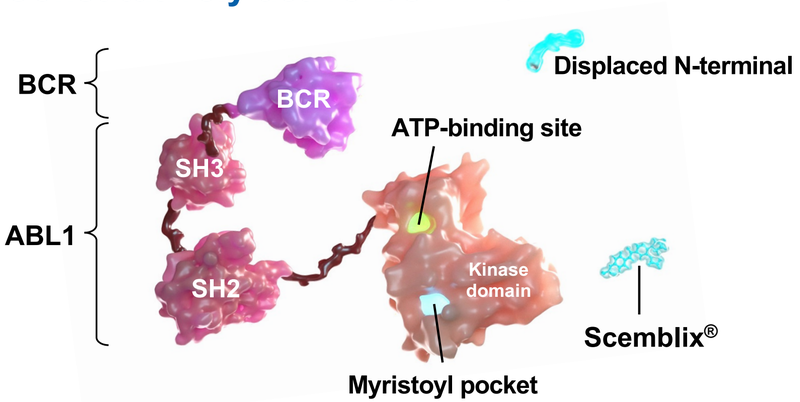


- Medium **duration of exposure** was over **3x longer** with asciminb (23.7 months) than bosutinib (7.0 months)
- Asciminib showed **improvements in symptoms and health-related quality of life** relative to baseline and relative to bosutinib

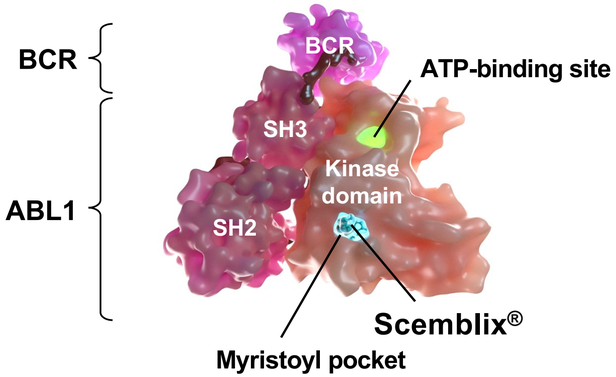
ASCEMBL Ph3, Hochhaus A. et al., Leukemia 2023; 37:617–626.

Scemblix®: First and only approved BCR-ABL inhibitor designed to address ATP-binding-TKI resistance and intolerance

Constitutively active BCR-ABL1



Inactive ABL1



Scemblix® is different from ATP-competitive TKIs – by **S**pecifically **T**argeting the **A**BL **M**yristoyl **P**ocket (**STAMP**) it maintains activity against cells expressing clinically observed ATP-binding TKI-resistant mutations

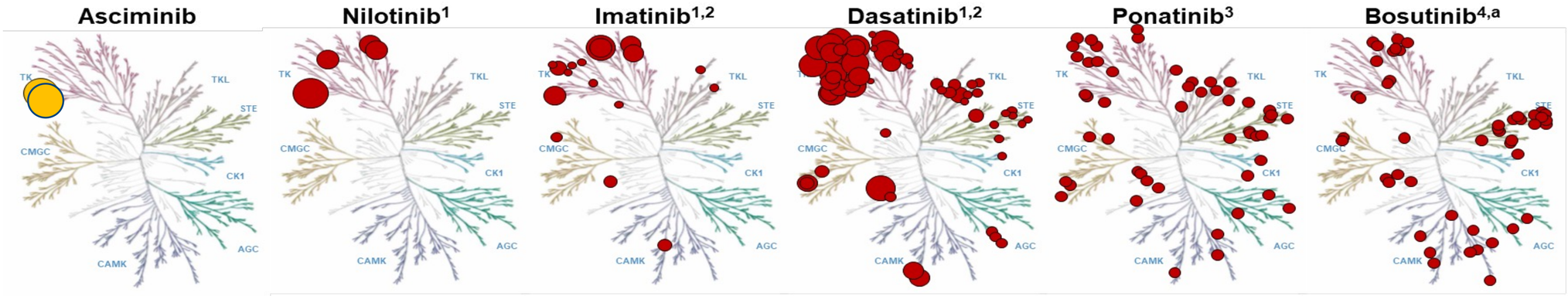
The specificity of Scemblix® for the ABL kinase family minimizes off-target activity, thus providing an improved tolerability profile vs. existing therapies

