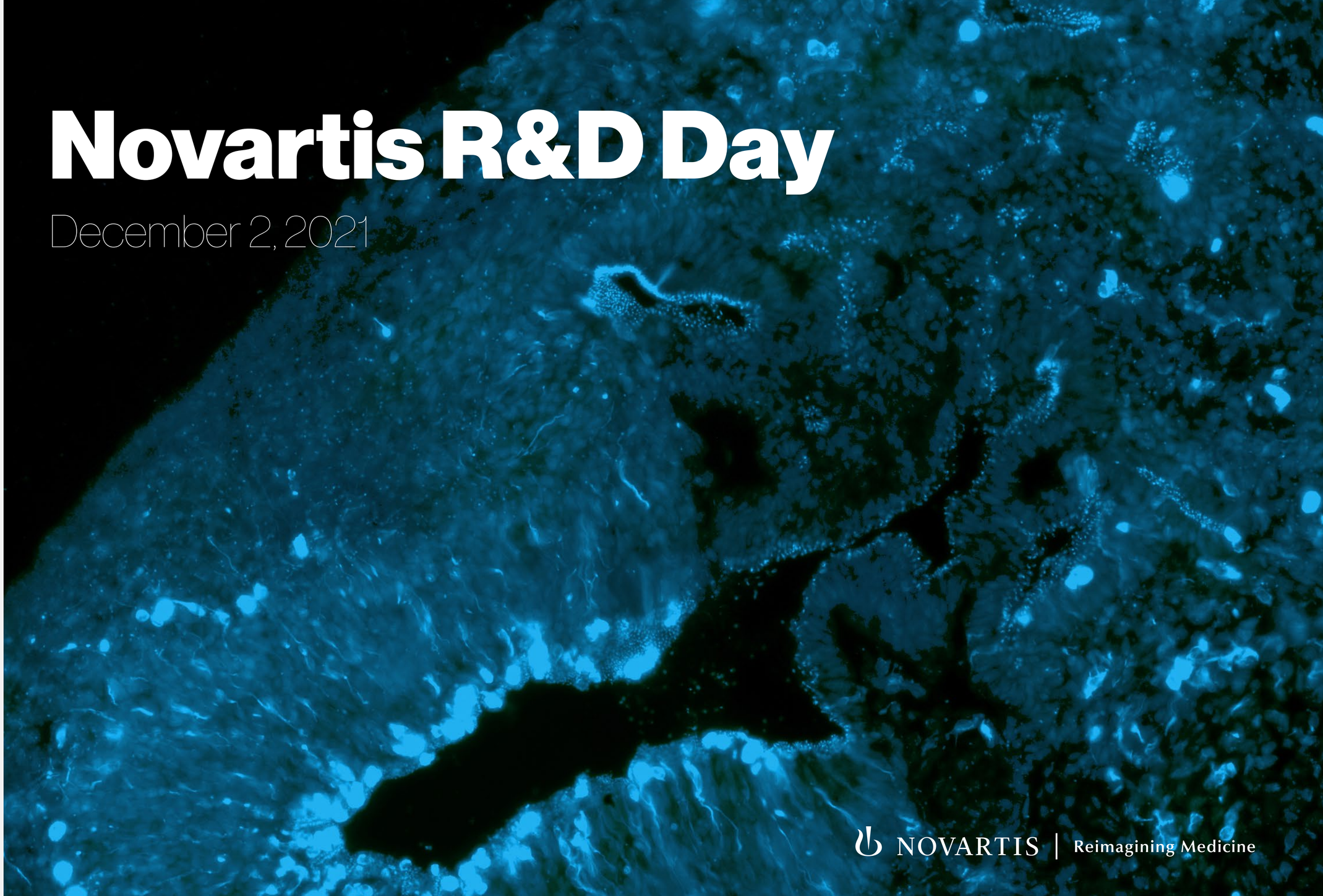
Novartis R&D Day

December 2, 2021



NOVARTIS | Reimagining Medicine

R&D Day 2021

December 2, 2021 (CET times)

14.00 – 14.50	**Novartis Strategy and Growth Story**
14.50 – 15.30	**Cardiovascular and Renal**
15.30 – 15.50	Break
15.50 – 16.45	**Immunology, Hepatology and Dermatology**
16.45 – 17.10	**Neuroscience**
17.10 – 17.30	Break
17.30 – 18.20	**Oncology**
18.20 – 18.50	**NIBR and Technology Platforms**
18.50 – 19.00	**Closing**

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Speakers

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Susanne Schaffert
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Angelika Jahreis
Global Head, Immunology, Hepatology and Dermatology Unit

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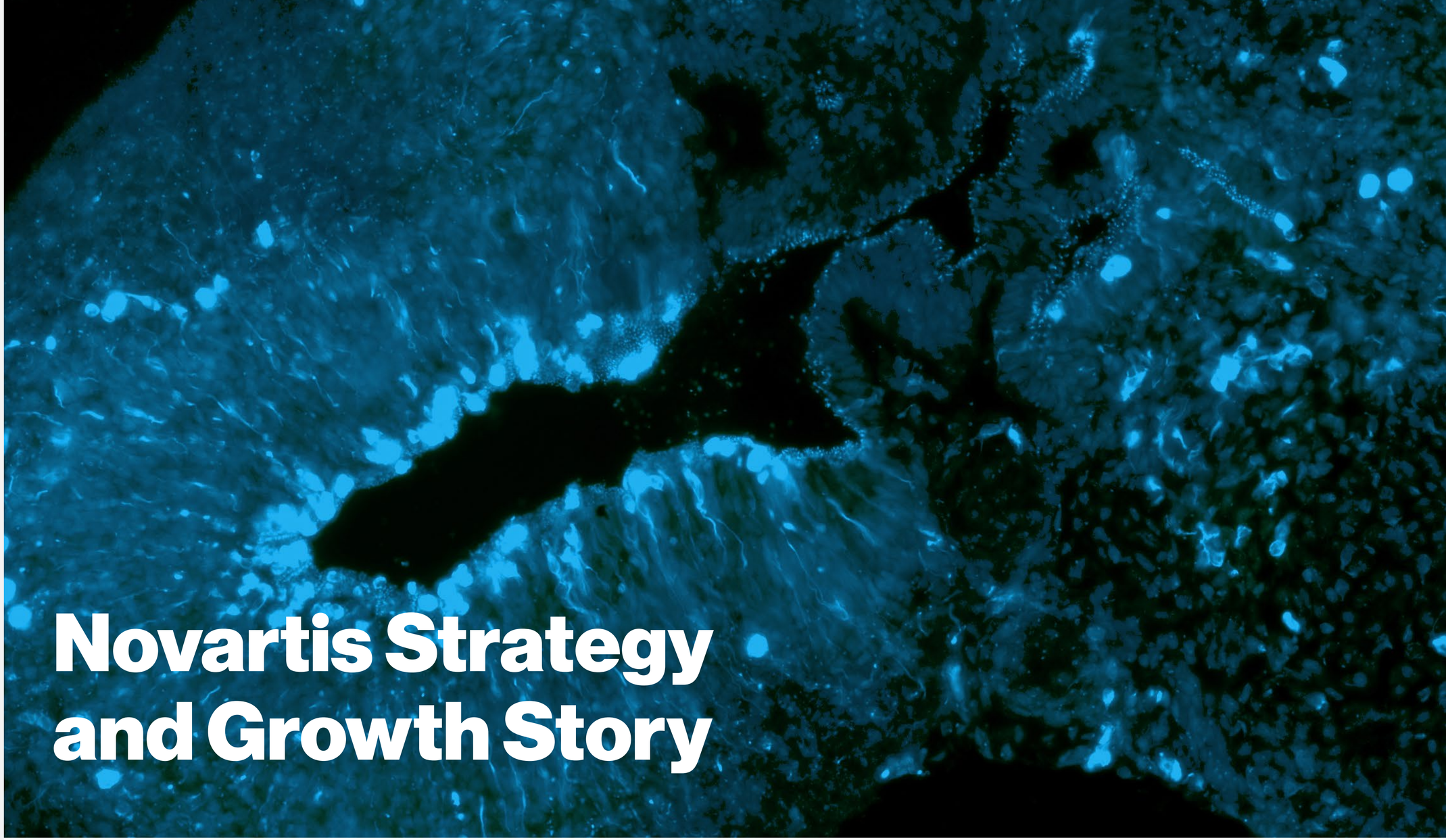
Global Head, Neuroscience Development Unit

Jeff Legos
Global Head, Oncology Development Unit

Alice Shaw
Global Head, Translational Clinical Oncology, NIBR

Jay Bradner
President, Novartis Institutes for BioMedical Research (NIBR)



Novartis Strategy and Growth Story

Our strategy

Focused medicines company powered by technology leadership in R&D, world-class commercialization, global access and data science

Where to play | our focus

Strengthen our core therapeutic areas

Advance our leading technology platforms

Accelerate our 4 priority geographies

Transform Sandoz

How to win | our five priorities

Embrace operational excellence every day

Unleash the power of our people

Deliver transformative innovation

Go big on data and digital

Build trust with society

Our aspiration

Innovation power
Top 3 innovator

Returns
High 30s IM margin, attractive ROIC[1]

Growth
Consistent above peer median average growth

ESG
Global leader in material ESG factors

1. Return on invested capital.

Today, we are a fully focused medicines company delivering consistent top-line growth with margin expansion

Diversified
Healthcare Group

1996 - 2014

Focused
Medicines Company

2015 - 2021

Actions 2015 – 2020

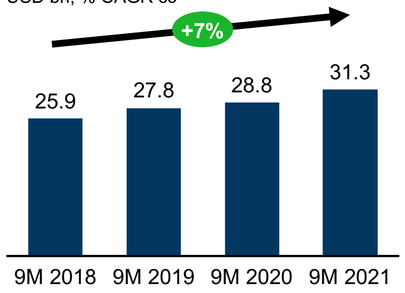
- Exit of Animal Health, Vaccines, Consumer Health
- Alcon spin | value creating, tax neutral, largest in EU market history
- Opportunistic bolt-on acquisitions

Actions 2021

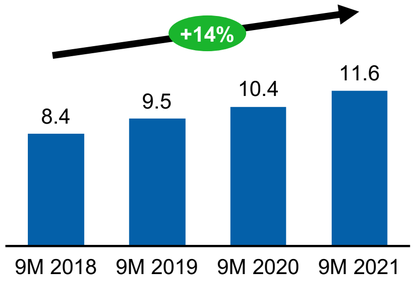
- Strategic Review of Sandoz to maximize shareholder value
- Sale of Roche stake | single bilateral transaction, ~USD 21bn, no tax leakage, IRR of 10.2% in USD

Consistent strong operating performance (Innovative Medicines)

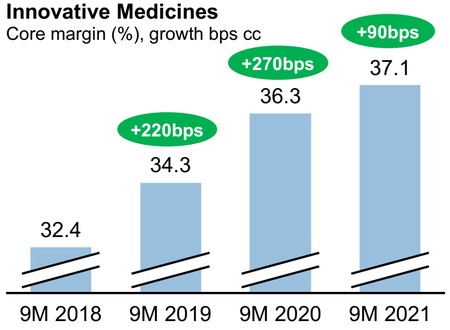
Sales
USD bn, % CAGR cc



Core OpInc
USD bn, % CAGR cc



Innovative Medicines
Core margin (%), growth bps cc



We remain disciplined and shareholder-focused in our capital allocation priorities

Capital allocation priorities

1	**Investments in organic business**	>	Continued focus on core medicines business
2	**Growing annual dividend in CHF**	>	Committed to maintain strong and growing dividend (in CHF), increased by CAGR 7.8% in CHF and 9.8% in USD between 1996-2020[1]
3	**Value-creating bolt-ons**	>	~USD 29bn M&A bolt-ons since 2018[2] (10+ deals, mean of ~USD 2bn)
4	**Share buybacks**	>	~USD 12bn of share buybacks[3] over past 5 years

1. Reflecting dividend payments up to and including the business year 2020 (paid out in March 2021), converted at historic exchange rates at the respective dividend payment dates as per Bloomberg. 2. Until Q3 2021. 3. Net of mitigation of dilution related to participation plans of associates.

We have therapeutic area depth, strength in technology platforms, and a balanced geographic presence

In-market and pipeline depth in 5 therapeutic areas

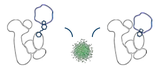
5 CRM, IHD, NS, ONC, HEM[1]
Opportunistic in others:
Ophthalmology & Respiratory

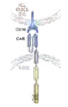
14 In-market blockbuster assets[2]

20 Potential bn-USD+ pipeline assets with approval by 2026

8% Limited binary risk on a single product[2]

Strong positions in technology platforms

TPD  Advance our broad portfolio of NMEs

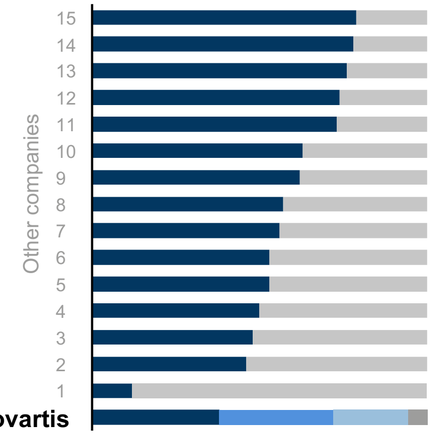
CELL THERAPY  Lead in next generation of CAR-Ts

GENE THERAPY  Advance next wave of assets

RLT  Expand across additional solid tumors

xRNA  Fully build up siRNA capabilities

Geographically diversified[3]



US | Low exposure to US pricing reforms[4]
EU | Maintain sales leadership
China | Sales on track to double by 2024

US | Asia, Africa, Australasia | ex-US
EU | Canada & Latin America

1. Cardio-Renal, Immunology, Neuroscience, Oncology, Hematology. 2. Based on 2020 Group sales actuals. 3. Source IQVIA Analytics Link (MIDAS database), sales numbers are estimated bottom up based on average wholesaler price and volume, and therefore deviates from net sales reported by companies in their annual reports. Includes branded and generics drugs as well as vaccines but no OTC. 4. Relative to peers. TPD: Targeted Protein Degradation, RLT: Radioligand Therapy.

Our innovative pipeline addresses unmet medical needs with a renewed focus to deliver high value assets

Scale

Projects[1]

70
NMEs

65
Phase 3 / Registration

100
Phase 1/2

Innovation

23
FDA breakthrough therapy designations in the past 6 years

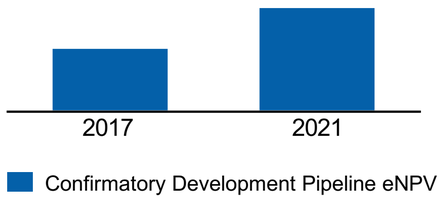
~85%
Pipeline[2] potentially first-in-class / first-in indication

>80%
Target areas of high unmet need[2]

Value

#1
NME US FDA approvals[3]

~1.5x
eNPV growth per asset since 2017[4]



Priorities

Focus on assets with **significant potential**

Early **expansion into multiple indications** (e.g. Iptacopan, Remibrutinib, Ligelizumab)

Rapid transitions to pivotal studies especially for **high value assets** (e.g. JDQ/TNO, NIS, YTB)

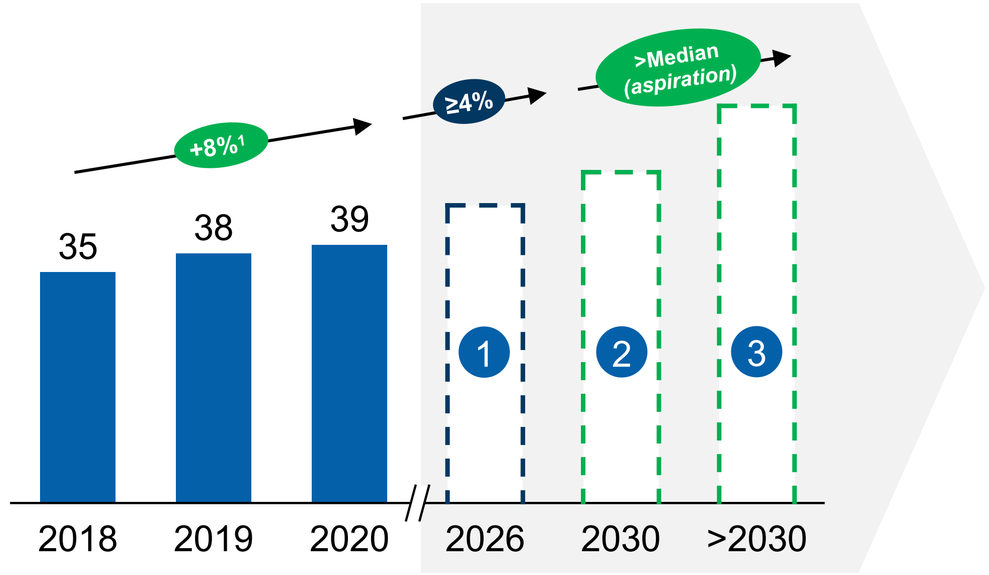
Early out licensure of **non-strategic internal assets**

1. As per IR Q3 2021 pipeline. 2. Confirmatory development pipeline. 3. Source: Evaluate Pharma, US NME FDA Approvals 2018 -2020. 4. Confirmatory development pipeline, IMB portfolio review May 2017 vs May 2021

Novartis is committed to driving consistent growth through 2030 and beyond

IM sales evolution

Illustrative, USD billion, % CAGR cc



1. **2020-2026 | ≥4%**
Focused resources on key growth brands and launches, upscaling next generation engagement models

2. **2026-2030 | >peer median**
Double-down on internal pipeline assets to unlock their full potential and add complementary BD&L

3. **>2030 | >peer median**
Focused investments in technology platforms while staying at the forefront of innovation in small and large molecules

1. 6% in USD

1

Novartis Growth Story
2020 - 2026

Six assets with multi-billion USD sales potential to drive growth

	Cosentyx®	Entresto®	zolgensma®	KISQALI®	Kesimpta®	LEQVIO®
Q3 sales annualized[1] **Q3 Growth**	USD bn **5.0** +22%	USD bn **3.7** +44%	USD bn **1.5** +28%	USD bn **0.9** +27%	USD bn **0.4** nm	USD bn **nm** nm
Peak sales **CAGR 2020-2026**	USD bn **>7.0** Low double-digit	USD bn **>5.0** Double digit until LoE	USD bn **Multi-billion[3]** Low to mid teens	USD bn **Multi-billion** Low 30s[4]	USD bn **Multi-billion** nm	USD bn **Multi-billion** nm
US LoE[2]	**2029+**	**2025-2036**	**2031+**	**2031+**	**2031+**	**2036+**

USD, all growth rates in constant currencies (cc). Excludes potential impact from US HC reform. 1. Reported Q3 net sales annualized. 2. Estimated based on relevant patents; further extensions possible. 3. Including Zolgensma IT. 4. Including Kisqali adjuvant.

Leqvio® on track for US launch with FDA action date January 1

US launch preparation on track

Enable ~200 prioritized health systems readiness

Drive awareness among HCPs leveraging strong CV footprint

Facilitate product acquisition through >1000 AICs[1]

H1 2022	H2 2022
High interest from early adopters	Permanent J-code available
Independent HCPs ready for buy-and-bill	Buy-and-bill capabilities established
AICs responding to demand	System P&T committee review complete
Temporary J-code	Finalization of payer coverage policies

Generating additional evidence

V-INITIATE Explore “Leqvio® first” directly after statins[2]

V-INCEPTION Investigate Leqvio® initiation after ACS events[2]

Ex-US launches continue

RoW | Approved in 50 countries, reimbursement reviews in >10 markets

UK | NHS population health agreement to treat ~300k ASCVD patients

1. Alternative Injection Centers. 2. In patients with elevated LDL-C despite treatment with maximally tolerated statin therapy. V-INITIATE NCT04929249; V-INCEPTION NCT04873934.

Additional key 2022 launches include Scemblix® and ^{177}Lu-PSMA-617

SCEMBLIX® (asciminib) 20 mg, 40 mg tablets

First STAMP inhibitor in 3L CML

FDA approval received in 3L CML and CML patients with T315I mutation

~25% of all CML patients addressable with current label

Potential to provide best benefit-risk profile in 1L CML

>50% of patients treated front line with imatinib

30-40% treated with 2nd generation TKIs

} develop resistance or intolerance

Initiated 1L pivotal study of asciminib vs. investigator-selected TKI (FPFV[1] achieved in Q4 2021)

^{177}Lu-PSMA-617[2]

Prognosis remains poor for patients with mCRPC[3]

2nd most diagnosed cancer in men

>80% of patients metastatic at the time of CRPC diagnosis

~10 months median OS on available treatment options

With FDA Priority Review, PDUFA[4] expected H1 2022

Submitted ^{68}Ga-PSMA-11 kit for PET imaging to FDA

Scaling community centers on RLT

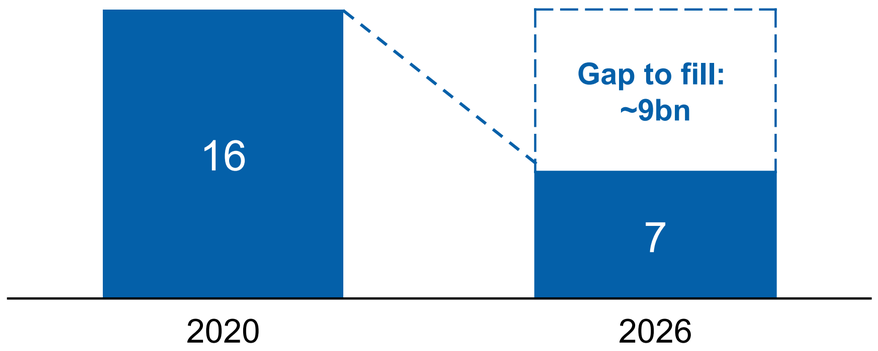
EMA submission completed and approval expected in H1 2022

1. First patient first visit. 2. Product and brand name are currently under FDA review. 3. Metastatic castration-resistant prostate cancer. 4. Prescription Drug User Fee Act.

Growth drivers and pipeline expected to exceed estimated USD 9bn gap from new generic entries through 2026

Sales from products with future Gx competition

Illustrative, USD billion @cc
Assumptions including Entresto US LoE (2025)[1]



Products with future Gx impact up to 2026: Entresto, Lucentis, Gilenya, Tasigna, Promacta, Sandostatin, Xolair, Afinitor, Q-Family and Votrient

Excludes potential impact from US healthcare reforms and decline of established medicines & existing generics

USD 9bn — Generic gap

≥USD 2.5bn — Potential upside to 2026 sales
If Entresto US LoE is beyond 2026[1]

Given our **global footprint**, LoE and erosion curves vary between geographies

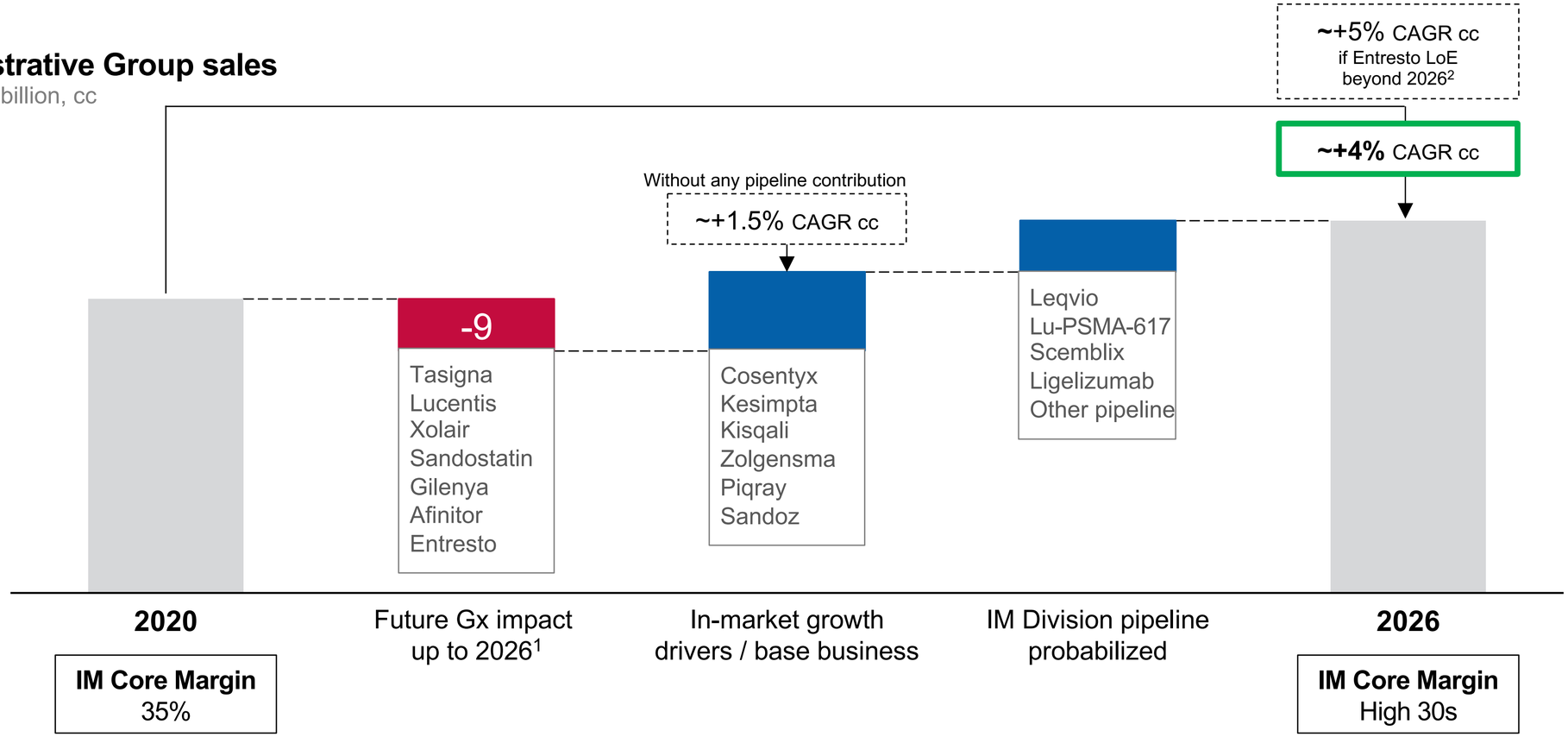
Significant potential sales for major brands remain for some time post genericization, e.g., Diovan family, Glivec

1. For internal forecasting purposes we do not expect Gx in US at least until 2025

Confident in delivering 4%+ sales CAGR 2020 - 2026

Illustrative Group sales

USD billion, cc



Excludes potential impact from US healthcare reform 1. Estimated based on relevant patents; further extensions possible. Additional products include Promacta, Q-Family and Votrient. 2. For internal forecasting purposes we do not expect Gx in US at least until 2025

In summary – our growth story to 2026

2020-2026 Sales Group CAGR (cc)

+1.5%	Overcoming USD 9bn Gx erosion gap and assuming **zero contribution** from pipeline
~+3%[1]	Current consensus
+4%	Our expectations with **probabilized pipeline sales** and Entresto LoE forecast assumption of 2025[2]
+5%	Our expectations with **probabilized pipeline sales** and potential Entresto LoE beyond 2026[2]

1. 2.7% -3.1% based on In-house, FactSet, Bloomberg consensus 2. For internal forecasting purposes we do not expect Gx in US at least until 2025

2

Novartis Growth Story
2026 - 2030

Up to 20 potential billion-USD+ pipeline assets with approval by 2026

Most are supported by high strength of evidence

Selected assets

	Strength of evidence **Moderate**	Strength of evidence **High**		
Unprobabilized peak sales **USD bn / multi-bn**	**Sabatolimab** MDS; AML	**Iptacopan** PNH; C3G; IgAN; aHUS	**Kisqali** Adj. BC (+endocrine th.) ◆	**Leqvio** Hypercholesterolemia
	NIS793 PDAC; Colorectal Cancer	**Remibrutinib** CSU; MS	**YTB323**[1] 2L DLBCL	**Cosentyx** Multiple indications ◆
	Pelacarsen CVRR	**Zolgensma** ◆ SMA IT	**Ianalumab** Sjogren's; SLE; AIH; Lupus Nephritis	**^{177}Lu-PSMA-617** mCRPC post & pre-taxane; mHSPC
	Canakinumab Adj. NSCLC	**Ligelizumab** CSU; FA; CINDU		**Scemblix** 3L+ CML; 1L CML
	UNR844 Presbyopia			**Tislelizumab** Multiple indications
	Libvatrep (SAF312) Chronic Ocular Surface Pain			**Piqray** PROS; HER2+ adv BC; TNBC; Ovarian cancer ◆
	TNO155, JDQ443[1] NSCLC; Colorectal Cancer; Combos			
Unprobabilized peak sales **up to USD 1bn**		**Lutathera** 1L G2/G3 NET ◆	**Kymriah** r/r Follicular Lymphoma ◆	**Beovu** DME ◆
			Tafinlar/Mekinist Solid Tumor Agnostic ◆	**Jakavi** SR GvHD ◆

Most advanced and key indication(s) **approved by 2026**

- Submission
- Phase III
- Phase II
- ◆ LCM

1. Ph3 to start in 2022. Assets are shown in the phase of the most advanced indication (listed first). Value based on the total of the listed indication(s). Strength of evidence based on the most advanced indication: High if in Ph3 or when Ph2 results available for the same MoA in the lead indication.

Promising pipeline assets to drive mid-term growth (1/2)

Pharmaceuticals

Selected assets, nearly all with exclusivity into 2030+

★ First-in-class

Cardio-Renal

Asset	Indication	Peak Sales	Next Milestone/ Status	Submission
★ Leqvio	Hyperlipidemia		FDA action date Jan 1st 2022	-
	CVRR-LDLC	●●●	Ph3 ORION-4 and VICTORIAN-2-PREVENT ongoing	2026+
★ Iptacopan[1]	IgAN		Ph3 APPLAUSE-IgAN ongoing	2023[2]
	C3G	●●●	Ph3 APPEAR-C3G ongoing	2023
	iMN		Ph2b ongoing	2026+
★ Pelacarsen	CVRR-Lp(a)	●●●	Ph3 ongoing	2025

Neuroscience

Asset	Indication	Peak Sales	Next Milestone/ Status	Submission
★ Zolgensma	SMA IT	●●●	Ph3 STEER initiating	2025
★ Branaplam	Huntington's disease	●●●	Ph2b start H2 2021	2026+
Remibrutinib[1]	Multiple sclerosis	●●●	Ph3 REMODEL-1 and 2 start H2 2021	2025

Unprobabilized peak sales (USD): ● <1bn ●● 1-2bn ●●● >2bn

Immunology

Asset	Indication	Peak Sales	Next Milestone/ Status	Submission
Cosentyx	HS		Ph3 SUNRISE, SUNSHINE positive readout H2 2021	2022
	GCA		Ph3 ongoing	2024
	jPsA/ERA	●●●	In registration	-
	Lupus Nephritis		Ph3 SELUNE ongoing	2026+
	Lichen Planus		Ph2b PRELUDE readout in 2022	2025
Ligelizumab	CSU		Ph3 PEARL 1, 2 readout 2021[3]	2022
	Food allergy[4]	●●●	Ph3 PEANUT start H2 2021	2025
	CINDU		Ph3 PEARL-PROVOKE ongoing	2025
Remibrutinib[1]	CSU	●●●	Ph3 REMIX-1 ongoing	2024
	Other indications being explored			
★ Ianalumab	Sjögren's		Ph3 start in 2022	2026+
	SLE		Ph2a ongoing	2026+
	Autoimmune hepatitis	●●●	Ph2b ongoing	2026+
	Lupus Nephritis		Ph3 start in 2022	2026+
★ Iscalimab	Liver Tx		Ph2b ongoing	2026+
	Sjögren's	●●	Ph2b ongoing	2026+
	HS		Ph2a ongoing	2026+

1. Peak sales potential based on all studied indications. 2. Based on 9 months UPCR readout (US accelerated approval). 3. Q4/2021-Q1/2022 potential COVID-19 impact. 4. Food Allergy indication falls within the Respiratory & Allergy therapeutic area.

Promising pipeline assets to drive mid-term growth (2/2)

Oncology

Selected assets, nearly all with exclusivity into 2030+

★ First-in-class

Solid Tumors

	Asset	Indication	Peak Sales	Next Milestone/ Status	Submission
	Kisqali	HR+/HER2- BC (adj)	●●●	Ph3 NATALEE readout event-driven, expected end 2022[1]	2023
★	Canakinumab	NSCLC adjuvant	●●	Ph3 CANOPY-A readout in 2022	2023
★	Lu-PSMA-617	mCRPC post-taxane	●●●	In registration	-
		mCRPC pre-taxane		Ph3 PSMAfore ongoing	2023
		mHSPC		Ph3 PSMAddition ongoing	2024
	JDQ443 KRAS inhibitor	2/3L NSCLC (mono)	●●●	Ph3 start in H1 2022	2024
		NSCLC (combo)		In Ph2	2026+
★	TNO155 SHP2 inhibitor	Solid tumors: multiple combinations being explored in ongoing trials			
	Tislelizumab	2L esophageal cancer	●●	In registration	-
		NSCLC		H1 2022 MAA submission, evaluation of US BLA submission options ongoing	2022
		Multiple other indications		Ongoing trials	

Hematology

	Asset	Indication	Peak Sales	Next Milestone/ Status	Submission
★	Scemblix (Asciminib)	CML 3L	●●●	US approved	-
		CML 1L		Ph3 ongoing	2025
★	Iptacopan[2]	PNH	●●●	Ph3 ongoing	2023
		aHUS		Ph3 ongoing	2025
★	Sabatolimab	HR-MDS	●●●	Ph2 STIMULUS-MDS-1 continues to PFS readout[3]	2022/2023
				Ph3 STIMULUS-MDS-2 ongoing	
		AML		Ph2 STIMULUS-AML-1 ongoing	2024
★	YTB323 CD19 CAR-T	Non-Hodgkin's Lymphoma	●●●	Ph3 start 2022	2024
★	PHE885 BCMA CART-T	Multiple myeloma	●	Ph2 start 2022	2024

Unprobabilized peak sales (USD): ● <1bn ●● 1-2bn ●●● >2bn

1. Could move to early 2023. 2. Peak sales potential based on all studied indications. 3. Planned DMC readout for CR completed, study continues blinded to PFS readout, with submission in 2022/2023 using PFS and/or OS outcomes of Ph2 and/or Ph3 trial.

Recent data releases support progression of our mid-stage pipeline

Cosentyx HS

Primary efficacy endpoint was met in both Ph3 studies SUNSHINE and SUNRISE

Iptacopan

C3G: 45% proteinuria reduction; EMA PRIME

PNH: Ph2 substantial reduction in intra- & extravascular hemolysis; FDA BTD

JDQ443

Entering Ph3 2L KRAS G12C mutant **NSCLC** in H1 2022, based on ongoing Ph1 study

Ianalumab

Sjögren's Ph2b primary endpoint met, confirming efficacy and good tolerability

Autoimmune hepatitis, SLE and **CLL** studies ongoing

Remibrutinib

Rapid and effective **CSU** disease activity control, with favorable safety in Ph2b

YTB323 / PHE885

T-Charge™ assets to be presented at ASH

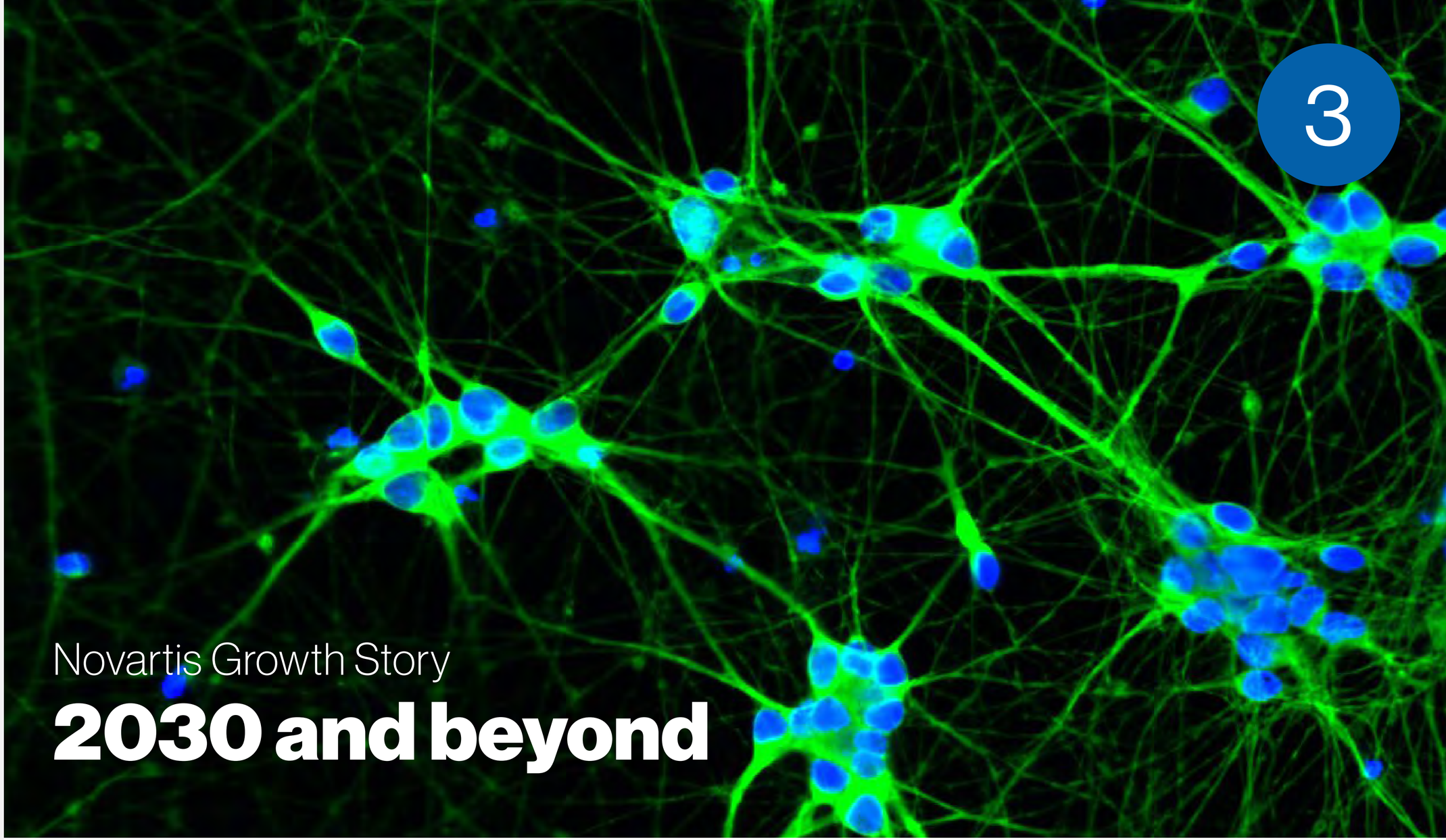
- Anti-CD19 YTB to Ph3
- Anti-BCMA PHE to Ph2

Branaplam

Potential FIC[1] for **Huntington's**

Ph2b initiated based on demonstrated PoC in pre-clinical, Ph1 (healthy volunteers) and SMA studies

1. First-in-class.



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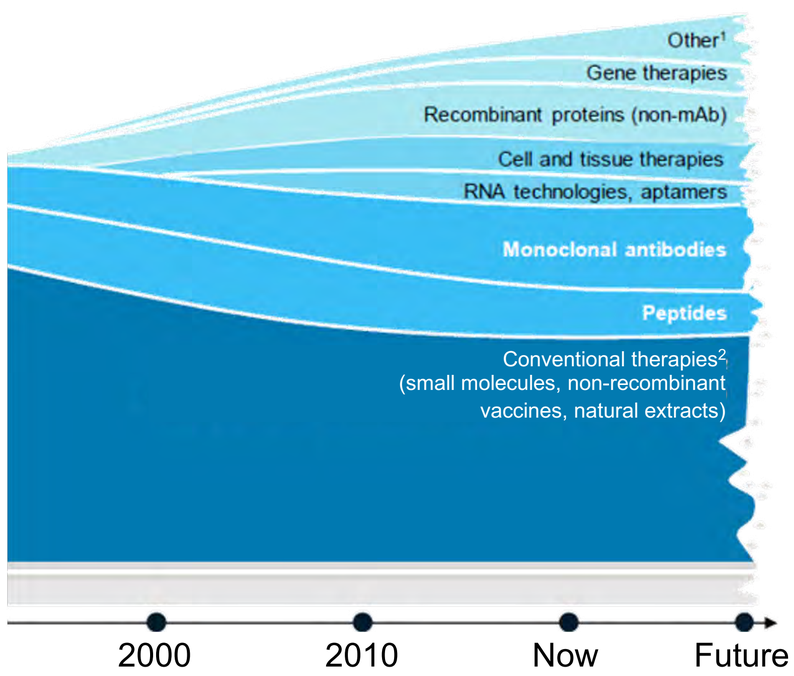
Novartis Growth Story

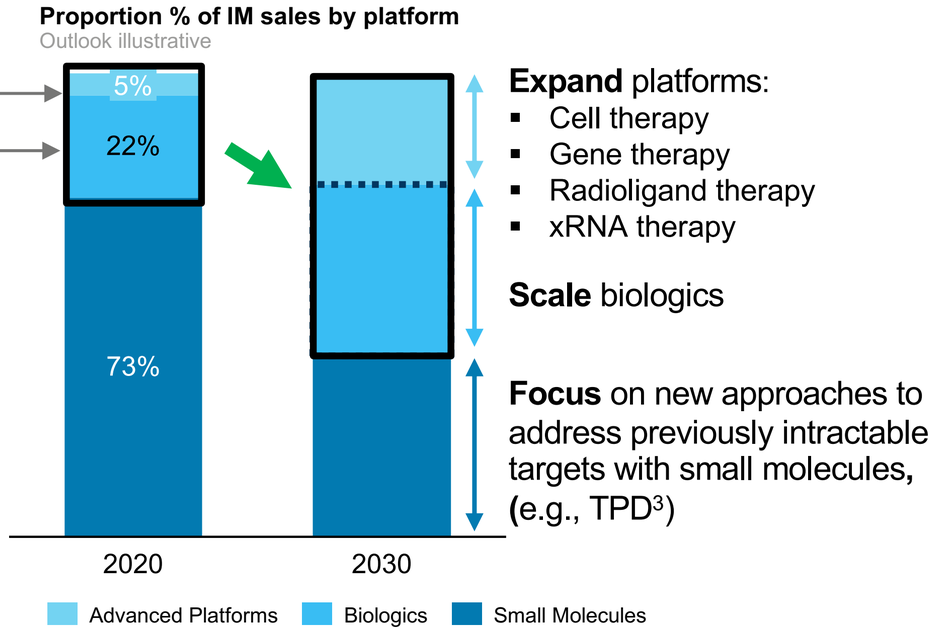
2030 and beyond

The Biopharmaceutical industry is shifting towards new platforms to find the next wave of medicines and we are investing to lead

Global pipeline composition, directional technology outlook



Novartis portfolio shift towards biologics & advanced platforms



Expand platforms:
- Cell therapy
- Gene therapy
- Radioligand therapy
- xRNA therapy

Scale biologics

Focus on new approaches to address previously intractable targets with small molecules, (e.g., TPD[3])

1. e.g. Microbiome, Nanotechnologies, Bioelectronics, Bioengineered vaccines, Protein extracts. 2. Currently ~60% of global clinical pipeline. 3. Targeted Protein Degradation. Source: McKinsey analysis, EvaluatePharma

We take a principled approach to selecting platforms and deploying them in our core therapeutic areas

Principles for platform investments

Broad applicability

Clear differentiation

Advances disease area strategy

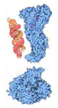
Scalability

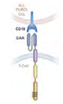
Integration of diverse expertise

Sustained competitive advantage

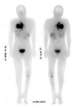
Major Novartis platforms


Chemistry & Chemical Biology | TPD[1]


Biotherapeutics | xRNA[2]


Stem-Progenitor Cell Therapy


Viral Gene Therapy


Radioligand Therapy

Applying our technology across other TAs

	Chemistry	Bio-therapeutics	Cell	Gene	RLT	xRNA
Oncology	■	■	■		■	
Cardio-Renal	■	■				■
Immunology	■	■				
Neuroscience	■	■		■		
Ophthalmology	■	■		■		
Respiratory	■	■				

■ Currently marketed products ■ Potential to expand

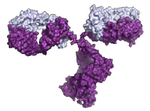
1. Targeted Protein Degradation. 2. xRNA includes RNA targeting LMWs, ASOs, siRNA, mRNA cancer vaccines.

Advancing our biologics / xRNA 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 additional indications

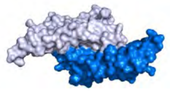
Cosentyx® (secukinumab)

ILARIS® (canakinumab)

15 products on the market[1]

Clinical portfolio
Scaling new therapeutic approaches to the clinic

Peptide therapeutic
(LNA043)



ANGPTL3 agonist for osteoarthritis

Antisense therapy
(Pelacarsen)

~70 projects[2]

Discovery pipeline
Innovating emerging technology

Antibody drug conjugates

Localize payload (small molecule, RNA, radiolabel, etc.) to the Ab's target

Multi-specific and multi-chain

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

~50 projects

1. Based on 2020 Actuals. 2. Clinical development Ph1 to submission.

Continue innovating on small molecules while building strong position in new technology platforms

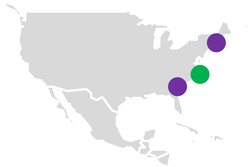
	TPD	Cell	Gene	RLT	xRNA[1]
Existing commercial assets		KYMRIAH	zolgensma® LUXTURNA®	LUTATHERA®	LEQVIO®
Key focus	Unlock previously undruggable targets	Enhance potency, durability and manufacturing efficiency	Explore novel cargos, targeting, and switchable expression	Expand the indication landscape	Explore new approaches in RNA therapeutics
# of projects[2]	12	15	22	12	9
Expected next filing	**2026+**	**2024**	**2025**	**2023**	**2026+**

1 xRNA includes RNA targeting LMWs, ASOs, siRNA, mRNA cancer vaccines. 2. Exploratory to Ph1/2

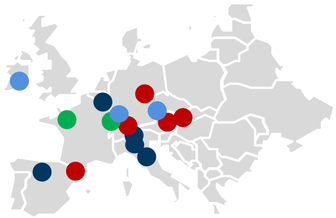
We are a global leader in technical and production capabilities in advanced therapy platforms

Advanced therapies manufacturing footprint

North Americas



Europe



Asia

Biologics (9)
Austria
Belgium
France
Slovenia
Singapore
Switzerland

Cell therapy (3)
France
Switzerland
USA

Gene therapy (2)
USA

RNA (3)
Austria
Ireland
Switzerland

RLT (5)
Italy
Netherlands
Spain

Scaled operations in biologics and advanced therapies

- Building leading supply network across Biologics, Cell therapy, Gene therapy, RNA and RLT
- Deep technical expertise enables support of internal pipeline and to be a partner of choice
- Growing CMO operations with multiple partnership agreements in place

Note: Number in parenthesis indicate count of Novartis' own sites.

Novartis path to leadership in technology platforms

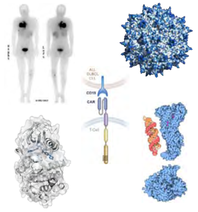
Building on the integrated technology platform strengths across our organization

Depth and breadth across platforms

~70 projects[1]

Development and regulatory experience

Technology platforms



Global footprint

Manufacturing scale and expertise

North Americas

Europe

Asia

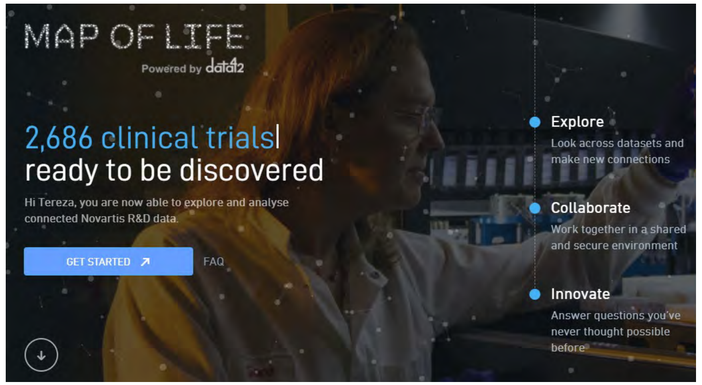
Experience in commercialization

KYMRIAH®
LEQVIO®
LUTATHERA®
LUXTURNA®
zolgensma®

1 Exploratory to Ph1/2

Harnessing the power of data science and AI, alongside external partners, to fuel longer-term growth

Launched Data42 as a data science platform to reimagine medicine, one of the most advanced platforms in the industry



~2,700
clinical trials harmonized

~220
investigations conducted

~700
users onboarded

Data
at our fingertips
days vs. years to find data

60%
active users

Faster
time to insights
weeks vs. months

Other examples include:

Microsoft
Anchor data and AI partnership with enterprise-wide activities

Tencent 腾讯
Digital healthcare solution across chronic heart disease and dermatology

aws
Develop next-generation patient services platform

Key takeaways

1

Clear strategy

Delivering on strategy as a focused medicines company

2

Attractive growth profile

Confident in 4%+ sales CAGR (2020 to 2026) and above peer median beyond 2026

3

Strong mid-stage portfolio

Breadth and depth, up to 20 assets with USD ≥1bn potential, fuel further growth to 2030 and beyond

4

Platform leadership

Continue to develop leadership across technology platforms

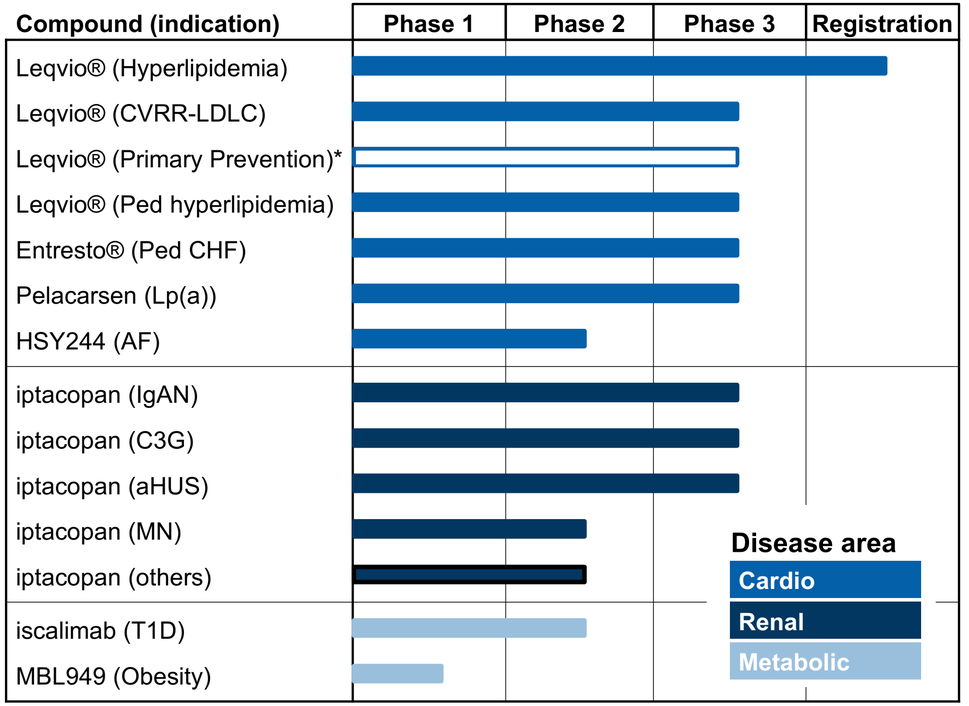
Cardiovascular and Renal

Our CRM strategy is focused on areas of high unmet need, with a strong mid and late-stage pipeline

CRM strategy

- Novel approaches that fundamentally improve **HF outcomes** at scale
- **Dyslipidemia treatments** that improve CV morbidity/ mortality in identifiable high-risk groups with high unmet need and leverage innovative commercial models
- New solutions for chronic and acute **renal specialty indications** with high unmet need and limited/no targeted therapies
- Disease modification therapies for **metabolic disorders**

Assets highlighted today:
Leqvio®, pelacarsen, iptacopan



Note: bars in Gantt chart indicate current phase of development. *Not yet started.

Leqvio®[1] (inclisiran)

First and only siRNA LDL cholesterol lowering treatment

Marketed (EU)

Key highlights

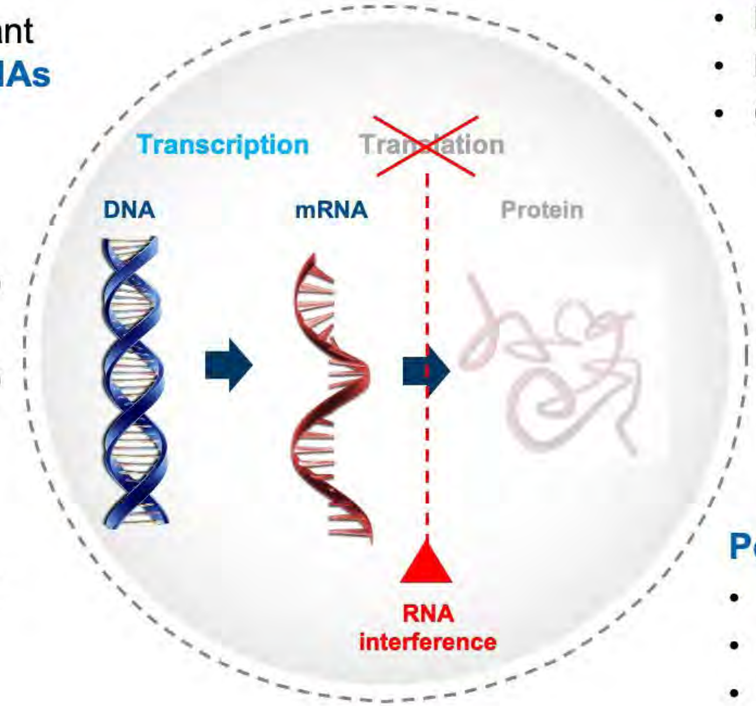
- More than 135m ASCVD patients worldwide and only ~20% reach LDL-C goal in real-world practice despite existing therapies[3,4,5]
- Leqvio® demonstrated effective and sustained LDL-C reduction up to 52% with only two doses a year[2,5] and safety comparable to placebo
- Inclisiran is approved in 50 countries worldwide incl. EU and UK. US FDA review ongoing, launch preparation aligned with expected FDA action date January 1, 2022
- Poised to overcome access, affordability and adherence challenges based on unique product features (twice yearly dosing, HCP administration) and commercial model
- Comprehensive study program including expansion into primary prevention
- US/EU: Patents on composition of matter and use 2035-2036 / Patent on composition of matter 2035[6]

ASCVD – Atherosclerotic Cardiovascular Disease LDL-C – Low Density Lipoprotein Cholesterol 1. Product and brand name are not FDA approved. Currently under FDA review. 2. Given as an initial dose, again at 3 months, and then every six months thereafter. 3. Roth GA, Johnson C, Abajobir A, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. J Am Coll Cardiol. 2017;70(1):1-25. 4. World Health Organization. Cardiovascular diseases (CVDs). https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds). Accessed May 28, 2020. 5. Ray KK et al. N Engl J Med. 2020;382(16):1507-1519. 6. Includes anticipated extended patent term in US and extended patent term in EU. For additional information, please refer to the Novartis 20F 2020.

RNA interference: harnessing a natural process to target LDL-C and Lp(a)

Only **~2%** of the human genome encodes proteins while a significant portion codes for **non-coding RNAs** (ncRNAs)

ncRNAs are involved in **gene regulation**, RNA maturation and protein synthesis



Inclisiran is a **small interfering RNA**

- Double strand (sense and antisense)
- RNA degradation through RISC
- GalNAc conjugated for targeted delivery to liver

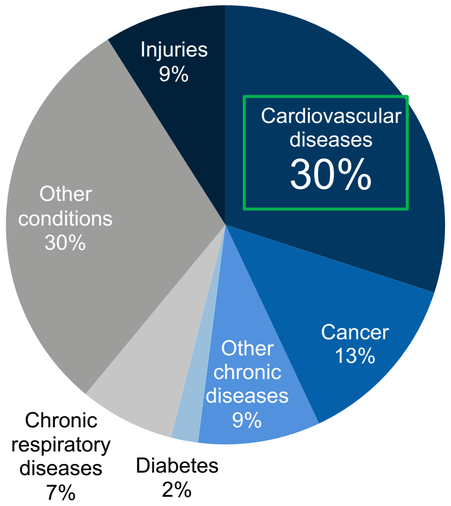
Pelacarsen is an **antisense oligonucleotide**

- Single strand (antisense only)
- RNA degradation by RNase H1
- GalNAc conjugated for targeted delivery to liver

Despite availability of effective treatments, the burden of cardiovascular disease on health systems continues to rise

CVD accounts for more deaths than any other disease[1]

% of deaths



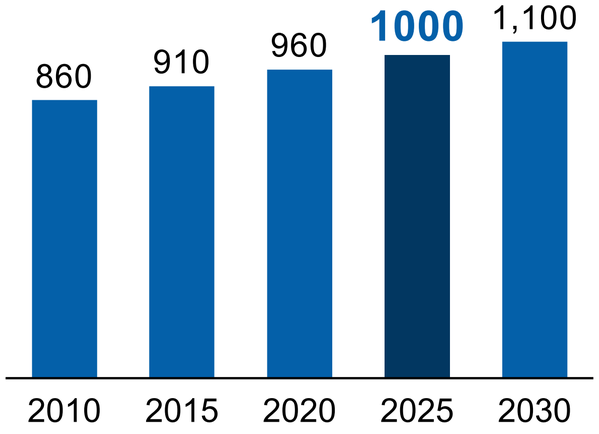
18m lives lost globally to CVD[2]

After years of decline, number of lives lost is on the rise again[3]

~60m patients with ASCVD in US and EU5[4]

Global CVD costs to surpass 1 trillion p.a. by 2025[1]

USD billion



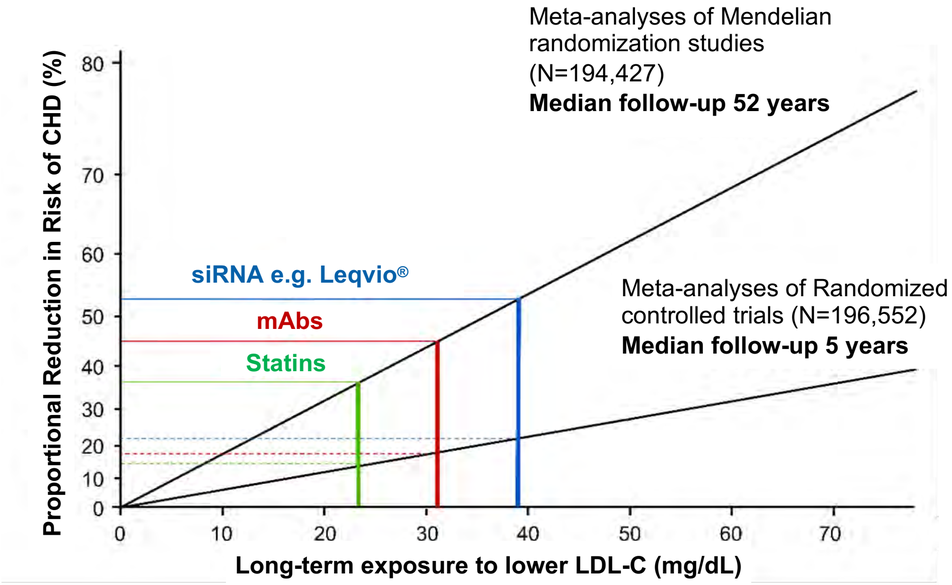
Recurrent heart attacks, strokes and death drive **healthcare costs** (55%) and result in productivity loss (45%)[1]

Total cost 2010-2030 = USD 20 trillion

CVD – Cardiovascular Disease. ASCVD – Atherosclerotic Cardiovascular Disease. 1. Bloom, D.E., et al. (2011). The Global Economic Burden of Noncommunicable Diseases. Geneva: World Economic Forum. 2. World Health Organization. Cardiovascular diseases (CVDs). Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [Last accessed: September 2020]. 3. McClellan M, Brown N, Califf RM, Warner JJ. Call to Action: Urgent Challenges in Cardiovascular Disease: A Presidential Advisory from the American Heart Association. Circulation. 2019;139(9):E44–E54. 4. Decision Resources Group, EU5: Germany, France, Spain, Italy, UK.
Note: The effect of Leqvio® on cardiovascular morbidity and mortality is currently being studied in the ongoing Phase III ORION-4 trial.

50 years of evidence demonstrate that effective and sustained LDL-C reduction improves cardiovascular outcomes*[1,2]

Log-linear association per unit change in LDL-C and the risk of cardiovascular disease[5]



Each mmol/L reduction in LDL-C
reduces the relative risk of ASCVD events by 20% after 3 years and 1.5% in each subsequent year[3]

Relationship between LDL-C and MACE
is supported by clinical trials involving ~500k patients[3,4]

Relation between LDL-C and outcomes
is well established

LDL-C – Low Density Lipoprotein Cholesterol ASCVD – Atherosclerotic Cardiovascular Disease MACE - Major Adverse Cardiovascular Events CV – Cardiovascular 1. Silverman MG, et al. JAMA. 2016;316(12):1289-1297. 2. CTT Collaboration. Lancet 2015;385:1397-1405. 3. Cholesterol Treatment Trialists' (CTT) Collaboration, et al. Lancet. 2010;376(9753):1670-1681. 4. Wang N, et al. Lancet Diabetes Endocrinol. 2020;8:36-49. 5. 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. *The effect of Leqvio® on cardiovascular morbidity and mortality is currently being studied in the ongoing Phase III ORION-4 trial.
Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status.

Guideline evolution recognizes evidence of link between lower LDL-C and improved outcomes[3]

AHA/ACC (2018)[1]

Clinical ASCVD	Very high CVD risk
LDL-C reduction **by ≥50%**	LDL-C reduction **to <70 mg/dL** (1.8 mmol/L)

ESC/EAS (2021)[2]

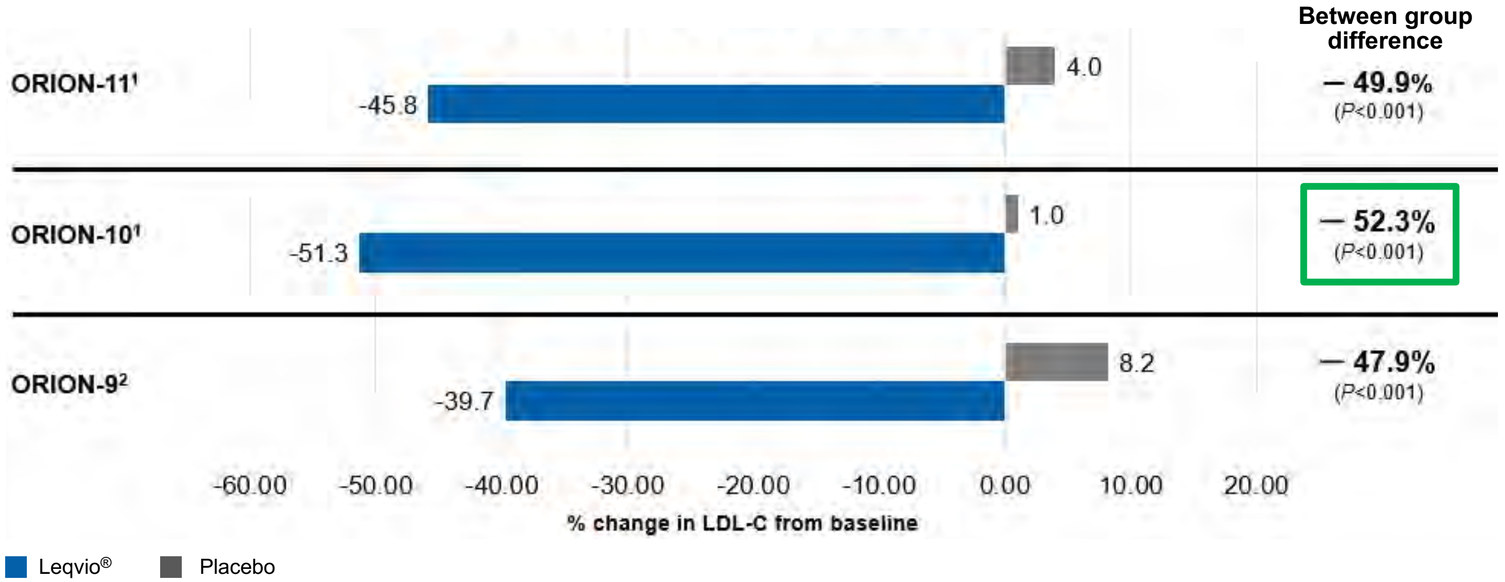
High CV risk	Very high CV risk
LDL-C reduction **to <70 mg/dL** (1.8 mmol/L) and LDL-C reduction **by ≥50%**	LDL-C reduction **to <55 mg/dL** (1.4 mmol/L) and LDL-C reduction **by ≥50%**

LDL-C – Low Density Lipoprotein Cholesterol. AHA – American Heart Association. ACC – American College of Cardiology. ESC – European Society of Cardiology. EAS - European Atherosclerosis Society. ASCVD – Atherosclerotic Cardiovascular Disease. CVD – Cardiovascular Disease. CV – Cardiovascular. 1. Grundy SM, et al. J Am Coll Cardiol. 2019;73(24):3237-3241. 2. Visseren FLJ et al. Eur Heart J. 2021; Sep 7; 42(34):3227-3337. 3. The effect of Leqvio® on cardiovascular morbidity and mortality is currently being studied in the ongoing Phase III ORION-4 trial.

Leqvio® delivers effective and sustained[3] LDL-C reduction of up to 52%[1,2] with twice-yearly[4] HCP-administered dosing

Leqvio® effected significant reductions in LDL-C vs. placebo at Day 510, on top of SoC

Range, -47.9% - 52.3%



Between group difference

— 49.9% (*P*<0.001)

— 52.3% (*P*<0.001)

— 47.9% (*P*<0.001)

Between group difference (in absolute values)

-49.7 mg/dL (P<0.0001)

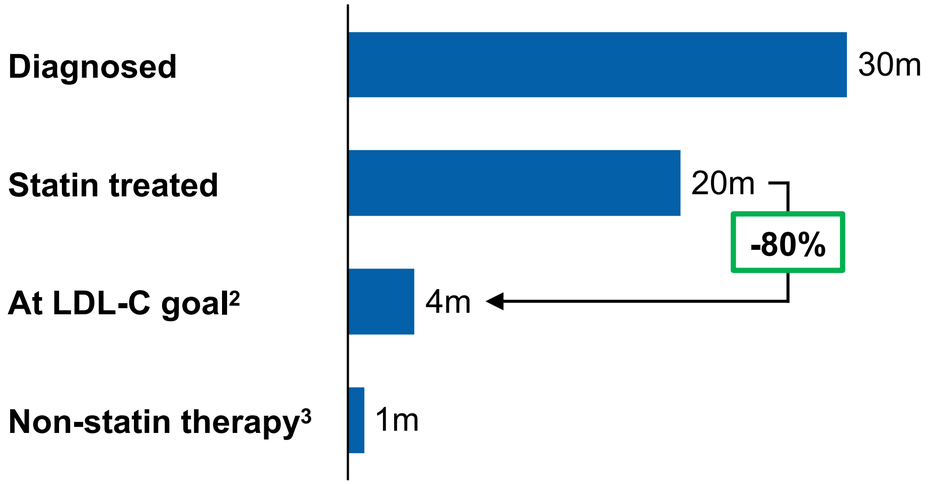
-56.8 mg/dL (P<0.0001)

-69.6 mg/dL (P<0.0001)

LDL-C – Low Density Lipoprotein Cholestero. ASCVD – Atherosclerotic Cardiovascular Disease. 1. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL CholesterolKausik K. Ray, M.D., M.Phil., R. Scott Wright, M.D., David Kallend, M.D., Wolfgang Koenig, M.D., Lawrence A. Leiter, M.D., Frederick J. Raal, Ph.D., Jenna A. Bisch, B.A., Tara Richardson, B.A., Mark Jaros, Ph.D., Peter L.J. Wijngaard, Ph.D., and John J.P. Kastelein, M.D., Ph.D., for the ORION-10 and ORION-11 Investigators*; March 18, 2020, at NEJM.org.DOI: 10.1056/NEJMoa1912387. 2. Inclisiran for the Treatment of Heterozygous Familial HypercholesterolemiaFrederick J. Raal, M.D., Ph.D., David Kallend, M.B., B.S., Kausik K. Ray, M.D., M.Phil., Traci Turner, M.D., Wolfgang Koenig, M.D., R. Scott Wright, M.D., Peter L.J. Wijngaard, Ph.D., Danielle Curcio, M.B.A., Mark J. Jaros, Ph.D., Lawrence A. Leiter, M.D., and John J.P. Kastelein, M.D., Ph.D., for the ORION-9 Investigators*; March 18, 2020, at NEJM.org.DOI: 10.1056/NEJMoa1913805. 3. Across the 6-month dosing interval. Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status. 4. After an initial dose, again at 3 months, and again every six months thereafter. As a strong complement to a maximally tolerated statin

In the US, Leqvio® is positioned to meet the needs of 80% of statin-treated ASCVD patients currently not at LDL-C goal

US ASCVD patient population[1]



Leqvio® is uniquely positioned to address unmet needs in ASCVD

A1 Adherence

Effective and sustained[5] LDL-C reduction with **two doses per year[4]**, generally well-tolerated[1,2]

A2 Access

Medical benefit coverage for majority of patients at launch

A3 Affordability

0 USD expected co-pay for 2/3 patients at launch

ASCVD – Atherosclerotic Cardiovascular Disease. LDL-C – Low Density Lipoprotein Cholesterol. 1. Data on file; American Heart Association. Center for Health Metrics and Evaluation. Accessed at: https://healthmetrics.heart.org/prevalence-and-number-of-us-adults-eligible-for-and-currently-using-statin-therapy-nhanes-2011-2014/; Wong ND. Journal of Clinical Lipidology. 2016;10(5):1109–1118; American Heart Association/American Stroke Association. Cardiovascular Disease: A Costly Burden. 2. <70mg/dL. 3. Non-statin lipid lowering therapies include ezetimibe and PCSK9i mAbs. 4. After an initial dose, again at 3 months, and again every six months thereafter. 5. Across the 6-month dosing interval. Note: Leqvio® is approved in Europe, in the US Leqvio® has investigational status

Inclisiran approved in 50 countries; US PDUFA date January 1, 2022

USA

- FDA review ongoing with PDUFA goal date Jan 1, 2022
- Launch preparation ongoing to enable readiness of health systems, drive awareness and facilitate access

Ex-US

- Approved in 50 countries
  - 30 EU/EEA countries and other countries including UK, Canada, Australia, and Switzerland
  - Launched in more than 10 countries
  - Reimbursement reviews ongoing
- Regulatory reviews ongoing in more than 20 countries

Large integrated program to establish Leqvio® as the standard of care in ASCVD management

Lipid lowering	Outcomes	Healthcare system partnerships	Implementation science and RWE
Registration trials	**Secondary Prevention**	**NHS collaboration**	**Initiation of treatment**
ORION-3 (Ph2 extension) ORION-5 (Ph3 HoFH) ORION-8 (Ph3 extension)	ORION-4 (Oxford) VICTORION-2-PREVENT	VICTORION-SPIRIT (UK)	VICTORION-INITIATE (US)
Geographic expansion	**Primary Prevention**		**Post-ACS**
ORION-14 (China) ORION-18 (China) ORION-15 (Japan)	ORION-17 (Oxford)		VICTORION-INCEPTION (US)
Diverse patient populations			
ORION-13 (V-YOUTH) ORION-16 (V-YOUTH)			

>75,000 patients in >50 countries; program expansion underway

Long-term investment to confirm benefit of Leqvio® on cardiovascular outcomes

Market potential

Indication	Asset potential
Hyperlipidemia[3]	
Secondary prevention (CVRR)	●●●
Primary prevention (CVRR)	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Long-term program involving **~70,000 patients** across **~50 countries**

ORION-4[1]
Secondary prevention

- Evaluate impact of treatment with inclisiran on MACE
- Patients with established ASCVD
- N = 15,000
- Countries: UK, US
- Conducted in collaboration with Oxford University
- Status: Ongoing
- Estimated completion: 2026

VICTORION-2-PREVENT[2]
Secondary prevention

- Evaluate impact of treatment with inclisiran on MACE and CV Death
- Patients with established ASCVD
- N = 15,000
- ~50 countries
- Status: Ongoing
- Estimated completion: 2028

ORION-17
Primary prevention

- Evaluate impact of treatment with inclisiran on MACE
- Subjects 55 years and older
- N = ~40,000
- Country: UK
- Conducted in collaboration with Oxford University
- Status: In planning
- Estimated completion: ~2030

1. ClinicalTrials.gov Identifier: NCT03705234. 2. ClinicalTrials.gov Identifier: NCT05030428. 3. Adult and pediatric hyperlipidemia..

Pelacarsen
(TQJ230)

Antisense oligonucleotide for the reduction of lipoprotein(a)

Phase 3

Key highlights

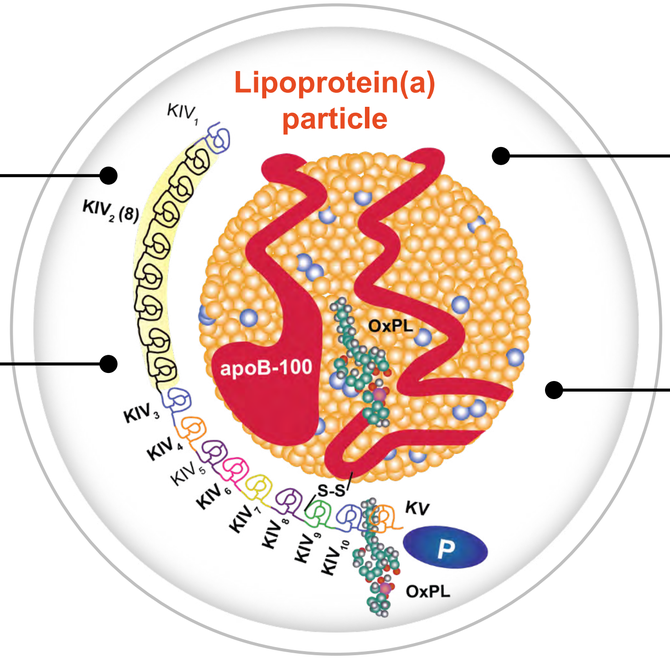
- **1/5 people have elevated Lp(a)** which increases cardiovascular risk ~2-fold[1]
- **No therapies available** to lower Lp(a)
- Pelacarsen is expected to be the **first disease modifying treatment for Lp(a)** and expected to reduce CV risk
- **Focus on population at highest risk** of ASCVD (8m in G7[2]) where pelacarsen has unique effect
- Ph2b data showed **potent and consistent reduction of Lp(a)** with excellent tolerability and safety
- Recruitment for Ph3 outcomes trial HORIZON extended to early 2022 due to COVID-19. Trial **readout expected 2025**
- **US/EU**: Patent on composition of matter (2034/2034)[3]

CV – Cardiovascular ASCVD – Atherosclerotic Cardiovascular Disease 1. Tsimikas S. J Am Coll Cardiol. 2017;69:692-711; Kamstrup PR et al. JAMA. 2009;301(22):2331-9; 2x fold increase if considering 50 md/dL as high. 2. Potential patients defined by the population studied in Lp(a)HORIZON: patients with elevated Lp(a) and MI, stroke or PAD. Potentially eligible population dependent on trial results and label 3. Patent term extensions and regulatory-based exclusivities are possible

Lp(a) is an independent risk factor for ASCVD[1] that cannot currently be treated

Lp(a) is an **independent, inherited and causal risk factor** for CVD, with elevated Lp(a) mediating MI, stroke, and PAD

Lp(a) consists of an **LDL-like particle** which is covalently bound to apo(a)



Lp(a) levels are primarily **genetically determined** and not influenced by diet or exercise

There are currently **no approved therapies** to treat elevated Lp(a)

ASCVD – Atherosclerotic Cardiovascular Disease. Lp(a) – Lipoprotein a. CVD – Cardiovascular Disease. LDL – Low Density Lipoprotein. MI – Myocardial Infarction. PAD – Peripheral Artery Disease. Apo(a) – Apolipoprotein(a). ApoB-100 – Apolipoprotein B-100. KIV – Kringle IV. Lp(a) figure adapted from Tsimikas S. J Am Coll Cardiol 2017;69:692–711. 1. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials. Note: pelacarsen is an investigational product.

Elevated Lp(a) is highly prevalent and one of the strongest genetic CVD risk factors[1-6]

1 in 5 people worldwide have elevated Lp(a)*[1,2]

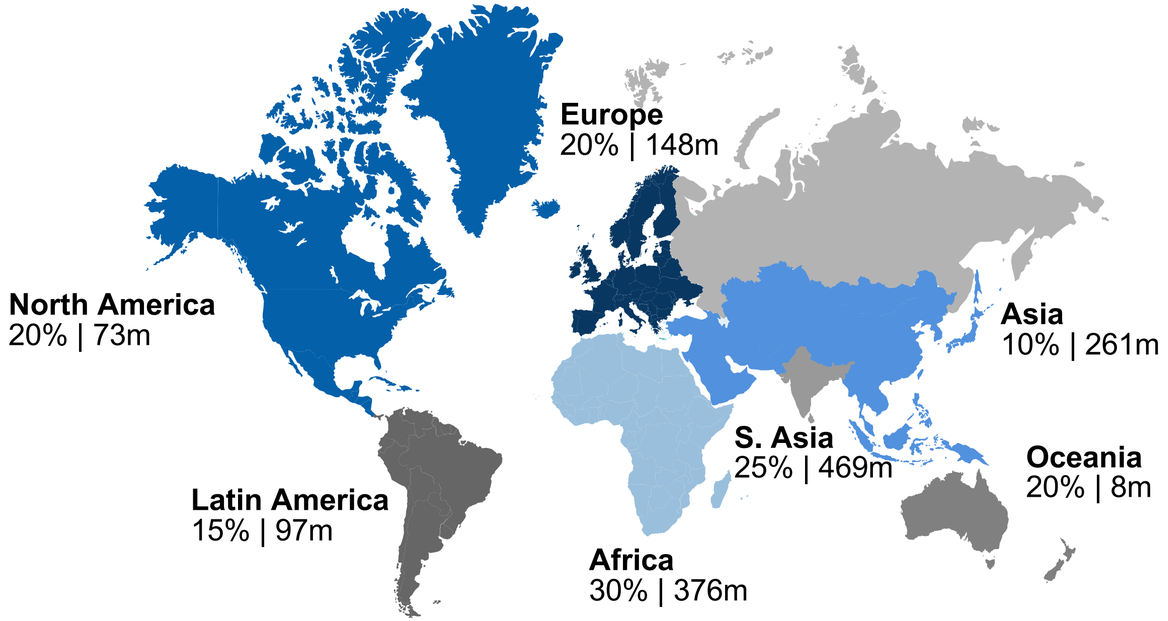
1.4 billion people have elevated Lp(a)*, increasing their ASCVD risk[1,2]

Lp(a) is both the **most common monogenic CVD risk factor** and one of the strongest genetic CVD risk factors[2–5]

Indication	Asset potential
CVRR (Lp(a)) [7]	●●●

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

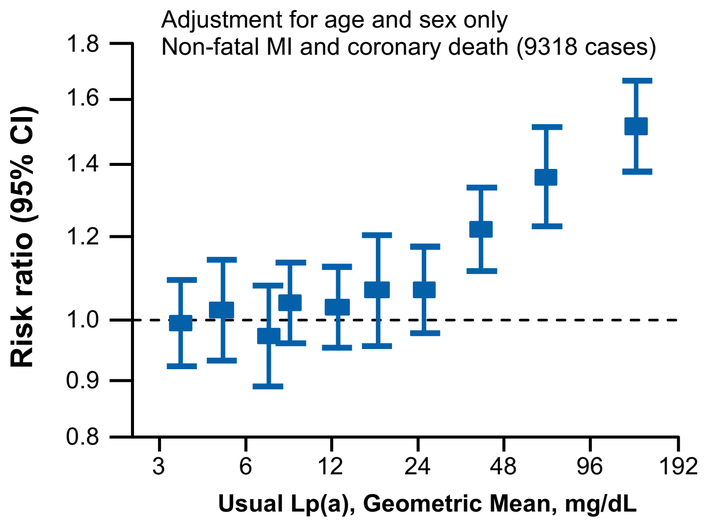
The prevalence of elevated Lp(a)* varies by geography



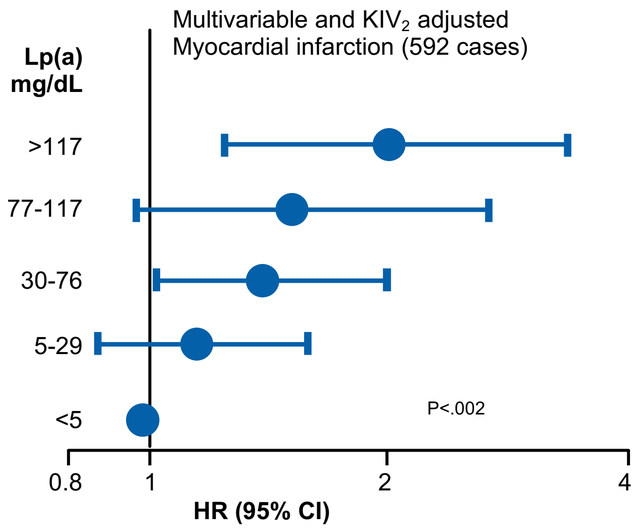
LP(a) – Lipoprotein a. CVD – Cardiovascular Disease. *Lp(a) >50 mg/dL or >125 nmol/L. 1. Tsimikas S et al. J Am Coll Cardiol. 2018;71(2):177–192. 2. Tsimikas S, Stroes ESG. Atherosclerosis 2020;300:1–9. 3. Nordestgaard BG, Langsted A. J Lipid Res. 2016;57:1953–75. 4. Tsimikas S. J Am Coll Cardiol. 2017;69(6):692–711. 5. Clarke R et al. N Engl J Med. 2009;361(26):2518–2528. 6. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trial. 7. Secondary prevention Note: pelacarsen is an investigational product.

Elevated Lp(a) increases cardiovascular risk[5] ~2-fold, a level similar to LDL-C

Lp(a) is an independent, genetic and causal risk factor for MI, stroke and PAD[1,2,3]



Elevated Lp(a) increases risk for CV-events ~2-fold[1,3,4]



CI – Confidence Interval. CV – Cardiovascular. KIV – Kringle IV. Lp(a) – Lipoprotein(a). 1. Tsimikas S. J Am Coll Cardiol. 2017;69:692-711 . 2. Erquo S et al. JAMA. 2009;302(4):412-23. 3. Kamstrup PR et al. JAMA. 2009;301(22):2331-9.
4. 2x fold increase if considering 50 mg/dL as high. 5. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trial. Note: pelacarsen is an investigational product.

Pelacarsen: An innovative approach to reducing Lipoprotein(a)

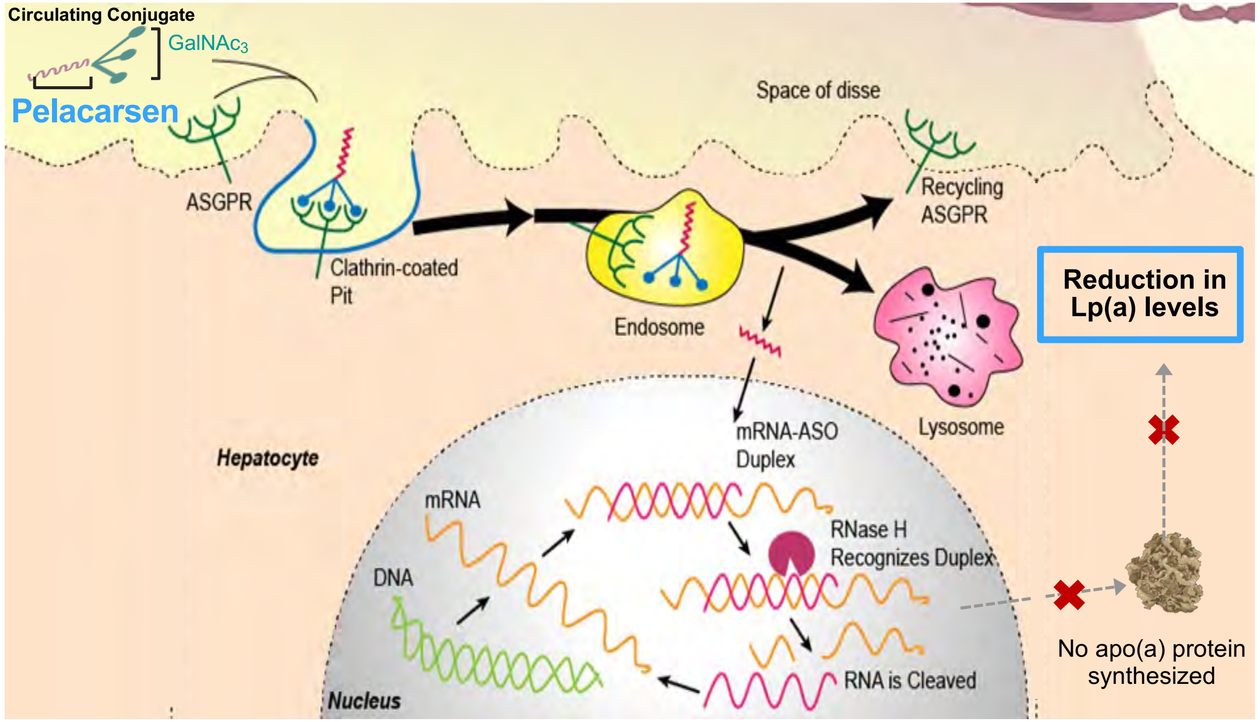


Illustration of Pelacarsen mechanism of action.

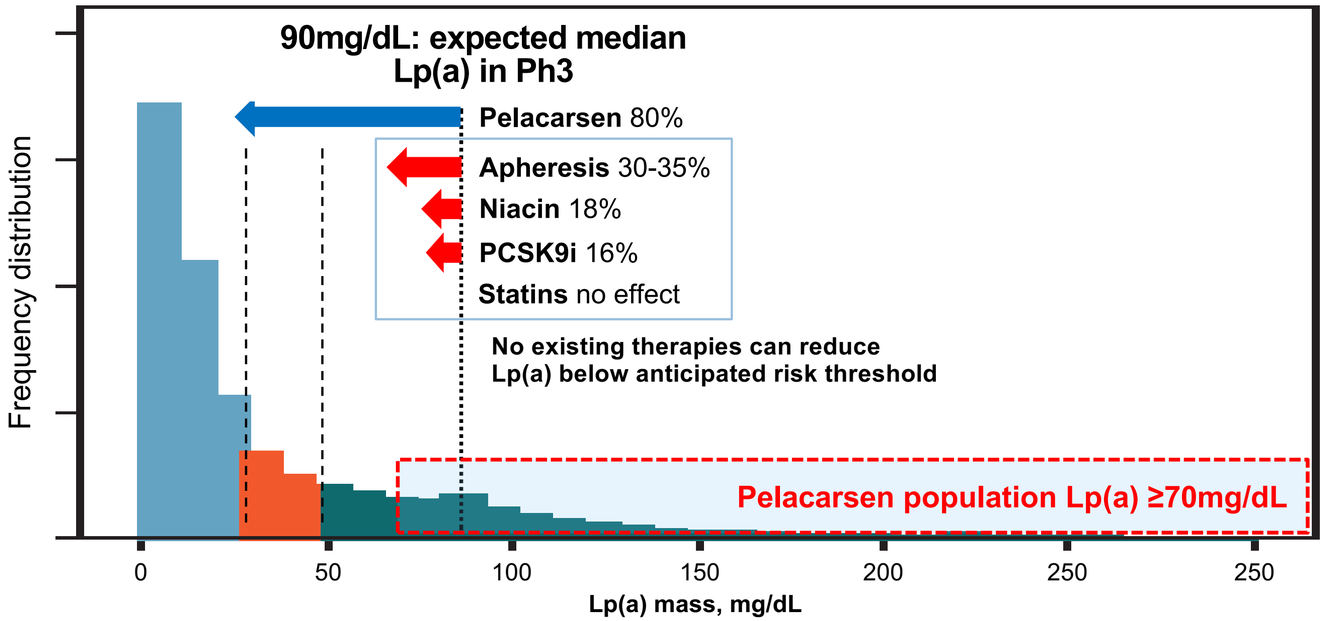
Apolipoprotein(a) is required for the assembly of Lp(a)

Pelacarsen specifically targets Lp(a) production

- Enters hepatocytes through ASGPR
- Binds to apolipoprotein(a) mRNA
- Prevents apolipoprotein(a) synthesis
- Lowers levels of circulating Lp(a)

Pelacarsen is the only therapy that can lower Lp(a) below risk threshold[1] compared to other approaches

Comparison of Lp(a) lowering effect[2]



<30mg/dL: negligible risk
30-50mg/dL: threshold for low risk (sec. prevention)
>50mg/dL: high risk

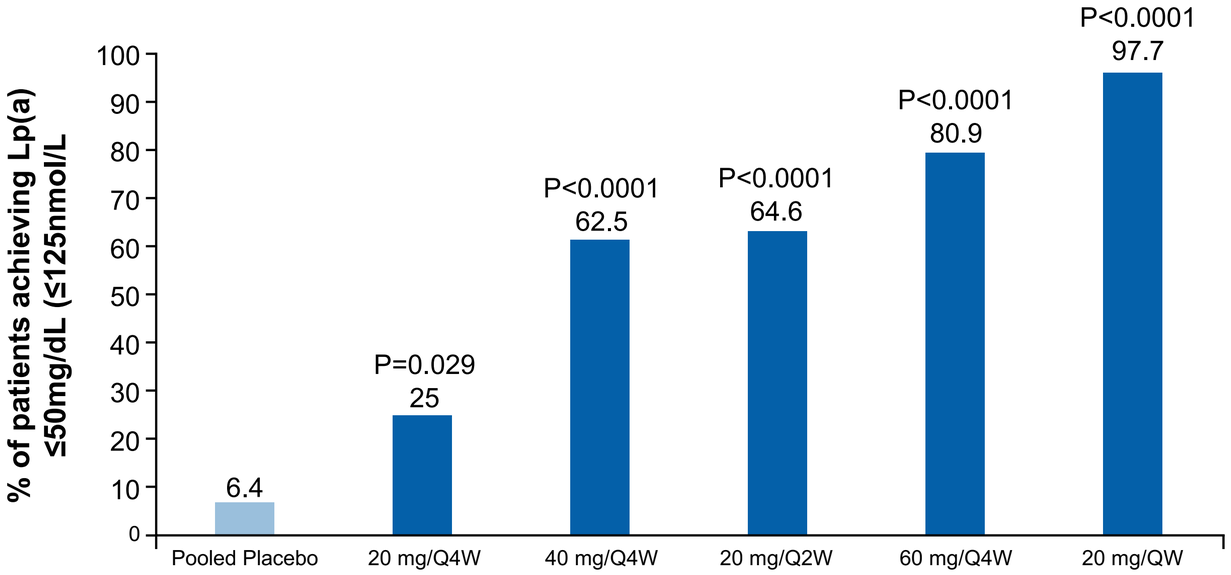
- ✓ In high-risk populations, pelacarsen can bring Lp(a) **below recognized risk thresholds**
- ✓ Focus is on the population at highest risk where powerful efficacy is needed to **show CVRR**[2]

1. Based on Ph2 results, Tsimikas S, et al. N Engl J Med. 2020;382:244–255. 2. Adapted from: Tsimikas, JACC 2017, 69:692–711; Willeit, Lancet 2018; O'Donoghue, EAS 2018; Parish et al, Circ Genom Precis Med. 2018.

Pelacarsen significantly reduced Lp(a) in CVD patients in Ph2b

Ph2b results – pelacarsen vs. placebo

NEJM Tsimikas, et al. 2020



P-values represent comparison to pooled placebo

Ph2b data showed:

- Lp(a) levels were reduced to ≤50mg/dL in 98% of CVD patients following treatment with pelacarsen 20mg once a week
- Dose-dependent Lp(a) reductions up to 80%
- Good tolerability and safety profile

80mg monthly is being evaluated in Ph3

Lp(a) - Lipoprotein a. CVD - Cardiovascular Disease. QW - once a week. Souce: Tsimikas, et al. N Engl J Med. 2020;382(3):244-255. Note: pelacarsen is an investigational product.

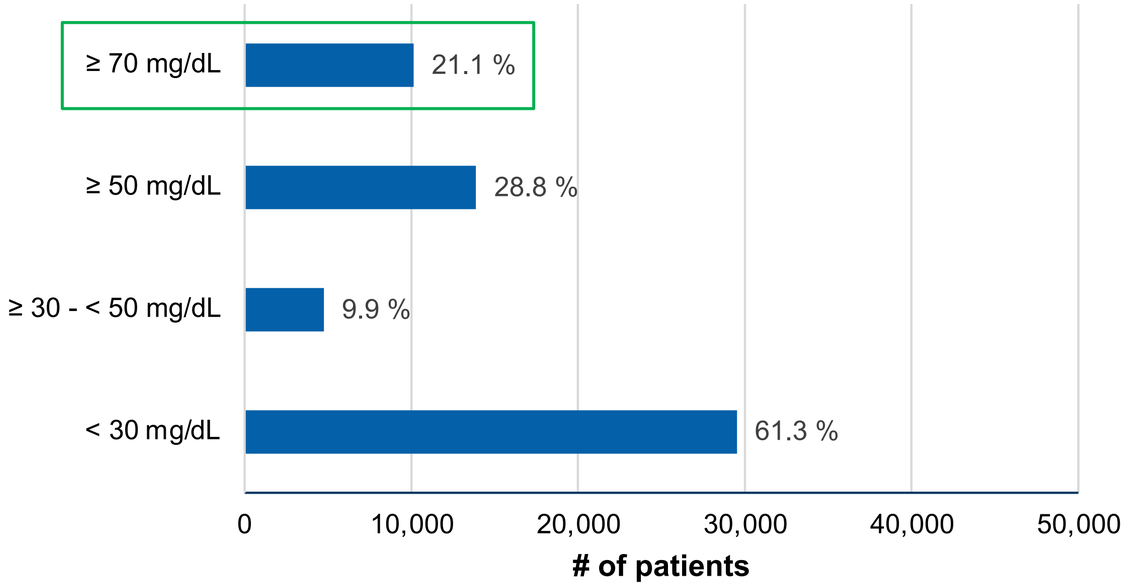
Lp(a) HERITAGE prevalence study found 21% of patients with Lp(a) with ≥ 70mg/dl (HORIZON cut off)

Prevalence study

Lp(a) Heritage Prevalence Study

- Study evaluated prevalence of elevated Lp(a) levels in patients with established CVD
- > 48,000 patients, > 900 sites across 48 countries
- Study initiated April 2019, completed July 2021
- Median Lp(a) levels observed were as expected[1]

Number and percentage of subjects in specific Lp(a) categories



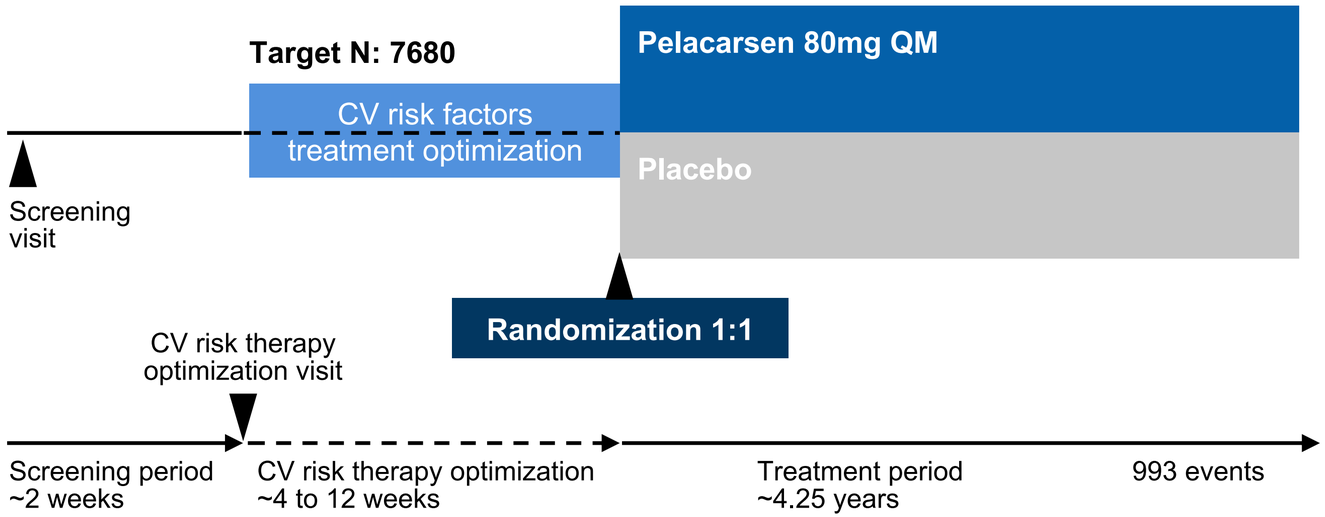
CV – Cardiovascular. MACE - Major Adverse Cardiovascular Event. Lp(a) – Lipoprotein a. 1. Varvel et al. Arterioscler Thromb Vasc Biol. 2016;36:2239-2245

Lp(a)HORIZON - Ph3 CV outcome study ongoing

Readout expected in 2025

Lp(a) Horizon Outcomes Study

Randomized double-blind, parallel group, placebo-controlled, multicenter study to assess effect of TQJ230 on MACE in patients with established CV disease[1]



Study population

Patients with established CV disease (prior MI, stroke, PAD) and Lp(a) ≥70mg/dL

Objectives

Primary endpoint: Time to first occurrence of expanded MACE in the overall study population and in a subpopulation of patients with Lp(a) ≥90mg/dL both tested concurrently.

Secondary endpoints include time to first occurrence of MACE, coronary events composite.

Readout expected in 2025

CV – Cardiovascular. MACE - Major Adverse Cardiovascular Event: MI, stroke, CV death or urgent coronary revascularization. Lp(a) – Lipoprotein a. 1. https://clinicaltrials.gov/ct2/show/NCT04023552. Note: pelacarsen is an investigational product

Urgency to test for Lp(a) is growing in guidelines

NLA, AHA

Awareness of the presence of **elevated Lp(a)** is important, because high Lp(a) increases atherosclerotic cardiovascular disease risk and could inform clinical decision-making regarding risk management

Lp(a) screening: All adults with personal or family history of premature ASCVD, severe hypercholesterolemia, suspected FH

Lp(a) threshold: >50 mg/dL (>100nmol/L) for ASCVD

Treatment: Consider intensification of treatment of LDL and other risk factors

ESC/ EAS

Lp(a) screening: All adults once in a lifetime

Lp(a) threshold: None for ASCVD. Primary prevention patients with >180mg/dL (>430nmol/L) CV risk equivalent to HeFH

Treatment: Consider intensification of treatment of LDL and other risk factors

Lp(a) – Lipoprotein a. NLA – National Lipids Association. AHA- American Heart Association ASCVD – Atherosclerotic Cardiovascular Disease. LDL-C – Low Density Lipoprotein Cholesterol. ESC/ EAS – European Society of Cardiology/ European Atherosclerosis Society. FH – Familial Hypercholesterolemia. CV – Cardiovascular. HeFH - Heterozygous Familial Hypercholesterolemia. Note. The effect of pelacarsen on cardiovascular morbidity and mortality is currently being studied in the HORIZON trials. Pelacarsen is an investigational product.

Iptacopan (LNP023)

Oral Factor B inhibitor targeting the alternative complement pathway

Phase 3

Key highlights

- **Across nephrology** and **hematology**, the iptacopan development program covers indications with limited (PNH[1], aHUS[2], LN[3], ITP[4]) or no approved treatments (IgAN[5], C3G[6], CAD[7], iMN[8])
- By inhibiting the complement pathway, iptacopan **addresses the underlying pathophysiology** of indications in scope with oral convenience, good safety and tolerability based on Ph2 data
- In renal, iptacopan has **disease-modifying potential** and could delay the need for dialysis and/or transplant[9]
- In PNH, iptacopan has 1L potential given it addresses **both intra- and extravascular hemolysis**
- **Pipeline in a pill** with potential to deliver multi-blockbuster revenue
- Positive Ph2 data in PNH, C3G and IgAN. **Ph3 data readouts in PNH (H2 2022), C3G (2023),** and **IgAN (2023[10])**. First filings expected 2023.
- **US/EU**: Patent on compound (2034/2034)[11]

1. PNH = paroxysmal nocturnal hemoglobinuria 2. aHUS = atypical hemolytic uremic syndrome 3. LN = Lupus nephritis 4. ITP = Immune Thrombocytopenic Purpura 5. IgAN = IgA nephropathy 6. C3G = C3 glomerulopathy 7. CAD = cold agglutinin disease
8. iMN = idiopathic membranous nephropathy 9. Orphan Drug Designations: C3G (US/EU), PNH (US/EU), IgAN (EU) 10. 9 months readout may support US submission for conditional approval 11. Patent term extensions and regulatory-based exclusivities are possible.