Scemblix® demonstrated rapid and deep molecular responses in newly diagnosed and previously treated CML (Ph3 ASCEMBL[1] and IIT ASCEND[2])

Proven activity against mutations that confer resistance to ATP-binding TKIs

ABL1 – Abelson tyrosine kinase. SH - Src homology. TKI – tyrosine kinase inhibitor. ATP – adenosine triphosphate. BCR – breakpoint cluster region. References for figure: Wylie AA, et al. Nature. 2017;543:733-737; Schoepfer J, et al. J Med Chem. 2018;61:8120-8135; Hughes TP, et al. Oral presentation at: 25th EHA Virtual Annual Meeting; June 11-21, 2020. Abstract S170; Manley PW, et al. Leuk Res. 2020;98:106458; Nagar B, et al. Cell. 2003;112:859-871; Hantschel O, et al. Cell. 2003;112:845-857; Colicelli J. Sci Signal. 2010;3:re6; Hantschel O. Genes Cancer. 2012;3:436-446. 1. Hochhaus A. et al., Leukemia 2023; 37:617–626. 2. Yeung DT, et al. Oral presentation at: ASH 2022 Annual Meeting; December 10-13, 2022; New Orleans, LA, and virtual. Abstract 79.

Scemblix®: Specificity for ABL kinase family minimizes off-target activity vs. ATP-competitive TKIs



Selectivity of kinase inhibitors

Kinases bound by ATP-competitive TKIs are indicated by **red** circles

Kinases bound by STAMP inhibitor are indicated by **yellow** circles

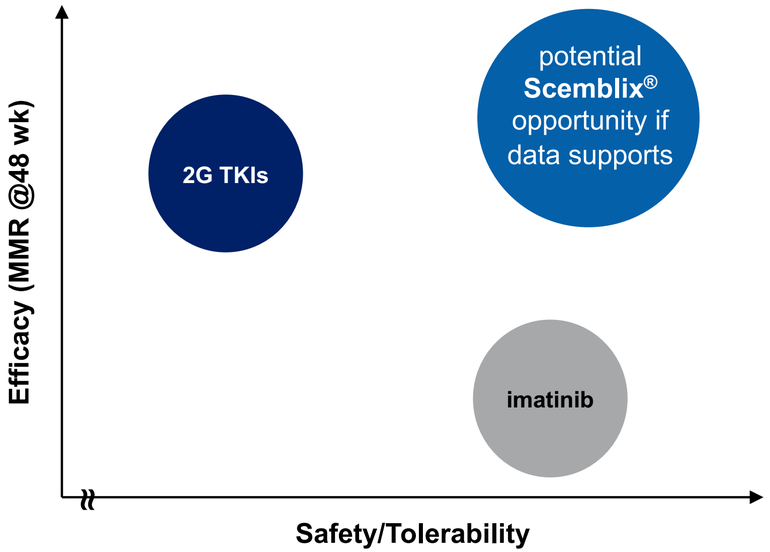
ATP – adenosine triphosphate. CAMK – calcium/calmodulin-dependent protein kinases; CK1, cell kinase. STAMP – Specifically Targeting the ABL Myristoyl Pocket. STE, serine/threonine kinases. TKL – tyrosine kinase-like.

1. Steegmann JL, et al. Leuk Lymphoma. 2012;53:2351-61. 2. Karaman MW, et al. Nat Biotechnol. 2008;26:127-32. 3. Lang JD, et al. Clin Cancer Res. 2018;24:1932-43. 4. Remsing Rix LL, et al. Leukemia. 2009;23:447-85. a. bosutinib inhibits additional kinases that are not depicted in the dendrogram.

Faster and deeper molecular response with good safety/tolerability remains unmet need for patients with CML

Limitations of current treatments

Illustrative



Inadequate control of CML and TKI-related AEs increase risk of progression

>60% of newly diagnosed CML patients **do not meet the 12-month MMR and DMR goals**, a key requirement for TFR attempt[1-6]

20% of CML patients **only** are successful in **achieving TFR** with time to attempt reaching ~8 years[7]

>50% of patients **relapse on imatinib or are refractory/intolerant to imatinib, >30%** suffer from TKI-related non-hematological AEs[8, 9]

Long-term use of 2nd generation TKIs is associated with **AEs** such as pleural effusion, GI and cardiovascular events[10]

Drug-related AEs remain the **most common reason for intentional non-adherence** to TKI treatment[11]