Pipeline in a pill with global multi-blockbuster potential across several nephrology and hematology diseases

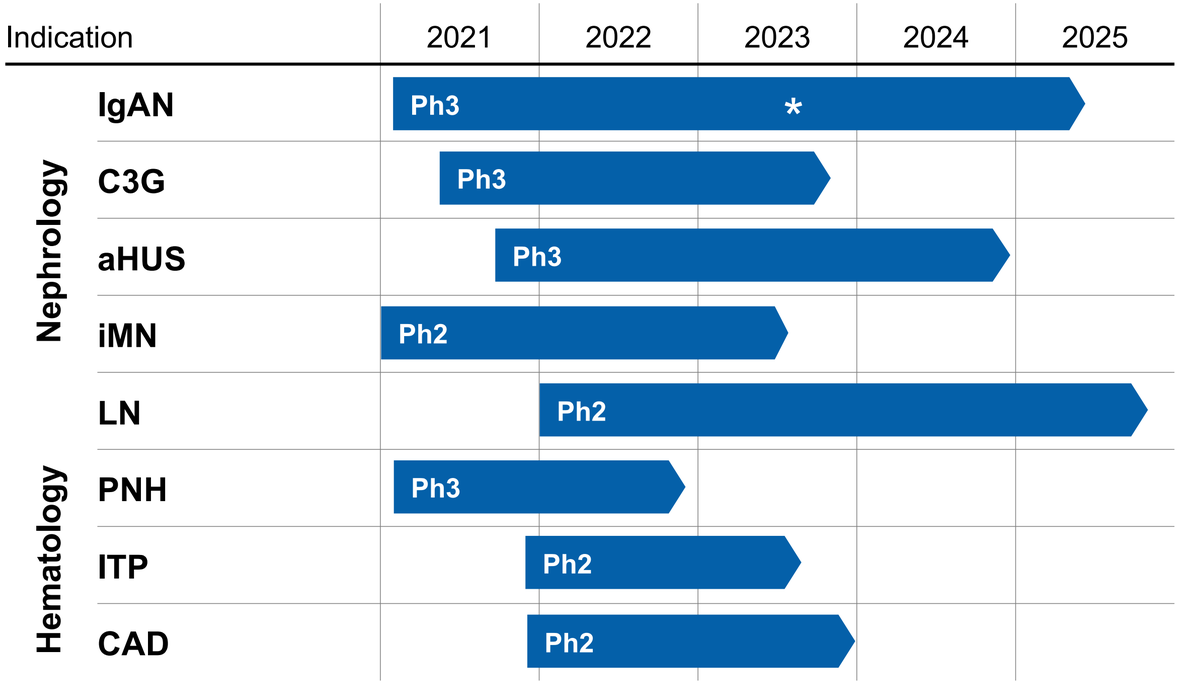
Market potential

Indication	Asset potential[2]
IgAN, C3G, aHUS, iMN, LN, PNH, ITP, CAD	●●●

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Addressable patients

Indication	US prevalence thousands
Ultra-rare	
PNH	<10
C3G	<10
aHUS	<10
CAD	<10
Rare	
IgAN	~46-55[1]
iMN	~80
LN	~100
ITP	~100



* 9 months readout may support US submission for conditional approval

IgAN = IgA nephropathy. C3G = C3 glomerulopathy. aHUS = atypical hemolytic uremic syndrome. iMN = idiopathic membranous nephrpopathy. LN = lupus nephritis. PNH = paroxysmal nocturnal hemoglobinuria. ITP = Immune thrombocytopenic purpura. CAD = Cold agglutinin disease. 1. Estimated number of patients at high risk of progression with proteinuria >1g/day (~25%-30%) Ultra-Rare: < 10 thousand patients 2. Across indications

Iptacopan selectively targets the alternate complement pathway leaving direct signaling through classical and lectin pathways intact

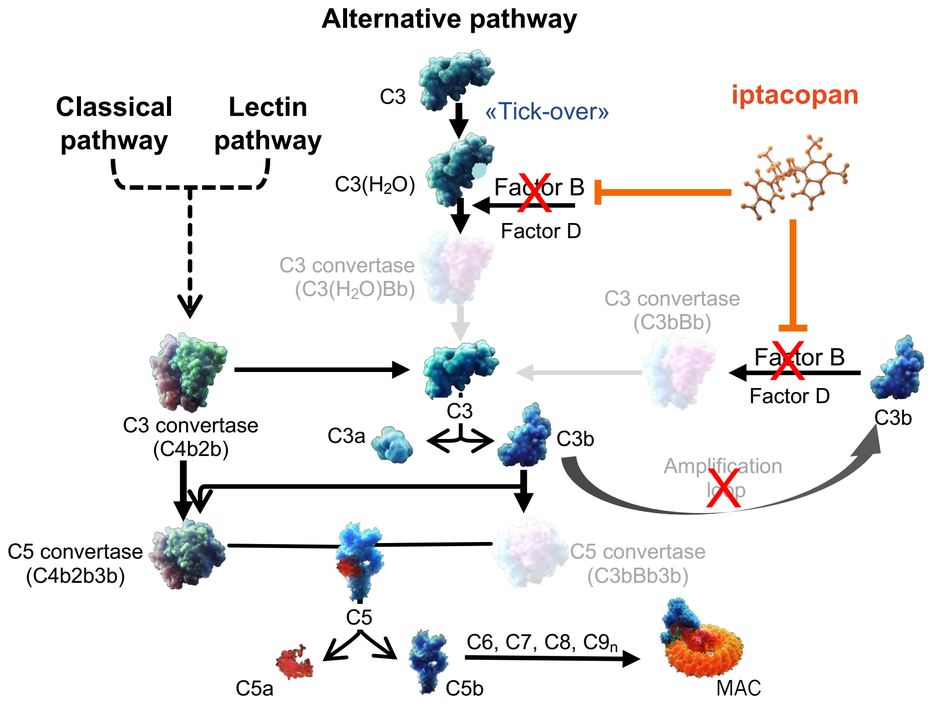
The complement pathway plays a role in a range of rare kidney and hematological diseases

Iptacopan (LNP023) is an **oral,** first-in-class, **potent** and selective small-molecule **inhibitor of factor B (FB)**

Iptacopan binds to FB to suppress the activity of C3 convertase and thus signaling from the alternative complement pathway (AP) and activation of the amplification loop

This prevents downstream generation of the C5 convertase complex, opsonization, and formation of C3a and C5a anaphylatoxins and membrane attack complex (MAC)

Direct classical and lectin pathway signaling remains intact, resulting in a potentially lower meningococcal infection risk in vaccinated patients compared to terminal complement pathway inhibitors

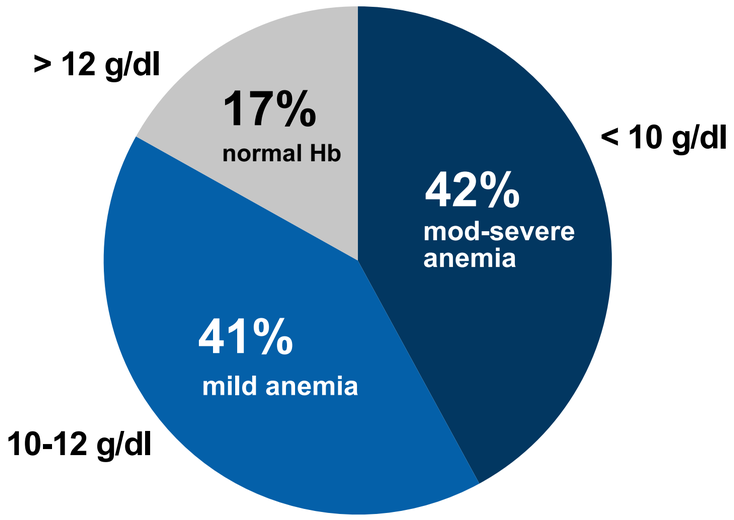


Schubart A et al. Proc Natl Acad Sci U S A 2019;116(16):7926-7931.

PNH

Iptacopan has the potential to be a first line oral anti-complement mono-therapy in patients with PNH

Hematological response to eculizumab[1]



Paroxysmal nocturnal hemoglobinuria (PNH) is a **rare, life-threatening blood disorder caused** by an acquired mutation in hematopoietic stem cells that leads to absence of complement-regulatory proteins

Prevalence: WW 7-16 cases/million; US 5-6k[2]

Many patients remain anemic and transfusion dependent despite eculizumab treatment

- C3-mediated **extravascular hemolysis not addressed** by anti-C5
- ~40% remain **anemic** (Hb[3] <10g/dl) of which ~50% are transfusion dependent[1]

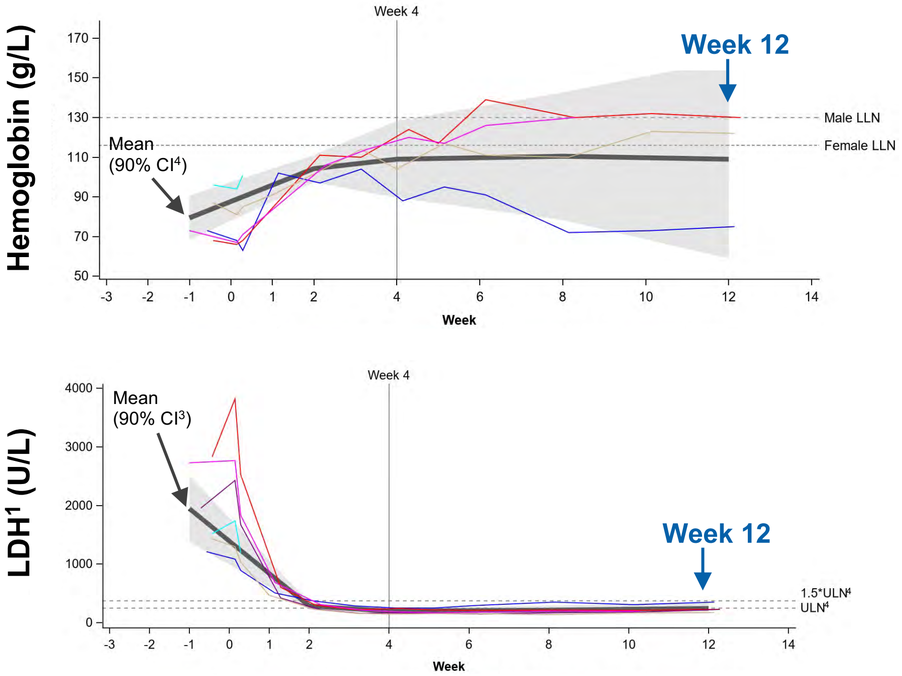
By specifically targeting the complement pathway proximally, **iptacopan could address both intra- and extravascular hemolysis** and thereby address the remaining unmet need in PNH

Interim Ph2 data already showed that iptacopan provides clinical benefits as add-on to eculizumab in patients with residual hemolysis

1. Blood (2019) 134 (Supplement_1): 3517. 2. Petropoulou AD 2010. 3. Hb = Hemoglobin.

Positive Ph2 study shows clinically meaningful increases in hemoglobin

Dose Cohort[1]: 50 → 200mg BID[3]



Data (anti-C5 naive) presented at EHA 2021

- **Primary endpoint** of reducing LDH[1] levels by ≥60% at Week 12 met; LDH reduction was **rapid and durable**
- Patients experienced **rapid, durable increase** in hemoglobin
- All patients except one (blue line) **remained transfusion-free** until Week 12
  - This patient had pre-existing MDS[2], requiring 13 RBC transfusions during the year prior to study entry

1. One patient was excluded for Hb analyses due to an RBC transfusion that occurred between screening and baseline, raising Hb from 71 to 110 g/L. 2. MDS = Myelodysplastic syndrome. 3. BID = twice a day. CI = confidence interval.

PNH

APPLY-PNH Ph3 to show superiority of iptacopan vs. SoC Anti-C5

Population (n ~91)

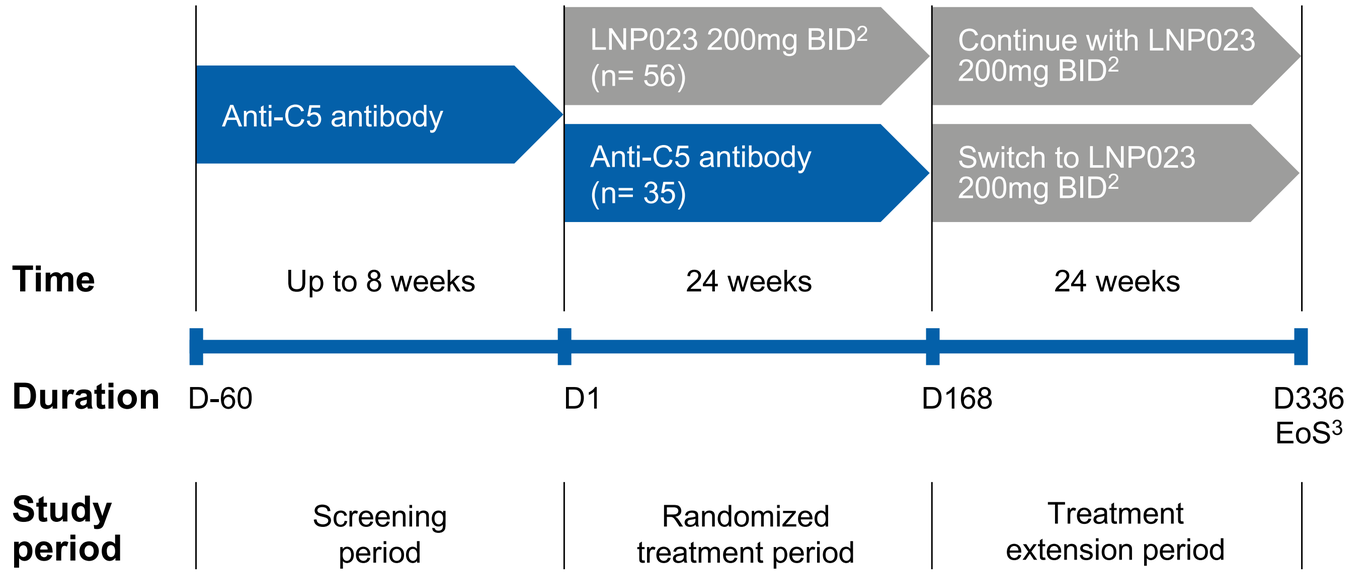
Adult PNH patients (Hb <10g/dL) on a stable regimen of anti-C5 therapy 6 months prior to randomization

Primary endpoints

Proportion of patients achieving increase in Hb ≥2g/dL from baseline in the absence of RBC[1] transfusion

Proportion of patients achieving Hb ≥12g/dL in the absence of RBC[1] transfusion

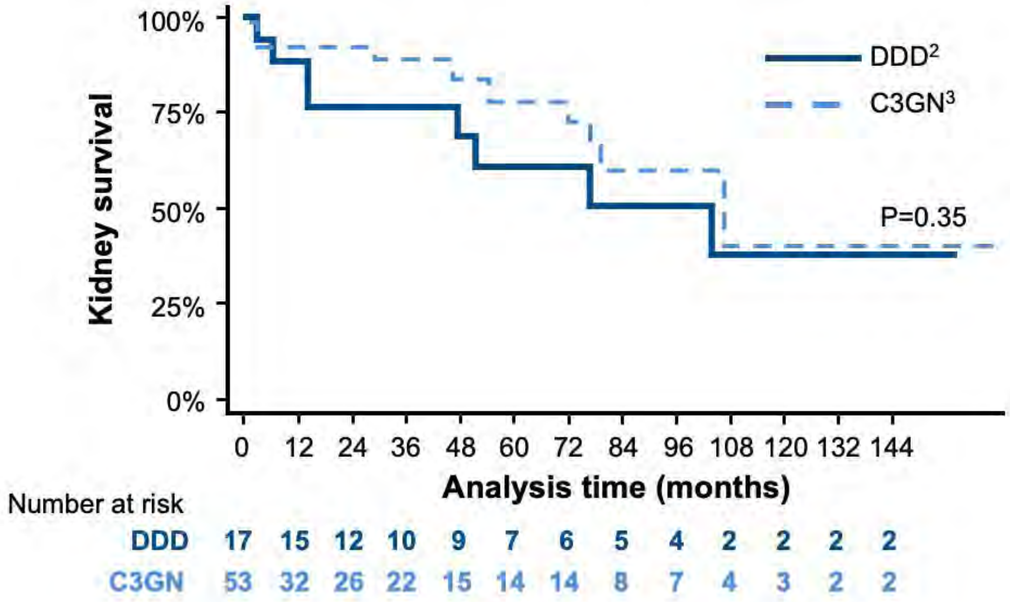
Primary readout expected in H2 2022



1. RBC = Red Blood Cell. 2. BID = twice a day. 3. EoS = end of study.

Iptacopan has potential to be disease modifying, delaying or preventing need for dialysis and/or kidney transplant

K-M analysis of kidney survival[1] by C3G subtype[4]

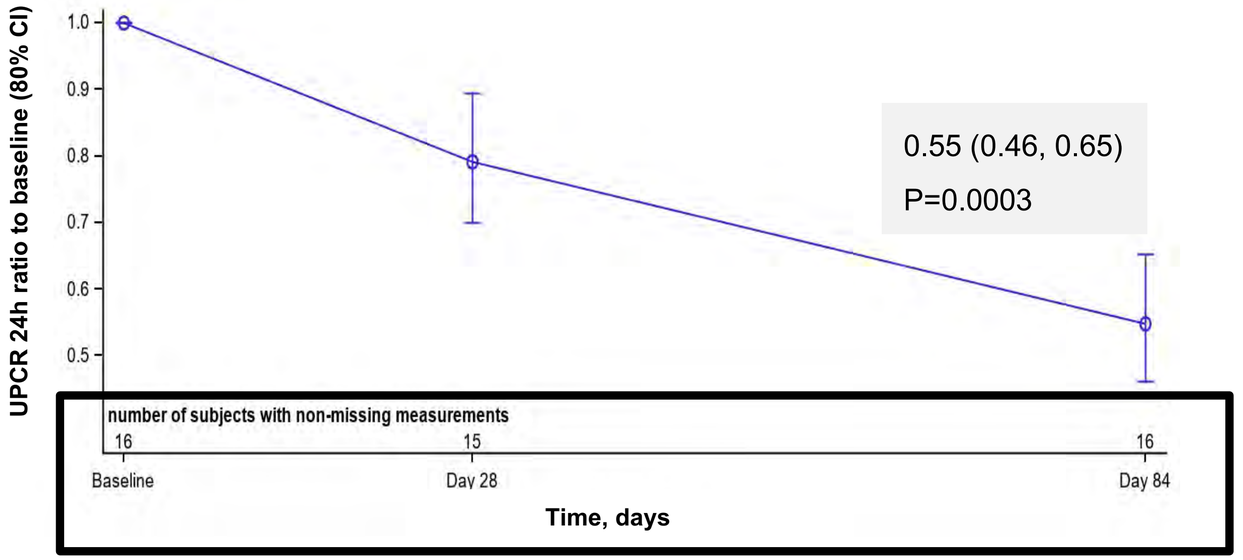


- **C3G** is an **ultra-rare**, severe form of primary glomerulonephritis and is commonly diagnosed in adolescents and young adults
- **Prevalence**: US: ~10k; EU5: ~1.5-2.5k; China: ~32k; Japan: ~3.2k
- There are currently **no approved therapies**
- **~50%** patients develop **kidney failure within 10 years** of diagnosis
- **Post-transplantation recurrence** and allograft loss **is common** (50% in DDD², 75% in C3GN³)
- Characterized by complement dysregulation and complement C3 deposition in the kidney
- In C3G, iptacopan has the **potential to be disease modifying** and to delay, or even prevent, the need for dialysis and/or transplant

1. End-stage kidney disease (ESKD) free renal survival. 2. Dense Deposit Disease. 3. C3 glomerulonephritis. 4. Medjeral-Thomas et al. Clin J Am Soc Nephrol. 2014;9(1):46-53.

Ph2 showed clinically meaningful 45% reduction in proteinuria...

UPCR[3] (24h urine collection) vs. baseline over time[1]



Primary endpoint data presented at ASN 2021

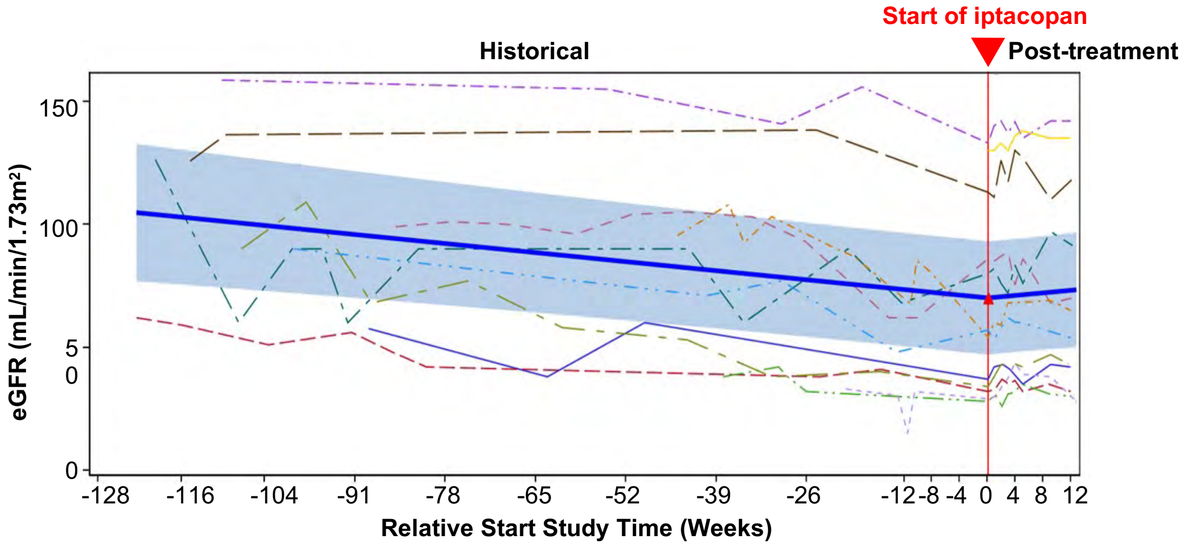
- **Significant and clinically meaningful reduction** in proteinuria of **45%** from baseline
- **Statistically significant reduction in C3 protein deposits** observed in transplanted kidneys
- Favorable safety and tolerability profile

1. Note: all patients from cohort A (with native kidney). 2. Caravaca-Fontan, Nephrol Dial Transplant 2021 Mar 29;gfab075. 3. UPCR = Urine protein to creatinine ratio.

C3G

... with improvements in trajectory of renal function decline compared to historical patients' trend

Mean eGFR[1] slope and 95% CI[2] indicated by bold blue line and surrounding shadowed area



Data presented at ERA-EDTA 2021

- Iptacopan treatment leads to **stabilization of renal function already at 3 months**
- Estimated effect corresponds to a mean predicted eGFR preservation of 6.4 mL/min/1.73m^2 over 12 weeks (p=0.0459)

Individual patient eGFR slopes (n=12) for up to 2 years prior to and following commencement of 12-week course of iptacopan

1. eGFR = estimated glomerular filtration rate. 2. CI = confidence interval.

APPEAR-C3G Ph3 ongoing to support global regulatory submissions

Population

Adult patients with **biopsy-confirmed C3G and native kidney**. Proteinuria ≥1g/g (24h UPCR[1])

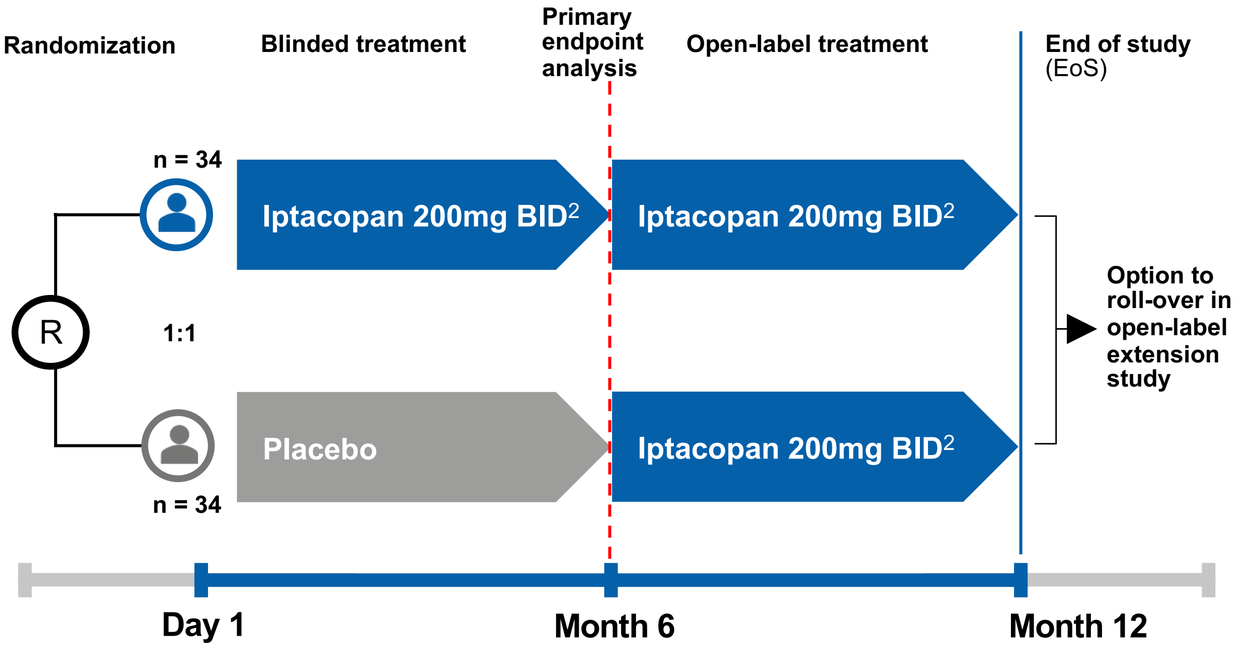
Primary objectives

Proteinuria reduction at 6 months

Secondary objectives

eGFR[3], proportion achieving a composite renal endpoint, reduction in glomerular inflammation, safety and tolerability

Readout expected in 2023

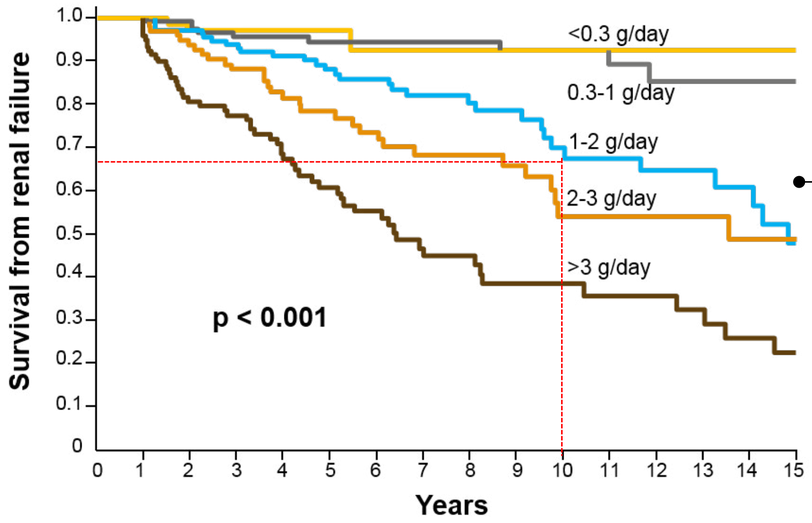


1. UPCR = urinary protein to creatinine ratio. 2. BID = twice a day. 3. eGFR = estimated glomerular filtration rate

IgAN

Iptacopan could potentially delay the need for dialysis and/or transplant

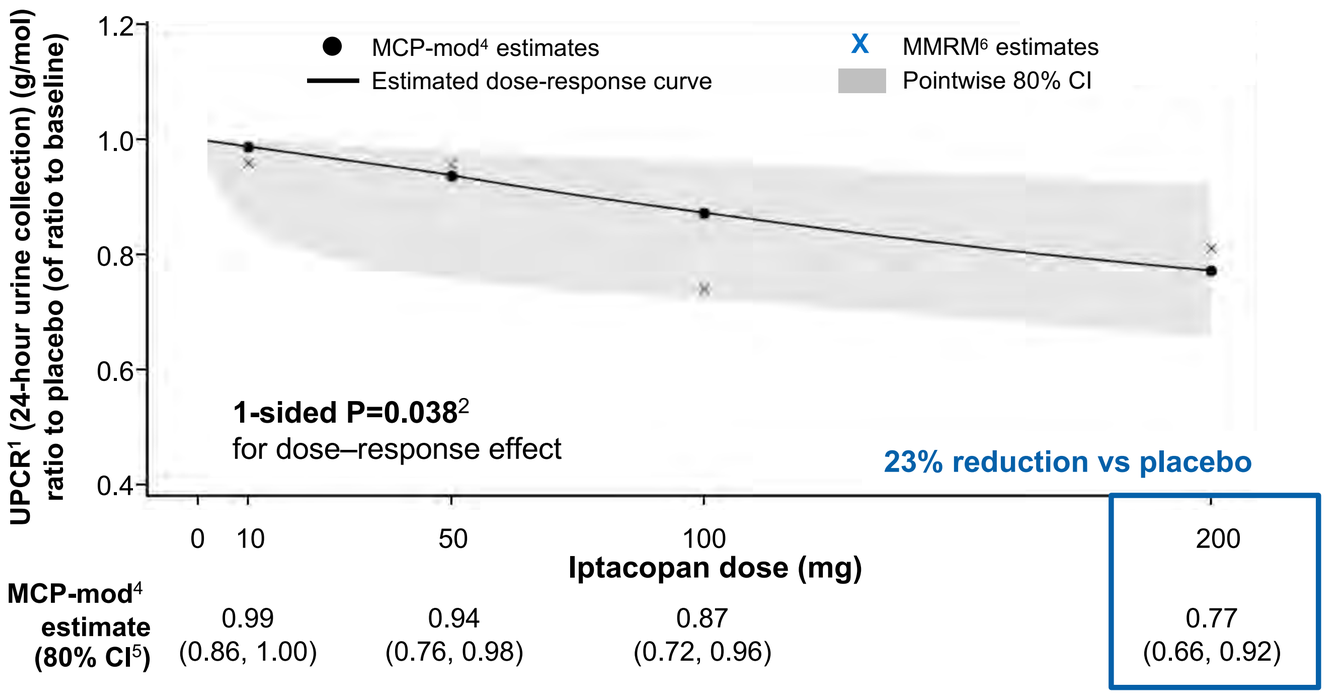
TA[3]-proteinuria: the strongest clinical predictor for IgAN kidney function decline[2]



- **Most common primary glomerulonephritis,** most common cause of kidney failure in young adult Caucasians[1]
- **Prevalence:** US: ~185k; EU5: ~32-51k; China: ~1m; Japan: ~130k
- **Standard of care (SoC):** currently no approved therapies, focus on supportive care
- **Proteinuria** ≥1g/day is the strongest risk factor for poor prognosis in IgAN: ~30% of patients with proteinuria 1-2 g/day progress to kidney failure within 10 years
- **Proteinuria reduction is an important clinical goal in IgAN** and a relevant endpoint for accelerated registration pathways by FDA and other authorities
- **Activation of the alternative pathway (AP)** is present in almost **90% of biopsies**
- By targeting the AP, iptacopan has the **potential to slow disease progression** and delay the need for dialysis and/or transplant

1. Nair R, Walker PD. Kidney Int 2006;69:1455-83. 2. Reich HN et al. J Am Soc Nephrol 2007;18:3177–183. 3. TA = time averaged.

Ph2 showed 200mg BID[3] led to a clinically meaningful proteinuria reduction of 23% at Day 90



Primary endpoint data presented at ERA-EDTA 2021

- Statistically **significant dose-response in proteinuria reduction**[8] versus placebo at 90 days
- **Iptacopan 200mg BID**[3] **led to a 23% proteinuria reduction** (80% CI: 8%, 34%)
- Encouraging trend to **early stabilization of renal function (eGFR**[7]**)**
- **Favorable safety and tolerability profile**; no serious infections
- **Further UPCR reduction at day 180** when compared to day 90

1. UPCR = Urine protein to creatinine ratio 2. Multiplicity-adjusted P-value; analysis adjusted for baseline UPCR (24-hour) and ancestry 3. BID = twice daily 4. MCP-mod = Multiple Comparison Procedure – Modelling
5. CI = confidence interval 6. MMRM = mixed model repeated measurements 7. eGFR = estimated glomerular filtration rate 8. 24-hour UPCR

APPLAUSE-IgAN Ph3 study provides the basis for potential filing on proteinuria reduction (IA)

Population

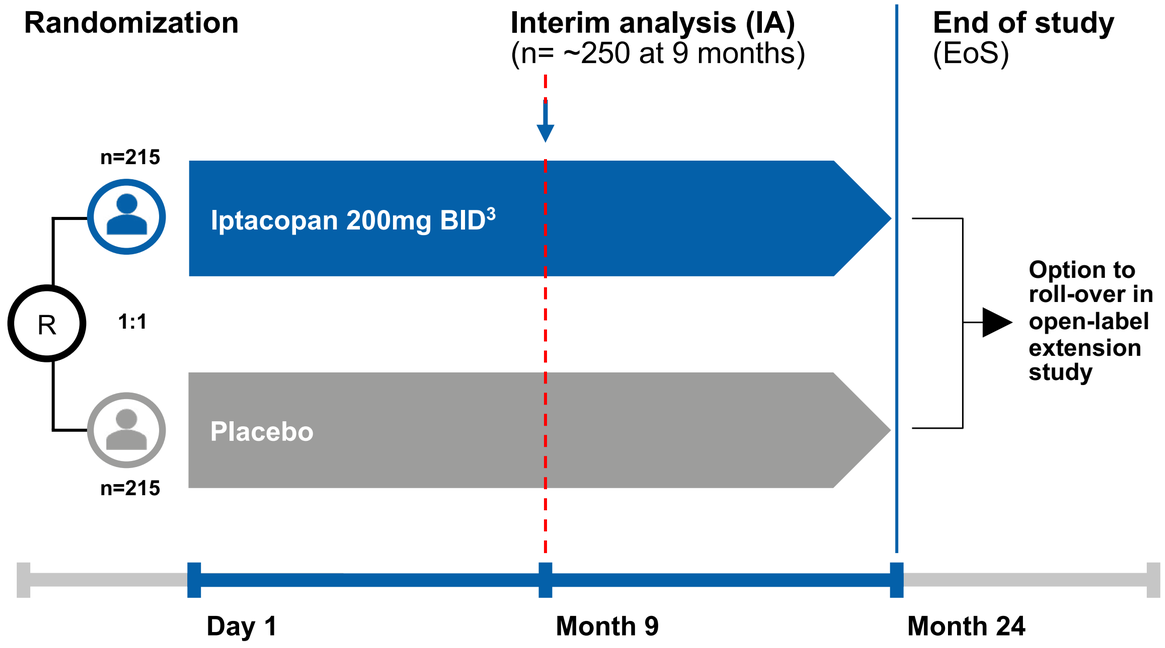
Biopsy-confirmed IgAN patients **at risk of progression** with elevated proteinuria (UPCR[2] ≥1g/g) **despite being on stable background therapy**[1]

Primary objectives

IA: Assess superiority of iptacopan vs. placebo in reduction of proteinuria[2] at 9 months; **to support regulatory submission for accelerated/conditional approval**

EoS: Assess superiority of iptacopan vs. placebo in **slowing progression of IgAN** measured by annualized total slope of eGFR decline over 24 months

Readout expected in 2023 (IA) and 2025 (EoS)



1. Including at least maximally tolerated dose of ACEi/ARB for at least 90 days. 2. UPCR (urine protein-to-creatinine ratio) from 24-h urine collection. 3. BID = twice daily.

Immunology, Hepatology & Dermatology

In IHD, we are deepening our presence in Rheumatology and Dermatology

IHD strategy

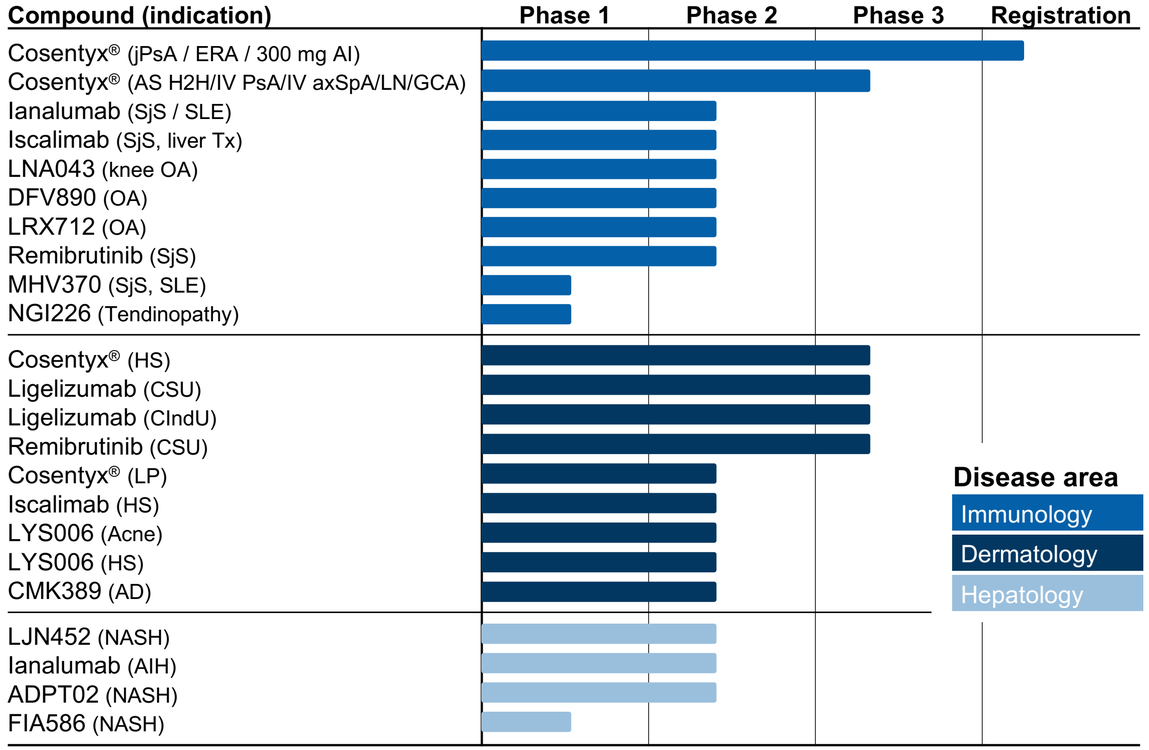
Focus on areas of highest need in rheumatology

- Deliver strong growth in SpA while capitalizing on LCM in areas of high unmet need
- Advance multiple assets in Sjögren's and Lupus to provide value to patients, HCP and HCS: ianalumab, iscalimab, remibrutinib, MHV370
- Fast-forward in osteoarthritis with LNA043

Become #1 in immuno-dermatology

- Expand Cosentyx leadership in dermatology through LCM e.g., in Hidradenitis Suppurativa
- Establish global leadership in CSU with ligelizumab and remibrutinib
- Accelerate Atopic Dermatitis portfolio

Assets highlighted today: Cosentyx®, ligelizumab, remibrutinib, ianalumab, LNA043



AD: Atopic dermatitis; AIH: Autoimmune Hepatitis; axSpA: axial Spondyloarthritis; CIndU: Chronic Induced Urticaria; CSU: Chronic Spontaneous Urticaria; ERA: Enthesitis related Arthritis; GCA: Giant Cell Arteritis; HS: Hidradenitis Suppurativa; IV PsA/axSpA: PsA and axSpA intravenous regimen; JPsA: Juvenile Psoriatic Arthritis; LN: Lupus Nephritis; LP: Lichen Planus; NASH: Non Alcoholic Steato-Hepatitis; OA: Osteoarthritis; PsA: Psoriatic Arthritis; SjS: Sjögren's Syndrome; SLE: Systemic Lupus Erythematosus; Tx: Transplant
Note: bars in Gantt chart indicate current phase of development.

Cosentyx® (secukinumab)

Fully human interleukin-17 inhibitor for psoriasis, psoriatic arthritis and axial spondyloarthritis

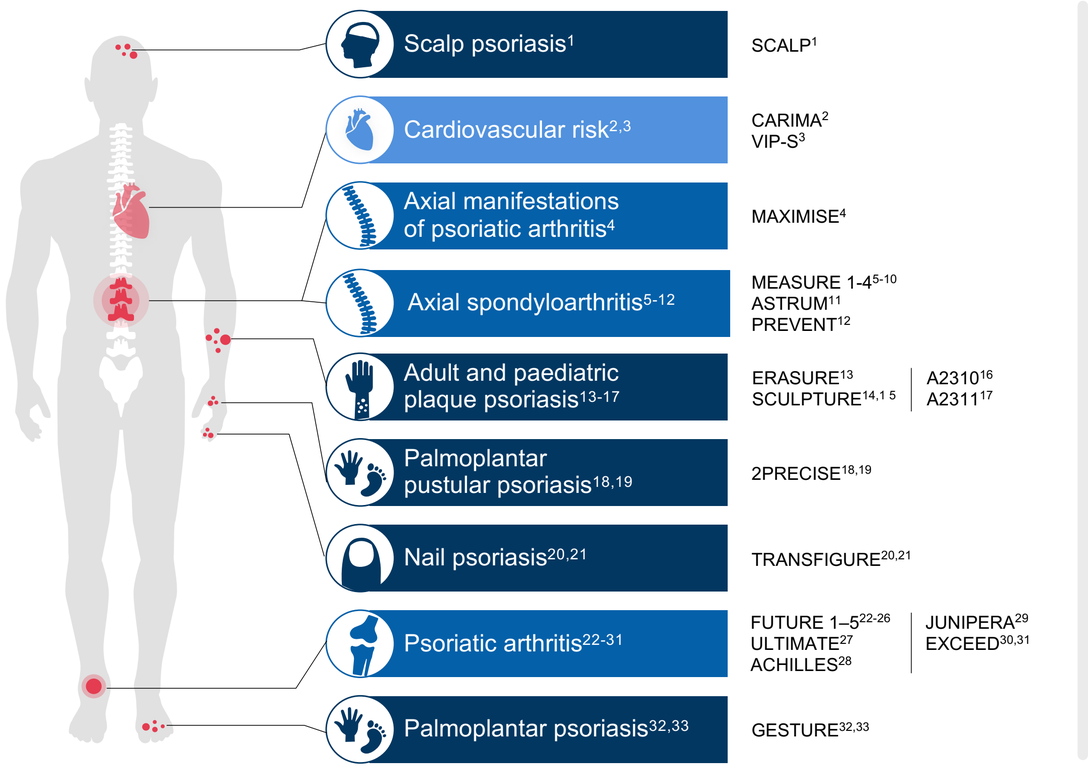
Marketed; LCM in Phase 2, 3

Key highlights

- Proven efficacy with **strong evidence in skin and joints**, >6 years of real-world experience, **reaching >500k patients** across 4 anchor indications (PsO, PsA, AS, nr-axSpA)
- LCM leading up to a **potential 10+ total indications** in areas of high unmet need (HS, LP, GCA, LN, JPsA and ERA), raising the **total addressable population to 10m patients**
- HS next growth opportunity. Ph3 studies met primary endpoint. Filing planned for 2022
- 3+ potential **formulation and dosing enhancements** with IV, 300mg autoinjector, PsO flexible dosing. IV submission in 2022
- **Peak sales expectations at least USD 7bn** driven by greater use of biologics, growth in China and comprehensive LCM
- **US/EU**: Patents on composition of matter and use (2029-2033/2030-2031)[1]

PsO = Psoriasis; PsA = Psoriatic Arthritis, AS = Axial Spondyloarthritis, axSpA = Axial Spondyloarthritis, HS = Hidradenitis suppurativa, LP = Lichen planus, GCA = Giant Cell Arteritis, LN = Lupus Nephritis, JPsA = Juvenile Psoriatic Arthritis, ERA = Enthesitis-related arthritis, LCM = Lifecycle Management, IV = Intravenous 1. Includes extended patent terms. For additional information, please refer to the Novartis 20F 2020.

100+ trials reinforcing Cosentyx' comprehensive efficacy and consistent safety across all key facets of PsO, PsA and axSpA



Scalp psoriasis[1]	SCALP[1]		
Cardiovascular risk[2,3]	CARIMA[2] VIP-S[3]		
Axial manifestations of psoriatic arthritis[4]	MAXIMISE[4]		
Axial spondyloarthritis[5-12]	MEASURE 1-4[5-10] ASTRUM[11] PREVENT[12]		
Adult and paediatric plaque psoriasis[13-17]	ERASURE[13] SCULPTURE[14,1 5]	A2310[16] A2311[17]	
Palmoplantar pustular psoriasis[18,19]	2PRECISE[18,19]		
Nail psoriasis[20,21]	TRANSFIGURE[20,21]		
Psoriatic arthritis[22-31]	FUTURE 1–5[22-26] ULTIMATE[27] ACHILLES[28]	JUNIPERA[29] EXCEED[30,31]	
Palmoplantar psoriasis[32,33]	GESTURE[32,33]		

Real-world Evidence[34-43]	PROSPECT[34] SERENA[35] REALIA[36] PURE[37]	AQUILA[38] HOPE[39] XPOSE[40] CANOVA[41]	PsO-REAL[42] PSOSAS[43]
Direct Compare[44-47]	FIXTURE[13] PRIME[44] CLEAR[45,46]	CLARITY[46,47]	
Administration[48-51]	FEATURE[48] JUNCTURE[49] ALLURE[50]	MATURE[51]	
Flexi-dose[52-54]	OPTIMISE[52] GAIN[53] A2324[54]		
Quality of Life[55-60]	PROSE[55] IPSI-PSO[56] SKIPPAIN[57,58]	PSORITUS[59] SUPREME[60]	
Early treatment[61,62]	STEPIn[61]	IVEPSA[62]	
Comorbidities[63-65]	METABOLYX[63] pINPOINt[64]	ObePso-S[65]	

PsO – Psoriasis PsA – Psoriatic Arthritis axSpA – axial Spondyloarthritis See references provided in the References section.

Developing Cosentyx® into a total of 10+ indications and adding multiple label enhancements – peak sales potential at least USD 7bn

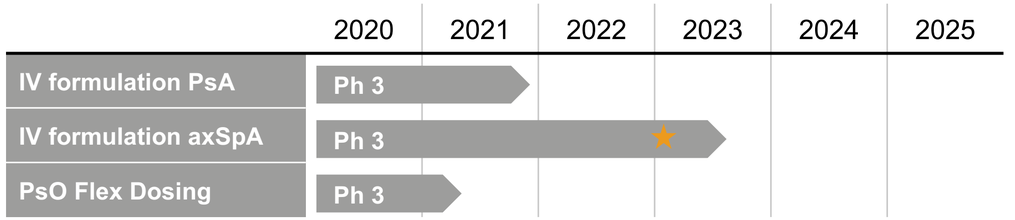
Indication	Asset potential
Hidradenitis Suppurativa (HS)	
Lichen Planus (LP)	
Juvenile Psoriatic Arthritis (JPsA) & Enthesitis Related Arthritis (ERA)	●●●
Giant Cell Arteritis (GCA)	
Lupus Nephritis (LN)	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

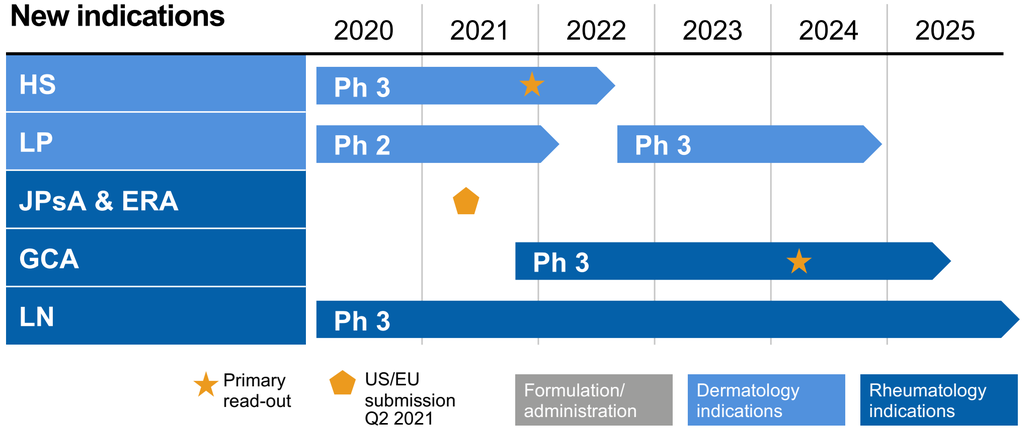
Diagnosed population[1] (G6)

Indication	Patients	Unmet need
HS	>400K[1]	Debilitating skin disease with significant QoL impact
LP	>2,500K	Inflammatory skin disease with impaired QoL
JPsA & ERA	>15K	Progressive, chronic pediatric diseases
GCA	>480K	Eye-sight threatening vasculitis in elderly
LN	>130K	Major cause of morbidity and mortality in SLE patients

Expansion in formulations and administration



New indications



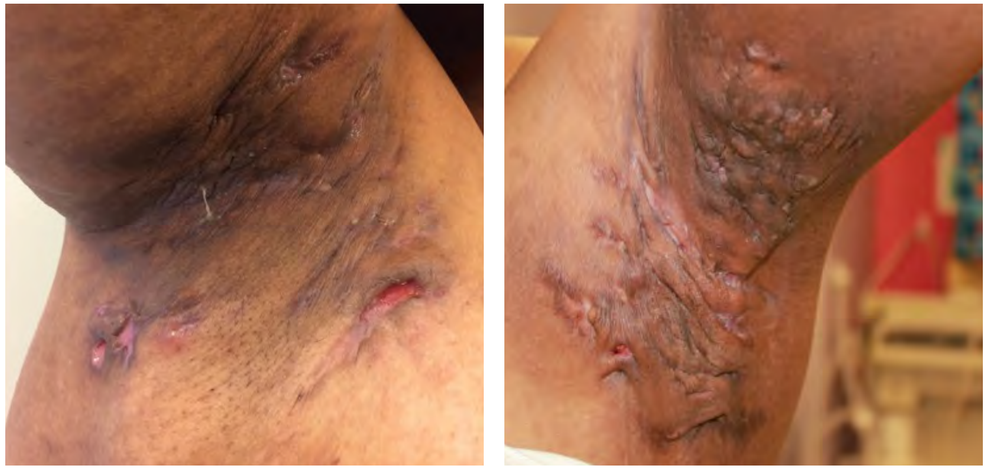
SLE – Systemic Lupus Erythematosus 1. Total diagnosed population – not accounting for potential restrictions in label/ treatment guidelines.