MMR – Major molecular response. DMR – Deep molecular response. TFR – Treatment-free remission. 1. Hochhaus A, et al. N Engl J Med. 2017;376: 917–927. 2. Hochhaus A, et al. Leukemia. 2016;30:1044-1054. 3. Brümmendorf TH, et al. Br J Haematol. 2015;168:69-81. 4. Cortes JE, et al. J Clin Oncol. 2018;36:231-237. 5. NCCN Clinical Practice Guidelines. Chronic Myeloid Leukemia. V2.2023. 6. Hochhaus A, et al. Leukemia. 2020;34(4):966-984. 7. Cortes J., Rea D., Lipton J.H. Treatment-free remission with first- and second-generation tyrosine kinase inhibitors. Am. J. Hematol. 2019;94:346–357. doi: 10.1002/ajh.25342. 8. Cortes and Lang, 2021. J Hematol Oncol 14:44 ELN recommendations 2019. 9. Garcia-Gutierrez V and Hernandez-Boluda JC, Front.Oncol. 2019. 10. Haznedaroglu IC. Drug Therapy in the Progressed CML Patient with multi-TKI Failure. Mediterr J Hematol Infect Dis. 2015. 11. Eliasson L, Clifford S, Barber N, Marin D. Exploring chronic myeloid leukemia patients' reasons for not adhering to the oral anticancer drug imatinib as prescribed. Leuk Res.

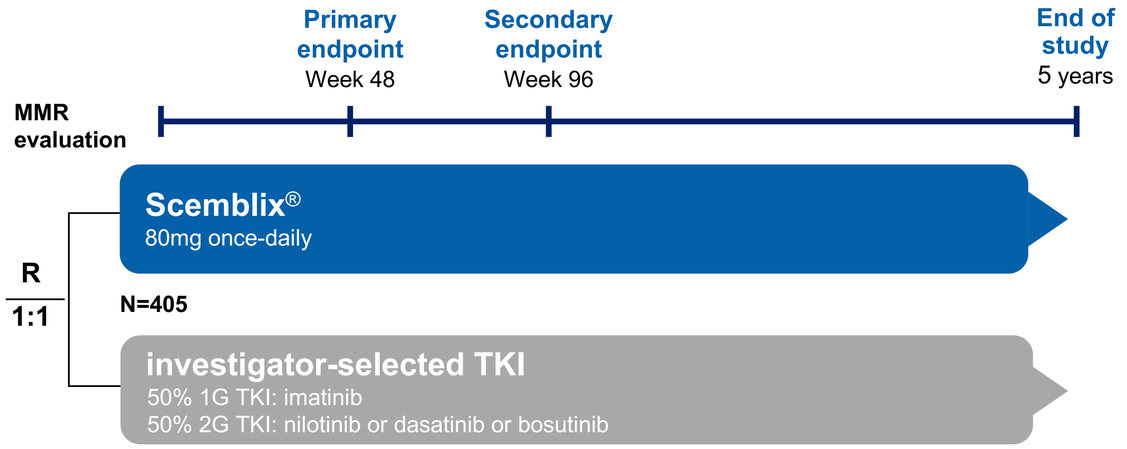
ASC4FIRST: Pivotal head-to-head trial testing Scemblix® in 1L CML-CP

- Objective of ASC4FIRST is to show that Scemblix® is providing **superior efficacy**, **more rapid** and **deeper responses**, and **improved tolerability** vs. current standard of care
- Head-to-head design comparing Scemblix® vs. investigator choice of 1st and 2nd generation TKIs
- **Primary analysis** at week 48 includes assessment of **MMR and extensive range of efficacy, safety, tolerability and patient reported outcomes**; basis for regulatory submission planned for 2024
- Trial aims to **deliver multiple subsequent analyses** with longer treatment duration with focus on 96 weeks and 5-year timepoints to demonstrate long term efficacy, safety and tolerability

Next steps 〉 **Readout expected in H1 2024**

Two primary endpoints

Superiority of Scemblix® vs. investigator choice TKI as assessed by MMR at 48 weeks
and/or
Superiority of Scemblix® vs. imatinib subgroup alone as assessed by MMR at 48 weeks



Achievement of MMR (BCR-ABL1 ≤ 0.1%) is associated with higher rates of EFS, PFS and OS[1]

CML-CP – chronic myeloid leukemia in chronic phase. MMR – major molecular response (BCR-ABL 1IS ≤0.1%). TKI – tyrosine kinase inhibitor. 1. Saussele S et al. Leukemia; 32(5):1222-8; 2018; Hochhaus et al., Leukemia; 34:966-84, 2020.

Kisqali®

NOVARTIS | Reimagining Medicine

Kisqali®

(ribociclib)

CDK 4/6 inhibitor

Market potential

● ● ● > USD 3bn

Unprobabilized peak sales of all asset indications in late-stage development

US/EU: Patent on compound (2031/2032)[1]

Continued strong momentum in metastatic breast cancer (mBC), now leader in NBRx (US), with increasing recognition of differentiated profile

- Consistent benefit regardless of combination endocrine therapy, menopausal status, site and number of metastases
- 1L OS benefit with preserved or improved quality of life, across all three Ph3 trials; longest median OS in postmenopausal HR+/HER2- mBC patients
- Included in NCCN guidelines as only Category 1 treatment for 1L mBC with AI, and only CDK4/6i with an ESMO-MCBS score of 5

Complemented by significant potential in early breast cancer (eBC)

- NATALEE trial met primary endpoint at interim analysis (ASCO 2023); final prespecified iDFS results to be presented at SABCS 2023
- In NATALEE, Kisqali® demonstrated consistent, clinically meaningful benefit (with 25% reduction in risk of recurrence) across broad population of patients with HR+/HER2- eBC, regardless of disease stage, menopausal or nodal status
- Filed in EU, US filing planned for Q4 2023

1. Granted extended patent terms. For additional information, please refer to the Novartis 20F 2022. 1L OS: First line overall survival.

NATALEE study builds on strong foundation in metastatic Breast Cancer (mBC), where Kisqali® has proven OS benefit

Kisqali® Ph3 OS results in 1L mBC

	Risk reduction	Median OS
MONALEESA-2	24%	63.9 months[1]
MONALEESA-7	24%	58.7 months[2]
MONALEESA-3	33%	67.6 months[3]

Proven OS benefit across all three Ph3 trials: Regardless of menopausal status, hormone therapy partner, or dose modifications[4]

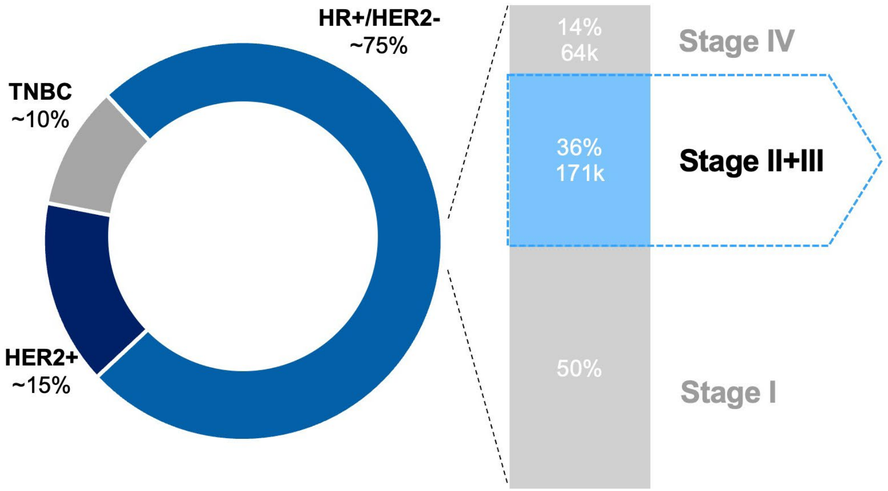
- **Kisqali® is the only CDK4/6i with statistically significant OS benefit** proven across all three mBC Ph3 trials, while maintaining or improving QoL
- **Kisqali® set a new benchmark for survival, with unprecedented median OS of ~5 years across 3 independent trials** when combined with letrozole or fulvestrant in 1L mBC
- **NCCN guidelines** recommend Kisqali® as the only Category 1 treatment for 1L mBC in combination with AI (~60% of 1L mBC patients)
- **Kisqali® is approved in HR+/HER2- mBC in 99 countries** including US, EU, and China

OS – overall survival. 1L – first line. AI – aromatase inhibitor. 1. In months vs. 51.4, P value: 0.008. Reference: Hortobagyi, GN et al., 2022. 2. vs. 48.0. Reference: Lu, YS et al., 2022. 3. vs. 51.8. Reference: Neven, P et al., 2022. 4. Based on an analysis of MONALEESA-2, -3 and -7.