Hidradenitis Suppurativa

Secukinumab: potential novel therapy to address a debilitating disease

High unmet need in Hidradenitis Suppurativa

- Inflammatory skin disease of the folliculopilosebaceous unit
  - Intertriginous skin areas of the axillary, groin, perianal, perineal, and inframammary regions
  - Recurrent, **painful nodules and abscesses, scarring, purulent discharge, odor** and loss of function
- Prevalence ~1%[1], ~400k patients (200k in the US, 200k in EU5) with moderate to severe HS
- Under-diagnosed: diagnosis rate ~20%[2]
- Available treatment options do not adequately reduce disease activity or prevent disease progression

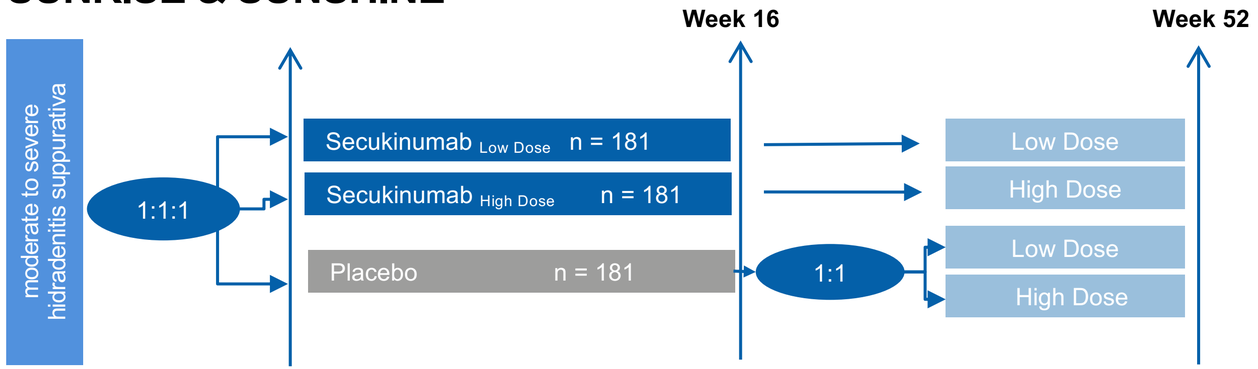


Images reproduced with permission from Kang et al.[3]

HS Hidradenitis Suppurativa 1. Ingram JR, British Journal of Derm, 2020. 2. Schrader et al., (2014) Journal of American Academy of Dermatology. 3. Kang S et al, eds. Fitzpatrick's Dermatology. 9th ed. McGraw-Hill; 2019

Ph3 program in Hidradenitis Suppurativa

SUNRISE & SUNSHINE[1]



- Two identical randomized, double-blind, placebo-controlled, multicenter studies
- Moderate to severe HS patients with or without prior biologic exposure
- Efficacy and safety[1]
- The primary endpoint is the HiSCR[2] at Week 16
  - HiSCR response: ≥50% decrease in Abscess and Inflammatory Nodule count with no increase in the number of draining fistulae

Primary endpoint, safety

Primary efficacy endpoint of HiSCR[2] at Week 16 was met in both studies

Safety data consistent with well established safety profile of Cosentyx

Study remains blinded and data will be presented after week 52

1. ClinicalTrials.gov identifier: NCT03713632. 2. HiSCR: Hidradenitis Suppurativa Clinical Response. 3. AN: abscesses and inflammatory nodules count

Lichen Planus

Impaired quality of life without approved systemic therapies

Unmet need in Lichen Planus

- Chronic inflammatory disorder of the skin, oral cavity, genitalia, scalp, nails, or esophagus
- Prevalence: 0.4% - 2.6%[1]
- Pruritic and painful
- Impact on quality of life comparable to psoriasis
- Current standard of care topical and systemic corticosteroids
  - Many patients refractory to SoC

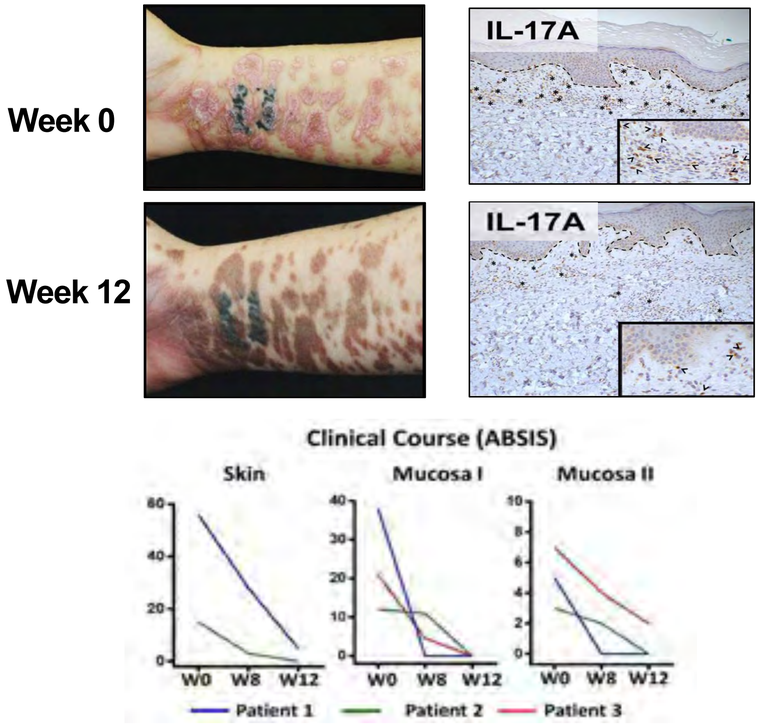
Th17-driven disorder[2]

Ex vivo scientific evidence

- Targeting of IL-17 pathway leads to a reduction of immune cell infiltrate in LP skin biopsies[2]

Secukinumab case reports

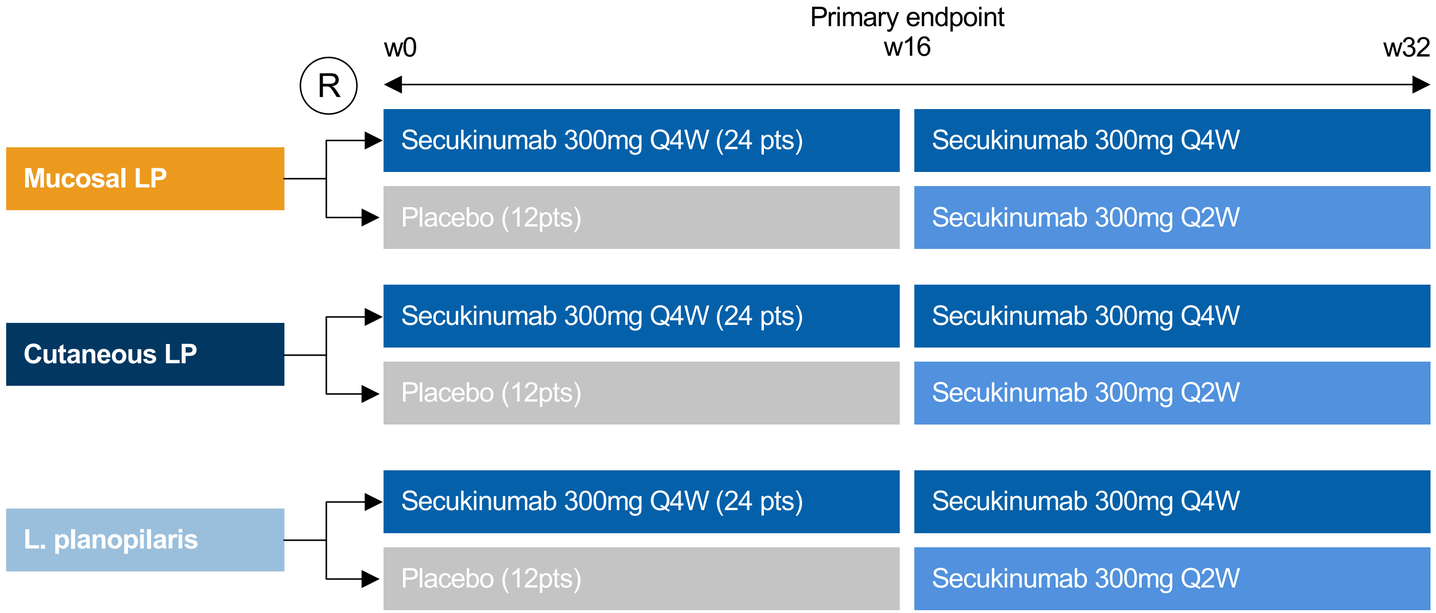
- Clinical improvement of skin and mucosal lesions within 12 weeks of treatment[2,3,4]



1. Gorouhi F et al. (2014) Scientific World Journal. 2. Solimani F, Schmidt T, Eming R, Mobs C, Pollman R, Hertl M. Therapeutic targeting of Th17/Tc17 cells leads to clinical improvement of LP. Front Immunol, 2019, 10:1018. 3. Rezzag-Mahcene C et al. Successful treatment of recalcitrant genital lichen planus with secukinumab. J Eur Acad Dermatol Venereol. 2021 May;35(5):e321-e323 4. Ismail F et al; The Australasian Journal of Dermatology, 2020; 61, e244-e275

Secukinumab Ph2 in Lichen Planus

PRELUDE[1]



- Randomized, placebo-controlled, double-blind, multi-center trial
- Innovative basket study design evaluating 3 subtypes of lichen planus
- Primary endpoint: Investigator's Global Assessment (IGA) score less or equal 2 (IGA ≤2) at Week 16
- Data expected H1 2022

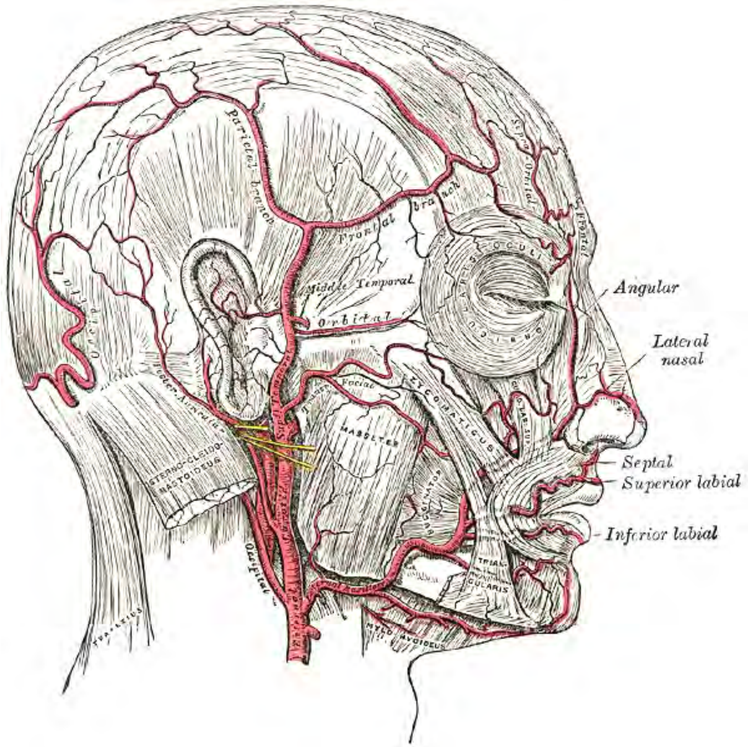
1. ClinicalTrials.gov identifier: NCT04300296.

Giant Cell Arteritis (GCA)

Vision threatening large vessel inflammatory rheumatic disorder

Unmet need in GCA

- Adult primary systemic large vessel vasculitis
- Elderly patients (mean age, 74 years)
- Lifetime risk of disease: 0.5-1%[1]
- Substantial morbidity due to irreversible vision loss, stroke[2] and toxicity of prolonged glucocorticoid treatment
- An unmet medical need remains for safe and effective steroid sparing treatments
- Standard of Care: high dose systemic steroids, MTX or tocilizumab[3]

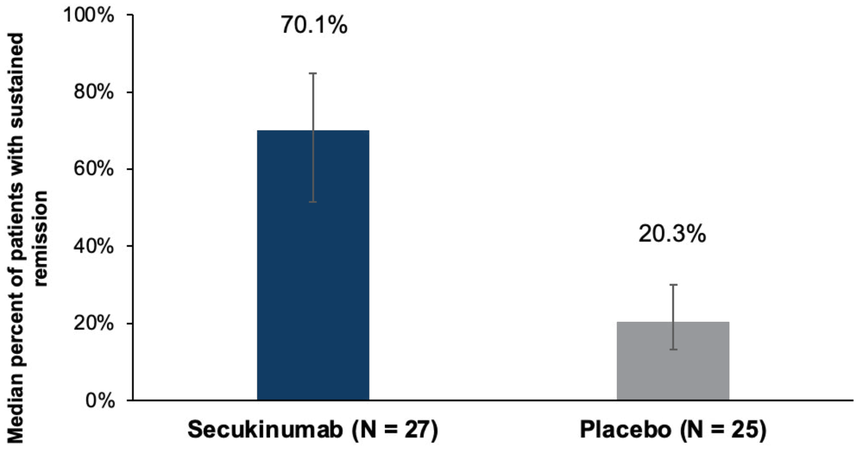


1. Crowson CS Arthritis Rheum. 2011 Mar;63(3):633-9. 2. Koster M, et al. Current Treatment Options in Rheumatology 2016. 3. Maz M et al. Arthritis Rheumatol.2021;73(8):1349–1365.

Secukinumab Ph2 study demonstrates sustained efficacy in Giant Cell Arteritis; met all primary and secondary endpoints

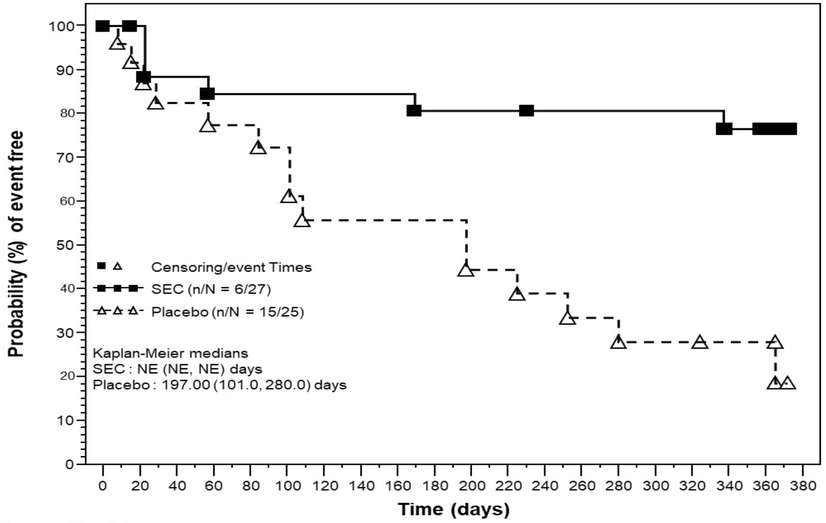
GCA Ph2 TiTAIN study[1] results

Primary endpoint: Proportion of patients in sustained remission until Week 28[2]



GCA, giant cell arteritis; N, number of patients in each treatment group, full analysis set

Time to first GCA flare after baseline up to Week 52[2, 3]



No. of subjects still at risk

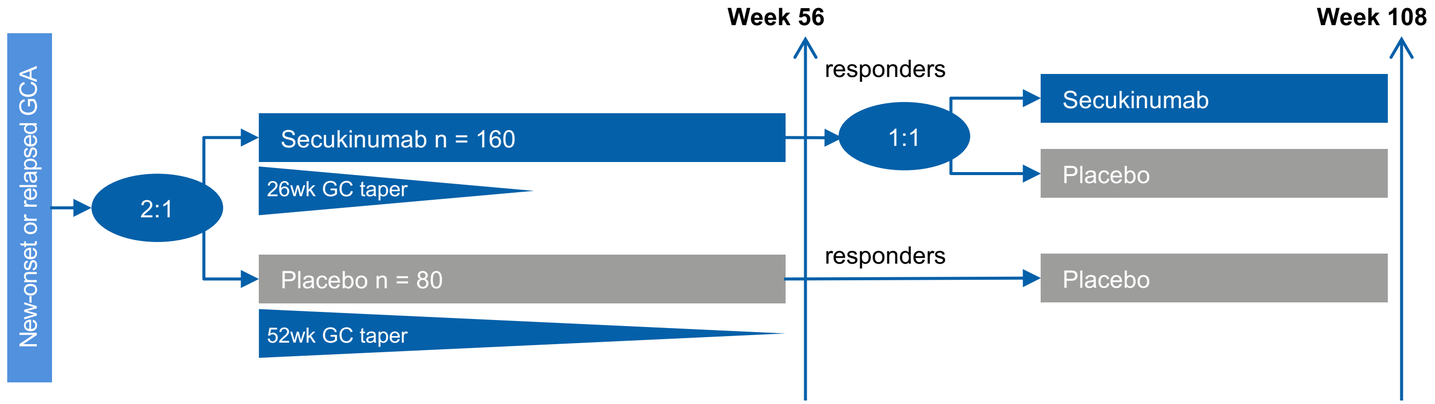
Time (days)	0	20	40	60	80	100	120	140	160	180	200	220	240	260	280	300	320	340	360	380
SEC	27	26	23	22	22	22	22	22	22	20	20	20	19	19	19	19	19	17	16	0
Placebo	25	20	16	15	15	13	10	10	10	10	8	8	7	6	6	5	5	4	4	0

n, total number of patients with a response (i.e., GCA flare);
N, number of patients in each treatment group; NE, not evaluable

ClinicalTrials.gov identifier: NCT04930094. 1. ACR Convergence 2021 Late-Breaking Abstracts. 2. Sustained remission is defined as being without a flare and in adherence to the protocol prednisolone taper regimen. A flare is defined as recurrence of signs and symptoms after remission and/or ESR ≥ 30 mm/h and/or CRP ≥ 10 mg/L attributable to GCA as per investigator's judgment. 3. Flares may occur during or after the steroid taper.

Secukinumab Ph3 program enrolled first patient in Oct 2021

GCA Ph3 study design[1]



- Efficacy and safety of secukinumab versus placebo, in combination with glucocorticoid taper regimen, in patients with Giant Cell Arteritis (GCA): faster glucocorticoid taper on secukinumab arm
- Primary endpoint: sustained remission at week 52
- First patient enrolled in October 2021
- Estimated primary completion 2024

1. ClinicalTrials.gov identifier: NCT04930094

IV regimen in Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA) with possible extension to other indications

A novel option for patients and HCPs

Unmet need in Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA) patients

IV regimen provides additional options

- Weight-based dosing
- Needle-phobic patients
- Patients with a preference for physician administration

Potential to expand patient access to treatment

- First IL-17i available in an IV formulation
- Of current PsA/axSpA patients on biologic treatment, ~20% receive IV biologic[1]

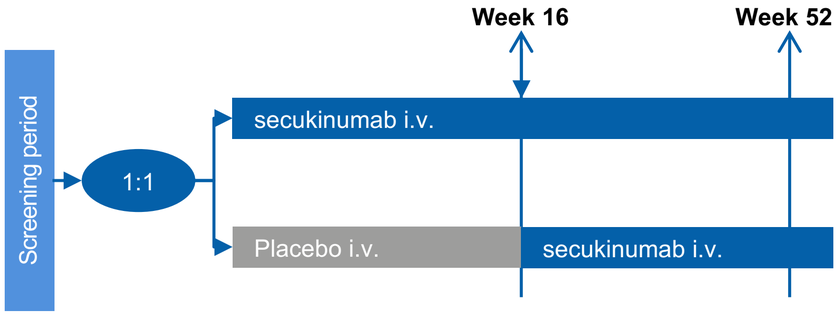
Scientific rationale for IV formulation

- Proven efficacy with s.c. dosing in axSpA and PsA
- Foundational IV safety dataset for future LCM indications
- Assessment of novel digital endpoints incl. sleep and activity

1. Source: US claims data and Novartis internal assumptions

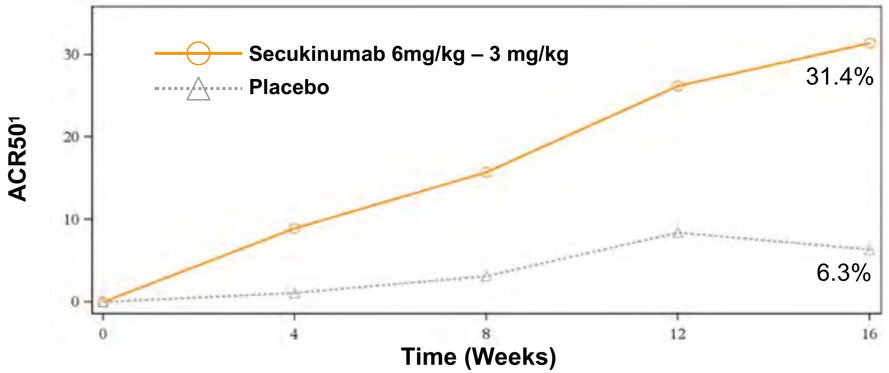
Secukinumab IV efficacious in Psoriatic Arthritis (PsA) Ph3

INVIGORATE-2 Ph3 PsA IV study design



- Efficacy and safety of intravenous secukinumab up to 52 weeks in subjects with active Psoriatic Arthritis[1]
  - Secukinumab 6mg/kg followed by 3mg/kg IV (N=191)
  - Placebo (N=190)
- Primary endpoint: ACR50 vs placebo at week 16

INVIGORATE-2 IV study results



- Demographics and baseline characteristics well balanced between treatment groups
- Primary and secondary efficacy endpoints
  - Statistically significant superiority of secukinumab IV compared to placebo
- Safety profile in line with well established safety profile of secukinumab

1. ClinicalTrials.gov Identifier: NCT04209205. 2. ACR50 (American College of Rheumatology 50) - is ≥ 50% improvement in measure of change in rheumatoid arthritis symptoms.

Ligelizumab (QGE031)

Humanized anti-IgE monoclonal antibody blocking IgE/FcεRI pathway

Phase 3

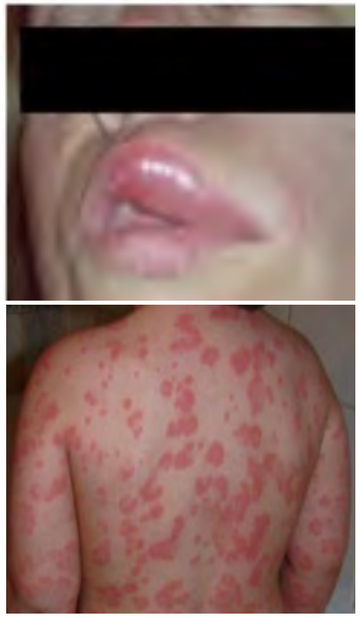
Key highlights

- **~740k CSU patients inadequately controlled** on antihistamines in G6[1]
- Ligelizumab targets IgE/FcεRI pathway with potential to **become new standard of care** based on higher selectivity and different binding site than Xolair®[2]
- Ph2b showed higher efficacy compared to Xolair® and a clear dose-response[3]. Results from Ph2b study in adolescent patients consistent with adult data
- **Ph3 superiority studies vs. current SoC Xolair®** underway (PEARL 1, 2); results expected Q4 2021 with submission in 2022
- **Initiating Ph3 studies** in CINDU and Food Allergy in Q4 2021
- **US/EU**: anticipated regulatory-based exclusivity from regulatory approval (12 years/10 years)

1. G6 = US+EU5 2. The mechanistic and functional profile of the therapeutic anti-IgE antibody ligelizumab differs from omalizumab, Gasser P., et al. Nature Communications 2020;11(1):165. 3. Maurer M., et al, N Engl J Med. 2019. 381(14): 1321–32.

"CSU does not kill you, but it also does not let you live"*

CSU consists of unpredictable onset itch, hives and angioedema which greatly diminish QoL



Almost half of people with moderate-to severe chronic urticaria suffer from painful angioedema[1]

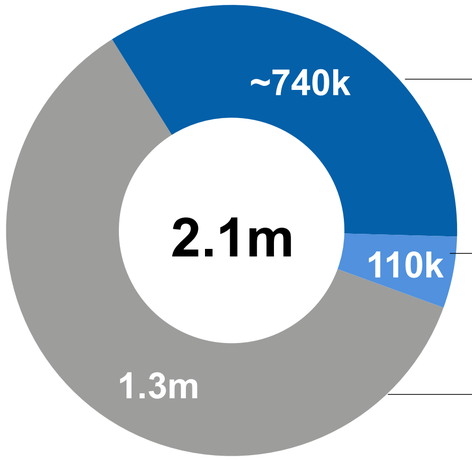
Up to 1 in 3 people with moderate to severe chronic urticaria have depression or anxiety[2]

Patients report **sleep** as one of the worse affected aspects of their life[3]

About **1 in 5 patients** report having to take time away from work due to their CSU[3]

Treatment gap: Untapped opportunity with low biologic penetration at 13%

2.1 million treated CSU patients in **G6 countries** in 2021[4]



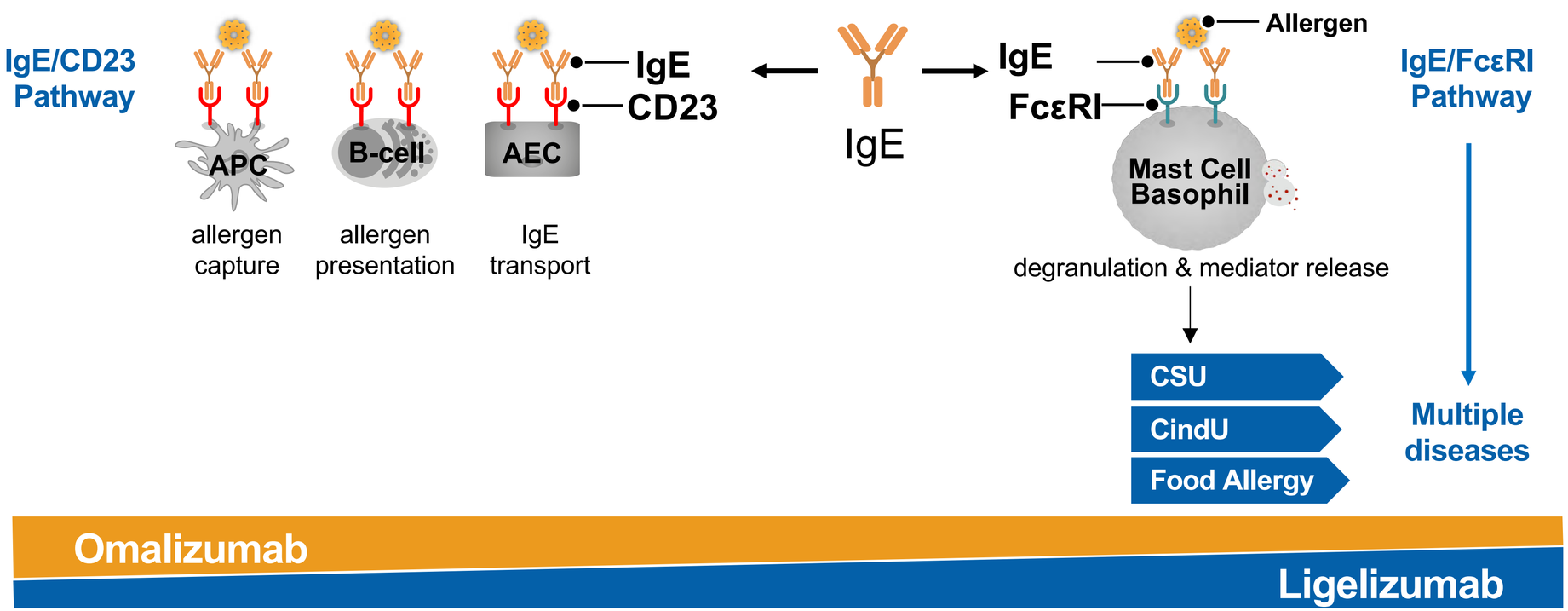
Treatment gap
Patients inadequately controlled, not receiving biologic

Only ~13% of eligible patients are on biologic treatment

Patients controlled with up to 4-fold second generation antihistamines

1. Maurer M, et al. June 19, 2017 2 BalpM-M et al. Patient. 2015 3 Maurer M et al. Allergy. 2017 4. Novartis internal information on file *Patient quote from Patient Journey Research, 2020; photos: © urticaria network e.V. (UNEV).

Ligelizumab best-in-disease potential driven by the IgE-FcεRI



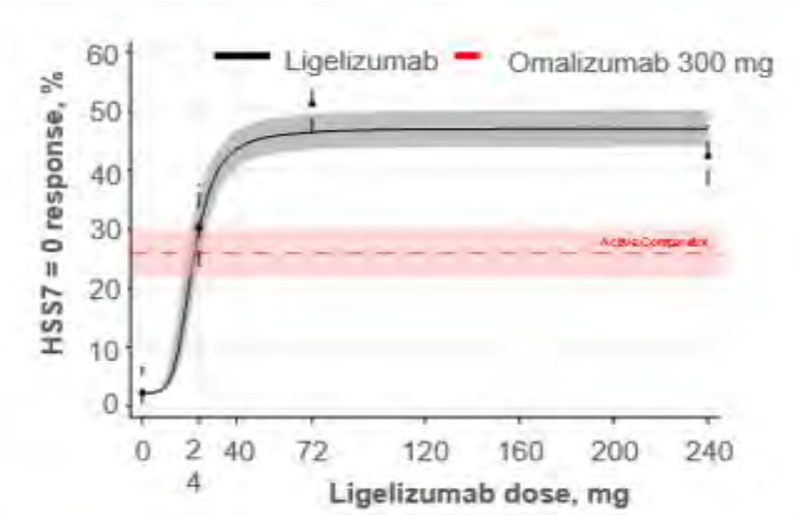
AEC, airway epithelial cell; APC, antigen presenting cell; CSU, chronic spontaneous urticaria; FcεRI, high affinity IgE receptor; IgE, immunoglobulin E. Eggel A and Bern U. European Academy of Allergy and Clinical Immunology symposium, June 6–8, 2020, Digital congress.

Chronic Spontaneous Urticaria

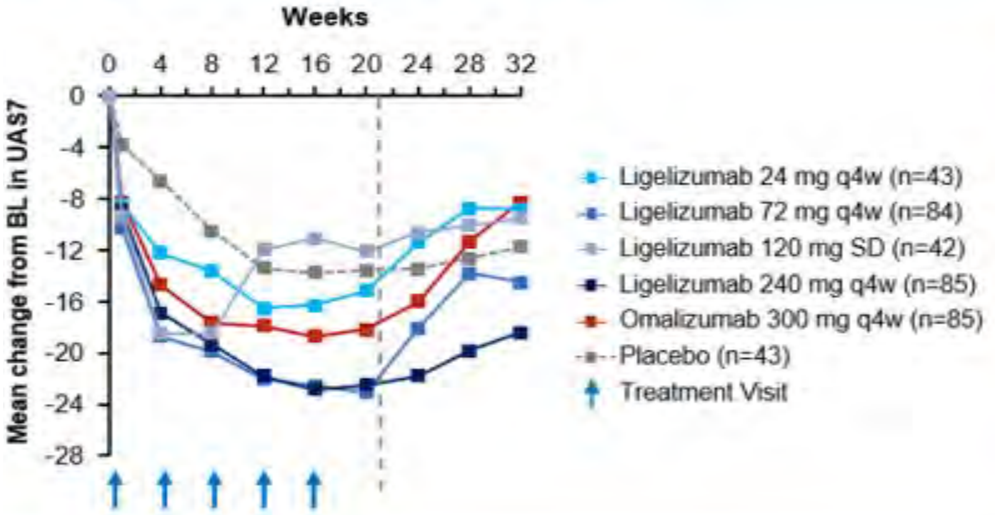
In Ph2b, ligelizumab showed better symptom control compared to Xolair®

Ph2b study with clear dose-response on complete hives control and UAS7[1] change from baseline[2]

A. Dose-response curve



B. Change from baseline in UAS7 over time



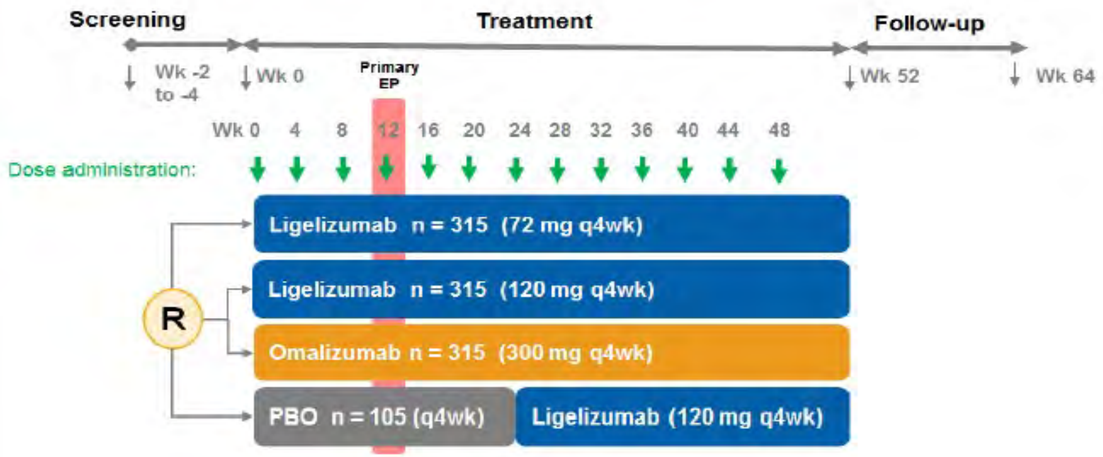
1. UAS7 = Urticaria Activity Score over 7 days. 2. Maurer M., et al, N Engl J Med. 2019. 381(14): 1321–32. 3. HSS7 = Hives Severity Score over 7 days.

Ligelizumab Ph3 CSU studies

Aim to demonstrate superiority vs Xolair®

PEARL 1 and 2 results expected Q4 2021

A press release will include the **combined** top line results of PEARL 1 and 2



2 multi-center, randomized, double-blind, active/placebo-controlled studies; recruited 2,059 adults and 93 adolescents

Head-to-head comparison vs SoC

(highest approved Xolair® dose 300mg)

1º endpoint:
UAS7[1] at week 12

2º endpoints at week 12:

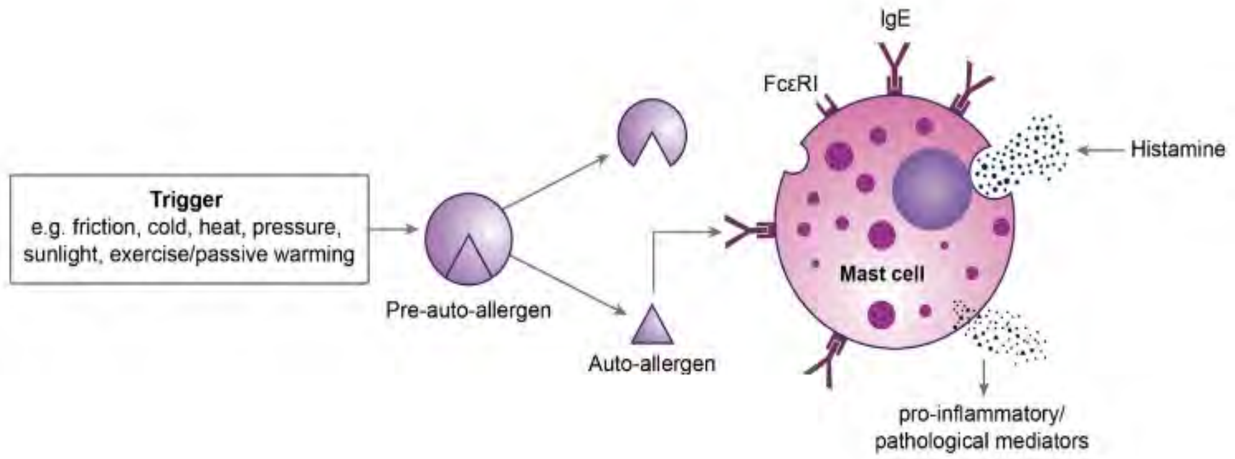
- % of subjects with **no** itch, no hives
- Improvement of itch severity score
- **No** impact on subject's quality of life[2]
- Cumulative number of weeks without angioedema

Expected submission: 2022

1. UAS7 = Urticaria Activity Score over 7 days. 2. Measured as DLQI = 0-1

Exploring ligelizumab in other IgE/FcεRI mediated diseases – Chronic Inducible Urticaria (CINDU)

IgE/FcεRI inhibition a promising therapeutic target in CINDU[2]

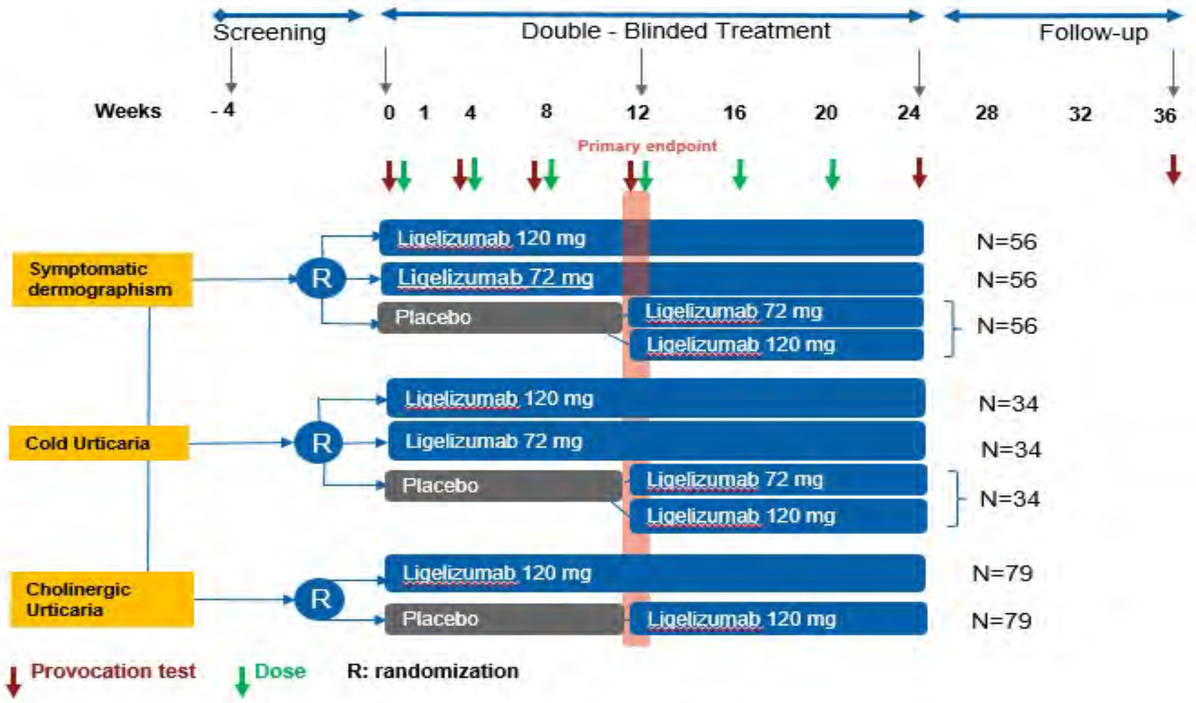


- ~1/3 of chronic urticaria patients have CINDU[1]
- SoC is antihistamines[2]
- Disease triggers often unavoidable
- No approved therapies for uncontrolled CINDU patients[2]
- Therapeutic goal: **complete symptom control**[2]

1. Maurer M et al. Unmet clinical needs in chronic spontaneous urticaria. A GA(2)LEN task force report. Allergy. 2011a;66:317-30. 2. Maurer M et al. Omalizumab treatment in CINDU. Systematic review. J Allergy Clin Immunol 2018.

Ligelizumab Ph3 CINDU study

Aim to investigate efficacy and safety in treatment of CINDU in adolescents and adults



Pearl-Provoke[1] Study attributes

- A randomized, double-blind, placebo-controlled study
- **Ph3 ongoing**
- IgE inhibition effective in CINDU patients inadequately controlled with H1-antihistamines[2-4]

Basket study design:

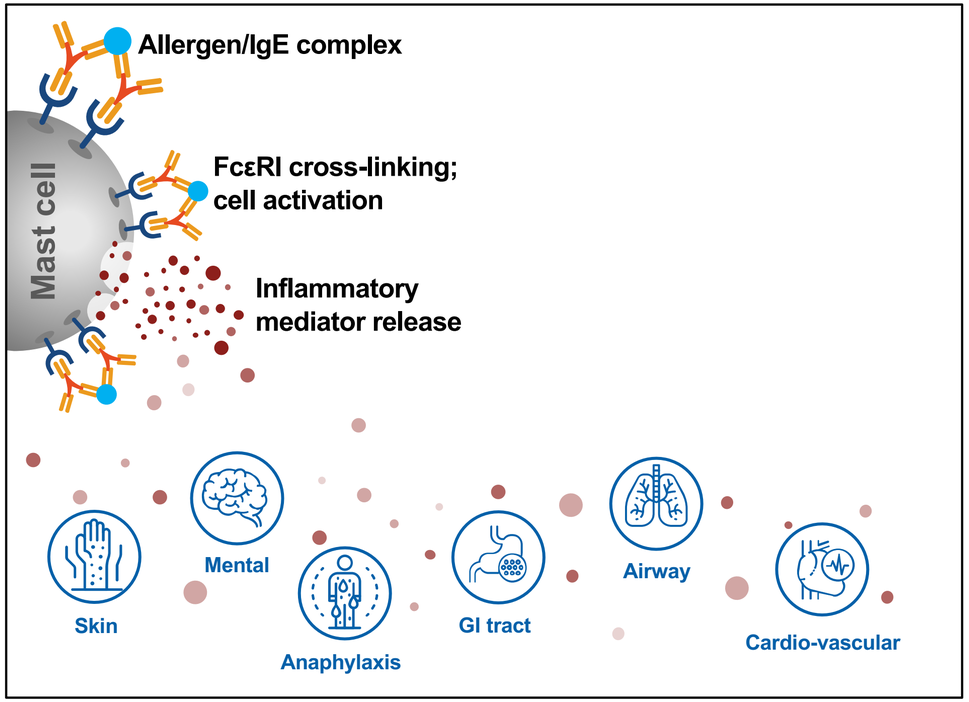
- 3 most common CINDU subtypes (N=348)

Submission planned 2025

CINDU = Chronic Inducible Urticaria. 1. ClinicalTrials.gov Identifier: NCT05024058. 2. Maurer M et al. J Allergy Clin Immunol. 2018 Feb;141(2):638-649. 3. Maurer M, et al. J Allergy Clin Immunol. 2017;140:870–3.e5. 4. Metz M, et al. J Allergy Clin Immunol. 2017;140:864–7.

Potential best-in-class therapy in Food Allergy

Protecting patients from reactions triggered by accidental exposure



- Prevalence: 3-8%
  - Allergy to multiple foods common[1]
    - 73% include peanut allergy
- 42% of children and 51% of adults with ≥ one convincing food allergies have experienced* ≥ one **severe** food-allergic reaction[4,5]
- Reactions can be triggered by tiny exposures (e.g., fraction of a peanut[6])
- Current standard of care:
  - Allergen avoidance and epinephrine[3]

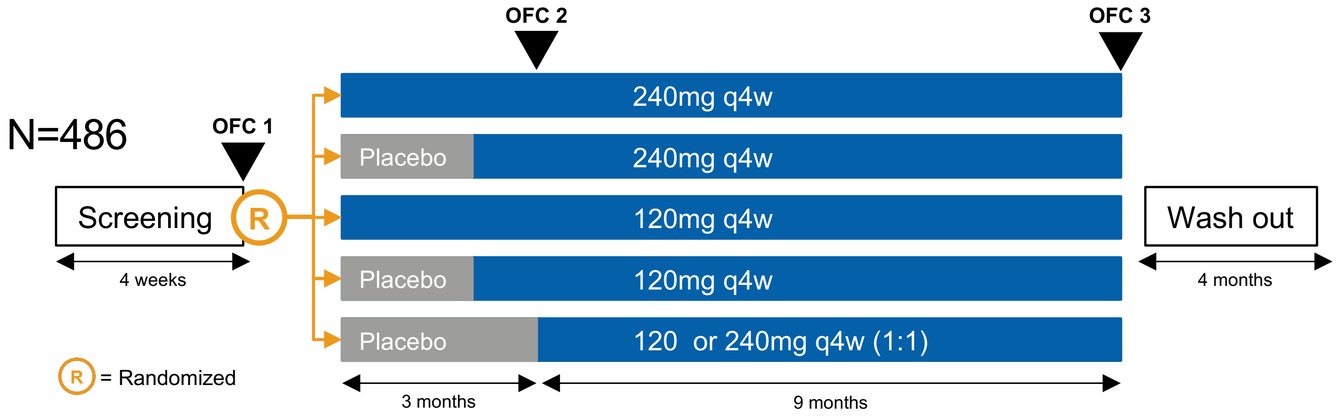
▶ High unmet need for effective and safe treatments[2] to improve quality of life of patients and families[3]

1. Warren et al. Epidemiology and Burden of Food Allergy. Current Allergy and Asthma Reports (2020) 20: 6 https://doi.org/10.1007/s11882-020-0898-7. 2. Interviews with 26 Allergy Specialists and 4 US Practice Managers in US, UK, France and Germany, July 2020. Novartis on file. 3. Asthma and Allergy Foundation of America. (2019). My Life With Food Allergy: Parent Survey Report. Retrieved from aafa.org/foodallergylife. 4. Gupta et al. Prevalence and Severity of Food Allergies Among US Adults JAMA Network Open. 2019(2):e185630. 5. Gupta et al. The Public Health Impact of Parent-Reported Childhood Food Allergies in US. Pediatrics. 2018;142(6):e20181235. 6. Hourihane et al. An evaluation of the sensitivity of subjects with peanut allergy to very low doses of peanut protein: A randomized, double-blind, placebo-controlled food challenge study J Allergy Clin Immunol 1997;100:596-600.
*Amended in May 2022

Ligelizumab Ph3 Food Allergy study

Aim to decrease reactivity to peanuts in patients with peanut allergy

Peanut[1]: Study to start Q4 2021



- A 52-week, multi-center, randomized, double-blind placebo-controlled study to assess the efficacy and safety of ligelizumab in decreasing the reactivity to peanuts in patients with peanut allergy
- Primary endpoint: Proportion of participants who can tolerate a single dose of ≥ 600mg (1044mg cumulative tolerated dose) of peanut protein without dose-limiting symptoms at Week 12

Study attributes

- Food allergy sensitive to IgE interacting with its high affinity receptor (FcεRI)[2]
- Peanut allergy study spearheading other food allergy studies
- IgE blockade effective in several studies [3-5]
- **First submissions planned 2025**

1. ClinicalTrials.gov Identifier: NCT04984876. 2. Zellweger F and Eggel A, Allergy 71 (2016) 1652–1661. 3. Leung, D. et al (2003). Effect of anti-IgE therapy (TNX901) in patients with severe peanut allergy. Journal of Allergy and Clinical Immunology 111 (1).
4. Hugh A. Sampson, et al. A phase II, randomized, double-blind, parallel-group, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy. Journal of Allergy and Clinical Immunology, Volume 127, Issue 5, 2011, Pages 1309-1310.e1.
5. Savage JH, et al. Kinetics of mast cell, basophil, and oral food challenge responses in omalizumab-treated adults with peanut allergy. J Allergy Clin Immunol. 2012;130(5):1123-1129.e2.

Developing ligelizumab in IgE/FcεRI pathway mediated diseases

Market potential

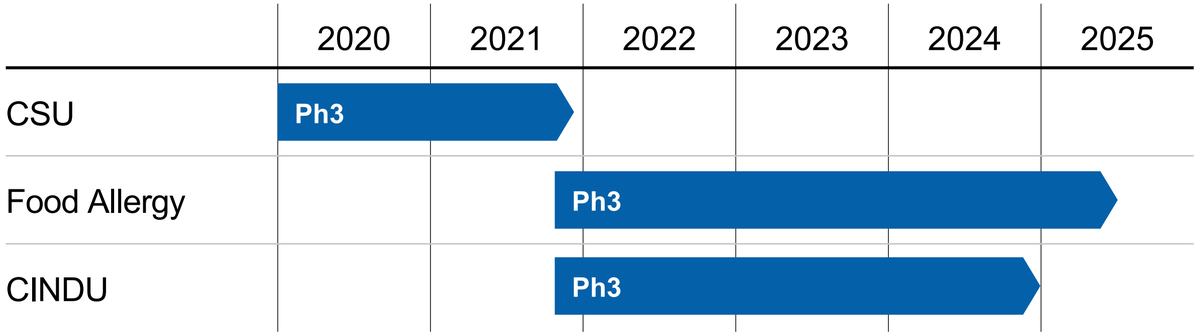
Indication	Asset potential
CSU	
Food Allergy	●●●
CINDU	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Addressable patients[1]

Indication	Patients
CSU	~740k
Food Allergy	3.40m
CINDU	300k

Upcoming milestones for development program



- CSU PEARLs readout in Q4 2021; submission 2022
- Food Allergy: Initiation of Ph3 program in Q4 2021
- CINDU: Ph3 ongoing

1. Approximate figures; Source: Novartis internal forecast for G6 countries

Remibrutinib (LOU064)

Oral, covalent BTK inhibitor targeting immune cell signaling

Phase 3

Key highlights

- **~740k CSU patients** inadequately controlled on antihistamines in G6[1]. **Biologic penetration only 13%**
- Remibrutinib is a highly selective, potent covalent BTK inhibitor with potential for **best-in-class efficacy and safety**
- Significant opportunity as **first option post H1-antihistamines** with oral convenience
- Ph2b showed **rapid and biologic-like efficacy** and favorable benefit/risk profile across entire dose range tested. **No clinically relevant AEs** associated with BTK class[2]
- On track as **first to market BTKi in CSU** with Ph3 enrollment ongoing, submission expected 2024
- **Direct-to-Ph3 initiated in RMS**. Exploring multiple other indications
- **US/EU**: Patent on compound (2034/2034)[3]

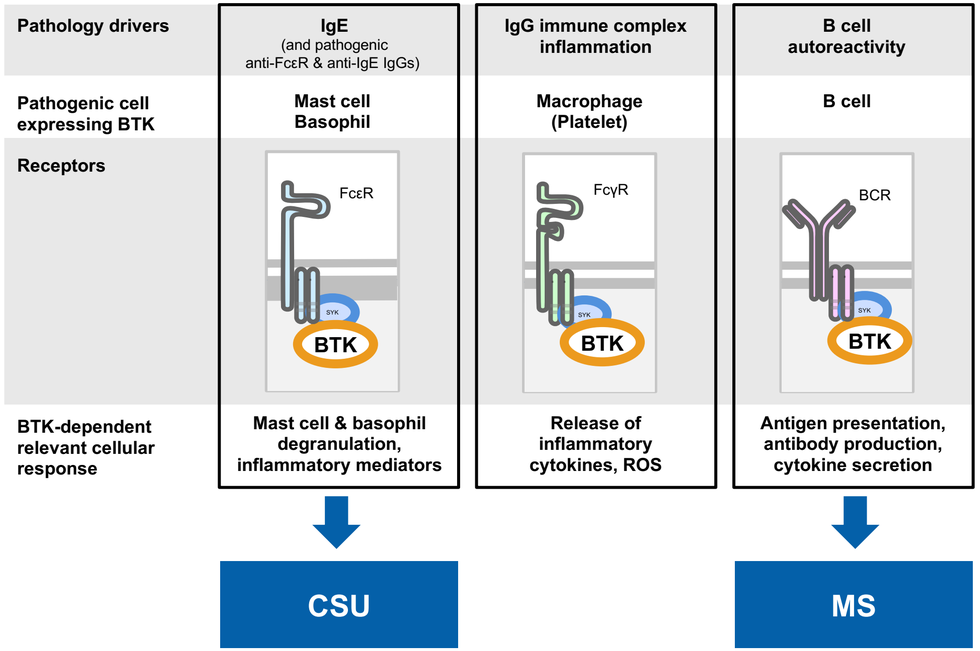
1. G6 = US+EU5. CSU: Chronic Spontaneous Urticaria RMS: Relapsing Multiple Sclerosis 2. e.g., infections, cytopenias, bleeding, hepatic events 3. Patent term extensions and regulatory-based exclusivities are possible

Remibrutinib: A highly selective and potent oral BTK inhibitor with best-in-class potential

BTK inhibition

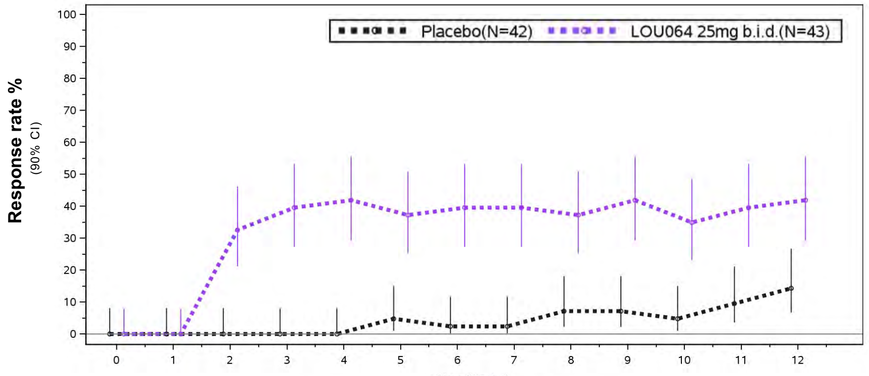
- Targeting immune cell signaling through FcεR, FcγR and BCR
- BTK selectively expressed in cells of adaptive and innate immune system including B cells, macrophages, mast cells and basophils
- **Novartis BTKi remibrutinib (LOU064)** differentiated by **high kinase selectivity** combined with **potent covalent BTK inhibition**
- No significant off target toxicity observed in clinical trials to date

BTK signaling overview



Favorable benefit/risk profile across the entire dose range, with no dose-dependent pattern of AEs

More patients achieved complete control (UAS7=0)



- **More patients** on remibrutinib achieved complete control, i.e. **complete absence of hives and itch** (UAS7=0) over 12-week treatment period
- **High response rate** maintained, up to end of treatment

Remibrutinib demonstrated good tolerability across the entire dose range tested with no safety signals

Key safety data include:

- ✓ No dose dependent increase of, treatment interruption or discontinuation due to LFT elevations
- ✓ No dose dependent cytopenias, treatment interruption or discontinuation due to low blood cell counts
- ✓ No clinically relevant adverse events associated with BTK inhibitor class (e.g., infections, cytopenias, bleeding, hepatic events) across the dose range tested

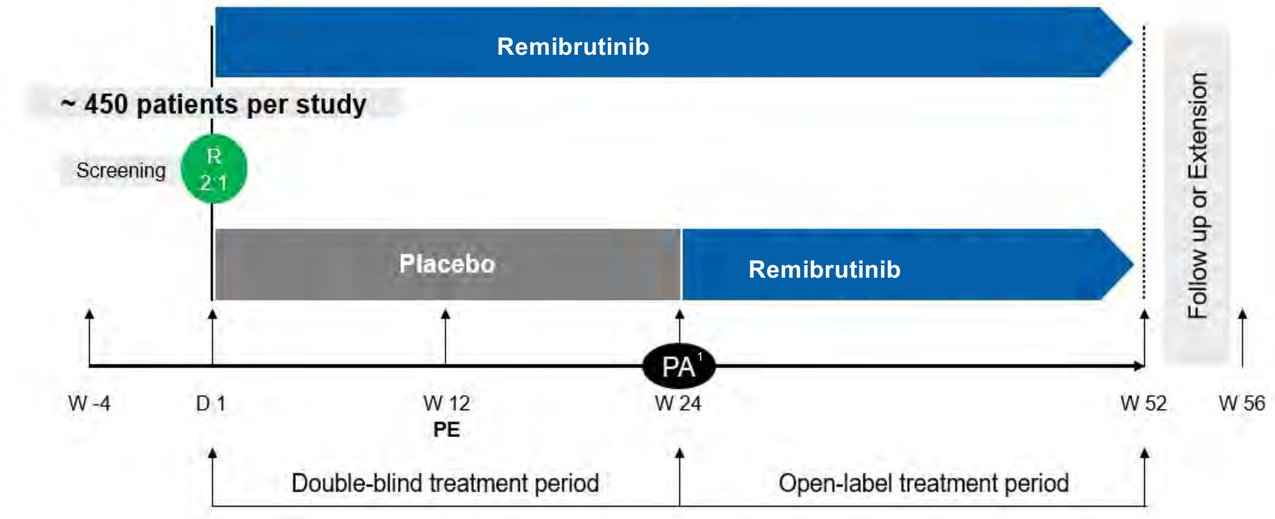
First oral therapy to advance to Ph3 in CSU in 2021 in H1 antihistamines inadequate responders.
Best-in-class profile based on positive benefit/risk profile. Ph3 in CSU ongoing

AE – Adverse events CSU – chronic spontaneous urticaria UAS7 – weekly Urticaria Activity Score b.i.d. – two times a day.

Remibrutinib CSU Ph3 program started in November 2021

Positive results from Ph3 studies REMIX-1 and REMIX-2 will enable submission of remibrutinib in CSU as first-in-indication BTK inhibitor in 2024

Multicenter, randomized, double-blind, placebo-controlled studies in patients with CSU inadequately controlled by H1-AHs



Co-primary endpoints (PE[2] @ week 12)

- Change from baseline in UAS7[3]
- Absolute change from baseline in ISS7[4] and HSS7[5]

Secondary endpoints (@ week 12)

- Disease activity control (UAS7 ≤6)
- Complete absence of hives and itch (UAS7 = 0)
- Reduction in ISS7 and HSS7 scores
- Achievement of DLQI = 0-1
- Sustained disease activity control
- Weeks without angioedema
- Safety and tolerability of remibrutinib (56 weeks)

ClinicalTrials.gov Identifier: NCT05030311/NCT05032157. 1. PA: Primary analysis. 2. PE: Primary endpoint. 3. UAS7 = weekly Urticaria Activity Score. 4. ISS7 = weekly Itch Severity Score. 5. HSS7 = weekly Hives Severity Score.

Remibrutinib is key to unlock full potential of CSU market, leveraging portfolio with ligelizumab

Xolair® omalizumab

Current SoC for patients uncontrolled on antihistamines

- Lower mean weekly itch severity vs. placebo
- More patients with complete control vs. placebo

Ligelizumab

Potential to become new biologic SoC

- More patients with complete control than Xolair®
- More convenient 1 injection per month

Remibrutinib

Potential first option after anti-histamines with oral convenience

- Biologic-like efficacy
- Favorable benefit/ risk profile
- No clinically relevant AEs associated with BTK class
- Oral convenience
- Only BTK in Ph3 in CSU

2014 — **2023** — **2025**

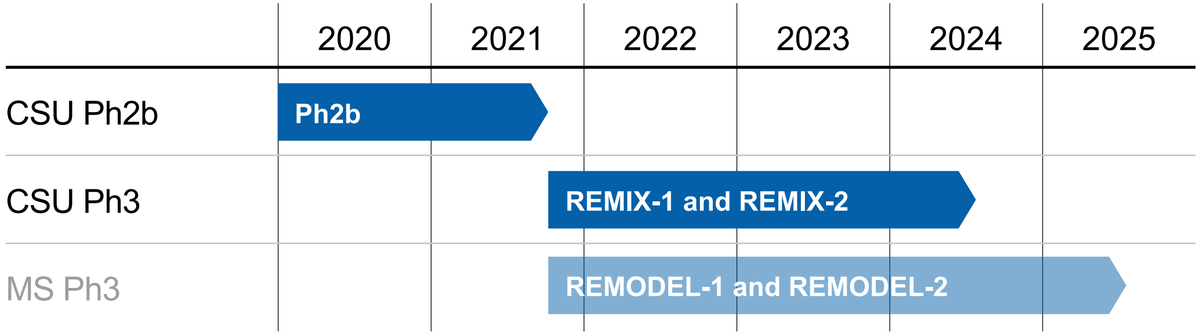
Remibrutinib has significant commercial potential across indications

Market potential

Indication	Prevalence[1]	Asset potential
CSU	~740k	●●●
RMS	> 0.5m	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Upcoming milestones for development program



REMIX-1 and REMIX-2

- Enrollment started November 2021
- Submission in 2024

REMODEL-1 and REMODEL-2

- Enrollment start December 2021
- Submission in 2025

1. G6 = US+EU5. CSU: Chronic Spontaneous Urticaria, MS: Multiple Sclerosis.

Ianalumab (VAY736)

Fully human monoclonal antibody binding to and blocking the function of the BAFF receptor

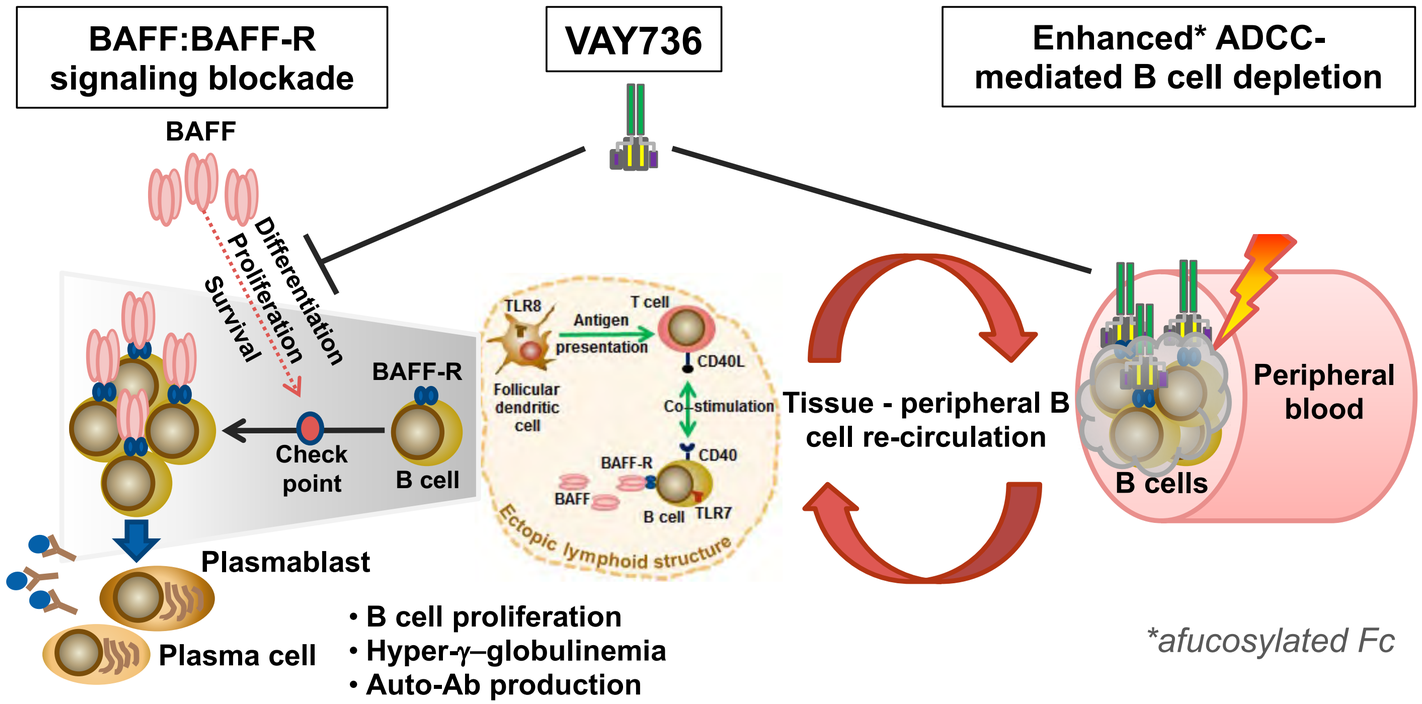
Phase 2

Key highlights

- **400k patients** with moderate to severe Sjögren's disease in G7
- **No disease-modifying treatment** available, systemic features in 40% patients, 5% develop Non-Hodgkin lymphoma
- Dual MoA expected to deliver **deeper, longer-term disease remissions** vs other B-cell depleting agents
- Potential to become **first disease modifying therapy** in Sjögren's based on **positive Ph2b** showing dose response and good tolerability. Filing expected in ≥2026
- Investigating ianalumab in **additional prototypical B cell associated diseases** including LN (Ph3 expected to start in 2022), SLE (Ph2a), autoimmune hepatitis (Ph2b), CLL (Ph1/2a)
- **US/EU**: Anticipated regulatory-based exclusivity from regulatory approval (12 years/10 years)

LN – Lupus Nephritis SLE – Systemic Lupus Erythematosus CLL - Chronic Lymphocytic Leukemia

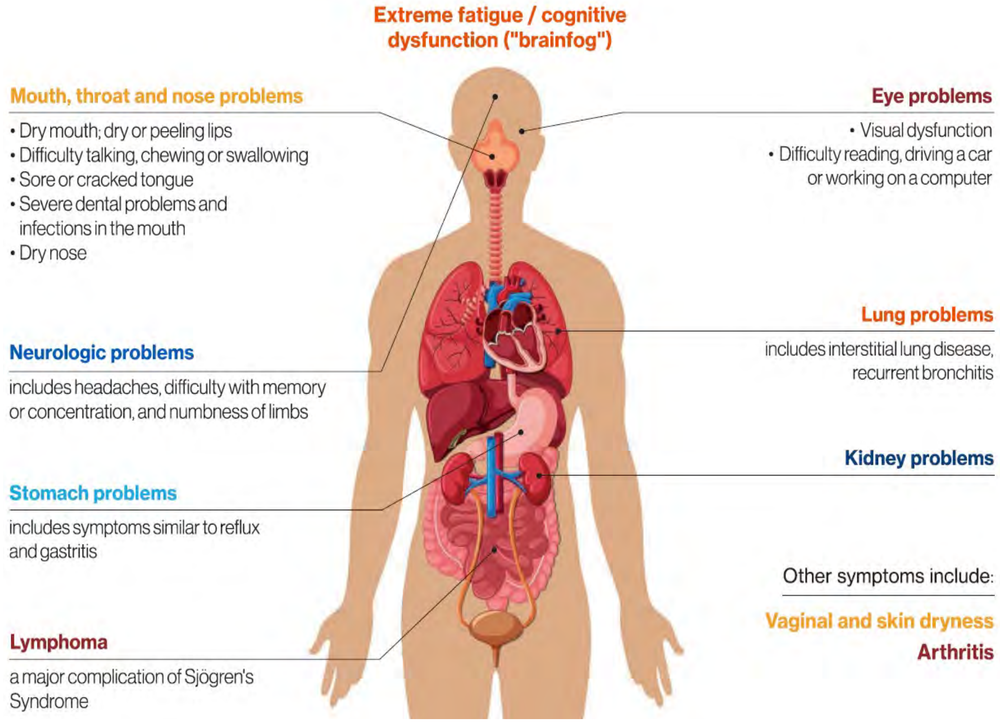
Ianalumab (VAY736) has unique dual MoA: Blocking BAFF-R and depleting B cells



Dual MoA and more profound B cell depletion expected to deliver deeper, longer term disease remissions vs other B-cell depleting agents

ADCC = Antibody-dependent cellular cytotoxicity

Sjögren's syndrome and rationale to target BAFF-R with ianalumab



Prevalence and treatment

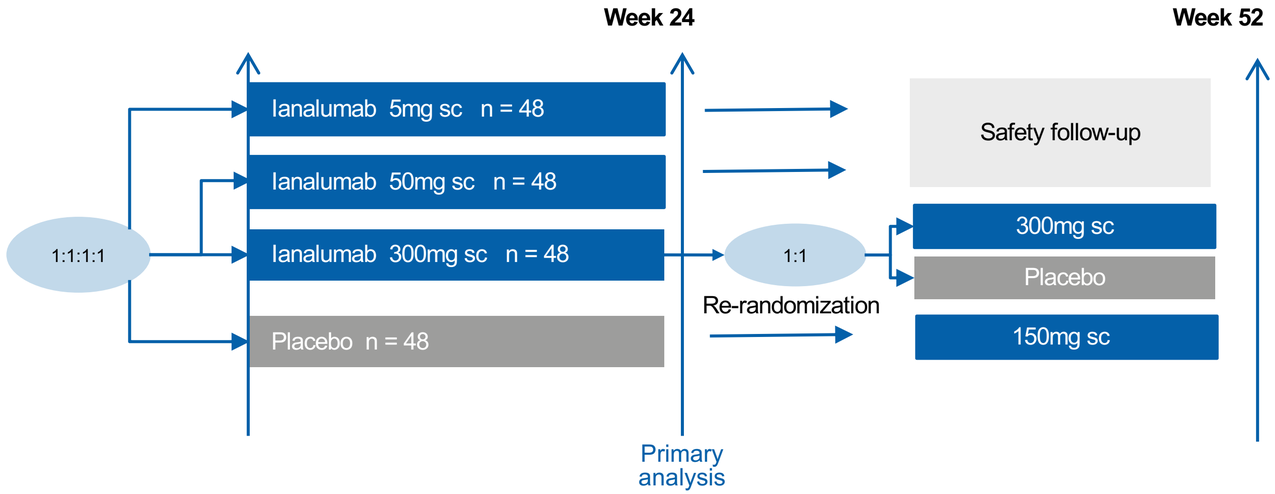
- Prevalence 0.2%
  - Systemic features in 40%
  - 5% develop Non-Hodgkin lymphoma[1-2]
- No disease modifying treatment[3]

Rationale for ianalumab

- Hallmark diagnostic features:
  - B-cell hyperreactivity and autoantibodies
  - Autoimmune inflamatory 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

1. Theander, 2006; 2. Voulgarelis, 1999; 3. X. Mariette and C. Criswell, Primary Sjögren's Syndrome. N Engl J Med 2018; 379:96-97

Ph2b study in Sjögren's disease: Efficacy on systemic disease manifestations



Randomized, double-blind, placebo-controlled, multicenter studies to evaluate the dose response on efficacy and safety of ianalumab, q4wk

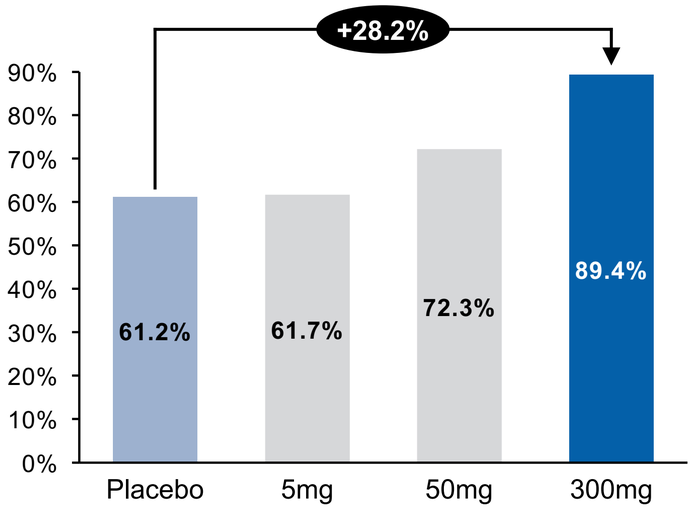
Study attributes

- Primary endpoint was met; dose response of ianalumab defined as change in ESSDAI from baseline at 24 weeks[1-3]
- Efficacy demonstrated on systemic extra-glandular manifestations of Sjögren's disease
- Secondary endpoint of ESSPRI not achieved
- Good tolerability with no dose dependency of adverse events except for local injection reactions

ClinicalTrials.gov Identifier: NCT 02962895 1. Seror et al., Arthritis Care Res 2013; 65:1358-64.; 2. Seror et al., Arthritis Res Ther 2015; 74:859-66. 3. S. Bowman et al, The Lancet 2021, in press

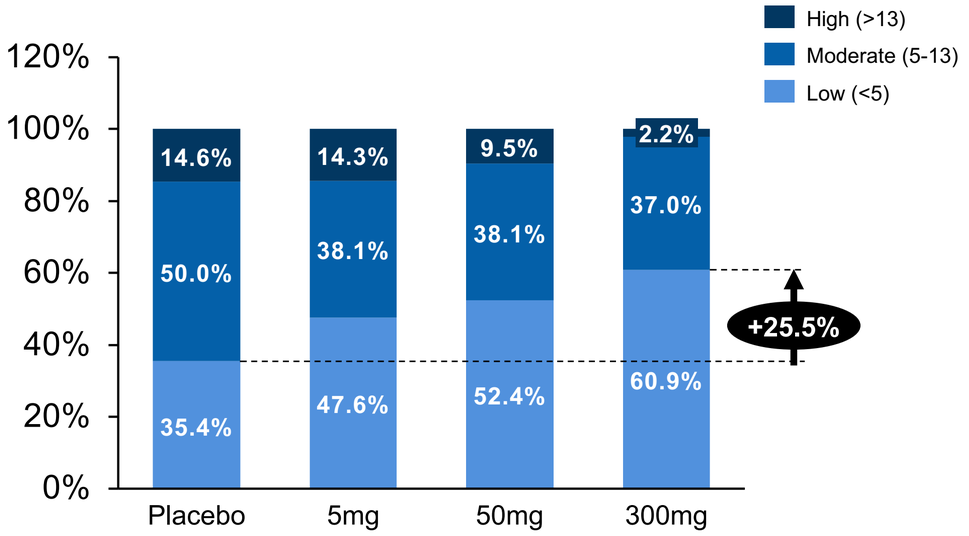
Ianalumab Sjögren's study showed dose dependent efficacy and good tolerability[1-2]

ESSDAI Responders w24



28% more responders vs placebo with 300mg ianalumab

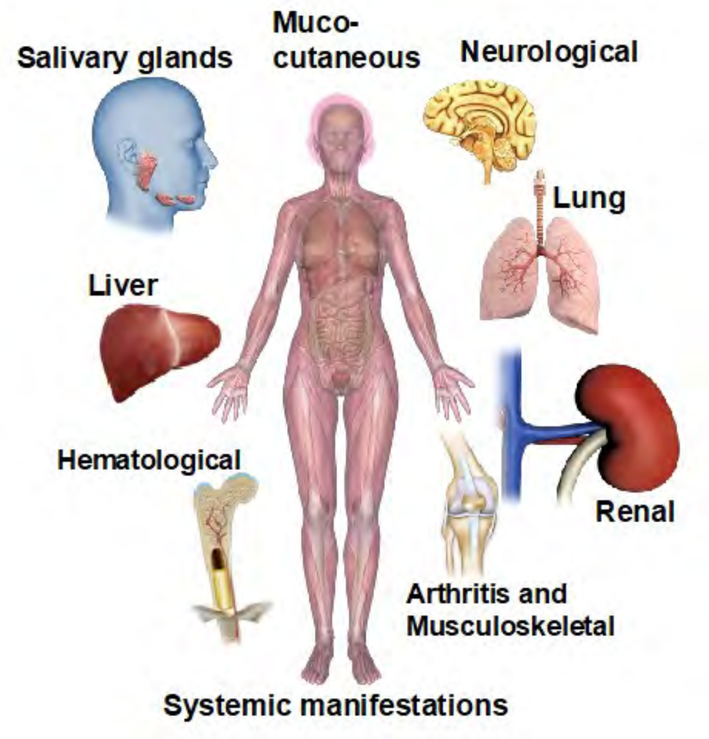
Disease activity w24



26% more patients improved to **low disease activity** and **only 2%** remained at high disease activity with 300mg ianalumab

1. S. Bowman et al, ACR Annual Congress 2019; 2. T. Dörner, EULAR Annual Congress 2020.

Systemic Lupus Erythematosus: A debilitating disease leading to permanent organ damage



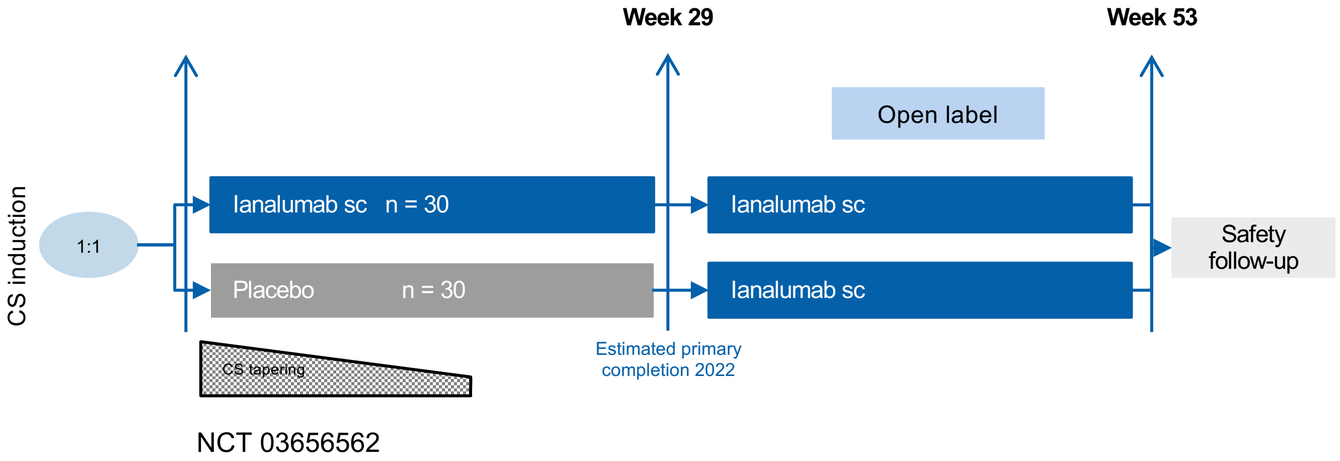
Prevalence and treatment

- Prevalence: 0.02-0.07%
- 9:1 f/m predominance
- Adolescents and younger adults
- Mortality: 2-3 times higher than in general population
- Limited disease modifying treatment option

Rationale for ianalumab

- Autoantibody-immune complexes produce organ tissue damage
- BAFF levels correspond to disease severity lupus autoantibody production
- Depleting B-cells and blocking BAFF-R targets underlying disease mechanism

Ph2a trial in Systemic Lupus Erythematosus (SLE)



NCT 03656562

Randomized, double-blind, placebo-controlled, multicenter studies to evaluate the efficacy and safety of ianalumab

Study attributes

Composite primary endpoint:

- SRI-4 reduction under sustained corticosteroid tapering at week 24

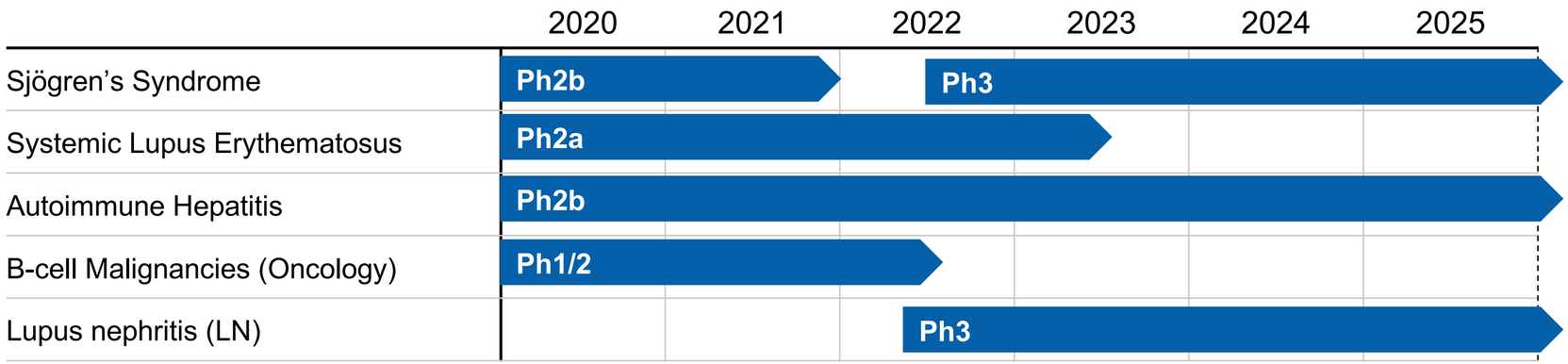
Secondary endpoint:

- Safety
- Lupus low disease activity status
- Flare incidence

Estimated primary completion 2022

ClinicalTrials.gov Identifier: NCT 03656562

Advancing ianalumab in a range of indications through 2020-25



Market potential (in G7 countries)

Indication	Prevalence (targeted population)	Asset potential*
Sjögren's Syndrome[1]	400,000+ (moderate to severe disease)	
Systemic Lupus Erythematosus[2]	200,000+ (moderate to severe disease)	
AIH[3]	120,000+ (non-responders to SoC)	●●●
B-cell malignancies[4]	170,000+ (incidence)	
Lupus nephritis	130,000+ (diagnosed patients)	

●○○ <USD 1bn
●●○ USD 1-2bn
●●● >USD 2bn

1. Data monitor Healthcare Report 2018; BMJ Best Practice, 2017; Cornec & Chiche, 2015; Maciel et al., 2017; Patel & Shahane, 2014 ; Kantar Health report 2014. 2. DRG Lupus Nephritis Disease report, Novartis internal analysis; SLE prevalence based on clinical definition (ACR≥4 or 3 with LN confirmed biopsy or ESRD diagnosis). 3. Gerven et al. Scand J Gastroenterol. 2014, and additional estimate; 4. Kantar CanerMPact Dec2020. *: Estimated peak sales

LNA043

WILD CARD

Modified recombinant human ANGPTL3 protein fragment that induces cartilage regeneration

Phase 2

Key highlights

- **300m people worldwide** suffering from osteoarthritis (OA), with knee OA most common form
- **No disease-modifying treatment** available
- Potential to become a **first-in-class disease modifying treatment** for osteoarthritis of the knee
- Early clinical trials showed **cartilage anabolic effects** and **repair of damaged cartilage** in patients with articular cartilage lesions in the knee
- Currently in Ph2b. FDA granted **fast track designation**. Filing expected ≥2026
- **US/EU:** Patent on composition of matter (2034/2034)[1]

OA = osteoarthritis 1. Patent term extensions and regulatory-based exclusivities are possible

Osteoarthritis a progressive, debilitating condition without disease modifying therapies

Unmet need in Osteoarthritis (OA)

- 300 million people worldwide have OA[1], most predominant is knee OA
- Single most common cause of disability in older adults[2]
- No treatments can slow or reverse the damage in the joints
- Existing pharmacologic treatments only address symptoms
- OA joints continue to degenerate – often leading to joint failure and joint replacement
- As many as 20% of patients undergoing surgical joint replacement may be unsatisfied with their outcome[3]
- High unmet need for disease modifying treatments

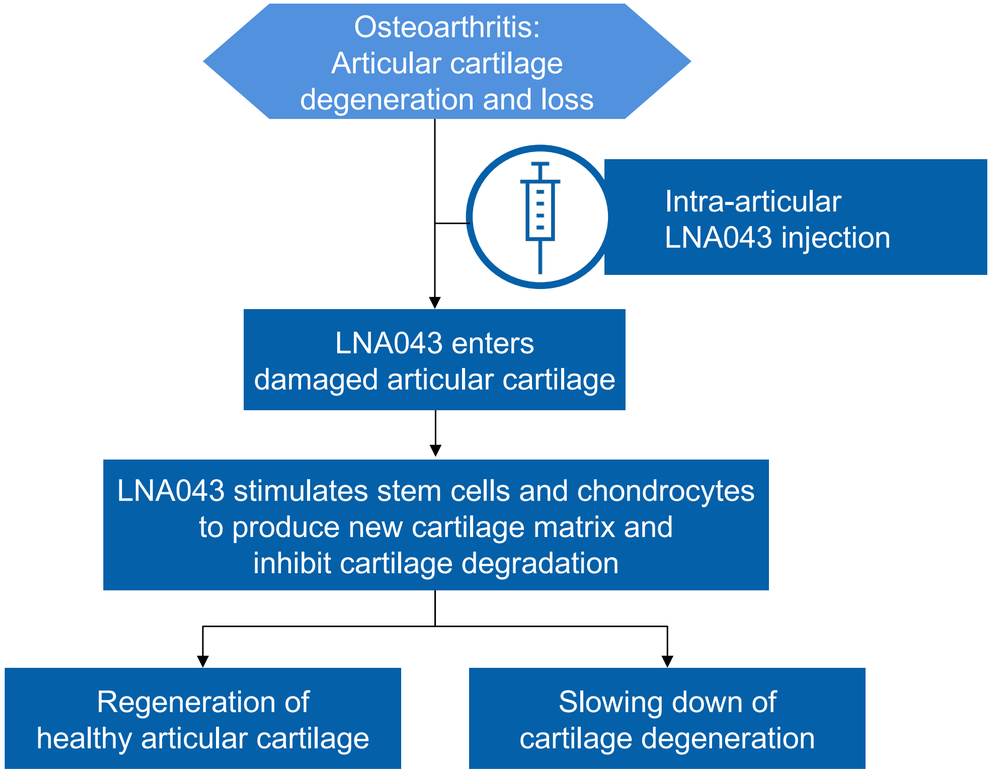
Goal

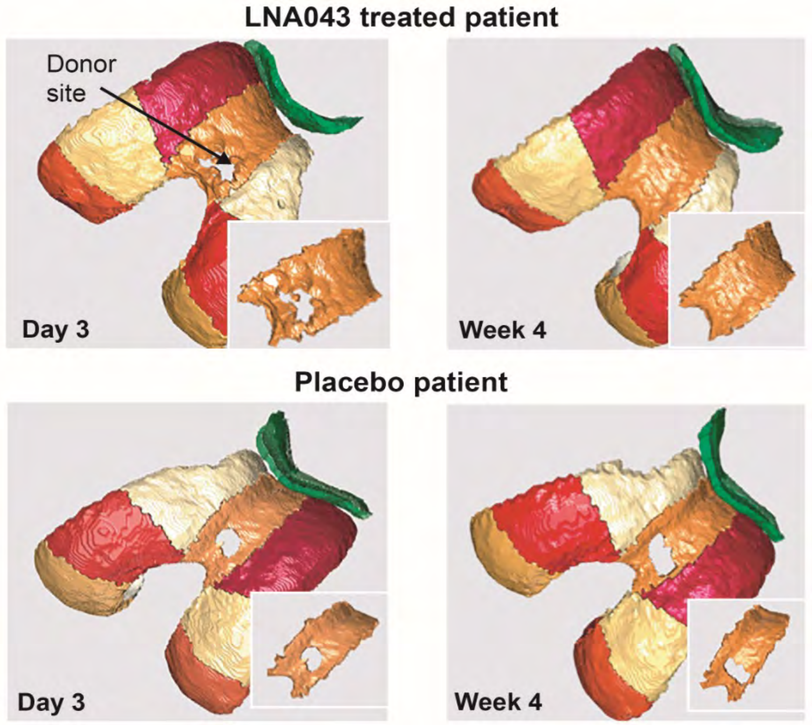
Develop disease-modifying treatment to:

- Reduce pain
- Improve function
- Prevent joint failure
- Prevent surgical joint replacement

1. Safiri S, Kolahi A, Smith E, et al. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. Annals of the Rheumatic Diseases 2020;79:819-8282. 2. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Annals of the Rheumatic Diseases. 2001;60:91-97. 3. Hofmann S, Seitlinger G, Djahani O, Pietsch M. The painful knee after TKA: a diagnostic algorithm for failure analysis. Knee Surg Sports Traumatol Arthrosc 2011; 19:1442–1452.

LNA043, a modified recombinant human ANGPTL3 protein fragment, induces cartilage regrowth

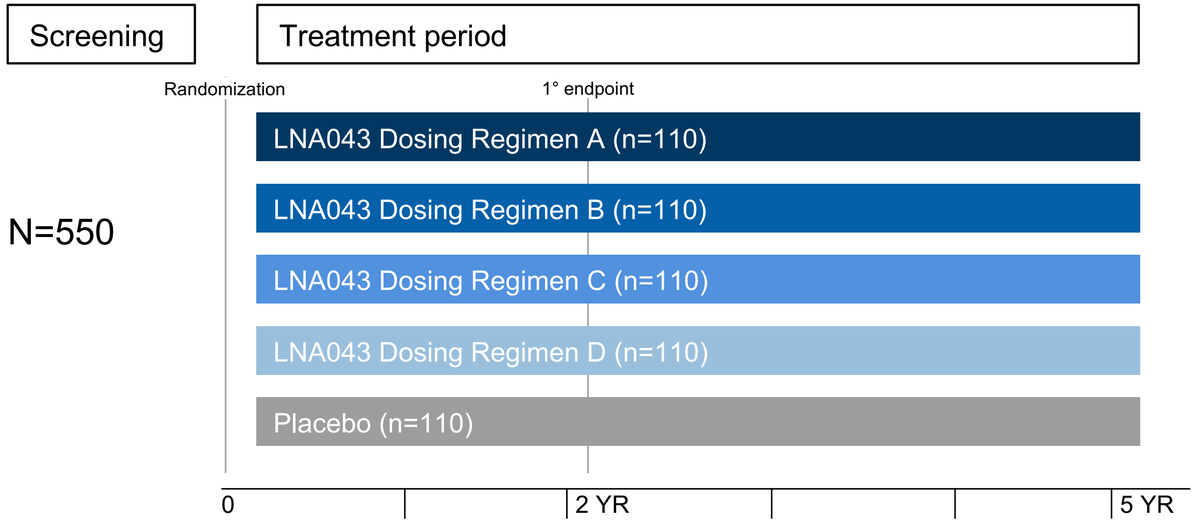




LNA043 displayed a **favorable safety profile** in studies to-date

1. Scotti C, Gimbel J, Laurent D, et al. First-in-human trial results of LNA043, a novel cartilage regenerative treatment for osteoarthritis. Osteoarthritis and Cartilage 29: S214, 2021.
2. Laurent D, Scotti C, Schreiner M, et al. Regeneration of hyaline cartilage in response to a single injection of LNA043, an ANGPTL3 mimetic, in the knee of patients with a focal cartilage defect. Osteoarthritis and Cartilage 29: S220-S221, 2021.

LNA043 Ph2b ONWARDS trial in patients with knee OA



ONWARDS[1]: A 5-year, randomized, double-blind, placebo-controlled, multi-center study assessing the efficacy, safety, and tolerability of intra-articular regimens of LNA043 in patients with symptomatic knee osteoarthritis

Study endpoints

Primary
Change from baseline at 2 years in the cartilage thickness of the medial compartment of the knee as assessed by imaging

Key secondary
Change from baseline in WOMAC pain and function at 2 years

1. ClinicalTrials.gov Identifier: NCT04864392. WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

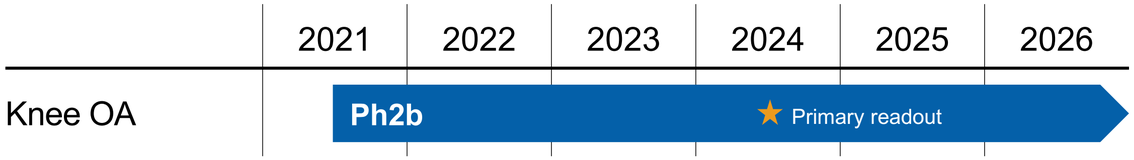
LNA043 has the potential to become a disease modifying drug for knee OA with a blockbuster potential

Market potential

Indication	**Prevalence** (G8)	Asset potential
Knee OA	165 m	●●●

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Upcoming milestones for development program



Neuroscience

Our NS development strategy is focused on areas of high unmet need, with a strong late and early-stage pipeline

Neuroscience strategy

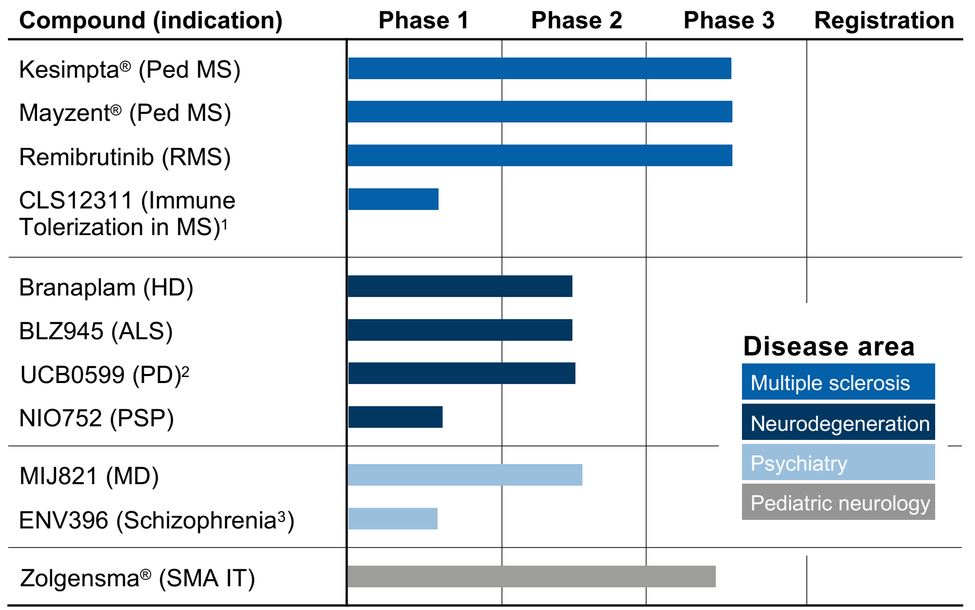
Ambition to deliver complete disease control for people living with **multiple sclerosis**

Slow disease progression for people with **neurodegenerative disease**

Deliver transformational symptomatic control and disease modification in **psychiatry**

Correct genetic deficits in children with **genetically driven** neurological conditions with Zolgensma®

Assets highlighted today:
remibrutinib, Zolgensma®, branaplam, UCB0599



Partnerships across multiple platforms: Cellerys in MS, UCB in PD, Sangamo in pediatric neurology

1. Option to acquire after Ph2 2 In partnership with UCB. 3.Cadent sponsor of schizophrenia Ph1 trial Note: bars in gantt chart indicate current phase of development.

Remibrutinib (LOU064)

Oral, covalent BTK (Bruton's tyrosine kinase) inhibitor targeting immune cell signaling

Phase 3

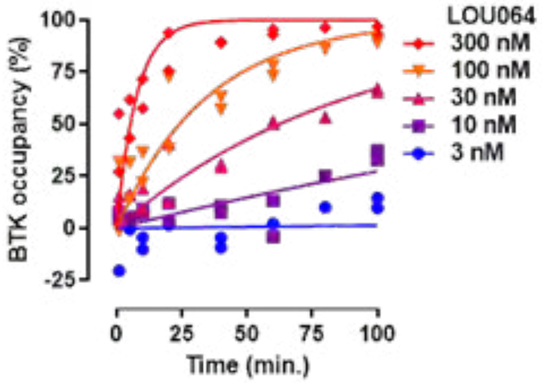
Key highlights

- Despite the availability of several DMTs for the treatment of MS, **patients continue to experience disease activity**
- **BTKi inhibit activation of B-cells** and other innate immune cells with oral convenience
- Remibrutinib is a highly selective, potent covalent BTK inhibitor with **best-in-class potential in MS** as it may offer **comprehensive and sustained BTK inhibition** that allows maximizing on efficacy without compromising safety
- Ph2b data in CSU showed rapid and biologic-like efficacy, a positive benefit/risk profile and **good tolerability across entire dose range tested**
- **Direct to Ph3 in RMS**. REMODEL-1 and 2 to begin enrollment in 2021
- **US/EU**: Patent on compound (2034/2034)[1]

DMT: Disease Modifying Therapy MS: Multiple Sclerosis CSU: Chronic Spontaneous Urticaria RMS: Relapsing Multiple Sclerosis DMT: Disease Modifying Therapy 1. Patent term extensions and regulatory-based exclusivities are possible

Remibrutinib: potent and rapid BTK inhibition expected to translate into clinical efficacy and favorable safety profile

Remibrutinib shows potent BTK inhibition in human blood *in vitro* at clinically relevant concentrations[1]



Data suggest that remibrutinib has **rapid reaction kinetics and rapidly reaches full BTK** inhibition in relevant matrices such as human blood

Remibrutinib demonstrated good tolerability across the entire dose range tested with no safety signals

Key safety data include:

- ✓ No dose dependent increase of, treatment interruption or discontinuation due to LFT elevations
- ✓ No dose dependent cytopenias, treatment interruption or discontinuation due to low blood cell counts
- ✓ No clinically relevant adverse events associated with BTK inhibitor class (e.g., infections, cytopenias, bleeding, hepatic events) across the dose range tested

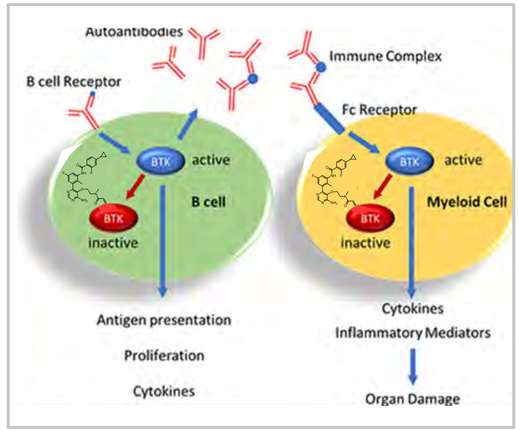
Potential best-in-class profile based on positive benefit/risk profile. Ph3 studies in RMS initiating

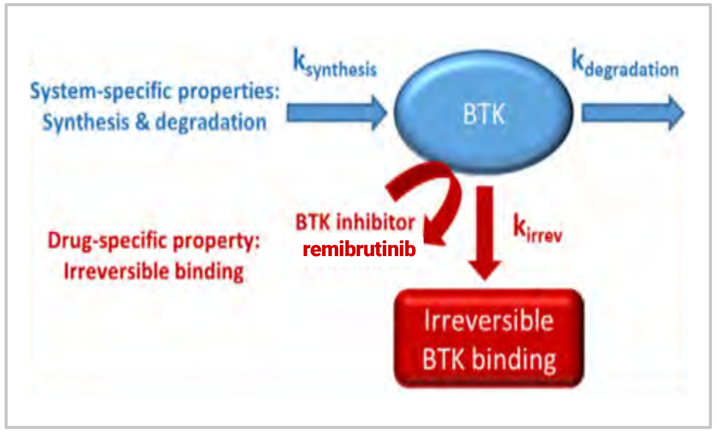
BTK - Bruton's tyrosine kinase RMS – Relapsing Multiple Sclerosis LFT – Liver Function Test.

Initiating Ph3 trials with remibrutinib in relapsing multiple sclerosis

Remibrutinib

Potential best-in-class potency, selectivity and safety. May offer a **more comprehensive and sustained BTK inhibition** that allows for **maximizing efficacy** without compromising patient safety





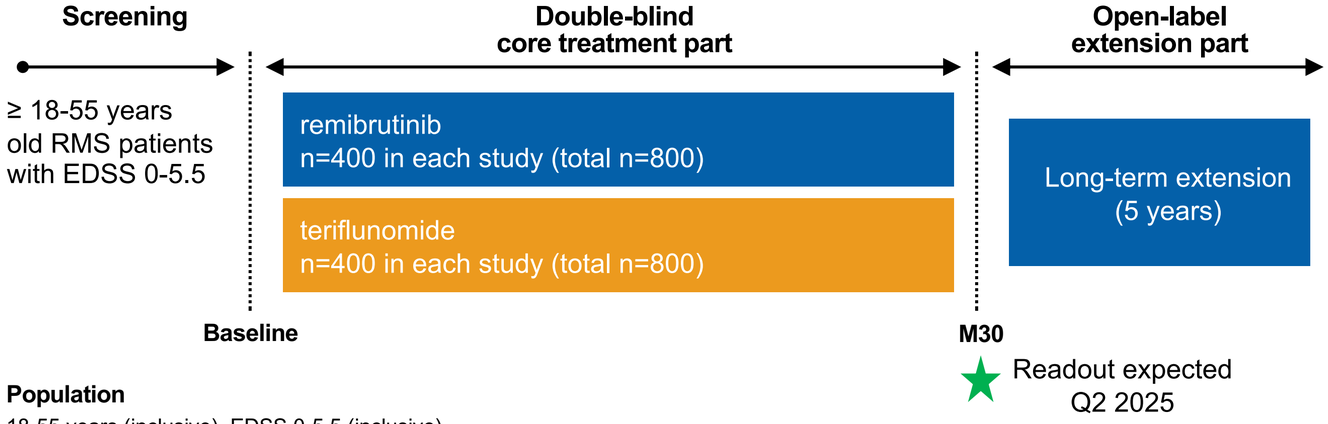
- **Covalently binds** to the intracellular enzyme BTK in B cells and myeloid cells
- **Potent BTK inhibition** with brief and low systemic exposure which **minimizes risk** for AEs and drug-drug interactions
- CSU data – **no dose-limiting side effects** in Ph2a trial
- **Move directly into Ph3** in MS, with trials to start in Q4 2021

BTK - Bruton's tyrosine kinase AE . Adverse Event CSU – Chronic Spontaneous Urticaria

REMODEL 1, 2 powered to show superiority vs teriflunomide

REMODEL 1 and 2 initiation expected in 2021

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

Objective

Compare the efficacy and safety of remibrutinib vs teriflunomide in Relapsing Multiple Sclerosis patients (adults)

1º endpoint

Annualized relapse rate (ARR)

Key 2º endpoints

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

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

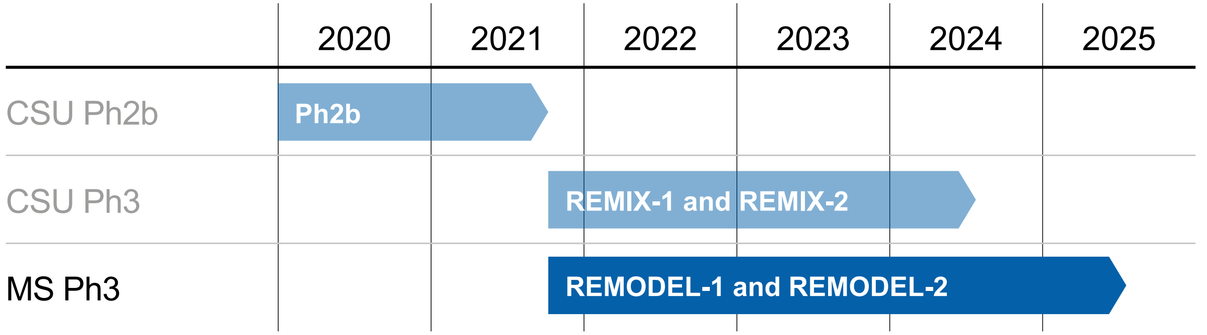
Remibrutinib with significant commercial potential across indications

Market potential

Indication	Prevalence[1]	Asset potential
CSU	~740k	●●●
RMS	> 0.5m	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Upcoming milestones for development program



REMIX-1 and REMIX-2

- Enrollment started November 2021
- Submission in 2024

REMODEL-1 and REMODEL-2

- Enrollment start December 2021
- Submission in 2025

RMS – Relapsing Multiple Sclerosis. CSU – Chronic Spontaneous Urticaria 1. US+EU5

Zolgensma®
(onasemnogene abeparvovec)

AAV gene therapy for the treatment of spinal muscular atrophy

Marketed (IV); Phase 3 (IT)

Key highlights

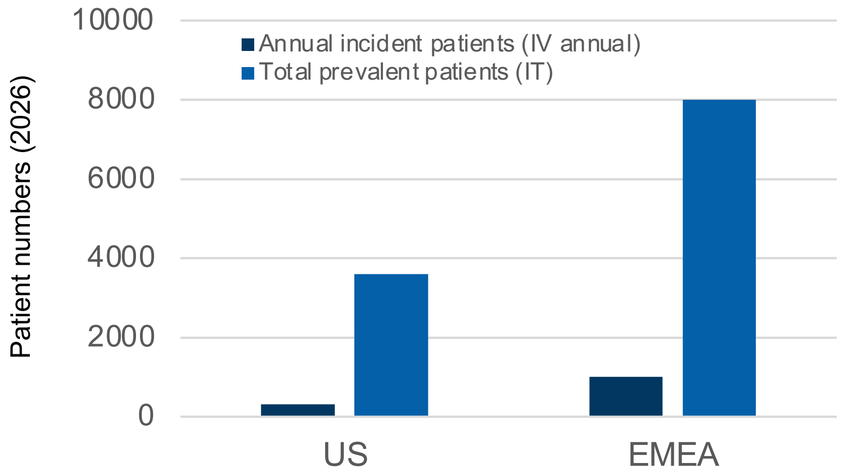
- Indications:
  - Worldwide Incident SMA Population (2022): 6,800
  - Worldwide Prevalent SMA Population in 2026: 60,000
- Zolgensma is an essential one-time treatment that replaces the function of the missing or non-working SMN1 gene
- Zolgensma demonstrated age-appropriate development when used presymptomatically; consistent, significant benefit in symptomatic children; and durability 5+ years post-treatment
- OAV101 IT (STRONG) demonstrated significant efficacy with a rapid and sustained improvement in motor function
- US/EU: Patent on composition of matter (2033)/Regulatory-based exclusivity (2030)[1]
- Key upcoming milestones:
  - SMART (IV): anticipate data readout in 2023
  - STEER (IT): anticipate beginning enrollment in coming weeks

AAV – Adeno Associated Virus SMA – Spinal Muscular Atrophy SMN – Survival Motor Neuron IV – Intravenous IT – Intrathecal 1. Patent term extensions and regulatory-based exclusivities are possible.

OAV101 IT would replace chronic administration for a large potential SMA population with significant unmet needs

Our goal is to make gene therapy foundational to all patients with SMA who may benefit

Potential patient population by 2026



Existing therapies have limitations

- Require chronic use over person's lifetime
- Work on the back-up *SMN2* gene
- Risks and compliance challenges with administration

*OAV101 IT expected to file in 2025

SMA – Spinal Muscular Atrophy SMN – Survival Motor Neuron IV – Intravenous IT – Intrathecal *Assumes priority review.

New clinical trials will build on STRONG data, which reinforced potential best-in-category profile for OAV101 IT for later-onset SMA

A 3-point increase in HFMSE is agreed by experts to represents the **minimum** change considered clinically meaningful[1–3]

Transformational efficacy with a 6-point mean increase in HFMSE[4], 2x the clinically meaningful threshold

Rapid and Sustained Hammersmith Scores with gains seen across all five domains of motor function

Safety profile consistent with IV program

Comprehensive data package resolved FDA non-clinical safety concerns with DRG, partial hold lifted Aug 2021

Sitting

Rolling

Transitioning/Crawling

Transitioning/Kneeling

Standing/Stepping

HFMSE – Hammersmith Functional Motor Scale-Expanded IV – Intravenous FDA – Food and Drug Administration DRG – Dorsal Root Ganglia 1. Swoboda KJ, et al. PLoS One. 2010;5:e12140. 2. Swoboda KJ, et al. PLoS One. 2009;4:e5268. 3. Mercuri E, et al. N Engl J Med. 2018;378:625–635. 4. A 6-point change in HFMSE from baseline impacts between 3 and 6 skills.

OAV101 IT clinical program aims to confirm potential best-in-category profile for prevalent SMA

	STEER – Ph3	STRENGTH – Ph3b
Population	Treatment-naive patients with SMA Type 2 aged 2-18 who can sit but have never walked (n=>100)	Patients aged 2-12 with SMA who receive OAV101 IT after discontinuing treatment with nusinersen and/or risdiplam
Overview	Global, Ph3, sham-controlled	Global, Ph3b, open-label study
Primary Objective	HFMSE change from baseline at 52 weeks	Safety and tolerability
Status	**Patient enrollment anticipated in coming weeks**	**Planning patient enrollment in 2H 2022**

SMA – Spinal Muscular Atrophy IT – Intrathecal HFMSE – Hammersmith Functional Motor Scale-Expanded

Zolgensma® expanding clinical data set across IV and IT formulations

Market potential

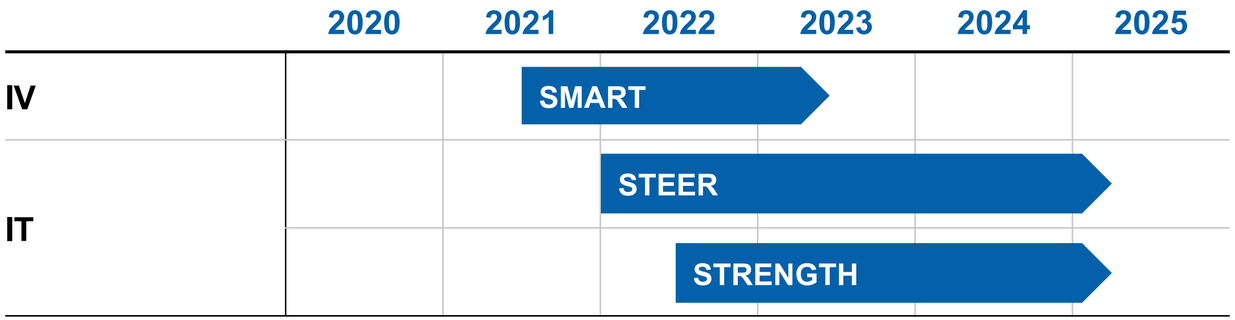
Formulation	Asset potential
IV	●●●
IT	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Addressable patients[1]

Indication	Patients
Incident (2022)	6,800
Prevalent (2026)	60,000

Upcoming milestones for development program[2]



SMART: currently enrolling SMA patients who are ≤21kg in global Ph3b trial; anticipate data readout in 2023.

STEER: anticipate beginning to enroll treatment-naive patients with SMA Type 2 (aged 2 -18) in coming weeks for global Ph3 trial

STRENGTH: enrollment of patients aged 2-12 with SMA to receive OAV101 IT after discontinuing treatment with nusinersen and/or risdiplam anticipated to begin in 2H22.

IV – Intravenous IT – Intrathecal SMA – Spinal Muscular Atrophy 1. Worldwide incident and prevalent populations. 2. End of arrow denotes estimated study completion.