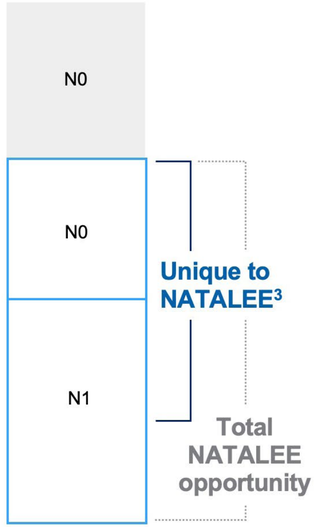
Early Breast Cancer (eBC) remains an area of high unmet need

Total Breast Cancer patient population

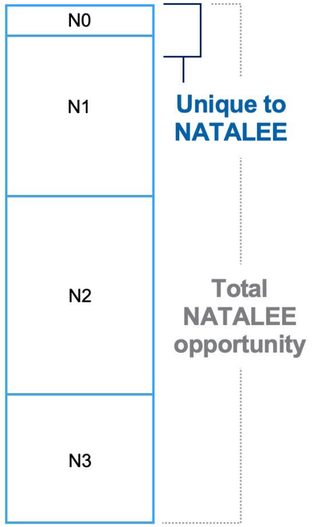
Annual incidence, US+EU5 ~620k



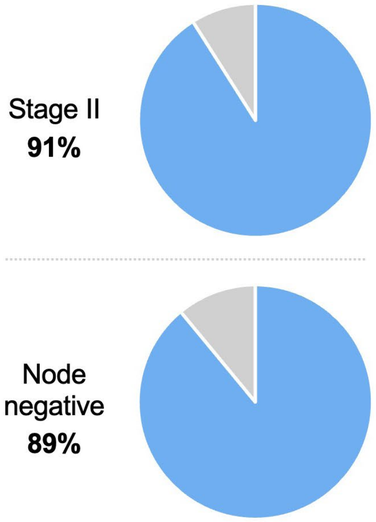
Stage II (132k)[1]



Stage III (39k)[1]



NATALEE control arm 3-y iDFS rates[2]



NATALEE control arm indicates ~10% of Stage II or N0 patients could expect to see their cancer recur within the first 3 years

Data Source: Kantar Health – US/ EU5 Patient Metrics 2023. 1. Estimated incidence data sources: DRG (US) and Kantar (EU5). 2. Bardia et al. ESMO 2023.

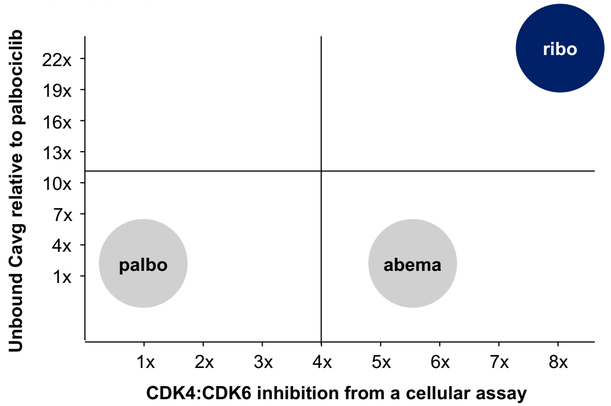
NATALEE was designed to leverage Kisqali® strengths and to address significant unmet needs in eBC

	Insights	NATALEE trial design
Treatment period	Longer on-target CDK4 inhibition may be critical to induce senescence to prevent both early and late recurrences	3-year treatment duration to address risk of recurrence
Population	Stage II and III patients are at significant risk of recurrence (~30-50% within 20 years)	Broad population of stage II and III eBC patients, including those with N0 disease
Dose	Tumor control achievable with lower drug concentration vs. mBC, given lower tumor burden	Lower dose (400mg) to improve tolerability and adherence while maintaining efficacy

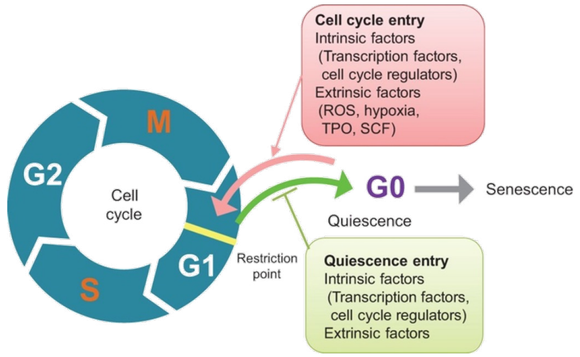
N – node. N0 – no nodal involvement.