Branaplam (LMI070)

Orally administered, small molecule RNA splicing modulator

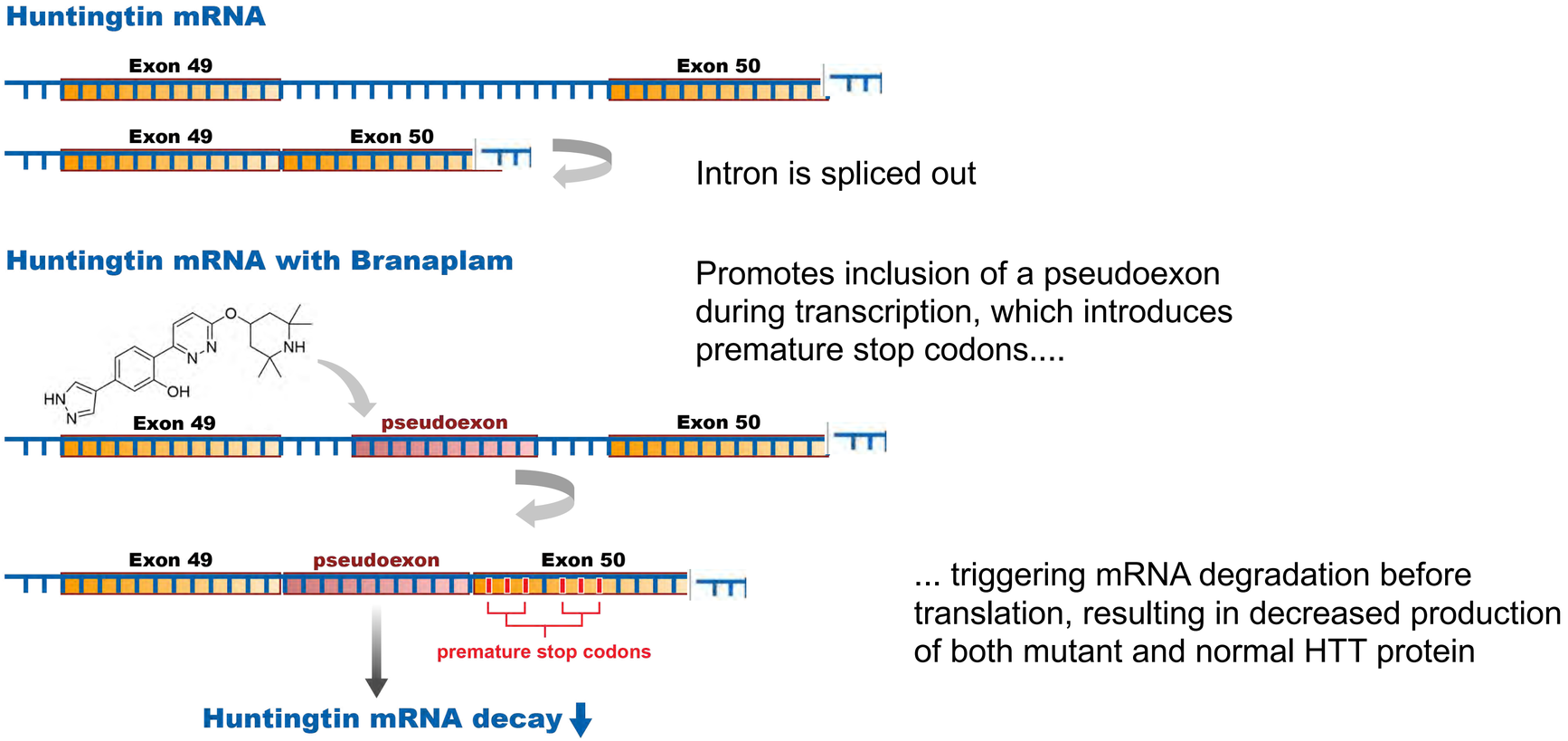
Phase 2

Key highlights

- **~70k people** with Huntington's Disease in G6 with high unmet need
- **No approved disease modifying therapies** that delay disease onset or slow progression
- Branaplam is an **oral RNA splicing modulator** that lowers HTT by driving HTT mRNA degradation and has the potential to be the **first disease modifying therapy for HD**
- Proof of concept demonstrated in pre-clinical and Ph1 studies and **clinical data in children with SMA**
- **Ph2b VIBRANT-HD study** aims to identify dose which reduces mHTT sufficiently to provide clinical benefit while maintaining adequate levels of HTT for normal function. To be initiated Q4 2021
- **US/EU**: Patent on compound (2033/2033)[1]

RNA – Ribonucleic Acid HTT – Huntingtin mHTT – Mutant Huntingtin SMA – Spinal Muscular Atrophy 1. Patent term extensions and regulatory-based exclusivities are possible

Branaplam lowers human HTT levels by driving HTT mRNA degradation



RNA – Ribonucleic Acid mRNA – messenger Ribonucleic Acid HTT – Huntingtin mHTT – Mutant Huntingtin

Huntington's disease is a devastating neurodegenerative disease

Our goal is to transform care with the first oral disease-modifying therapy

Huntington's disease

- Inherited disease affecting multiple generations of families, those with a mutated gene develop the disease
- Patients typically diagnosed age 30-50, disability leads to death within 15-20 years
- Characterized by progressive worsening in motor, cognitive and psychiatric symptoms
- Rare disease, ~70,000 diagnosed patients in US and EU
- No approved disease modifying therapies to delay disease onset or slow progression
- Earlier diagnosis by genetic testing expected as disease-modifying therapies become available

Branaplam

- Oral branaplam lowers Huntingtin protein, an opportunity for disease modification
- Non-invasive oral splice modulator for at-home administration
- Convenience of once weekly dosing
- May provide uniform HTT lowering throughout brain based on mouse models
- Broad exposure in peripheral tissues

HTT – Huntingtin

Proof of concept demonstrated in Huntington's Disease

Ph1 results consistent with earlier preclinical data and clinical findings in SMA

Ph1 healthy volunteer results support proof of concept and Ph2 initiation

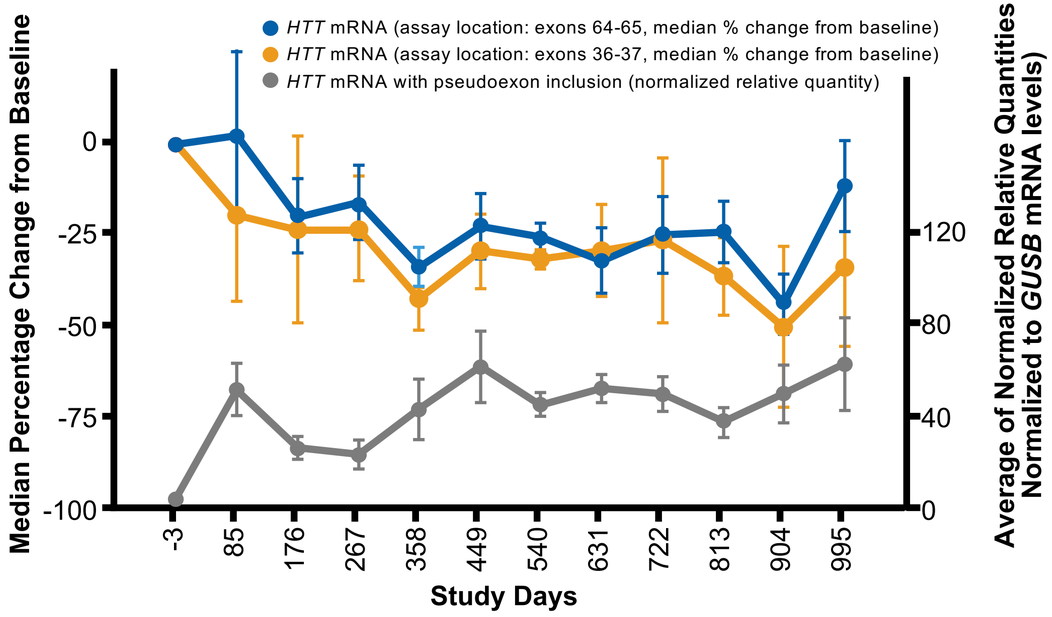
- Dose-dependent target engagement shown by inclusion of pseudoexon 50a in blood
- HTT mRNA and protein levels reduced in blood after single doses in healthy volunteers
- PK/PD supports weekly oral dosing
- Well-tolerated

Market potential

Indication	Asset potential
Huntington's Disease	●●●

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

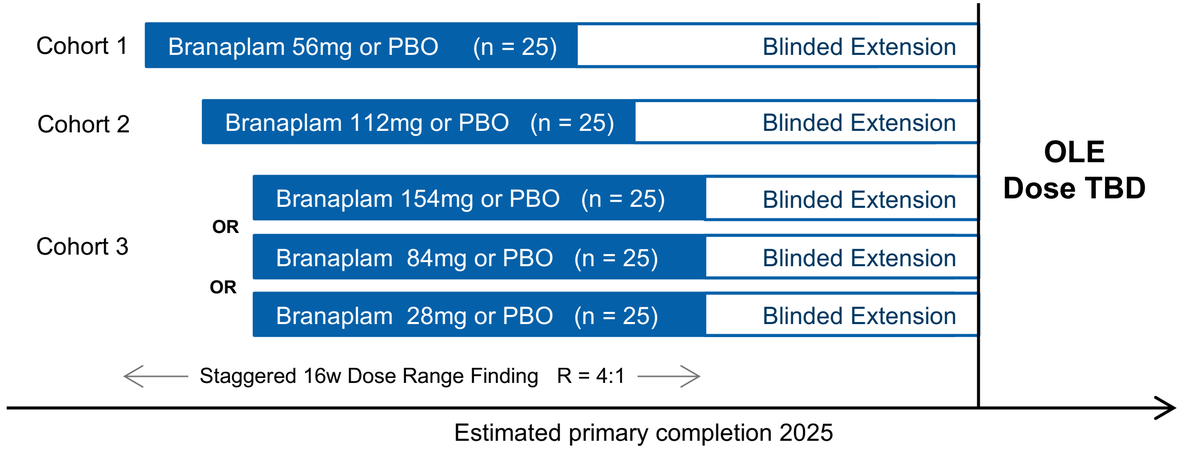
Branaplam lowering of HTT mRNA in SMA patients demonstrates target engagement and mechanism



SMA – Spinal Muscular Atrophy HTT – Huntingtin mRNA – messenger Ribonucleic Acid PK – Pharmacokinetics PD – Pharmacodynamics

Ph2b VIBRANT-HD study to begin enrollment by year end

VIBRANT-HD[1]



- Randomized, double-blind, placebo-controlled dose range finding study with open-label extension
- Primary end-points: % reduction in mHTT protein in CSF, number of treatment emergent adverse events and serious adverse events

Study attributes

Evaluating safety, tolerability, pharmacokinetics and pharmacodynamics of branaplam when administered as weekly oral doses in participants with early manifest HD

Goal is to identify a dose of branaplam which is safe and well-tolerated, and lowers mHTT sufficiently in CSF to expect a clinical benefit in HD (35-50%)

PBO – Placebo mHTT – mutant Huntingtin CSF – Cerebrospinal Fluid OLE – Open Label Extension HD – Huntington's Disease 1. ClinicalTrials.gov Identifier: NCT05111249

UCB0599

Potential first-in-class, small molecule, alpha-synuclein misfolding inhibitor

Phase 2

Key highlights

- **10m people** with Parkinson's Disease (PD) worldwide[1]
- High unmet need given **lack of disease-modifying therapies** with Parkinson's disease the fastest growing neurological disorder in prevalence, disability, and deaths[2,3]
- Novartis and UCB have entered into a co-development and co-commercialization agreement for **UCB0599** (alpha-synuclein misfolding inhibitor), with opt-in for **UCB7853** (anti-alpha-synuclein antibody)
- With UCB0599, potential to transform care with **first oral disease modifying therapy for PD**[4]
- Alpha-synuclein misfolding most prominent **neuropathological hallmark** of PD and primary step in disease progression[5]
- **In a preclinical model,** UCB0599 reduced α-synuclein pathology and downstream neurodegeneration, as well as improved functional motor endpoints[6]
- UCB0599 in **Ph2 clinical development**. UCB7853 in Ph1

1. Parkinson's Foundation. Parkinson's Disease Statistics. https://www.parkinson.org/Understanding-Parkinsons/Statistics. Accessed November 2021. 2. Bloem BR, Okun MS and Klein C. Parkinson's disease. The Lancet Neurology. 2021; 397 (10291), 2284-2303. 3. Ray Dorsey E, Elbaz A, Nichols E et al. Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2018;17(11):939-953. 4. Smit JW, Maguire RP, Avbersek A et al. UCB0599 transition to the clinic: An orally available brain-penetrant inhibitor of αsynuclein (ASYN) misfolding in Ph1 development for Parkinson's disease (PD). MDS Virtual Congress September 12–16 Late-breaking abstract;LBA4. https://www.movementdisorders.org/Congress-Branded/Congress-2020-Files/MDSVirtualCongressLateBreakingAbstracts1.pdf. Accessed November 2021. 5. Bendor JT, Logan TP, Edwards RH. The function of alpha-synuclein. 2013, 79: 1044-1066. . 6. UCB, Data on file.

Oncology

We are building on the strength of our Oncology pipeline to maximize impact for patients

Oncology strategy

Leading Oncology pipeline
with >30 NMEs in clinical development, reaching >1.2m patients

Strengthen our core
by maximizing existing and accelerating new assets

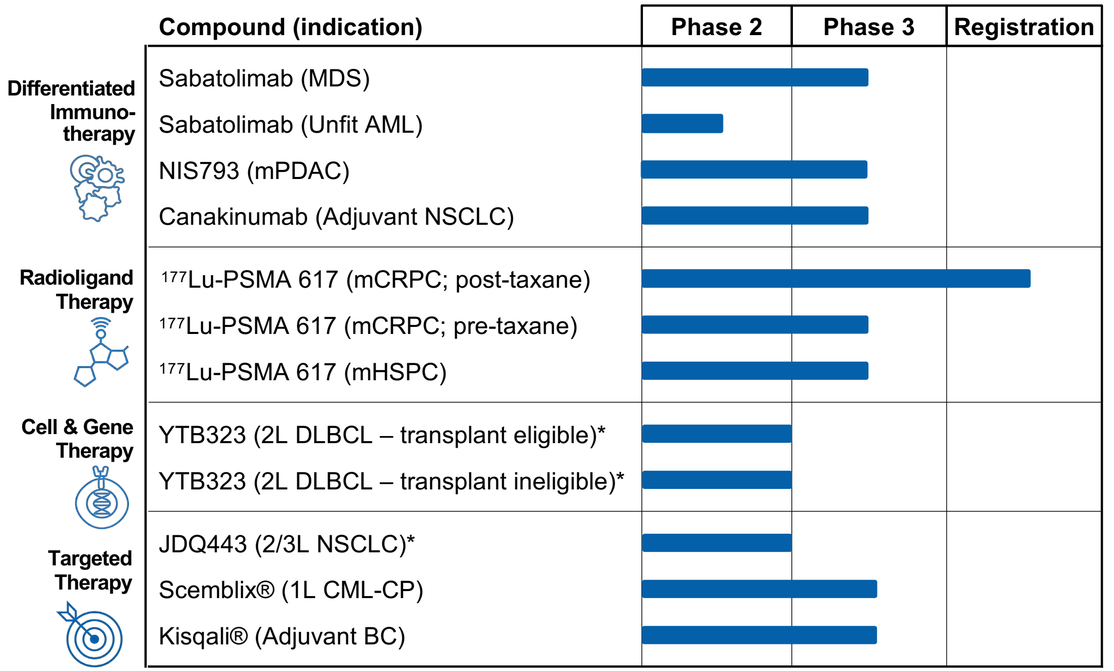
- Prioritize development in Breast, Prostate, Lung, AML/MDS and NHL
- Additional investment in asset-driven opportunities with breakthrough potential (e.g. NIS793)
- Expanding indications in areas with highest unmet need and moving into earlier lines of therapy – ultimately with curative intent

Invest in innovative combinations and advanced therapy platforms

- Explore innovative combinations across platforms to deepen responses and overcome resistance
- Expand our leading position in RLT with Lu-PSMA 617 in Prostate and beyond
- Invest in next generation of our C&G pipeline (e.g. YTB323)

Assets highlighted today:
Kisqali, ^{177}Lu-PSMA-617, sabatolimab, JDQ443, TNO155, YTB323 & PHE885, Scemblix, NIS793

Key late-stage programs in 2022 across platforms



* Planned Phase 3 programs initiating in 2022

CANOPY-1 Ph3 data support further evaluation of canakinumab in lung cancer

CANOPY-1

- Did not meet primary endpoints: OS and PFS in previously untreated locally advanced or metastatic NSCLC[1]
- **Potentially clinically meaningful improvements in both PFS and OS** among pre-specified subgroups of patients with inflammatory biomarkers; additional analyses ongoing[1]
- Results support **continued study of canakinumab in earlier stages** of lung cancer, further evaluation of Pro-Tumor Inflammation in all lung cancer settings[1].
- **CANOPY-A** study more closely reflect the CANTOS study population vs. CANOPY-1[2,3,4.] CANTOS the 1st study to suggest that IL-1β inhibition may play a role in lung cancer[3]
- **No unexpected safety signals** when combined with pembrolizumab plus platinum-based chemotherapy

Study	Patient population	Hypothesis	Findings
CANOPY-2 2/3 L NSCLC	Metastatic NSCLC treatment failed. Canakimumab with docetaxel	Reduce progression of treatment resistant tumors	Primary endpoint OS not met. No benefit observed.
CANOPY-1 1L NSCLC	Metastatic NSCLC, treatment naive. Canakimumab combined with pembrolizumab	Reduce progression of treatment naive tumors	Primary endpoints of OS + PFS not statistically significant. Potentially clinically meaningful OS +PFS improvements in pre-specified subgroups (hs-CRP, other biomarker-defined subgroups)
CANOPY-A Adjuvant NSCLC	Stage II-III NSCLC. Canakimumab after complete resection and adjuvant chemotherapy	Reduce development of tumors from micro-metastatic disease.	To be determined
CANTOS	Stable post MI with elevated hsCRP > 2mg/L	Alter tumor development in high risk population	Dose-dependent reduction in fatal/non-fatal lung cancer incidence

Developing other potential pro-tumor inflammation pathway inhibitors, which are at various stages of development, incl. gevokizumab[5,6]

1. Novartis Data on File 2.ClinicalTrials.gov. Brief Title: Study of Efficacy and Safety of Canakinumab as Adjuvant Therapy in Adult Subjects With Stages AJCC/UICC v. 8 II-IIIA and IIIB (T>5cm N2) Completely Resected Non-small Cell Lung Cancer 3. Ridker PM, Thuren T, Zalewski A, et al. Interleukin-1β inhibition and the prevention of recurrent cardiovascular events: rationale and design of the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS). Am Heart J. 2011;162:597–605 4. ClinicalTrials.gov. Study of Efficacy and Safety of Pembrolizumab Plus Platinum-based Doublet Chemotherapy With or Without Canakinumab in Previously Untreated Locally Advanced or Metastatic Non-squamous and Squamous NSCLC Subjects (CANOPY-1) 5. ClinicalTrials.gov. Gevokizumab With Standard of Care Anti-cancer Therapies for Metastatic Colorectal, Gastroesophageal, and Renal Cancers. 6. Jayaraman. P. Targeting IL-1β pathway for cancer immunotherapy. Proceedings of the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics; 2019 Oct 26-30

Kisqali®

Cyclin-dependent kinase 4/6 inhibitor

Marketed;
LCM in Phase 3

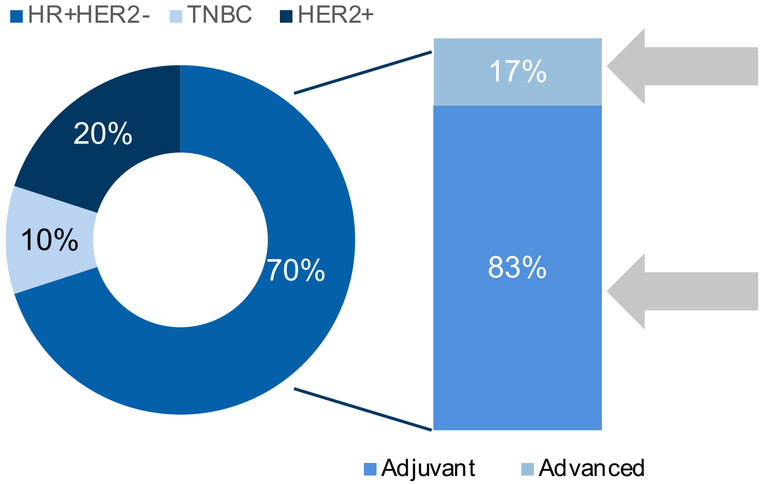
Key highlights

- **Kisqali® has the most robust and rigorous body of evidence to be positioned as the standard of care (SOC)** in 1L postmenopausal HR+/HER2- aBC, the largest patient population (~25K patients in the US each year, and up to ~370K patients globally)
- **Kisqali® achieved the longest median overall survival (OS) ever reported in aBC (>5 years);** it is the only CDK 4/6i with statistically significant OS across three Ph3 trials
- **Kisqali® is being investigated in early BC in the Ph3 NATALEE study**
- If successful, Kisqali® will be the only CDK4/6i with evidence supporting use in the **intermediate and high-risk populations** (>200K patient in the US & EU)
- NATALEE trial readout is event driven and expected in **2022**
- US/EU: Patent on compound (2031/2032)[1]

1. Includes extended patent terms. For additional information, please refer to the Novartis 20F 2020

HR+/HER2- BC, the largest segment in BC, remains an area of high unmet need

Estimated percentages of total breast cancer population



"...Improving patient outcome without putting additional burden on the patient is the challenge. ... you would not accept a treatment which reduces quality of life.'"

US Oncologist (Market Research Study 2020)

Metastatic Breast Cancer

- **Extending OS without impacting quality of life (QoL)** is the #1 treatment goal
- Kisqali® is the only CDK 4/6 inhibitor that **significantly improved OS** while maintaining or **improving QoL** consistently across all patient subgroups in three pivotal trials

Early Breast Cancer (eBC)

- **83%** of breast cancers are diagnosed as eBC
- The treatment goal in eBC is to **prevent disease recurrence while maintaining QoL**
- Kisqali® is being investigated in eBC in the Ph3 NATALEE study
- The study is uniquely designed to assess benefit in both **intermediate and high-risk populations**

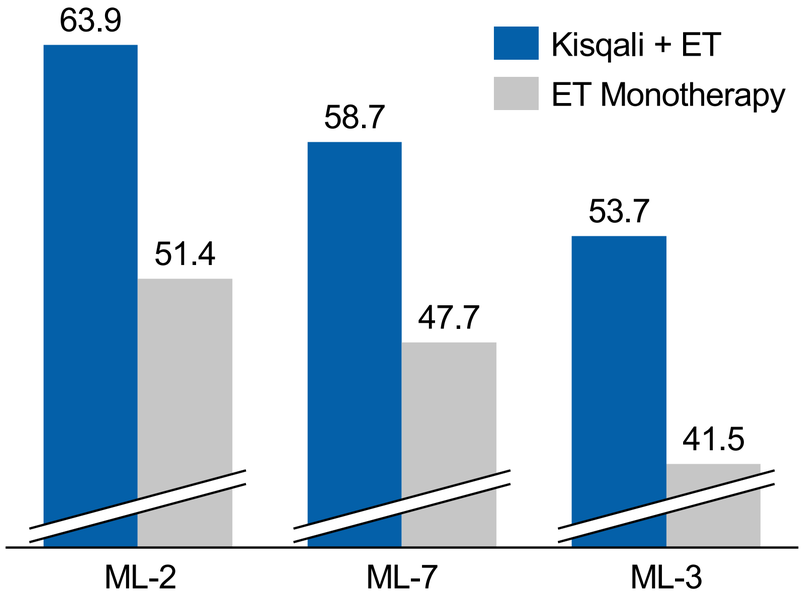
>3x	More intermediate risk patients diagnosed vs. high risk

Data Source: Kantar Health – US/ EU5 Patient Metrics 2020

Kisqali® has demonstrated significant OS benefit regardless of ET partner, line of therapy or menopausal status

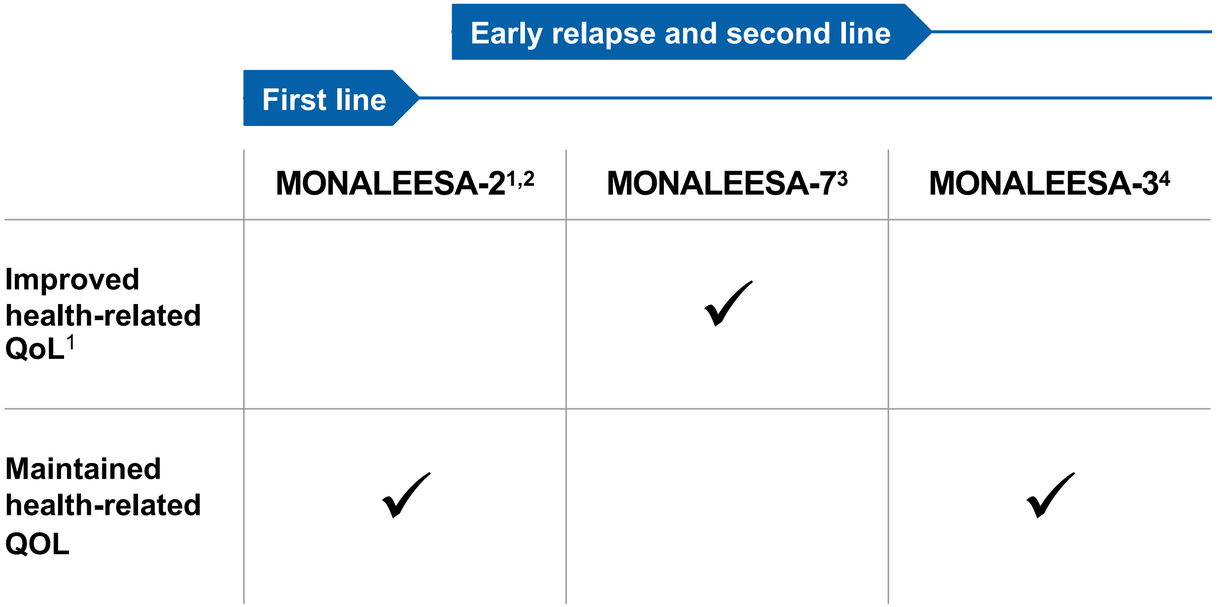
Overall survival across HR+/HER2- Ph3 trials

Months



- Kisqali is the only CDK 4/6 inhibitor with statistically significant overall survival proven across all three Ph3 trials
  - MONALEESA-2: the longest overall survival ever reported in KISQALI + AI (letrozole) in 1L postmenopausal patients *P*=0.004 (HR=0.765 [95% CI: 0.628-0.932])
  - MONALEESA-7: the longest overall survival reported in KISQALI + AI (NSAI + goserelin) in 1L premenopausal patients *P*=0.00973 (HR=0.71 [95% CI: 0.54-0.95])
  - MONALEESA-3: the longest overall survival reported in KISQALI + fulvestrant in 1L and 2L postmenopausal patients *P*=0.00455 (HR=0.726 [95% CI: 0.588-0.897])
- Overall survival increase of ~1 year or more across the trials

Overall QoL was maintained or improved across all MONALEESA trials



	MONALEESA-2[1,2]	MONALEESA-7[3]	MONALEESA-3[4]
Improved health-related QoL[1]		✓	
Maintained health-related QOL	✓		✓

Kisqali®-based combinations maintained or improved QoL and **delayed time to CT by at least 4 years (incl. 1 year improvement vs. ET alone)** in MONALEESA trials

AEs with Kisqali® are generally asymptomatic and do not impact activities of daily life

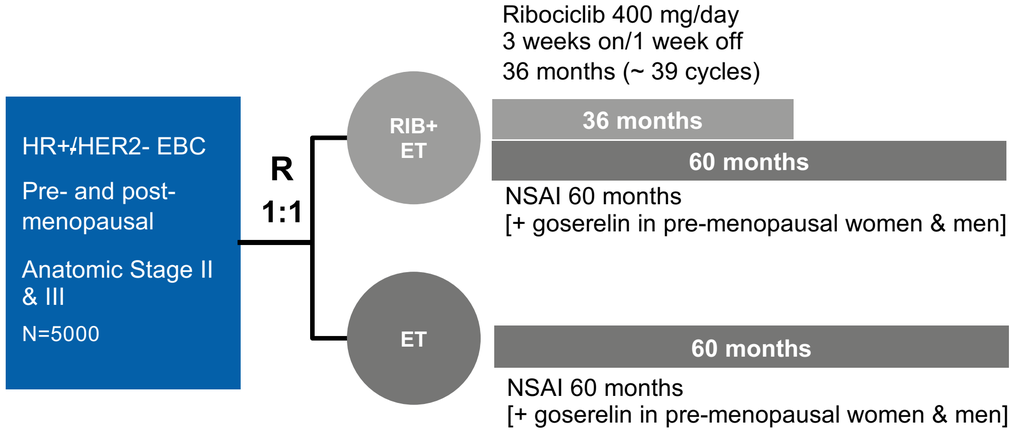
As eBC is a disease-free setting, QoL considerations become even more relevant

Additional data collection underway to assess **patient preferences** and **long-term QoL on Kisqali®**

1. Verma et al. Breast Cancer Res Treat. 2018;170(3):535-545. 2. Janni et al. Breast Cancer Res Treat. 2017;169(3):469-479. 3. Harbeck N, et al. Ther Adv Med Oncol. 2020;12:1758835920943065. 4. Fasching P, et al. Breast. 2020;54:148-154.

NATALEE adjuvant trial could address large unmet need in eBC

NATALEE study design



Indication	Asset potential	Population
Early breast cancer	●●●	218K (US & EU)[1]

●○○ <USD 1bn ●●○ USD 1bn – 2bn ●●● >USD 2bn

What makes NATALEE unique?

- Broad patient population that includes **patients with high and intermediate risk** of recurrence[2] (60% Stage III and 40% Stage II; stratification factor)[3]
- **Longer treatment duration** of 3 vs. 2 years (monarchE)
- **Lower dose compared to metastatic setting** (400mg vs. 600mg) to potentially improve overall tolerability without compromising efficacy in a disease-free setting

Study status

- Enrollment is **complete**
- **Discontinuation rate remains within expectations** based on current aggregate data
- Final readout is event-driven and **anticipated in 2022**

1. eBC Patient - Adjuvant Breast Cancer Opportunity Assessment June 2020. 2. based on AJCC prognostic staging. 3. The trial did not require Ki-67% or other CDx for patient identification or stratification, but Ki-67% is part of the statistical analysis plan

^{177}Lu-PSMA-617

Radioactive lutetium-labelled small molecule targeting the prostate specific membrane antigen (PSMA)[1]

Registration

Key highlights

- ^{177}Lu-PSMA-617 anticipated to address a **broad set of prostate cancer disease stages**
  - **Post-taxane mCRPC** (VISION trial, in registration)
  - Pre-taxane **mCRPC** and **mHSPC** patients in ongoing Ph3 studies PSMAfore and PSMAddition
- ^{177}Lu-PSMA-617 is expected to be the **first-to-market radioligand therapy targeting >80% of prostate cancer patients who express PSMA**[4-11]
- In the VISION trial, ^{177}Lu-PSMA-617 **reduced the risk of death by 38%**, **radiographic progression or death by 60%** in patients with mCRPC compared to SoC alone[2], and ad-hoc analyses showed it delayed worsening of health-related quality of life and pain[3]
- **US and EU approvals expected in 2022** (FDA granted Priority Review and BTD)
- US: Patents on composition of matter (2028-2034); patents in EU pending

mCRPC: metastatic castration-resistant prostate cancer; **mHSPC**: metastatic hormone-sensitive prostate cancer.

1. Benešová M, et al. J Nucl Med. 2015;56(6):914–920. 2. Sartor O et al. N Engl J Med. 2021;385:1091-1103. 3. Fizazi K et al. Ann Oncol 2021;32(Suppl): S627-S628. 4. Hofman MS, et al. Lancet Oncol. 2018;19(6):825–833. 5. Violet J, et al. J Nucl Med. 2019;60(4):517–523. 6. Kratochwil C, et al. J Nucl Med. 2016;57(8):1170–1176. 7. Hope TA, et al. J Nucl Med. 2017;58(12):1956–1961. 8. Hupe MC, et al. Front Oncol. 2018;8:623. 9. Pomykala KL, et al. J Nucl Med. 2020;61(3):405–411. 10. Minner S, et al. Prostate. 2011;71(3):281–288. 11. Bostwick DG, et al. Cancer. 1998;82(11):2256–2261

^{177}Lu-PSMA-617 RLT enables targeted delivery of radiation to tumor while limiting damage to surrounding normal tissue[1-5]

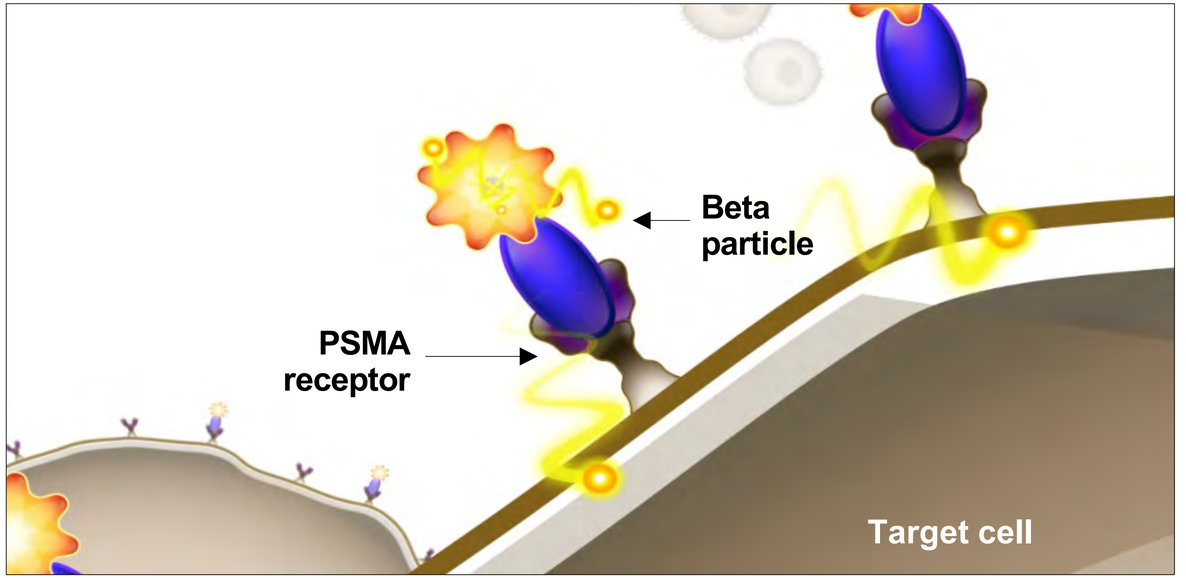
Why ^{177}Lu-PSMA RLT?

Binds to PSMA, highly expressed on >80% prostate cancer cells[6-9]

Once bound and internalized, the Lutetium-177 radioisotope **releases an energetic beta particle**[8,10-12]

This causes DNA breaks, **disrupting target cell's ability to replicate and/or triggering cell death**[13-14]

Designed to deliver radiation to target cells; may also impact neighboring cells[2-3,15]



1. Hofman MS, et al. Lancet Oncol. 2018;19(6):825–833. 2. Violet J, et al. J Nucl Med. 2019;60(4):517–523. 3. Kratochwil C, et al. J Nucl Med. 2016;57(8):1170–1176. 4. Boyd M, et al. Gene Ther. 1999;6(6):1147–52. 5. Current K, et al. Clin Cancer Res 2020;26(12):2946–55. 6. Hupe MC, et al. Front Oncol 2018;8:623. 7. Bostwick DG, et al. Cancer 1998;82(11):2256–61. 8. Rahbar K, et al. J Nucl Med. 2017;58(1):85–90. 9. Benešová M, et al. J Nucl Med. 2015;56(6):914–920. 10. Liu H, et al. Cancer Res. 1998;58(18):4055-4060. 11. Grupen C. Introduction to radiation protection. Springer-Verlag Berlin Heidelberg 2010. Doi: 10.1007/978-3-642-02586-0. 12. EMA. EndolucinBeta. Assessment report. EMA/CHMP/404078/2016: lutetium chloride. https://www.ema.europa.eu/en/documents/assessment-report/endolucinbeta-epar-public-assessment-report_en.pdf (accessed December 2020). 13. Ruigrok EAM, et al. Eur J Nucl Med Mol Imaging. 2020. https://doi.org/10.1007/s00259-020-05057-6 [Epub]. 14. Fendler WP, et al. J Nucl Med. 2017;58(11):1786–1792. 15. Kassis AI, et al. Semin Nucl Med. 2008;38(5):358–366.

High remaining unmet medical need for patients with Prostate Cancer requires treatments with novel mechanisms of action

Prostate cancer is the

2nd

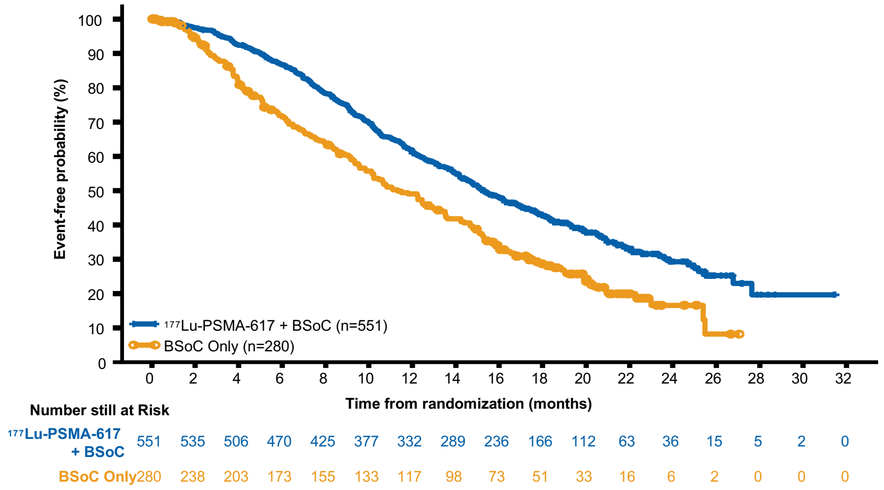
most diagnosed cancer in men[1]

Stage of disease	Non-metastatic		Metastatic	
	BCR-PC	nmCRPC	mHSPC	mCRPC
Key facts	**~35%** develop metastases within 2 years of diagnosis[2]		**~30%** 5-year **survival** prognosis[3] **~10** months median OS[4]	
Novel MoAs are needed to	**Delay progression to metastatic disease**		**Prolong survival**	

1. Ferlay J EM, et al. Global cancer observatory: cancer today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today. 2. in non-metastatic castration-resistant prostate cancer: Sternberg et al 2020 N Engl J Med. 2020;382:2197–206. 3. SEER. Cancer stat facts: prostate cancer April 2021. [https://seer.cancer.gov/statfacts/html/prost.html]. 4. In men with progressive mCRPC after docetaxel and abiraterone and/or enzalutamide, Smith et al., Phase III Study of Cabozantinib in Previously Treated Metastatic Castration-Resistant Prostate Cancer: COMET-1, J Clin Oncol 34:3005-3013 ;

^{177}Lu-PSMA-617 reduced risk of death by 38%, and radiographic progression or death by 60% in patients with mCRPC (VISION)[1,2]

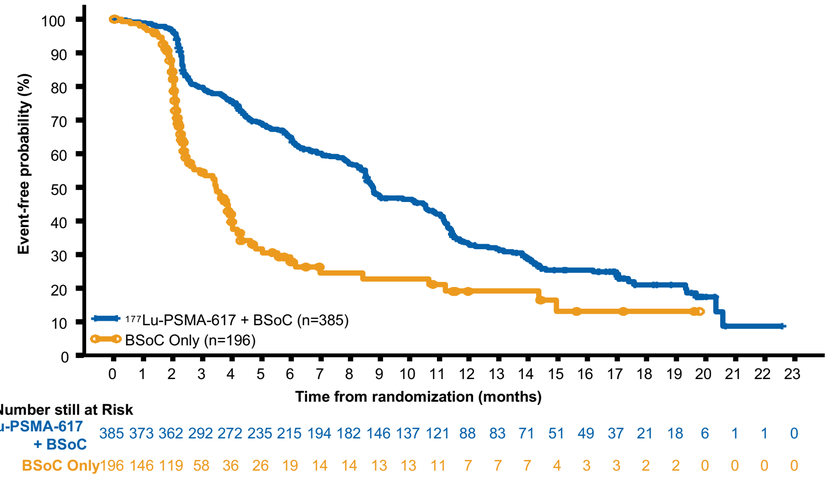
OS HR[3]: **0.62** (95%CI: 0.52, 0.74)
Median OS: **15.3 months** (14.2, 16.9)[4] vs. **11.3** (9.8, 13.5)[4]



Number still at Risk

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

rPFS HR[3]: **0.40** (99.2%CI: 0.29, 0.57)
Median rPFS: **8.7 months** (7.9, 10.8)[5] vs. **3.4** (2.4, 4.0)[5]



Number still at Risk

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

Data support investigating ^{177}Lu-PSMA-617 in earlier lines of therapy

Two Ph3 studies in pre-taxane 1L / 2L mCRPC **PSMAfore** and mHSPC **PSMAddition** already underway

Studies in earlier disease stages under consideration

1. Morris M. et al, Phase 3 study of 177Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION); ASCO 2021 plenary. 2. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. New England Journal of Medicine 2021. doi: 10.1056/NEJMoa2107322. 3. p<0.001, stratified log-rank test 1-sided. 4. 95% CI. 5. 99.2% CI, in line with hypothesis testing strategy.

Why explore ^{177}Lu-PSMA-617 RLT in earlier lines of prostate cancer?

Target expression

PSMA is expressed 100 to 1000-fold higher in prostate cancer cells than in normal tissue, even at earlier stages of prostate cancer[1]

Synergy with existing standard of care

^{177}Lu-PSMA-617 RLT to be used with **Androgen Deprivation Therapy** (ADT) and **Androgen-Receptor Pathway Inhibitors** (ARPI) which are reported to **increase PSMA expression by 45 to 55% in mCRPC patients**[2]

Safety

The acceptable safety profile demonstrated in the VISION study supports providing ^{177}Lu-PSMA-617 RLT to patients with **better performance status in combination with active (ADT/ARPI) therapy**

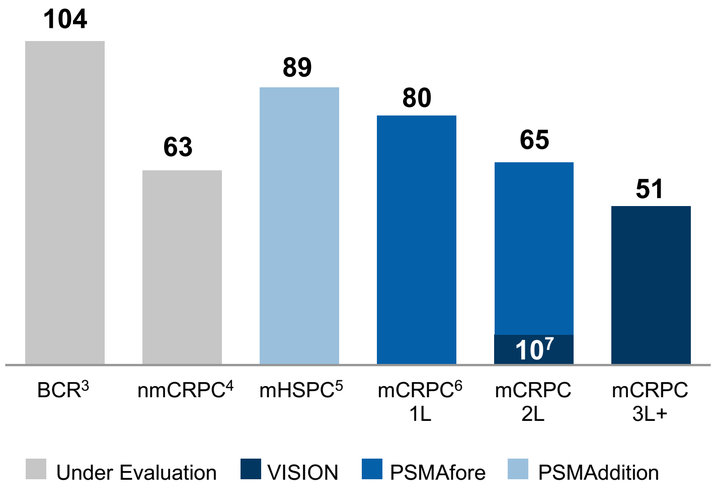
1. Heston WD. Urology. 1997;49 (suppl):104-1121. 2. Rosar F, et al. Eur J Nucl Med Mol Imaging. 2020;47(3):687-694.

Significant unmet need in earlier lines and stages of prostate cancer; two Phase 3 studies ongoing

Prostate cancer incidence[1]

US, EU5, JP ('000)

>80% of patients express PSMA



Aim to expand in earlier lines of prostate cancer treatment

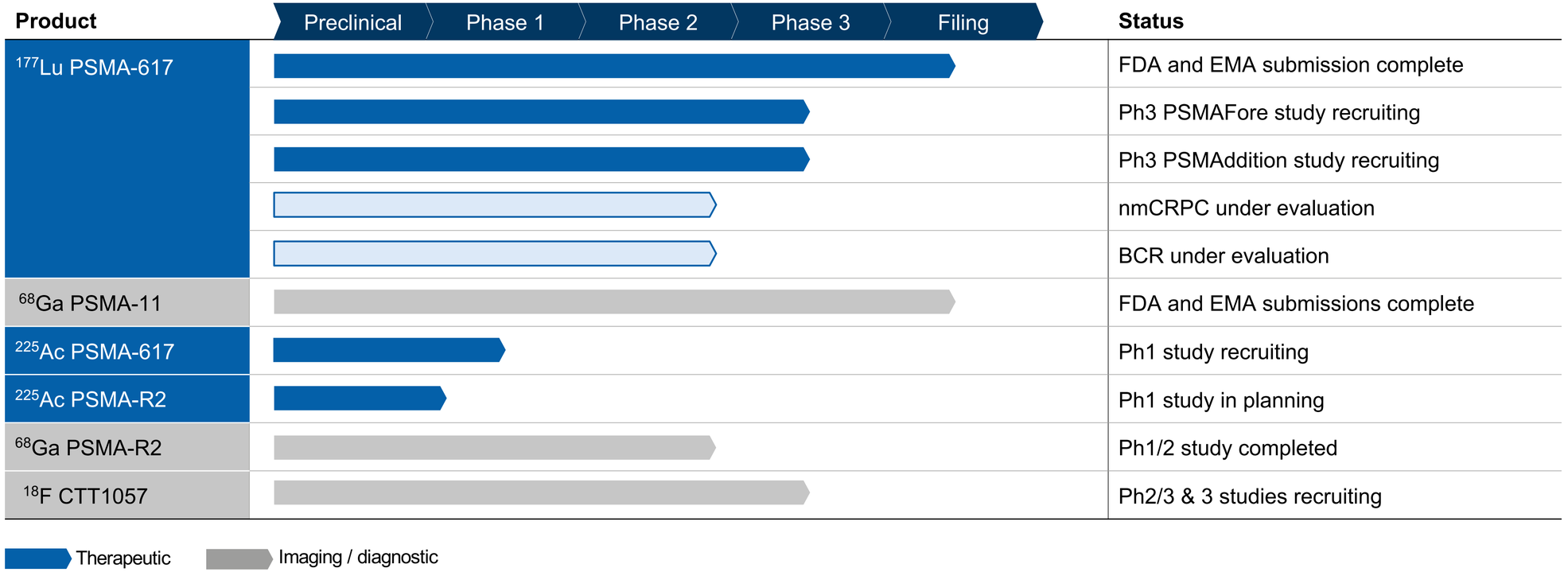
Setting	Study	Status	Expected filing	Asset potential
mCPRC 3/4L (post-taxane)	VISION	Completed	FDA complete EMA complete	
mCRPC 1L/2L (pre-taxane)	PSMAfore	Recruiting	2023	
mHSPC	PSMAddition	Recruiting	2024	●●●
nmCRPC	Under evaluation			
BCR	Under evaluation			

Market size: ●○○ <USD 1bn ●●○ USD 1bn – 2bn ●●● >USD 2bn

1. 2020 Incidence Based on Kantar Health CancerMPact Treatment Architecture US, EU5, JP (February 2021). Incidence incl. patients in long-term response from prior line, who die before receiving therapy, progress but do not receive therapy, and receive systemic therapy. 2. Localised high risk prostate cancer including adjuvant and neoadjuvant eligible. 3. Biochemically recurrent. 4. Non-metastatic castration-resistant prostate cancer. 5. Metastatic hormonal-sensitive prostate cancer. 6. Metastatic castration-resistant prostate cancer. 7. NVS estimation based on current treatment rates with 15% of 2L patients assumed to have progressed on both a fist ARDT and taxane treatment.

Growing Prostate Cancer RLT pipeline

Potential to address different prostate cancer disease stages via PSMA-targeted therapy



Sabatolimab (MBG453)

Anti-TIM-3 monoclonal antibody

Phase 3

Key highlights

- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) are related myeloid disorders with very high unmet medical need
- Sabatolimab is a potential **first-in-class immuno-myeloid therapy** that binds to TIM-3, a target expressed on immune and leukemic cells[1-5]
- Early clinical data show that **sabatolimab + HMA is safe and well tolerated**, and demonstrated **durable clinical benefits** in patients with vHR/HR-MDS and ND-AML, including patients with adverse risk mutations
- Pivotal study in **HR-MDS** ongoing, readout and **submission expected 2022-2023;** Ph3 recruitment is ahead of target, and close to completion
- Ph2 study in Unfit AML ongoing since 2020; readout projected for 2023 will inform subsequent Ph3
- US/EU: Patent on composition of matter (2035/2035)[6]

1. Pardoll DM. Nat Rev Cancer. 2012. 2. Das M, et al. Immunol Rev. 2017. 3. Kikushige Y, Miyamoto T. Int J Hematol. 2013. 4. Kikushige Y, et al. Cell Stem Cell. 2010. 5. Ngiow SF, et al. Cancer Res. 2011. 6. Patent term extensions and regulatory-based exclusivities are possible

Myelodysplastic syndrome and acute myeloid leukemia are related myeloid disorders with high unmet medical need

Limited durability

Poor prognosis and lack of durable benefits (e.g. responses, survival, QoL)

Median Overall Survival (mOS):
~12 months for HR-MDS[1]
~15 months for Unfit AML[2]

Tolerability

Significant toxicity impacts the benefit of current therapies (intensive chemotherapy, hypomethylating agents, HSCT)

Lack of innovation

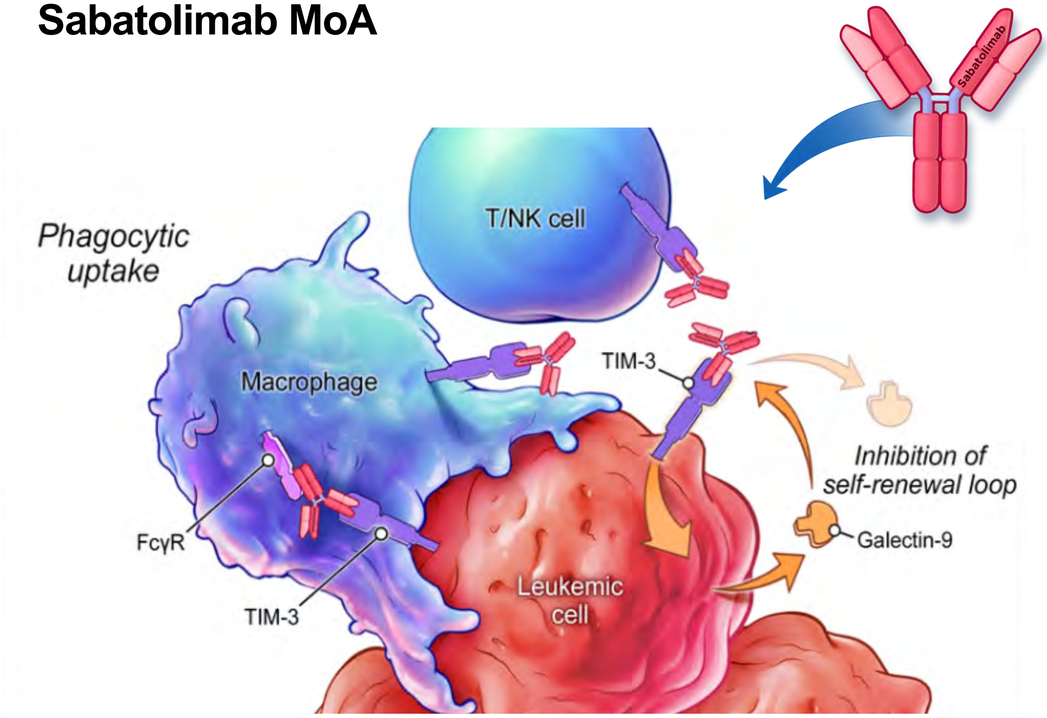
No treatment innovation in over **15 years**[3] **in HR-MDS**

	MDS	AML
Median Age of Diagnosis	~76 years[1]	~68 years[4]
Annual Incidence in US[5]	~ 19K/year	~ 20K/year
Patient Population with High Unmet Medical Need	Higher Risk-MDS (HR-MDS) is a more aggressive type with worse prognosis and a higher chance of progressing to AML	Unfit AML patients are often older and have a general health status that precludes intensive chemotherapy

MDS = Myelodysplastic Syndromes; AML = Acute Myeloid Leukemia. IPPS (International Prognostic Scoring System) risk categorization in MDS. "Higher Risk" ~34% (11% High Risk, 23% Intermediate-2 risk). 1. Zeidan, A. et al., et al. Blood Reviews 2019. 2. VIALE-A phase 3 study, C D. DiNardo et al. NEJM 2020 AML. 3. Vidaza EMA approval 2008, FDA 2004. 4. Shallis R, et al. Blood Reviews 2019. 5. SEER 2014-2018.

Sabatolimab is a novel immuno-myeloid therapy that targets TIM-3 on immune and leukemic cells

Sabatolimab MoA



TIM-3 is an **immuno-myeloid regulator of adaptive and innate immune responses** in myeloid malignancies

- **Expressed on myeloid immune cells and leukemic stem cells** (LSC) but not on normal hematopoietic stem cells[1-5], making it a promising target in MDS/AML[2,4,6]

Sabatolimab is a **potential first-in-class IgG4 anti-TIM-3 monoclonal antibody** (mAb), which is hypothesized to:

- **Bind TIM-3 on immune cells**, enhancing antileukemic immune activation and phagocytic killing of LSCs and blasts[9-12]
- **Directly target TIM-3 on LSCs**, inhibiting TIM-3/galectin-9–driven self-renewal[9,10]

AML, acute myeloid leukemia; FcγR, Fc gamma receptor; HSC, hematopoietic stem cell; LSC, leukemic stem cell; MDS, myelodysplastic syndrome; NK, natural killer; TIM-3, T-cell immunoglobulin domain and mucin domain-3.

1. Pardoll DM. Nat Rev Cancer. 2012. 2. Das M, et al. Immunol Rev. 2017. 3. Kikushige Y, Miyamoto T. Int J Hematol. 2013. 4. Kikushige Y, et al. Cell Stem Cell. 2010. 5. Ngiow SF, et al. Cancer Res. 2011. 9. Acharya N, et al. J Immunother Cancer. 2020;8(1):e000911. 10. Sabatos-Peyton C, et al. SITC 2020. Abstract 439. 11. Borate U, et al. HemaSphere. 2020;4(suppl 1):Abstract S185. 12. Borate U, et al. EHA 2020. Oral presentation

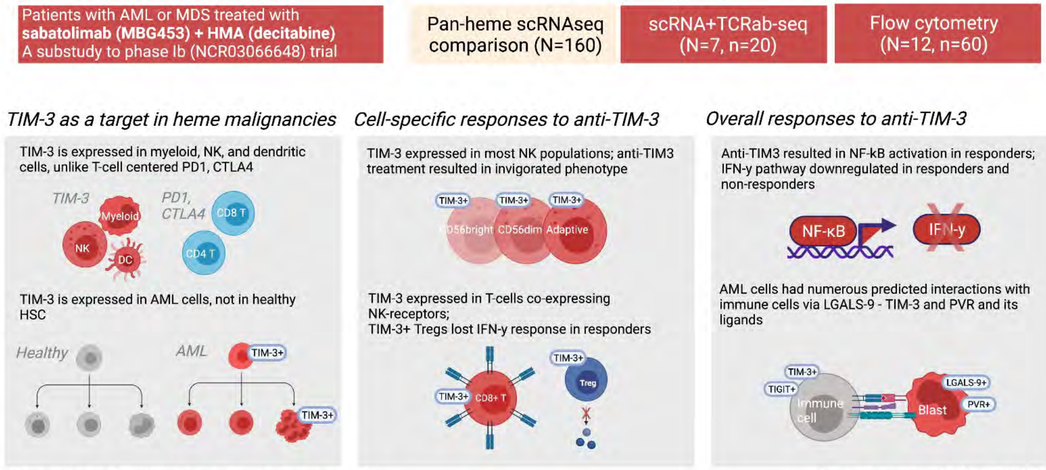
EHA and ASH newsflow 2021: Durable clinical benefit with sabatolimab, unique MoA as an immuno-myeloid therapy

Final analysis of sabatolimab + HMA Ph1 study[1]

- **Durable responses**, including in patients with adverse risk mutations (TP53, RUNX1, ASXL1)
- Clinically significant immune-mediated **AEs were rare**

Biomarker analysis of Ph1 patient samples

- **Single cell RNAseq analysis[2]**: Unlike PD-1 and CTLA-4, TIM-3 is expressed on leukemic, dendritic, myeloid, and NK cells. The effects of TIM-3 blockade were mainly observed in these cells
- **Implication of IL-1β[3]**: Sabatolimab + HMA downregulates pro-inflammatory cytokine IL-1β in leukemic blast cells, but conversely upregulates IL-1β in myeloid immune cells



N=number of patients, n=number of samples

Huuhtanen et al., ASH 2021

Figure was created with Biorender by Jani Huuhtanen. 1. Brunner A et al, ASH2021 oral presentation, Abstract #244. 2. Huuhtanen J et al., ASH2021 oral presentation, Abstract #801. 3. Wei A. et al, EHA2021 oral presentation, Abstract #S168

STIMULUS program fully deployed to establish sabatolimab as a backbone across myeloid diseases

HR-MDS

STIMULUS-MDS1
Ph2, HMA combination, enrollment complete

STIMULUS-MDS2
Ph3, HMA combination, enrollment ahead of schedule, and expected to complete by 2021

STIMULUS-MDS3
Ph2, HMA + venetoclax combination

STIMULUS-MDS-US
Ph2, combination with any approved HMA including the oral decitabine (INQOVI)

AML

STIMULUS-AML1
Ph2, HMA + venetoclax combination, Unfit AML

AML post-aHSCT
Ph1b/2, monotherapy and HMA combination, AML post-aHSCT, in remission but MRD+)

Novel combinations

MDS/AML
Ph1b, HDM201 combination

LR-MDS
Ph1b, mono and combination with NIS793, canakinumab

Myelofibrosis
Ph1b/2, ruxolitinib combination

Indication	G7 incidence[1]	Asset potential
HR-MDS	~22,000	●●●
Unfit AML	~15,000	

●○○ <USD 1bn
●●○ USD 1bn – 2bn
●●● >USD 2bn

- **STIMULUS-MDS1**: Ph2 randomized, double-blind, 2 primary endpoints: CR, PFS (event-driven)
- **STIMULUS-MDS2**: Ph3 randomized, double-blind, primary endpoint: OS (event-driven)
- Ph3 recruitment ahead of target, and very close to completion; readout and first submission expected 2022-2023

NCT03946670, NCT04266301, NCT04150029, NCT03940352, NCT04283526, NCT04097821, NCT04810611. STIMULUS-MDS1: Ph2 randomized, double-blind, 2 primary endpoints: CR, PFS (event driven); STIMULUS-MDS2: Ph3 randomized, double-blind, primary endpoint: OS (event-driven). CR – Complete Remission. PFS – Progression-free Survival. OS – Overall Survival. aHSCT: allogeneic hematopoietic stem cell transplantation. LR-MDS Lower Risk (Very Low, Low, or Intermediate Risk) MDS. MRD+: positive measurable residual disease. HDM201: HDM2 inhibitor. NIS793: Anti-TGF-β monoclonal antibody canakinumab: Anti-IL-1β monoclonal antibody ruxolitinib: Janus kinase inhibitor 1. Kantar Health EPI incidence 2020; Kantar Health CancerMPact® Treatment Architecture 2020

JDQ443

KRAS^{G12C} inhibitor

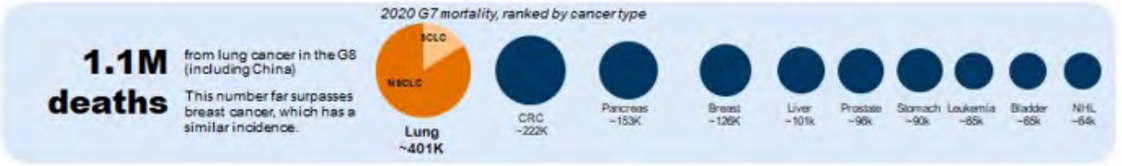
Phase 1

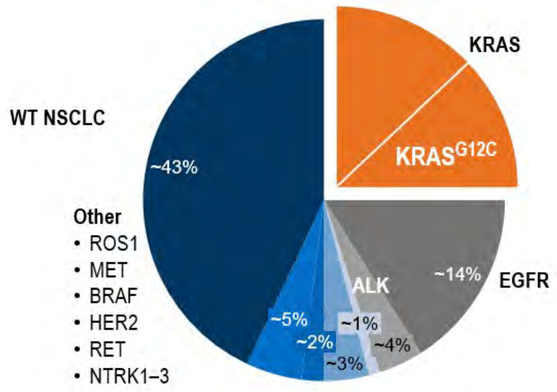
Key highlights

- KRAS^{G12C} occurs in **~13% of NSCLC** and is a clinically validated target
- JDQ443 is a **selective, covalent and orally bioavailable KRAS^{G12C} inhibitor** that binds the mutant cysteine residue, and irreversibly traps KRAS^{G12C} in a GDP-bound, inactive state
- In preclinical studies, JDQ443 potently **inhibits KRAS^{G12C}-driven oncogenic signaling** and **demonstrates dose-dependent activity**
- Emerging data from our ongoing Ph1 study supports **initiation of a pivotal Ph3 randomized study in 2L KRAS^{G12C} mutant NSCLC in H1 2022**
- FIH data will be presented at an upcoming cancer congress in **H1 2022**
- **JDQ443 will serve as the anchor for multiple combination strategies** designed to significantly enhance efficacy of G12C therapy and improve outcomes of patients with KRAS^{G12C}-driven cancers
- Patents pending

Lung cancer remains the deadliest cancer among all cancer types; KRAS^{G12C} mutation represents ~13% of NSCLC

- Lung cancer is the leading cause of cancer death worldwide[1]
- KRAS mutation occurs in 1 of 4 NSCLC patients; G12C accounts for ~50% of KRAS mutations
- The clinical activity of sotorasib (Lumakras) in KRAS^{G12C} mutant NSCLC is relatively modest (ORR 37%, median PFS 6.8 mos)[2]
- Multiple KRAS^{G12C} inhibitors are in clinical development

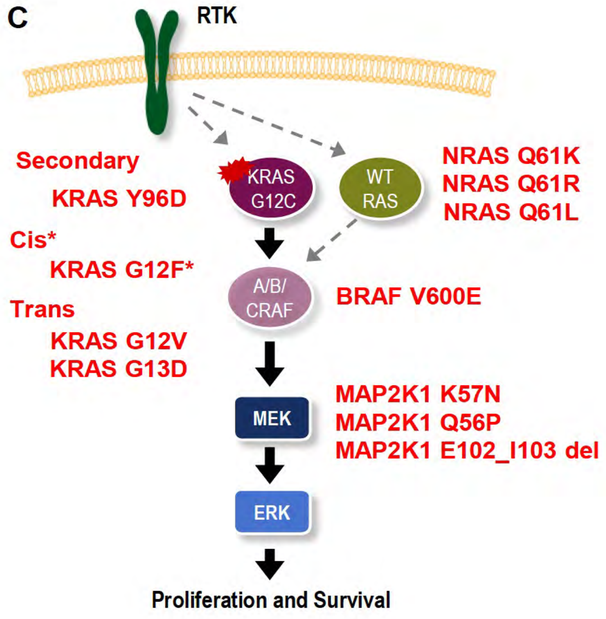




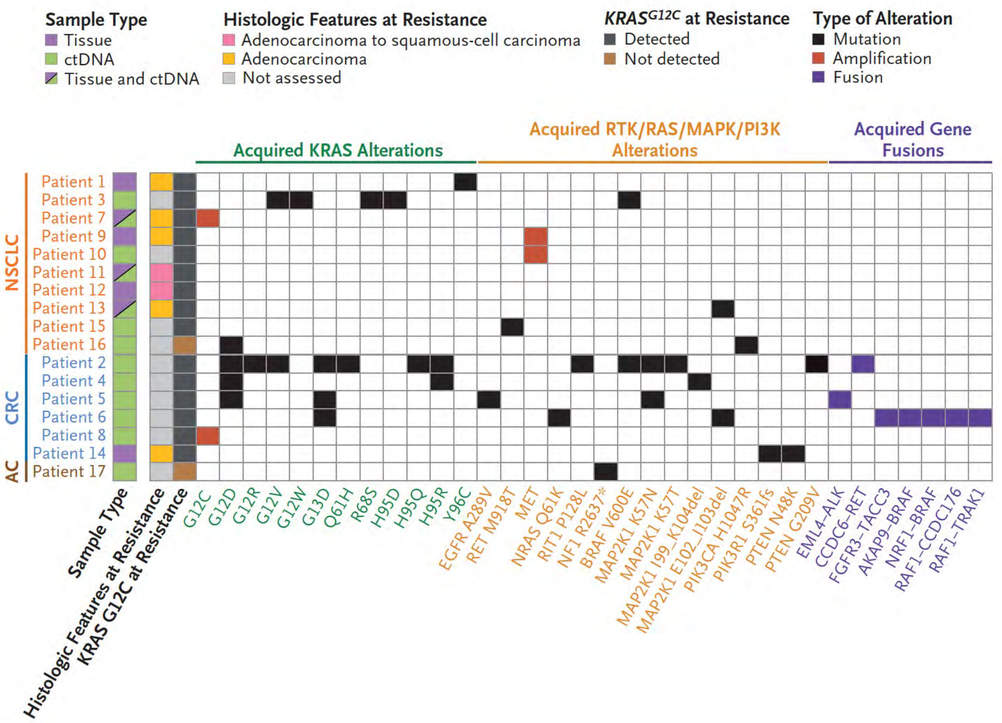
Sources: 1. GLOBOCAN 2020; [2]Skoulidis et al., NEJM 384(25): 2371-81, 2021.

Resistance to KRAS^{G12C} inhibitors emerges early and is polyclonal

One G12Ci-resistant patient with 10 distinct genetic alterations



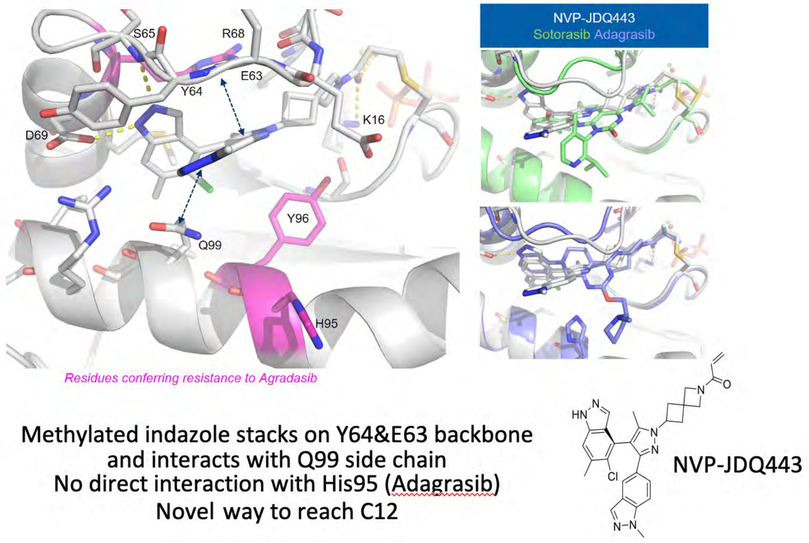
Heterogeneity of resistance mechanisms in G12C-driven cancers



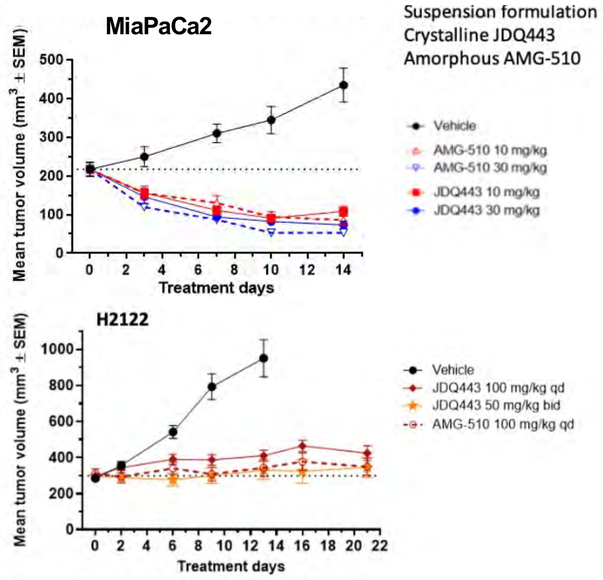
Tanaka N, et al. Cancer Discov. 2021;11:1913–22.

Awad et al., NEJM 384(25): 2382-93, 2021

JDQ443: MoA and preclinical studies



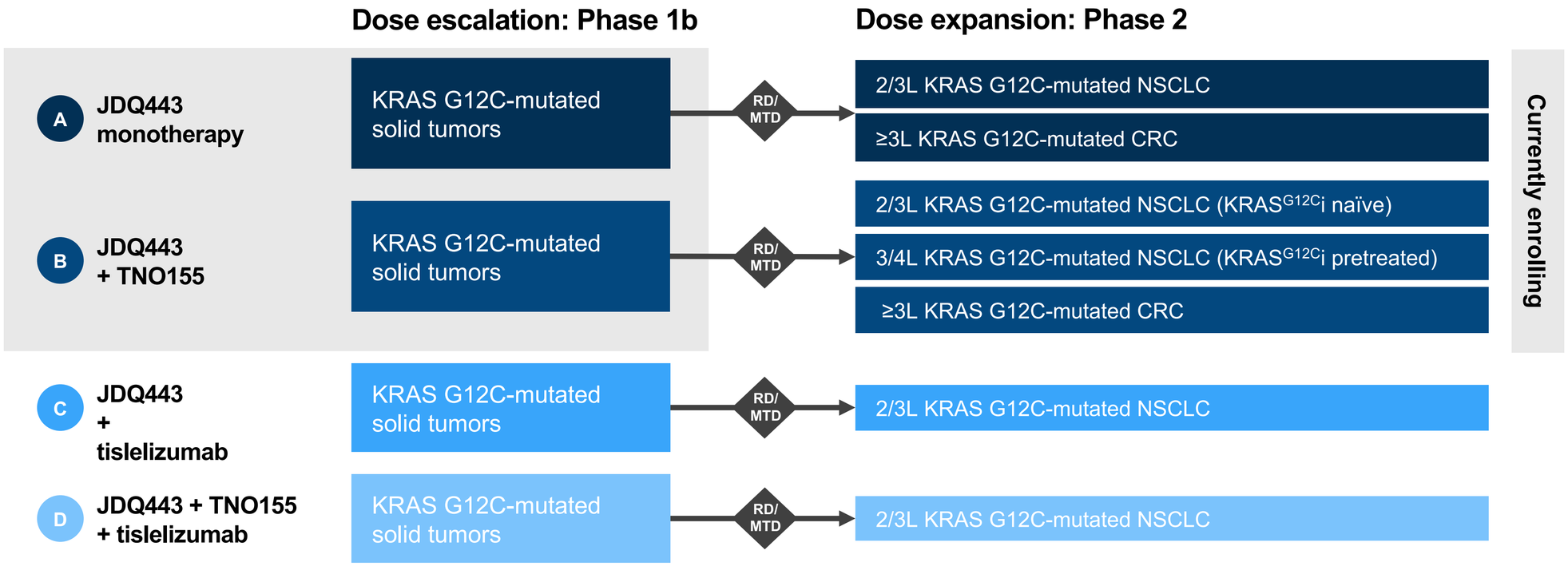
JDQ443 (NVP-JDQ443) is a selective, covalent and orally bioavailable investigational KRAS^{G12C} inhibitor that binds under the switch II loop, and irreversibly traps KRAS^{G12C} in a GDP-bound, inactive state



In preclinical models, JDQ443 potently inhibited KRAS^{G12C} cellular signaling and proliferation in a mutant-selective manner, and demonstrated dose-dependent anti-tumor activity, with comparable efficacy as sotorasib in KRAS^{G12C} mutant tumor xenografts

Brachmann et al., AACR-NCI-EORTC 2021.

KontRASt|01: Ph1 JDQ443 study



MTD, maximum tolerated dose RD, recommended dose

The KontRASt program will enable launching JDQ443 mono and combos for KRAS^{G12C} NSCLC patients

JDQ443 monotherapy for KRAS^{G12C} mutant NSCLC	JDQ443 combinations for KRAS^{G12C} mutant NSCLC (G12Ci naïve or pretreated)	Expansion to 1L KRASG12C mutant NSCLC
KontRASt |01 (Ph1/2)	KontRASt |01 (Ph1/2)	Studies to be defined based on emerging data
KontRASt |02 (Ph3)	KontRASt |03 (Ph1/2)	

TNO155

Low molecular weight SHP2 inhibitor

Phase 2

Key highlights

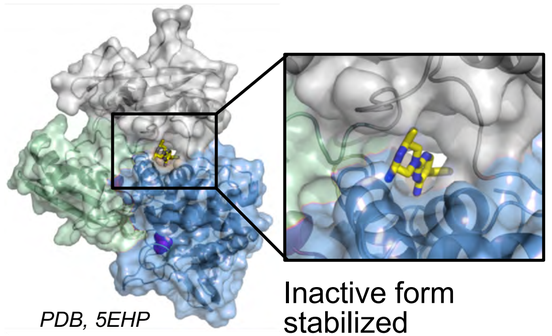
- SHP2 is a protein tyrosine phosphatase that drives cancer growth signaling in collaboration with receptor tyrosine kinases (RTKs) and KRAS; it is also a transducer of PD-1 signaling
- **TNO155 is a first-in-class inhibitor of SHP2** that acts as an intramolecular glue to effect allosteric inhibition
- Pre-clinical data support combination of TNO155 with a range of tyrosine kinase inhibitors as well KRAS^{G12C} inhibitors, and we have adopted a broad clinical combination strategy to blanket the MAPK pathway with **8 ongoing combination trials in solid tumors**
- The Ph1 study of TNO155 has established safety, PK/PD and RDE, enabling the investigation of multiple combination strategies
- TNO155 has shown preliminary promising activity in combination with KRAS^{G12C} inhibitors in G12C-driven cancers
- US/EU: Patent on compound (2035/2035)[1]

1. Patent term extensions and regulatory-based exclusivities are possible

TNO155: A first-in-class inhibitor of SHP2 and ideal combination partner for targeted and checkpoint therapies

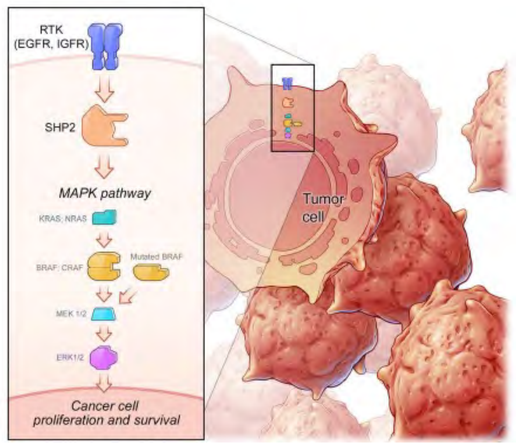
AACR American Association for Cancer Research

First SHP2i to enter the clinic



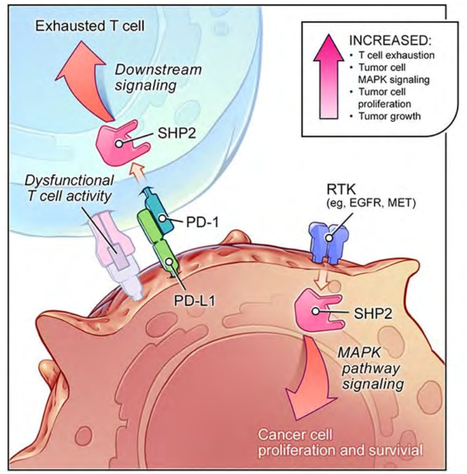
Ideal drug-like properties (e.g. high permeability, solubility, no CYP450 inhibition, ideal preclinical PK profile)

Required for RTK signaling



RTK-SHP2-RAS-MAPK pathway activation has been implicated across the majority of human cancers

Downstream transducer of PD-1

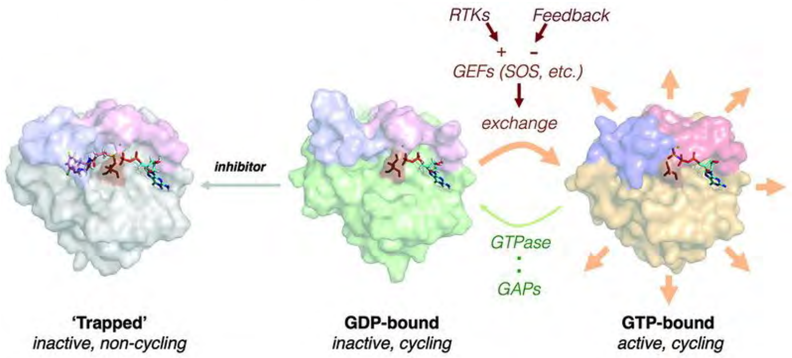


SHP2 is a downstream transducer of PD-1 signaling, a critical immune checkpoint in human malignancies

LaMarche, M., AACR 2020.

Strong pre-clinical synergy between SHP2i and KRAS^{G12C}i supports TNO155 + G12Ci combination approach

Mechanism of synergy

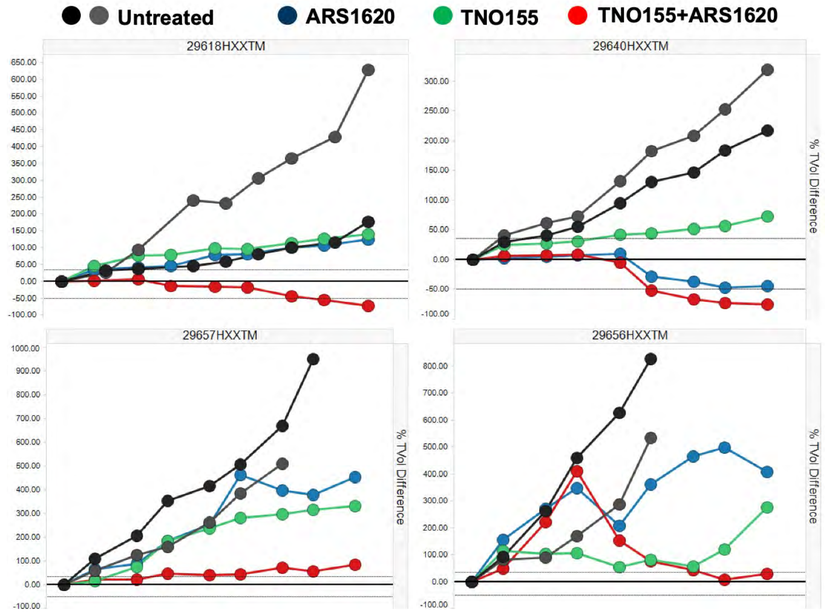


Science. 2016 Feb 5;351(6273):604-8.

KRAS^{G12C} still cycles between GTP- and GDP-bound states and SHP2i enriches the GDP-bound KRAS^{G12C}, which G12Ci binds (**enhances target engagement**)

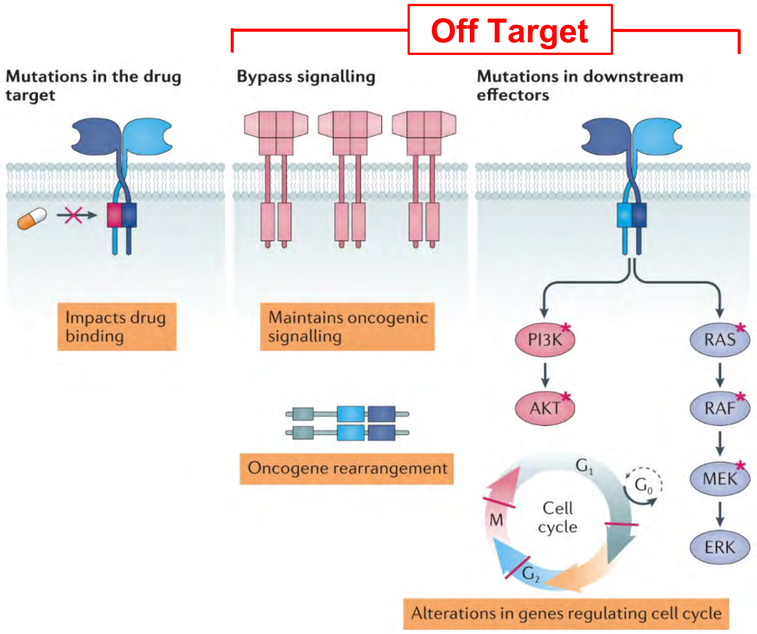
SHP2i suppresses feedback activation of wildtype KRAS, NRAS, HRAS post ERK inhibition by G12Ci (**prevents pathway re-activation**)

TNO155 + KRAS^{G12C}i shrink tumors in KRAS^{G12C} NSCLC PDX pre-clinical models



Other oncogene-driven cancers may be susceptible to SHP2i based combinations

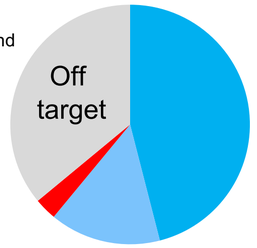
Major classes of resistance mechanisms to targeted therapies



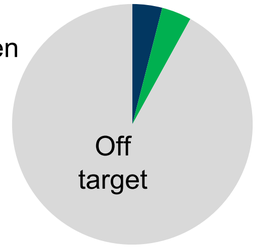
Off-target mechanisms drive the majority of resistance to next generation targeted therapies

EGFR

Post 1st/2nd gen TKI

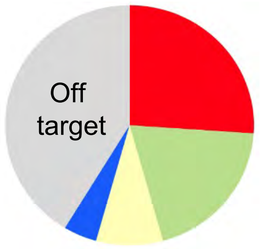


Post 3rd gen TKI (1L)

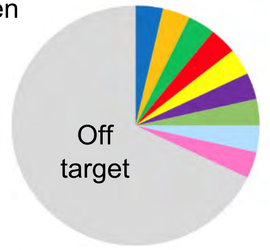


ALK

Post 2nd gen TKI



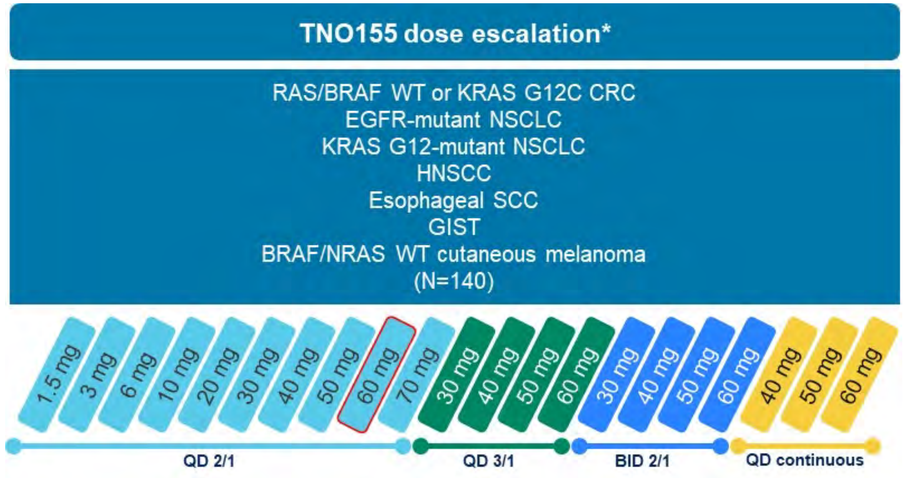
Post 3rd gen TKI (3L+)



Cohen P, et al. Nat Rev Drug Discov. 2021;20:551–69.

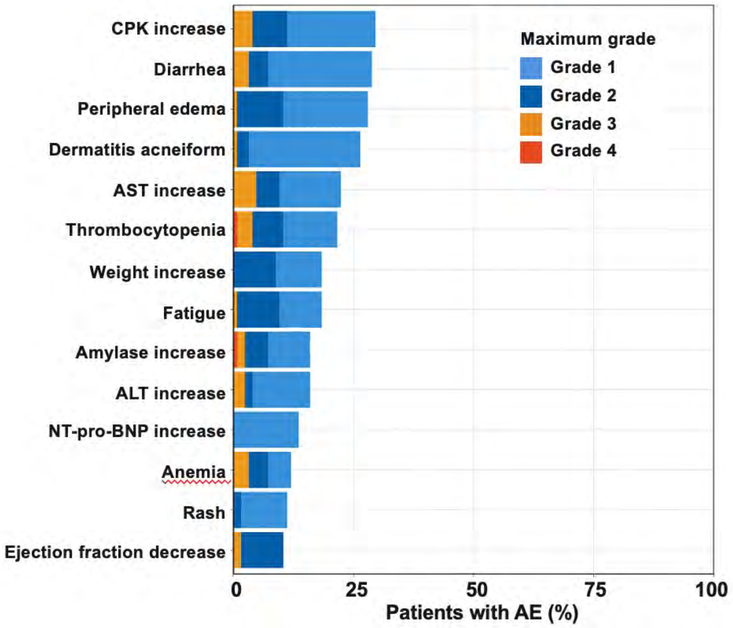
Ph1 first-in-human study of TNO155: Optimizing dose and schedule to enable combinations

Comprehensive dose escalation establishes safety, PK/PD and RDE of TNO155



Data cut-off: August 17, 2021
Primary objective: DLTs, safety, tolerability
Secondary objective: ORR, DCR, PFS, DOR, PK, pharmacodynamics
Treatment until unacceptable toxicity, disease progression, or patient/physician decision

Manageable safety profile with mostly low grade AEs enable TNO155 combinations

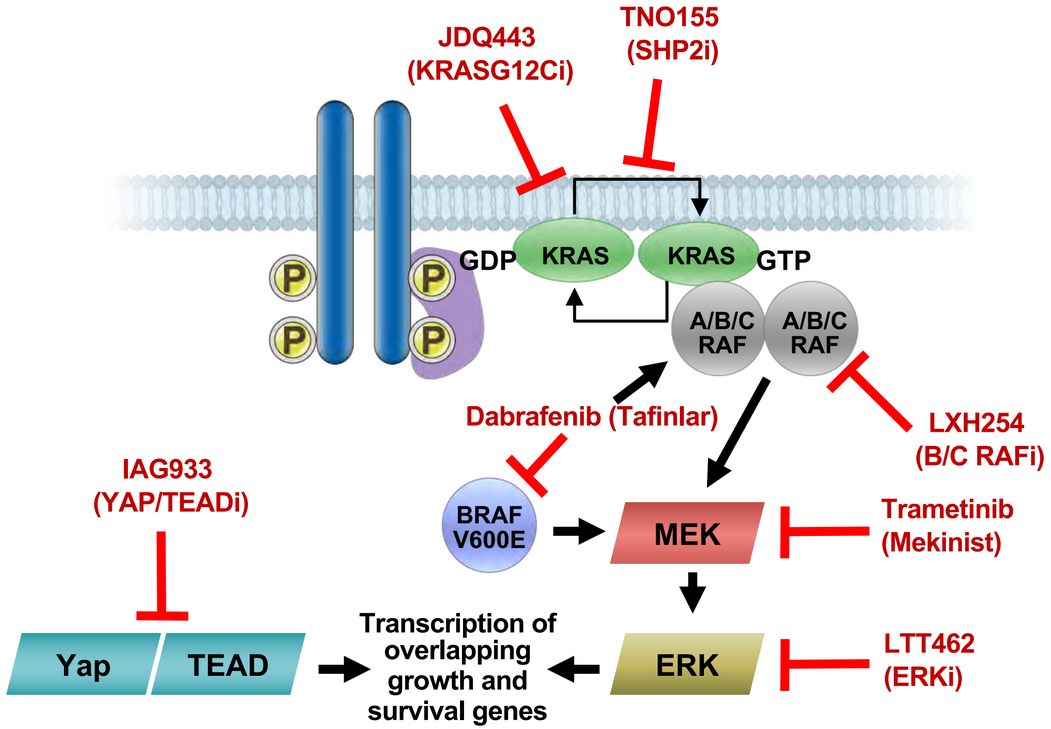


*NCT03114319. Source: Brana et al., ASCO 2021.

Multiple TNO155 combinations are being explored clinically

	Combination	Disease	Est. frequency	FPFV
	TNO155 + EGF816	EGFR mutant NSCLC, post osimertinib	10-40% of NSCLC	September 2020
MGH 1811	**TNO155 + lorlatinib**	ALK+ NSCLC, post next generation ALK TKI	3-5% of NSCLC	March 2021
	TNO155 + dab/tram **TNO155 + dab/LTT462**	BRAF V600-mut CRC	~10% of CRC	July 2021
	TNO155 + PDR001	KRAS^{G12C} NSCLC, ≥1% PD-L, post-chemo and aPD-(L)1	~13% of NSCLC	August 2019
	TNO155 + ribociclib	KRAS-mut CRC, post-SoC, per local standard	30-40% of CRC	August 2019
	TNO155 + JDQ443	KRAS^{G12C} NSCLC and CRC	~13% of NSCLC ~4% of CRC	June 2021
MIRATI THERAPEUTICS	**TNO155 + MRTX849**	KRAS^{G12C} NSCLC and CRC	~13% of NSCLC ~4% of CRC	April 2020
AMGEN	**TNO155 + sotorasib**	KRAS^{G12C} NSCLC and CRC	~13% of NSCLC ~4% of CRC	November 2021

Expanding the Novartis MAPK pipeline to enable innovative combination strategies



- KRAS-MAPK is one of the most **highly validated oncogenic pathways** in human cancer
- Novartis is exploring multiple combination strategies, including:
  - **JDQ443-based combinations** in KRAS^{G12C}-driven NSCLC, CRC and other solid tumors
  - **TNO155-based combinations** in multiple different indications, including KRAS^{G12C}-driven cancers
  - **LXH254-based combinations** in NRAS or BRAF mutant melanoma, KRAS mutant NSCLC, atypical BRAF mutant NSCLC
  - **Dabrafenib/LTT462 and dabrafenib/trametinib triplet combinations** in BRAF V600 mutant CRC
- **IAG933**, a YAP/TEAD inhibitor, has entered the clinic with FPFV October 2021 (NCT04857372)

T-Charge™

YTB323
CD-19 CAR-T therapy

PHE885
BCMA CAR-T therapy

Phase 1

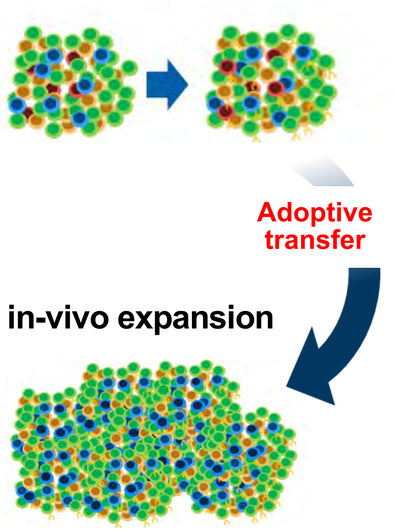
Key highlights

- The T-Charge™ platform **aims to revolutionize CAR-T cell therapy** with a rapid, expansion-less manufacturing process, expected to **increase CAR-T potency and reduce turnaround time and COGS**
- Preclinical studies demonstrate that YTB323 and PHE885, our lead candidates on the T-Charge™ platform, **retain the naive and stem cell memory T-cell subpopulations from the original patient apheresis**; these are associated with improved antitumor efficacy
- **YTB323** is a novel autologous anti-CD19 CAR-T cell therapy for B-cell malignancies, including DLBCL, which is the most common type of NHL, accounting for ~31% of all NHL in Western countries
- **PHE885** is a novel autologous fully human BCMA-directed CAR-T cell therapy investigated in Multiple Myeloma (MM), which comprises ~10% of hematologic malignancies
- Emerging safety and preliminary efficacy data support ongoing Ph1 studies; updated data will be presented at the upcoming ASH meeting
- Novartis is developing T-Charge™ as the **foundation for multiple new CAR-T therapies**
- YTB323: US/EU patent on composition of matter/use (2031/2031)[1]; PHE885: Patents pending

1. Patent term extensions and regulatory-based exclusivities are possible

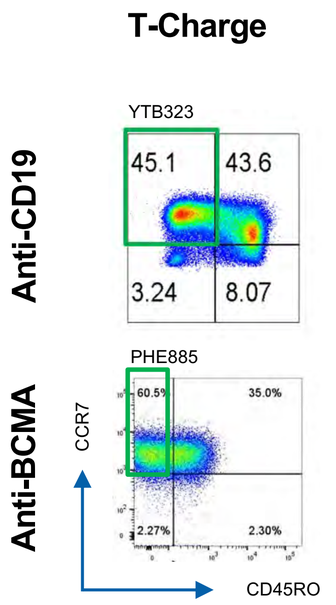
T-Charge™: NIBR developed, novel CAR-T technology platform serving new therapies in Novartis pipeline

Minimal ex vivo culture to maximize in vivo expansion



- T-Charge manufacturing process time will be less than 2 days
- With T-Charge, CAR-T cells can expand within their natural environment when infused into the patient
- 10-50 fold fewer CAR-T cells infused compared to existing CAR-T therapies

T-Charge preserves T-cell "stemness," an important T-cell characteristic closely tied to its therapeutic potential



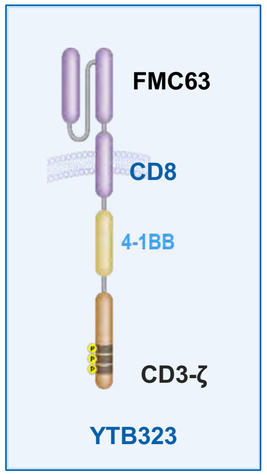
Flow cytometry shows:

- T-Charge retains naïve / Tscm cells (CD45RO-/CCR7+)
- In contrast, the traditionally generated product consists mainly of central memory T-cells (Tcm) (CD45RO+/CCR7+)

Two lead constructs in development on T-Charge™

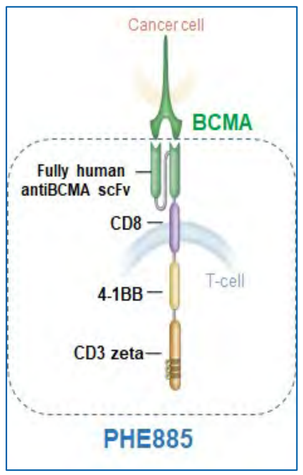
Designed to provide fast access to therapy, increased rates of response and longer durability

YTB323 is an autologous CD19-directed CAR-T cell therapy



- YTB323 is in Ph1 for B-cell malignancies such as r/r DLBCL and adult ALL
- Utilizes the FMC63 domain for CD19 recognition and 4-1BB costimulatory domain
- While using the same CAR transgene as tisagenlecleucel, the innovative T-Charge manufacturing process of YTB323 leads to a differentiated product with unique characteristics

PHE885 is an autologous BCMA-directed CAR-T cell therapy



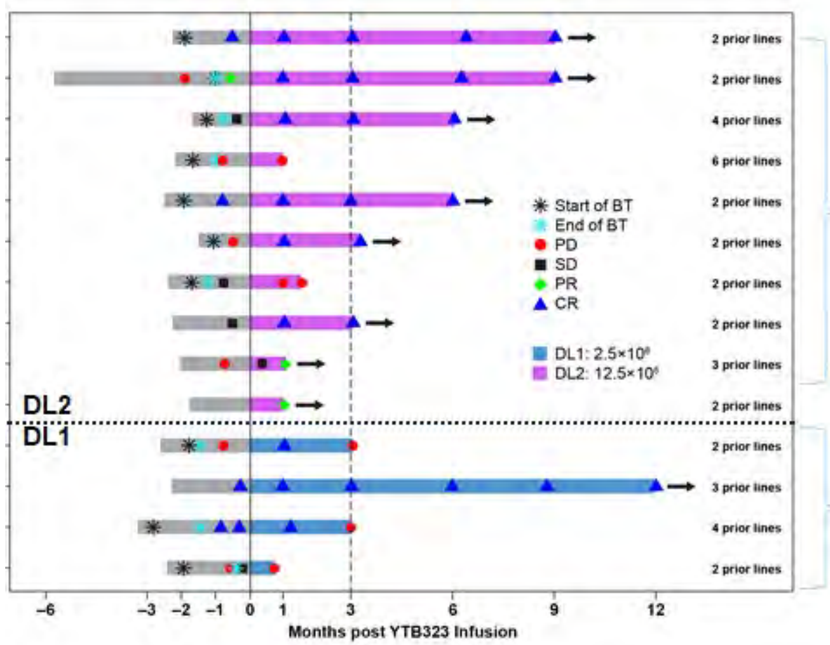
- PHE885 is a *fully human* investigational CAR-T cell therapy in Ph1 for multiple myeloma
- Utilizes a novel, highly potent extracellular scFv targeting B-cell maturation antigen (BCMA), and includes the 4-1BB co-stimulatory to enhance T-cell survival

YTB323 for B-cell Malignancies: 75% CR at ASH

Revolutionary autologous CD19 CAR-T cell therapy with novel biological attributes

Ph1: YTB323 in r/r DLBCL, N=14

- FIH study in r/r DLBCL and adult ALL is ongoing
- Promising preliminary efficacy: All patients dosed at 12.5 x 10^6 are ongoing and have responded to treatment (PR, cCR[1] or CR)[2]
- Preliminary safety profile similar to that reported for tisagenlecleucel in JULIET study



Presented at ASH 2021

6 out of 8 (75%) patients with DL2 and 3m FUP achieved CR

1 out of 4 (25%) patients with DL1 and 3m FUP achieved CR

1. cCR: continuous CR for patients in CR post bridging therapy. 2. 2 patients in DL2 with PD were given a lower than planned dose (6.8 and 7.4x10e6). Reference: 1. Flinn et al. American Society of Hematology Annual Meeting; December 11-14, 2021; Atlanta, GA. Oral 740.

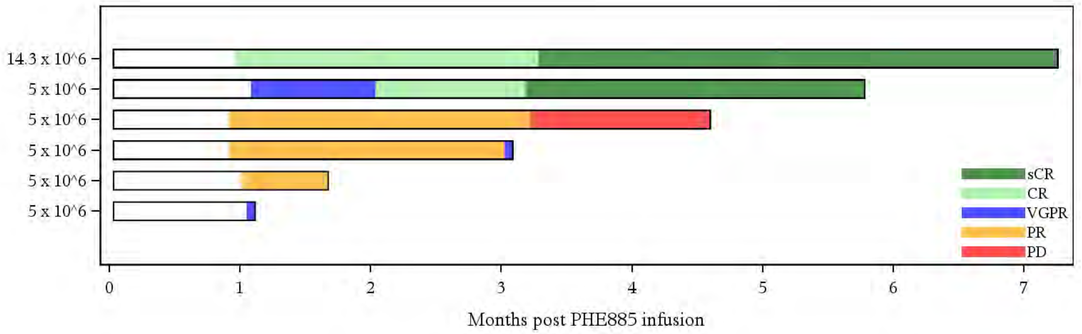
PHE885 in Multiple Myeloma: 100% ORR at ASH

Revolutionary autologous BCMA CAR-T cell therapy with novel biological attributes

Ph1: PHE885 in r/r MM, N=7

Presented at ASH 2021

- Preliminary data shows encouraging clinical activity in patients with r/r MM
  - 6/6 patients (100%) that were infused had a clinical response, that was achieved quickly and deepened over time
  - MRD was evaluable for 3 patients at 1 month after treatment, all were MRD negative (2 MRD negative 10^{-6} and 1 MRD negative 10^{-5})
  - The dose-finding phase of the FIH study is ongoing
- 6/6 patients (100%) experienced CRS, 2/6 (33%) had a grade 3 event (Lee et al 2014)
- Two patients experienced grade 2 neurotoxicity related to PHE885; both events were non-serious and temporally associated with grade 3 CRS



2/6 patients achieved sCR at 3 months

BCMA, B-cell maturation antigen; CR, complete response; MRD, mean residual disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. Reference: 1. Sperling A et al. American Society of Hematology Annual Meeting; December 11-14, 2021; Atlanta, GA. Poster 3864.

SCEMBLIX® (asciminib)

First STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor

Phase 3

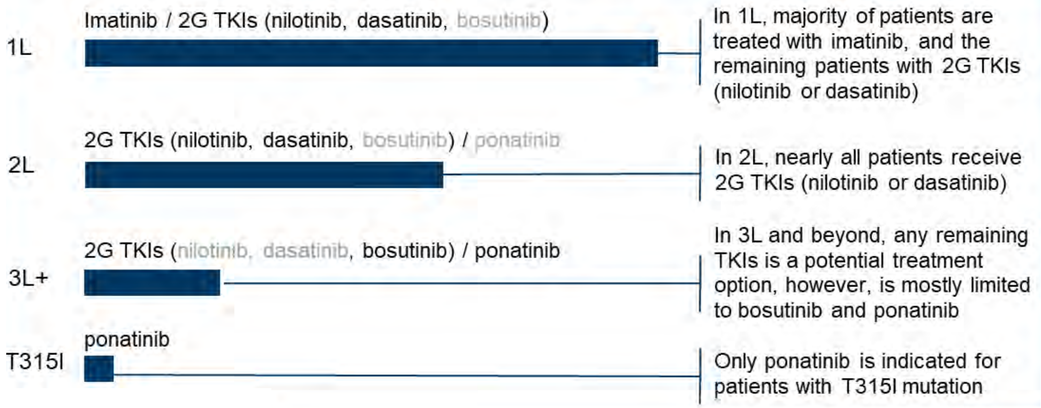
Key highlights

- Despite advances in chronic myeloid leukemia (CML) care, many patients are at risk of disease progression and sequential tyrosine kinase inhibitor (TKI) therapy may be associated with increased resistance and intolerance
- By **S**pecifically **T**argeting the **A**BL **M**yristoyl **P**ocket (**STAMP**), asciminib specifically inhibits the growth of BCR-ABL1-dependent cancer cells and is designed to overcome resistance and minimize off-target activity
- **FDA accelerated approval, based on ASCEMBL trial, granted in Oct 2021**
  - Approved in adult patients with Philadelphia chromosome positive (Ph+) CML in Chronic Phase (CP), previously treated with two or more TKIs (~10K patients)
  - Full approval for the treatment of adult patients with Ph+ CML in CP with T315I mutation (~1K patients)
- **ASC4FIRST** study investigating asciminib vs. investigator-selected TKI in 1L CML patients has started and is in the recruitment stage
- US/EU: Patent on compound (2033/2033)[1]

1. Patent term extensions and regulatory-based exclusivities are possible

SCEMBLIX®: A novel treatment approach to address high unmet need in CML

Patient Journey in CML, treatment options and preferences[1]



Blue bars denote decreasing treatment options, as patients move across lines of therapy (not to scale)

Indication	Addressable patients[5]	Asset potential
1L CML-CP	64K	
3L+ CML-CP	10.5K	●●●
T315I CML-CP	1.1K	

●○○ <USD 1bn
●●○ <USD 1bn – 2bn
●●● >USD 2bn

Approximately 24K patients worldwide (G7) are receiving 2L treatment and many may need a switch to 3L due to resistance and/or intolerance

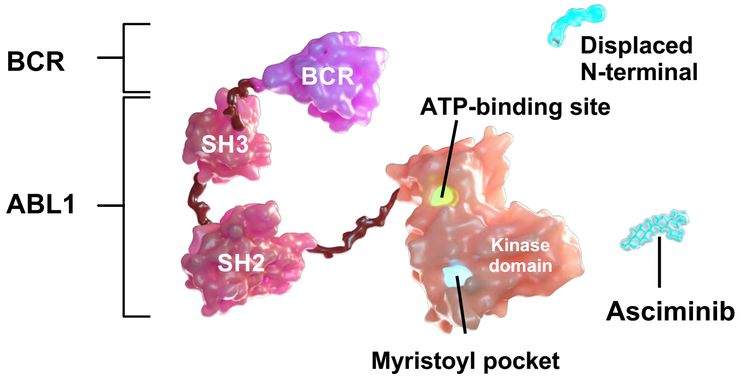
SCEMBLIX® will address high unmet medical need

- Currently, **10-15% of CML patients progress to 3L**, where failure rate can be as high as 75%[2]
- Additionally, a significant number **remain in 2L** due to lack of appropriate options
- **T315I mutation confers resistance to all ATP-binding TKIs except ponatinib[3]**
- **Potential to provide another treatment option in 1L CML**, as ~50% of patients relapse on imatinib or are refractory/ intolerant to imatinib, and >30% of patients suffer from TKI-related non-hematological AEs[3,4]

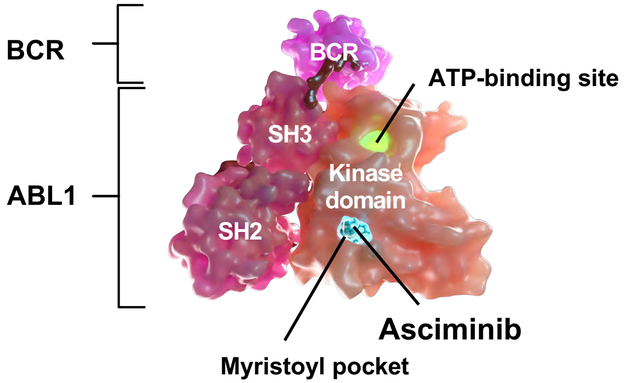
1. Applicable globally where therapies are approved, Ipsos, February 2020, EU5 countries. 2. Hochhaus et al. 2020, Leukemia 34, pages1495–1502 3. Cortes and Lang, 2021. J Hematol Oncol 14:44 ELN recommendations 2019. 4. Garcia-Gutierrez V and Hernandez-Boluda JC, Front.Oncol. 2019; 9:603. 5. Patient population from G7 countries

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

Constitutively active BCR-ABL1



Inactive ABL1



Asciminib 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

In earlier lines of treatment, asciminib may combat emergence of mutations at the BCR-ABL1 ATP-binding site

The specificity of asciminib for the ABL kinase family minimizes off-target activity

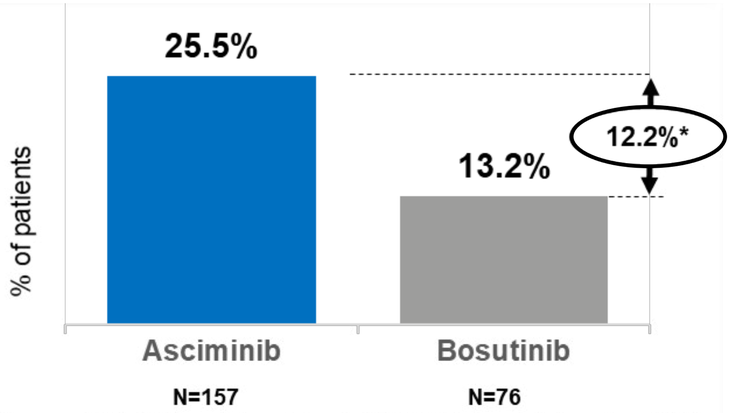
ABL1, Abelson tyrosine kinase 1; ATP, adenosine triphosphate; BCR, breakpoint cluster region; SH, Src homology; TKI, tyrosine kinase inhibitor.