Unique mechanism of action and three-year duration of therapy may be critical in preventing late recurrence

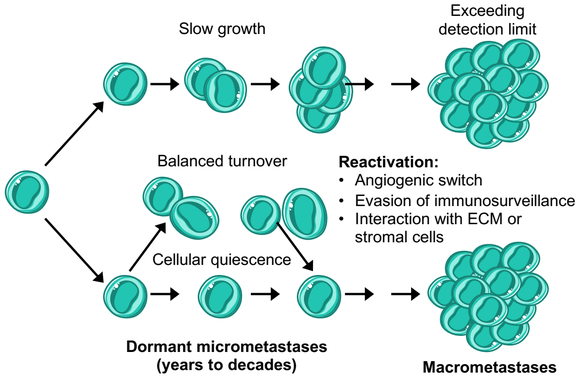
On-target CDK4 inhibition[1-4]



Lock cancer cells into senescence[5,6]



Reduce micrometastasis and prevent recurrence[7]



At clinically relevant doses, **ribociclib provides greater CDK4 inhibition** in vivo than competitors

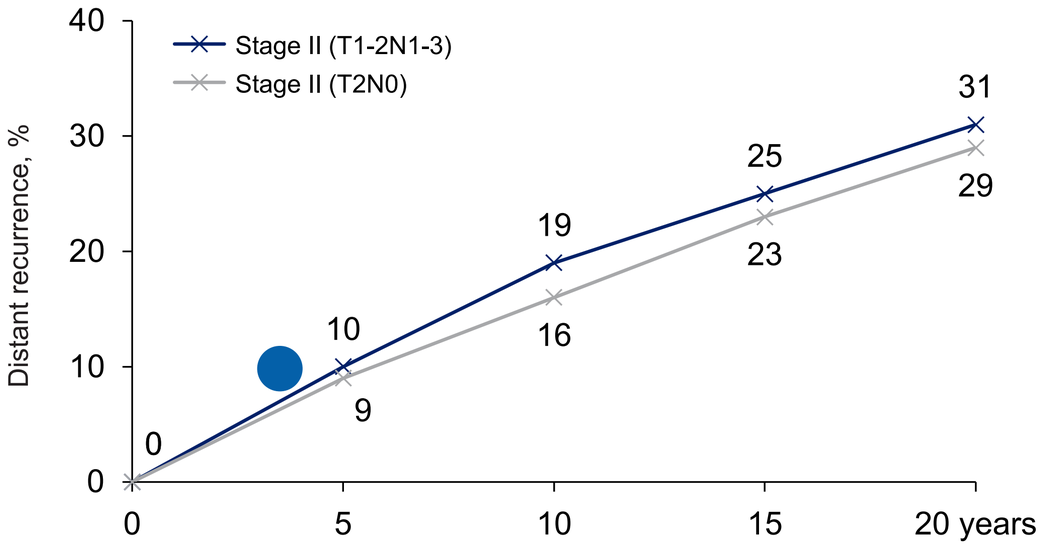
Higher unbound C_{avg} means **more drug available** to act on tumor cells[1-4]

More time for on-target CDK4 inhibition enables **irreversible cell growth arrest (senescence)** of micro-metastases and immuno-modulation

1. Yu Q, Sicinska E, Geng Y, et al. Requirement for CDK4 kinase function in breast cancer. Cancer Cell. 2006;9(1):23-32. 2. An H-X, Beckmann MW, Reifenberger G, Bender HG, Niederacher D. Gene amplification and overexpression of CDK4 in sporadic breast carcinomas is associated with high tumor cell proliferation. Am JPathol. 1999;154(1):113-118. 3. Kim S, Tiedt R, Loo A, et al. The potent and selective cyclin-dependent kinases 4 and 6 inhibitor ribociclib (LEE011) is a versatile combination partner in preclinical cancer models. Oncotarget. 2018;9(81):35226-35240;(suppl). 4. Sammons SL, Topping DL, Blackwell KL. HR+, HER2-advanced breast cancer and CDK4/6 inhibitors: mode of action, clinical activity, and safety profiles. Curr Cancer Drug Targets. 2017;17(7):637-649. 5. Faget DV, et al. Nat Rev Cancer. 2019;19:439-453. 6. Nakamura-Ishizu A, et al. Development. 2014 Dec 15;141:4656-66. 7. Zhang XH, et al. Clin Cancer Res. 2013;19(23):6389-6397.

Anatomical stage II and III patients with HR+/HER2- eBC are at risk of recurrence

Distant recurrence by nodal involvement[1]



Risk of recurrence

Stage II and III eBC patients are at significant risk of recurrence[1]:

- Unlike most solid tumors, **HR+ breast cancer may recur 5–30 years after initial diagnosis**[2]
- **Between ~30-50% will see their cancer recur** in their lifetime[1]

NATALEE control arm confirms that the patient population is at risk of recurrence, including those with N0 (11% at 3 years) and stage II (9% at 3 years) disease[3]

Quality of life (QoL)

Improving patient outcomes without putting additional burden on the patient is essential[4]

~30% of patients with or without nodal involvement will have recurrence within 20 years

1. Adapted from Pan H, et al. N Engl J Med. 2017;377:1836-1846. 2. Pederson RN, et al. J Natl Cancer Inst, 2022;114(3): djab202. 3. Bardia et al. ESMO 2023. 4. Cerner Enviza CancerMpact surveyed data as of Sep'22.

Consistent iDFS benefit across key subgroups in NATALEE at primary analysis (426 iDFS events)

MADRID 2023 ESMO congress

iDFS per key subgroup	HR	(95% CI)
Total population	**0.75**	(0.62, 0.91)
Stage II	**0.76**	(0.53, 1.10)
Stage III	**0.74**	(0.59, 0.92)
Pre-menopausal women and men	**0.72**	(0.53, 0.98)
Post-menopausal women	**0.78**	(0.61, 1.00)
Node negative	**0.63**	(0.34, 1.16)
Node positive	**0.77**	(0.63, 0.94)
<65 years	**0.77**	(0.62-0-94)
≥65 years	**0.72**	(0.46-1.14)
Ki-67≤20%	**0.80**	(0.59-1.08)
Ki-67>20%	**0.75**	(0.56-1.00)

To be presented at SABCS:

Invasive disease-free survival (iDFS) protocol pre-specified final analysis from the NATALEE trial

- ~500 iDFS events; ~6 months more follow-up
- Will reflect substantial share of patients having completed 3 years of treatment

Overall, the iDFS benefit with RIB + NSAI vs. NSAI alone was consistent across all clinically relevant subgroups, which in turn was consistent with that observed in the overall trial population

Limited treatment modifications with Kisqali® up to three years in NATALEE

No new safety signals

400mg dose **well tolerated**, with **limited need for dose reductions**

AE-related discontinuations (19%) were mostly protocol-mandated **due to asymptomatic lab findings**

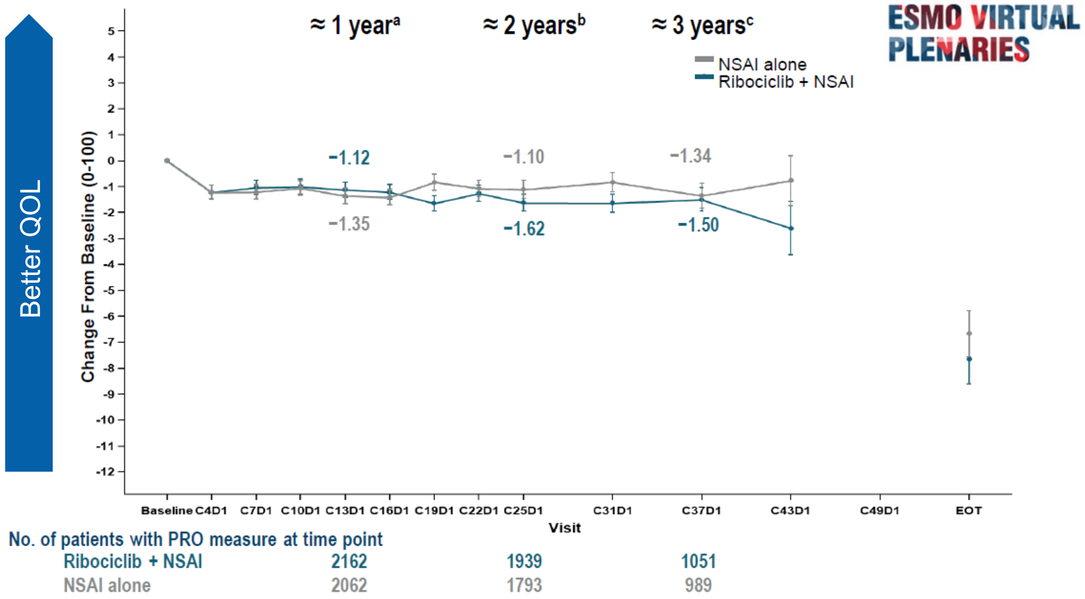
Most of the AE-related discontinuations occurred early in treatment (4 months median)

Low rates (<1%) of symptomatic AEs such as G3 diarrhea and fatigue

G3 VTE and ILD also low (<1%)

AE – adverse event. VTE – venous thromboembolism. ILD – interstitial lung disease.

Quality of life maintained in a broad population of Stage II & III patients with HR+/HER2- eBC with Kisqali®



- Global health status not impacted over time in both arms
- No difference in social functioning from baseline observed in both arms
- Breast cancer symptoms reduced quickly and improved at a slower rate over the study
- Anxiety and depression scores did not change meaningfully over time in either treatment arm

Physical functioning was maintained with the addition of Kisqali® to standard-of-care NSAI

a Week 49/day 1, C13D1. b Week 97/day 1, C25D1. c Week 145/day 1, C37D1.

Next steps for Kisqali®

NATALEE final iDFS analysis

incl. ~6 months of additional follow-up will be presented at SABCS 2023 (will reflect substantial share of patients having completed 3 years of treatment)

Filing in EU, CH, and others achieved in Q3 2023

Filing in US targeted for Q4 2023 and Novartis will use priority review voucher

Pursuing broad label

reflecting the ITT population studied in NATALEE

Collectively, NATALEE results have the potential to more than double the number of patients who could benefit from treatment with a CDK4/6 inhibitor in the eBC setting

Closing

NOVARTIS | Reimagining Medicine

Strong pipeline across our core therapeutic areas with planned submissions by 2027

Select examples

Kisqali® ●●●
Adjuvant breast cancer filed in EMA in **Q3 2023.** FDA regulatory submission expected in **Q4 2023**

Pluvicto® ●●
mCRPC (post-ARDT, pre-taxane), FDA regulatory submission expected in **2024**

mHSPC readout expected in **2025**

Iptacopan ●●●
PNH filed with FDA and EMA in **Q2 2023**

IgAN submission expected in **2024**[1]

C3G readout expected in **Q4 2023**

Atrasentan ●
IgAN submission expected in **2024**[1]

Remibrutinib ●●●
CSU submission expected in **2024**

Multiple sclerosis and CINDU readouts expected in **2026**

Lutathera® ●
GEP-NET 1L G3 EU submission expected in **2024**

Scemblix® ●●
1L CML-CP readout expected in **2024**

OAV-101 ●●
SMA IT readout expected in **2024**

Pelacarsen ●●●
CVRR readout expected in **2025**

Ianalumab ●●●
1L and 2L ITP readouts expected in **2025**

Sjögren's readout expected in **2026**

Zigakibart ●
IgAN readout expected in **2026**

1. US submission for accelerated approval. Unprobabilized estimated peak sales of all asset indications in late-stage development: ● > USD 1bn ●● > USD 2bn ●●● > USD 3bn

Confident that Novartis pipeline assets and R&D capabilities will drive mid-single-digit growth to 2027 and beyond

	2022 - 2027 +5% CAGR	>2027 mid-single digit
De-risked in-market brands	KISQALI®, PLUVICTO®, Kesimpta®, LEQVIO®, Cosentyx®, zolgensma®, SCEMBLIX®	KISQALI®, PLUVICTO®, Kesimpta®, LEQVIO®, SCEMBLIX®, zolgensma®
Pipeline assets	iptacopan, ianalumab, remibrutinib, atrasentan, pelacarsen	iptacopan, ianalumab, JDQ443, remibrutinib, atrasentan, AAA614 (FAPi), pelacarsen, zigakibart, XXB750, YTB323