1. Wylie AA, et al. Nature. 2017;543:733-737. 2. Schoepfer J, et al. J Med Chem. 2018;61:8120-8135. 3. Hughes TP, et al. Oral presentation at: 25th EHA Virtual Annual Meeting; June 11-21, 2020. Abstract S170. 4. Manley PW, et al. Leuk Res. 2020;98:106458. 5. Nagar B, et al. Cell. 2003;112:859-871. 6. Hantschel O, et al. Cell. 2003;112:845-857. 7. Colicelli J. Sci Signal. 2010;3:re6. 8. Hantschel O. Genes Cancer. 2012;3:436-446.

Launching SCEMBLIX®, a STAMP inhibitor with potential to transform the standard of care in CML

In ASCEMBL study, asciminib showed a nearly two-fold improvement in MMR rate supporting its clinical benefit in heavily pre-treated patients

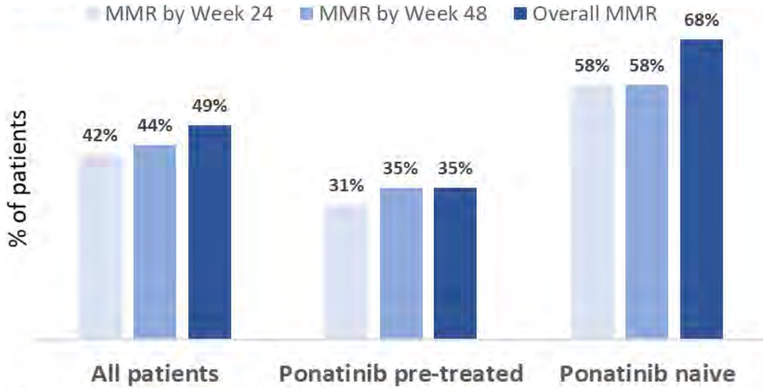
Major Molecular Response (MMR) rate at Week 24



Rea D et al. Blood 2021

Clinically meaningful efficacy of asciminib in patients with CML-CP harboring the T315I mutation

Major Molecular Response (MMR) by Wk 24 and Wk 48

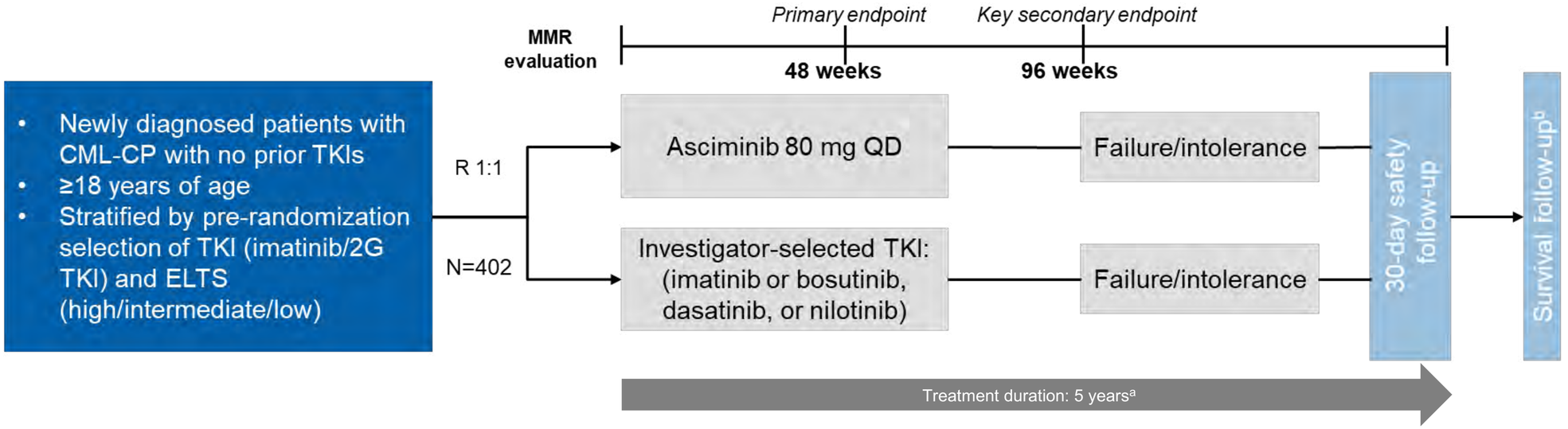


Confidence interval by week 24: Ponatinib pre-treated (16.3 – 48.7); Ponatinib naïve (36.8 – 77.0), All patients (27.7 – 57.8)

Data on file, not published

* Difference: **12.2%** (95% confidence interval: 2.19, 22.30, **two-sided p-value: 0.029**) (per the Cochran-Mantel-Haenszel test which is stratified by baseline major cytogenetic response status

ASC4FIRST: Pivotal trial testing asciminib in 1L CML-CP



The trial has **multiple primary endpoints**:

- Superiority of asciminib vs investigator choice TKI as assessed by MMR at 48 weeks and/or
- Superiority of asciminib vs IMA 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]

FPFV achieved in Q4 2021

CML-CP, chronic myeloid leukemia in chronic phase. ELTS, EUTOS long-term survival score. EUTOS, European Treatment and Outcome Study. QD, once daily. MMR, major molecular response (BCR-ABL 1IS ≤0.1%). TKI, tyrosine kinase inhibitor.
a. Patients will remain on study for 5 years after the last patient first dose. b. Patients who discontinue early will continue to be followed up for survival and disease progression until the end of the study. 1. Saussele S et al. Leukemia; 32(5):1222-8; 2018; Hochhaus et al., Leukemia; 34:966-84, 2020

NIS793

WILD CARD

Transforming Growth Factor β (TGFβ) monoclonal antibody

Phase 2/3

Key highlights

- Annually, approx 500k pts worldwide are diagnosed with PDAC and 1.9M with CRC[1]
- **TGFβ is critical to the maintenance of the fibrotic capsule**, characterized in tumors such as Pancreatic Ductal Adeno Carcinoma (PDAC); this fibrosis is believed to limit access and effectiveness of standard of care chemotherapy
- NIS793 is a potential **first-in-class neutralizing antibody specific for TGFβ**
- NIS793 demonstrates compelling preclinical evidence, target engagement and acceptable safety profile in early clinical studies
- **daNIS clinical trial program** initiated, focused on role of NIS793, in combination with chemotherapy, in 1L PDAC (daNIS-2) and 2L CRC (daNIS-3)
- FDA granted **orphan drug designation** NIS793 in PDAC in July 2021
- Global regulatory submissions could occur as early as **2025**
- **Multi-blockbuster peak sales potential** in 1L pancreatic cancer and in CRC
- US/EU: Patent on composition of matter (2032/2032)[2]

1. GLOBOCAN 2020 2. Patent term extensions and regulatory-based exclusivities are possible

Pancreatic Ductal Adenocarcinoma (PDAC): One of the worst prognoses of all cancers

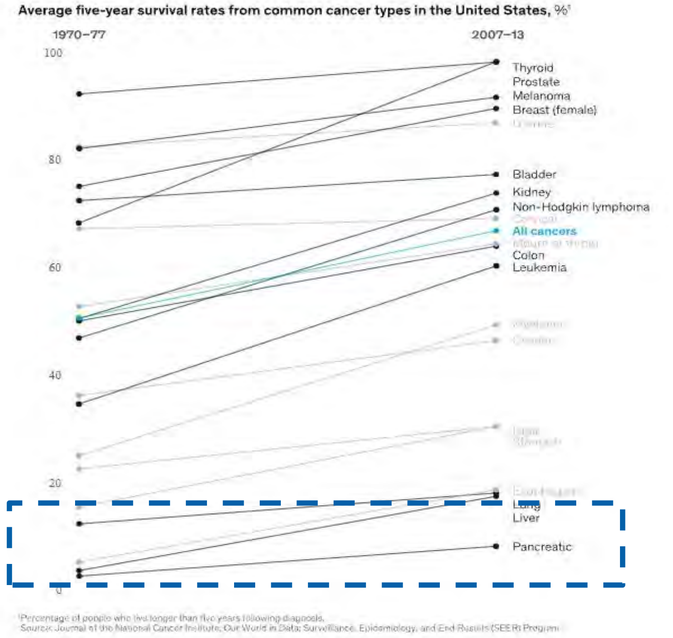
Pancreatic cancer is one of the **leading causes of cancer death** due to poor prognosis and limited treatment options

Majority of patients are diagnosed with metastatic disease with the **lowest rate of survival amongst all major cancers**[2]

- Five-year survival for metastatic PDAC ~3%[1]

Chemotherapy remains standard of care for PDAC with few to no new treatment approvals in 10+years

Outcomes across tumor types have improved significantly since the 1970s, but pancreatic remains among the deadliest[3]



1. Globocan database (2020 data). Available at: https://gco.iarc.fr/today 2.Pancreatic Cancer UK. Pancreatic Cancer Statistics 3. McKinsey & Company

NIS793: First-in-class TGFβ with potent and specific inhibition of all TGF isoforms

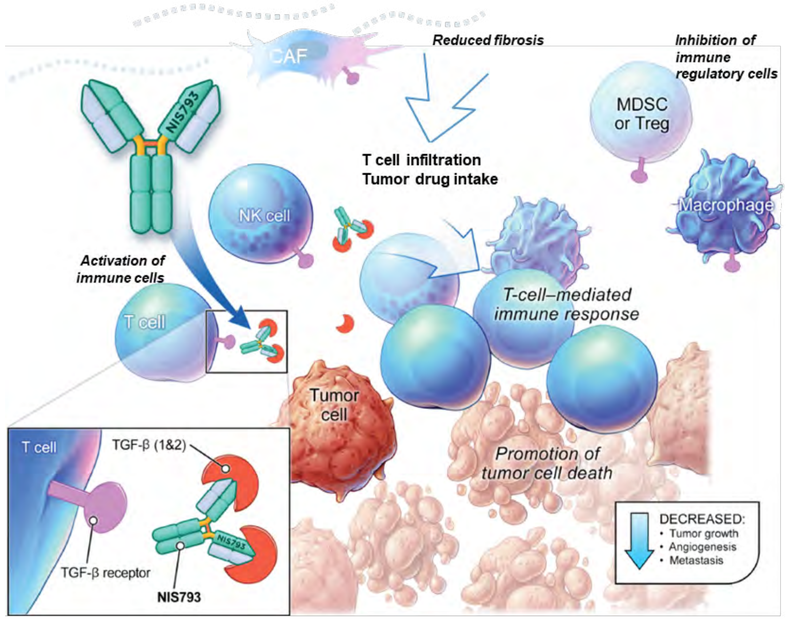
Inhibition of TGFβ has opportunity to:

- **Reduce** the formation of the fibrotic capsule that limits the activity of chemotherapy
- **Restore** endogenous anti-tumor immunity
- **Reduce** tumor growth, angiogenesis, and metastasis

NIS793:

- **Saturates** binding of all TGFβ isoforms in patients
- **Optimized** to target TGFβ signaling in the tumor itself, the tumor microenvironment, as well as immune cell matrix
- **Enables flexibility** in combining with multiple modalities

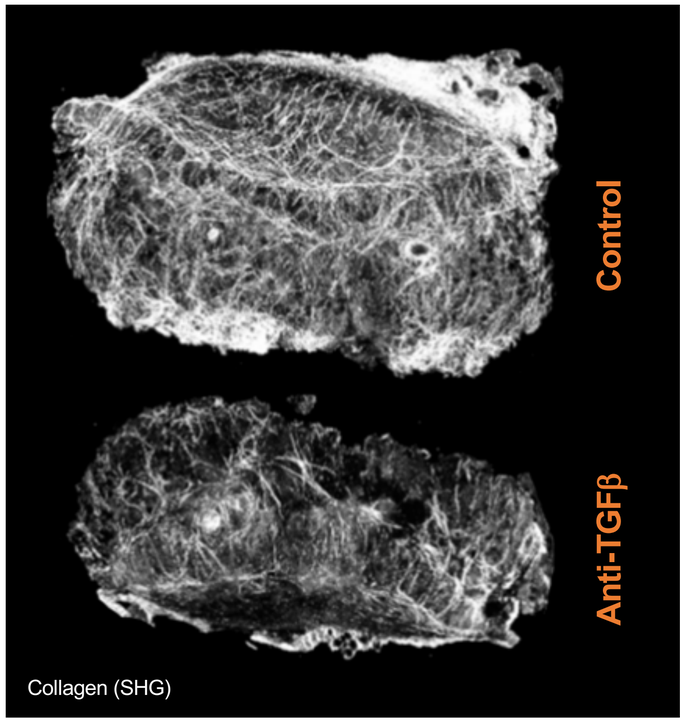
NIS793, a first-in-class TGFBβ inhibitor



CAF, cancer-associated fibroblast; EMT, epithelial to mesenchymal transition; MDSC, myeloid-derived suppressor cell; NK, natural killer; TGFβ, transforming growth factor beta, Treg, regulatory T cell.

Bauer TM, et al. Phase 1b study of the anti-TGF-β monoclonal antibody (mAb) NIS793 combined with spartalizumab (PDR001), a PD-1 inhibitor, in patients (pts) with advanced solid tumors. Oral presentation at: ASCO Annual Meeting; June 4, 2021

TGFβ-blockade halts fibrosis development in models of cancer



In animal models of PDAC (left panel):

- Anti-TGFβ **reduces fibrosis** in animal models of cancer
- Anti-TGFβ in combination with gemcitabine/nab-paclitaxel demonstrated **synergistic reduction in tumor volume** in a mouse model of pancreatic cancer
- In the same mouse-model, the combination **extended survival**

In the FIH study:

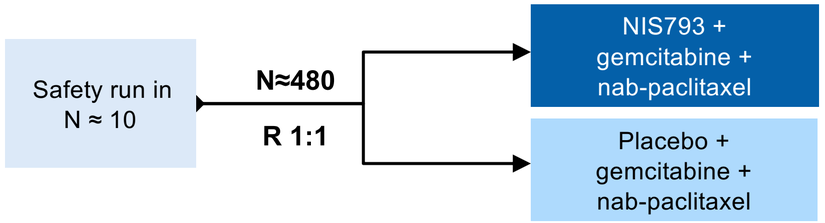
- Inhibition of TGFβ signaling shown in peripheral blood and tumor tissue
- **Free TGFβ levels were reduced to undetectable levels at all NIS793 doses tested**
- In paired tumor biopsies, NIS793 showed inhibition of the TGFβ signaling pathway by a reduced expression of PMEPA1, a known TGFβ signaling target

Grauel AL et al, Nat Commun 2020

daNIS-2 Ph3 study of NIS793 + SOC in 1L pancreatic cancer

daNIS-2 currently enrolling, expected completion early 2026

- Metastatic pancreatic ductal adenocarcinoma (PDAC), not amenable for curative surgery
- No prior treatment in metastatic setting (1L treatment)
- ECOG PS 0-1



Primary endpoint

OS

Secondary endpoints

- Efficacy: PFS, ORR, DCR, TTR, DOR (per RECIST1.1 by investigator)
- Safety and tolerability
- Health-related QOL
- PK and immunogenicity

daNIS clinical trial program underway

daNIS-1 (n=156) NCT04390763
Ph2 of NIS793 ± PD1 + SOC[1] in 1L mPDAC

- Testing hypothesis of addition of PD1 in PDAC
- Estimated completion: early 2023

daNIS-3 (n=190) NCT04952753
Ph2 of NIS793 + bevacizumab + chemotherapy[2] in 2L MSS mCRC

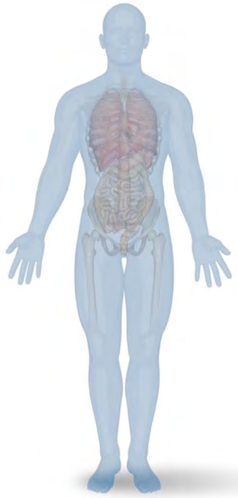
- Testing hypothesis of NIS793 + chemo in additional tumor type with fibrotic morphology
- Estimated completion: late 2023

[1] Gemcitabine + nab-paclitaxel. [2] Modified FOLFOX6 or FOLFIRI.

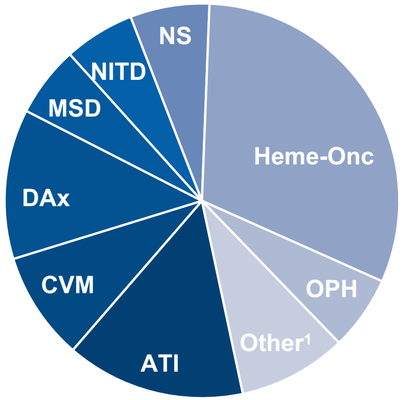
NIBR and Technology Platforms

NIBR discovers and develops medicines across a broad range of disease areas with an increasingly focused portfolio of projects

Distribution of projects across areas



- Autoimmunity, Transplantation & Inflammation
- Cardiovascular & Metabolism
- Hematology-Oncology
- Musculoskeletal Disease
- Neglected & Tropical Diseases
- Neuroscience
- Ophthalmology
- Disease Area X (DAx)



~5,600
Scientists, physicians and business professionals

~275
Research and early development programs

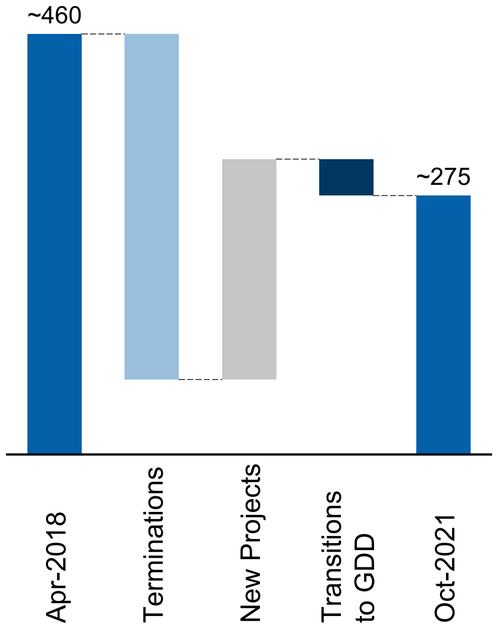
8
Disease areas

~90
New molecular entities in early research

USD 2.6bn
Research & early development spend

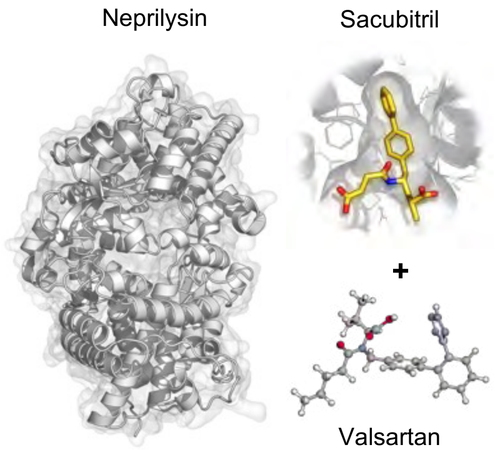
Portfolio choices

of projects

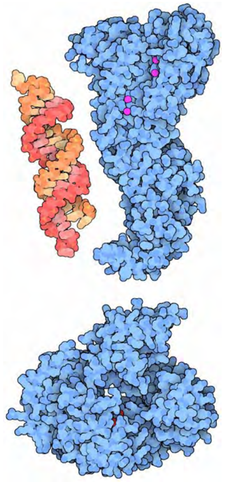


1 Other includes early stage projects where indication is not yet known

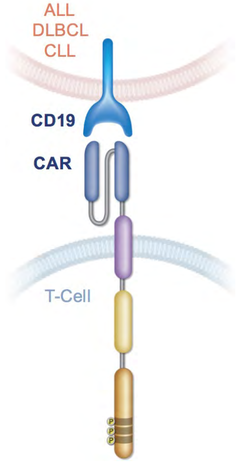
NIBR deploys a technology-forward approach to unlock therapeutic opportunities across five platforms



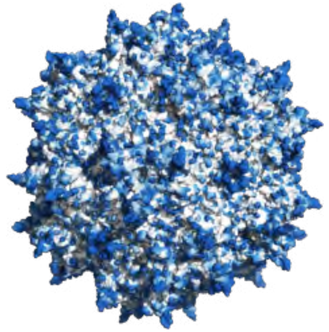
Discovery Chemistry
Entresto | HFrEF



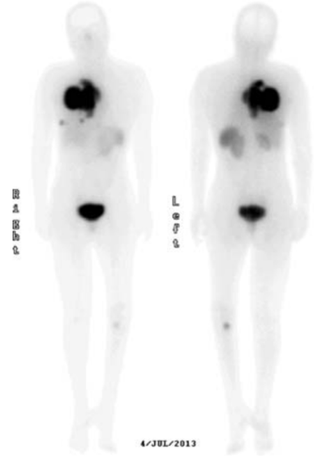
Biotherapeutics
Leqvio | CVRR



Stem-Progenitor Cell Therapy
Kymriah | B-ALL



Viral Gene Therapy
Zolgensma | SMA

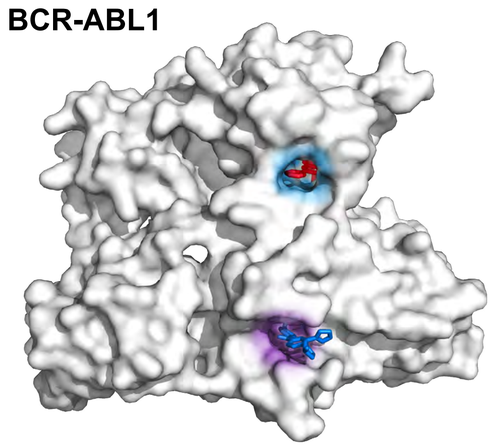


Radioligand Therapy
Lutathera | NET

Crespo-Jara A. et.al., Clinical Nuclear Medicine, 2016; PDB 2ffl, 2f8s, 1u04.

Chemistry platform unlocks new opportunities to address undruggable targets

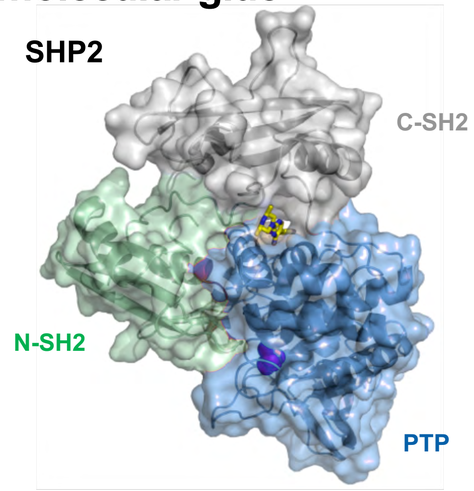
Exploiting allostery to overcome drug resistance



Myristoyl pocket binding to inhibit ABL1 kinase | ABL001 (Scemblix)

CML patients not responding to other tyrosine kinase inhibitors

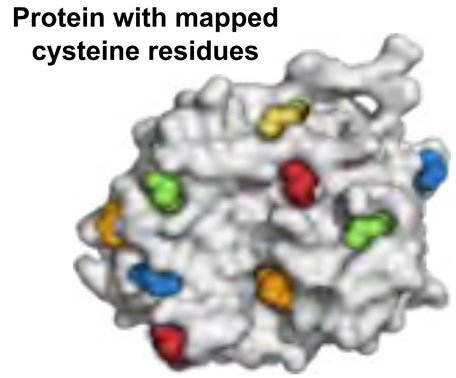
Next generation intra-molecular glue



Potent and highly selective conformational restriction | TNO155

Cancer: Lung, Head/Neck

Mapping ligandable sites across the proteome



Covalent drug discovery

Identification and prosecution of high value targets

We continue to innovate on small molecules while building strong position in new technology platforms





	TPD (Discovery Chemistry)	RLT	Gene	Cell	xRNA[1] (Biotherapeutics)
Key focus	Unlock previously undruggable targets	Expand the indication landscape	Explore novel cargos, targeting, and switchable expression	Enhance potency and durability	Explore new approaches in RNA therapeutics
# of projects[2]	12	12	22	15	9

Source: Novartis early pipeline as of November 2021. Projects are active NIBR portfolio (excludes GDD pipeline); Early-stage NME are post development candidate milestone. 1 xRNA includes RNA targeting LMWs, ASOs, siRNA, mRNA cancer vaccines. 2. Exploratory to Ph1/2

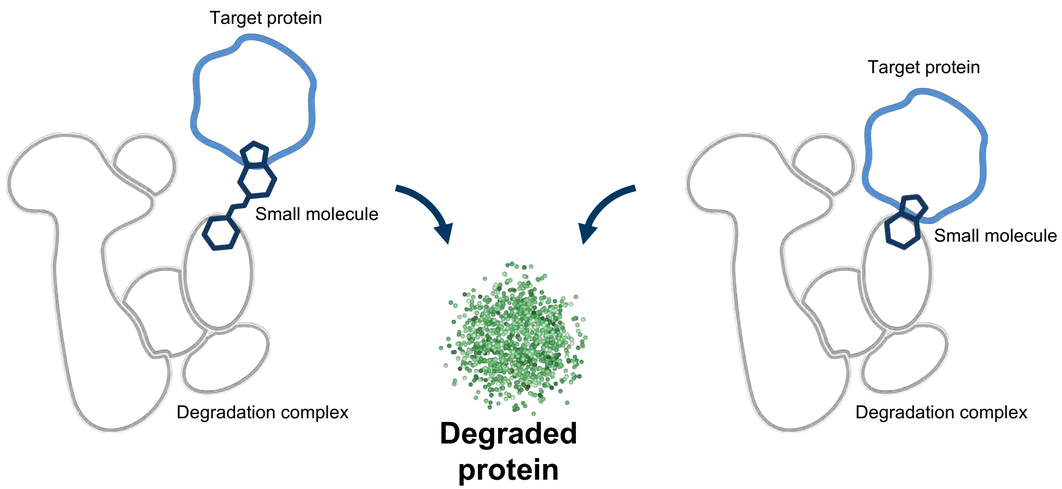
Targeted Protein Degradation

A new science of therapeutics and pharmacology

TPD platform overview

- Target degradation to achieve therapeutic benefit
- TPD reflects induced proximity of a target and a ubiquitin ligase by a molecular glue or bifunctional degrader
- Enterprise scale investment in TPD innovation platforms drives glue discovery, chemical libraries and structural insights
- FIC potential for multiple glue and bifunctional degraders of previously undruggable targets

Two distinct classes of Degrader Molecules

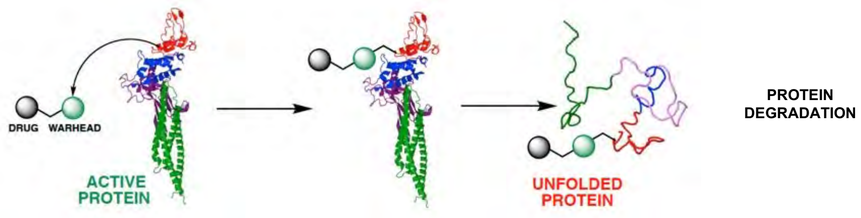


FIC – First In Class

Novartis is enhancing a strong position in TPD with external partnerships

Tunable and selective platform to generate novel and TPD drugs

DUNAD therapeutics



Next-generation targeted protein degradation
Proprietary covalent warhead induces target unfolding

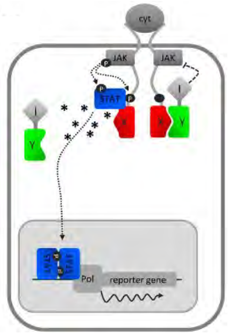
Favorable pharmacology
Compatible with oral delivery and CNS exposure

License and collaboration agreement
Signed to Dunad's covalent degrader platform and other technologies to develop and commercialize oncologic and other therapeutics specific for certain protein targets

High-throughput discovery of novel glue degraders

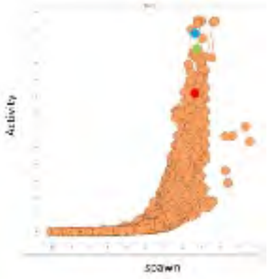
ORIONIS™ BIOSCIENCES

Collaboration to access a molecular glue discovery library



Reverse-MAPIT

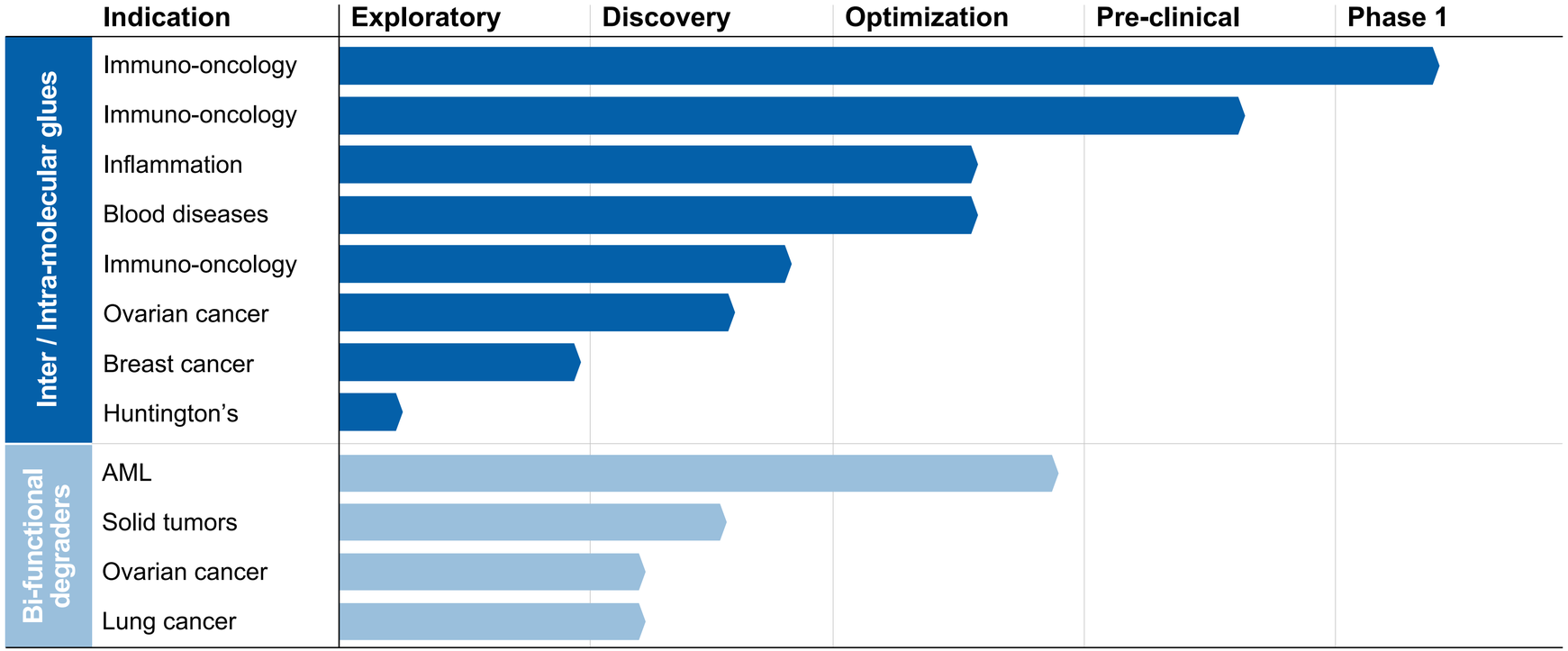
Detects small molecule induced protein-protein interactions



NEK7-CRBN recruitment screen at Orionis

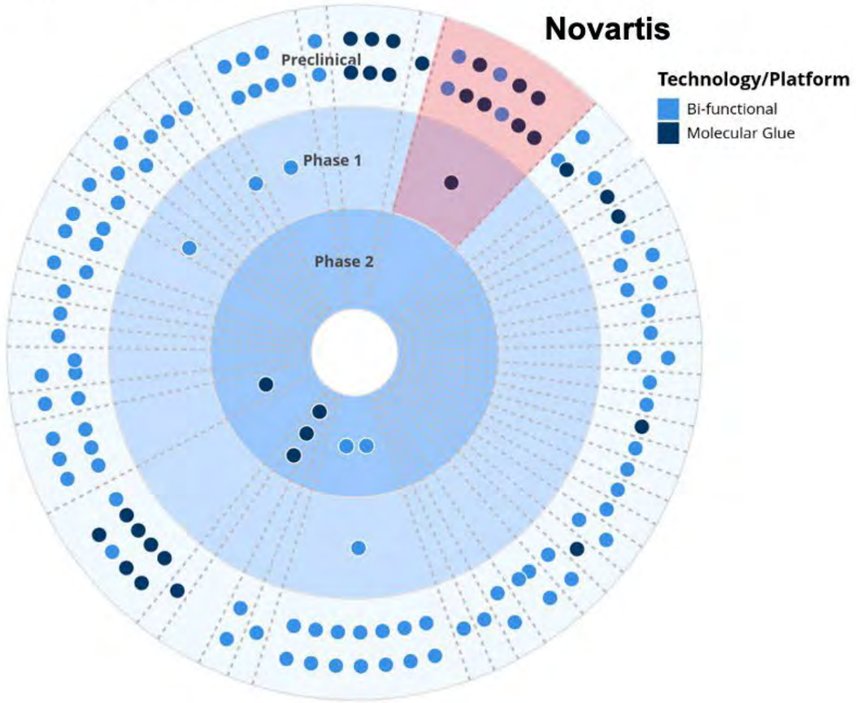
62+ targets screened with 10K+ library in CRBN Reverse-MAPPIT assay

NIBR TPD and glues pipeline covers a wide range of indications

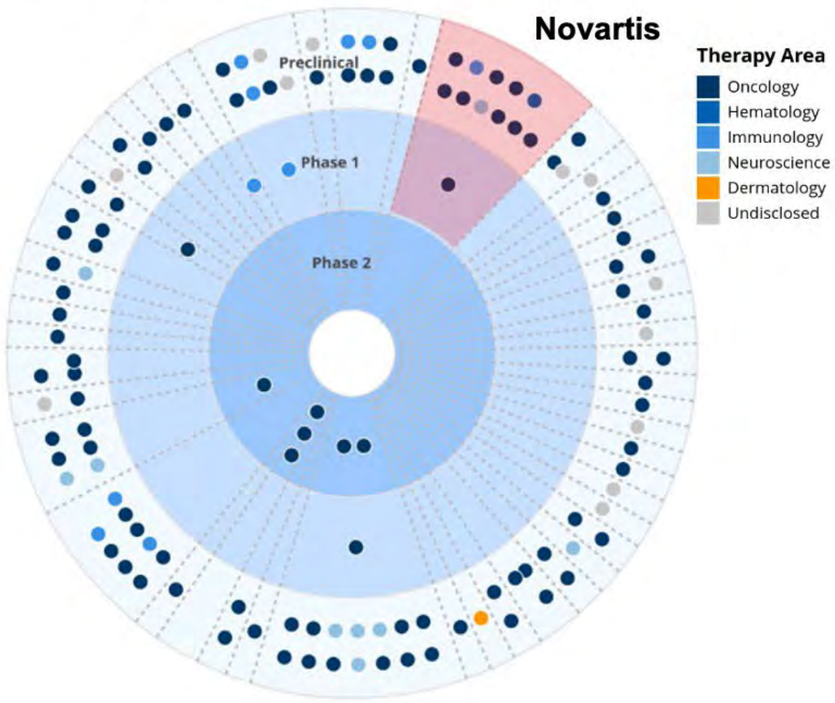


Novartis is the only large pharma with significant homegrown TPD pipeline

TPD pipelines by originator

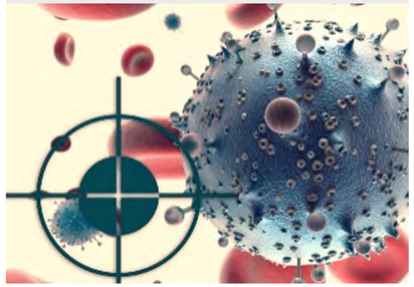
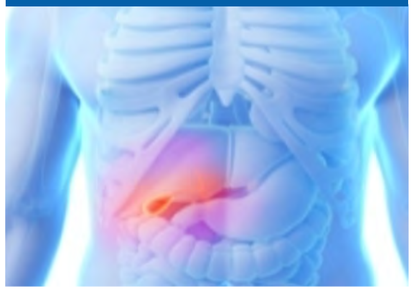
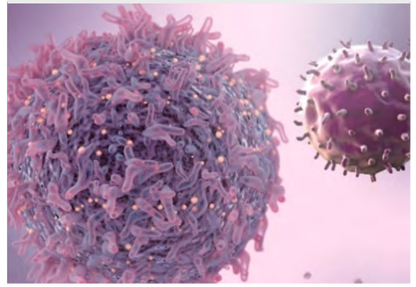
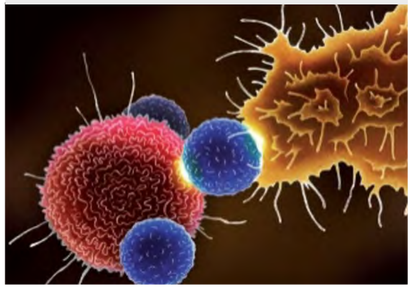


TPD pipelines by therapy area



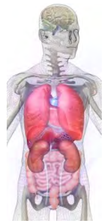
Novartis pipeline as of November 2021, competitor pipelines as of March 2021

RLT is a priority modality for the oncology portfolio

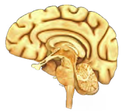
	Targeted Therapy	Radioligand Therapy	Cell & Gene	Differentiated Immunotherapy
				
Key commercial assets	PROMACTA® (eltrombopag) 25mg, 50mg, 75mg tablets JAKAVI® ruxolitinib KISQALI® ribociclib Tafinlar® (dabrafenib) + Mekinist® (trametinib) PIQRAY® ADAKVEO® crizanlizumab tmca TABRECTA® (capmatinib) tablets	Advanced Accelerator Applications LUTATHERA® (lutetium Lu 177 dotatate) injection, for intravenous use	KYMRIAH® (tisagenlecleucel) Suspension for IV infusion	

Further enhancing our position in RLT

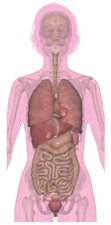
Expanding the indication space



Neuroendocrine tumors and other solid tumors (SSTR and GRPR)

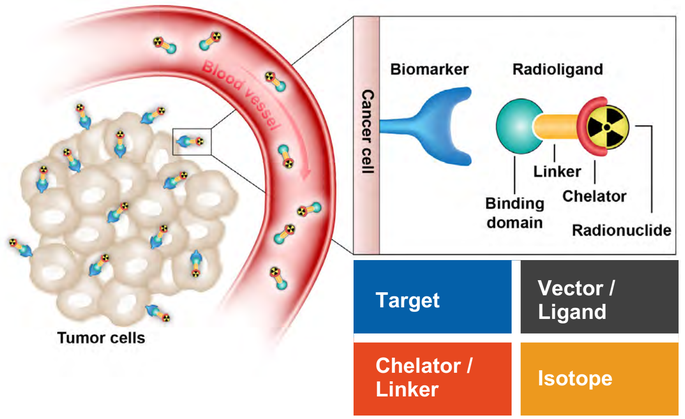


Glioblastoma



Breast cancer

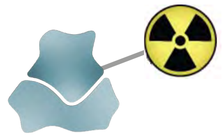
Rapid drug design



Improve target understanding, durability, localization, and potency

Enhancing precision targeting

Enhanced targeting via LMW and peptides



New linker chemistries

External partnerships help sustain Novartis' strong position in RLT

Priority Area	Partner	Deal / Collaboration
Combinations	artios DNA DAMAGE RESPONSE	**License and collaboration** DDR screening and identification of combination therapies
Targeting ligands	PeptiDream	**Partnership** Macrocyclic/constrained peptides generated with PeptiDream's proprietary platform for RLT and peptide-drug-conjugate use
Targeting biologics	ADIMAB AbCellera	**Collaborations** Discovery and optimization of biologics against priority Novartis targets

DDR – DNA Damage Response

Growing RLT research pipeline
Potential to address a range of solid tumors

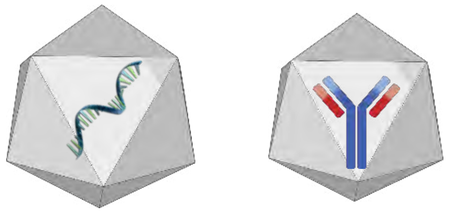
Product	Disease (target)	Status
^{177}Lu PSMA-617	Prostate cancer (PSMA)	FDA and EMA submission complete
		Ph3 PSMAFore study recruiting
		Ph3 PSMAddition study recruiting
		nmCRPC under evaluation
		BCR under evaluation
^{68}Ga PSMA-11		FDA and EMA submissions complete
^{225}Ac PSMA-617		Ph1 study recruiting
^{225}Ac PSMA-R2		Ph1 study in planning
^{68}Ga PSMA-R2		Ph1/2 study completed
^{18}F CTT1057		Ph2/3 & 3 studies recruiting
^{177}Lu-Dotatate	Neuroendocrine tumors (SSTR)	Ph3 NETTER-2 in 1L GEP-NET enrolling
		Pediatric study in GEP-NET and PPGL recruiting
	Other solid tumors (SSTR)	Other SSTR+ solid tumors in planning
^{177}Lu NeoB	Multiple solid tumors[1] (GRPR)	Ph1 basket study enrolling
^{68}Ga NeoB		IIT in GIST completed; Ph2 basket study completed
^{177}Lu FF-10158	Glioblastoma (integrin alphavbeta 3/5)	Study planned upon imaging results
^{68}Ga FF-10158		Ph1 study recruiting
FAPi		Deal closed with SOFIE Biosciences Q1 2021
Other (preclinical)	Additional targets	Targets under investigation

1. Breast cancer, GIST, GBM, neuroblastoma, ovarian, head & neck, esophageal

Our gene therapy platform innovates in three core areas

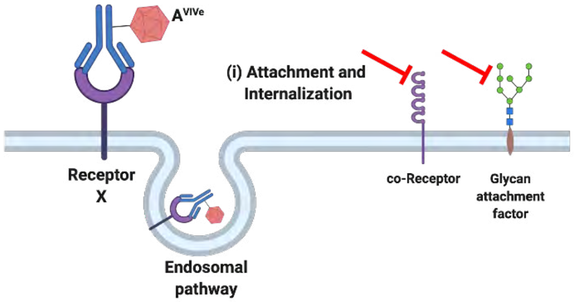
Natural or engineered gene transfer

Direct gene replacement (Zolgensma and CPK850)

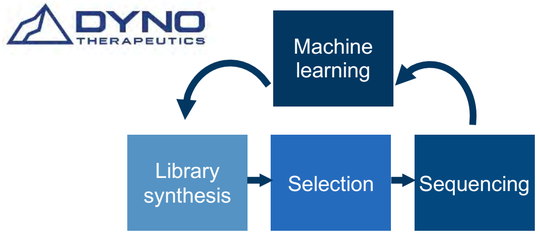


Deliver novel cargos (e.g. anti-sense oligonucleotides and anti-bodies)

AAV Tropism

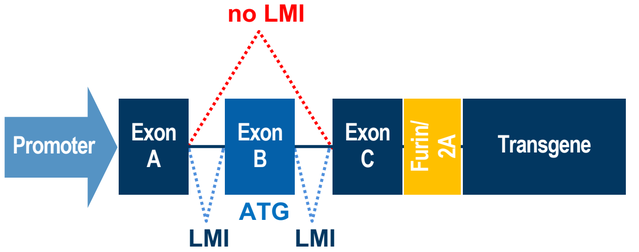


Antibody targeting



Capsid evolution for optimal tropism

Switchable gene expression



Switchable expression of transgene

Beyond our internal pipeline, acquisitions and partnerships consolidate our position in viral gene therapies

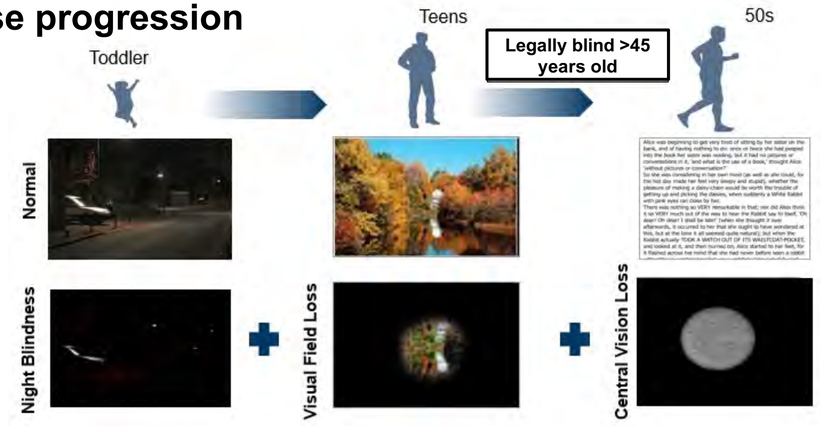
Priority Area	Partner	Deal / Collaboration
Ocular Gene Therapies	DYNO THERAPEUTICS	**License and collaboration** utilizing multi-cycle AI-driven optimization of AAV capsids for ocular delivery
	vedere™	**Acquisition** of optogenetics gene therapy programs, novel AAV capsids, and licenses to optogenetics intellectual property
	ARCTOS medical	**Acquisition** of optogenetics-based technology and one pre-clinical optogenetic AAV gene therapy program in new MOA
Neuroscience Gene Therapies	Sangamo THERAPEUTICS	**Collaboration and license** to develop gene regulation therapies for three neurodevelopmental targets

AAV gene therapy for inherited retinal dystrophy due to mutations in RLBP1 gene

Retinitis Pigmentosa

- A progressive inherited retinal dystrophy that results in early night blindness, gradual loss of visual fields and visual acuity, leading to complete blindness in one's 40s
- RLBP1 mutation cause a specific form of autosomal recessive retinitis pigmentosa
- Prevalence = 1:800,000 patients

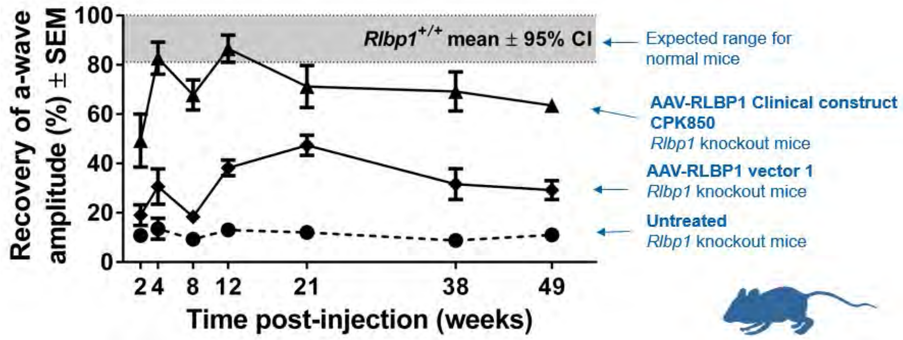
Disease progression



CPK850

- AAV treatment that restores a functional copy of the RLBP1 gene to cells of the retina
- Ph1/2 clinical trial is ongoing

AAV treatment improves long-term dark adaptation in a mouse model of RLBP1 dystrophy

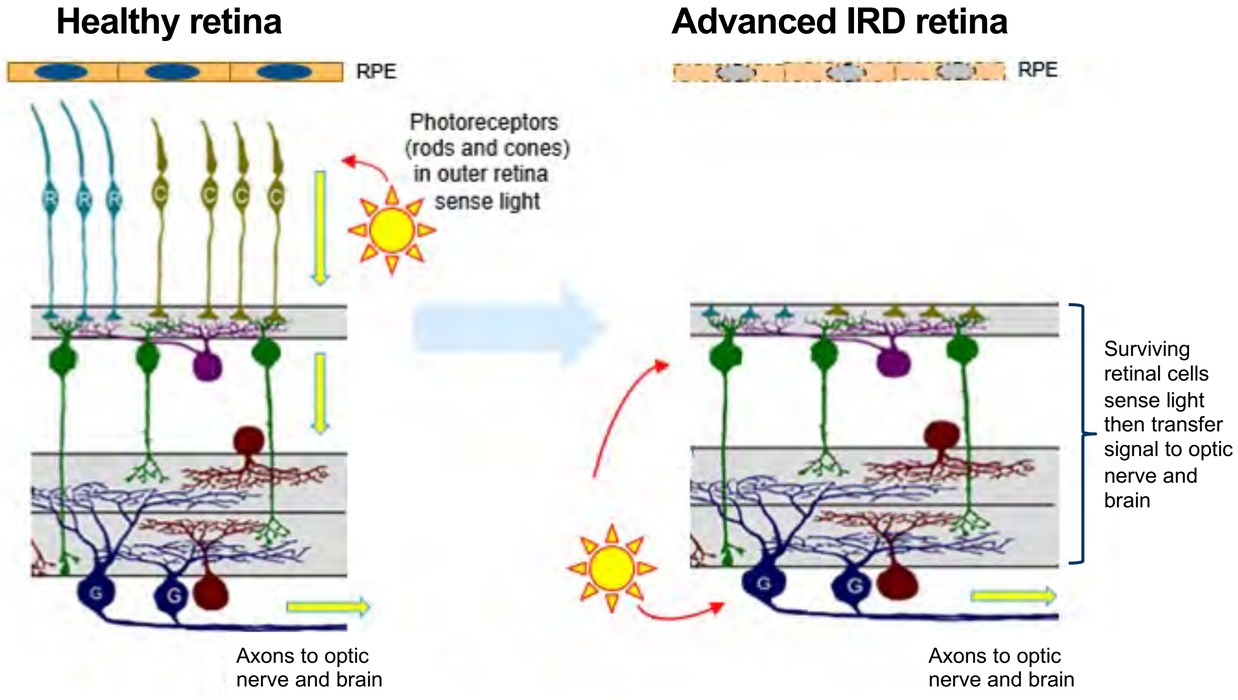


Optogenetics as the basis for a gene-agnostic AAV treatment for blindness

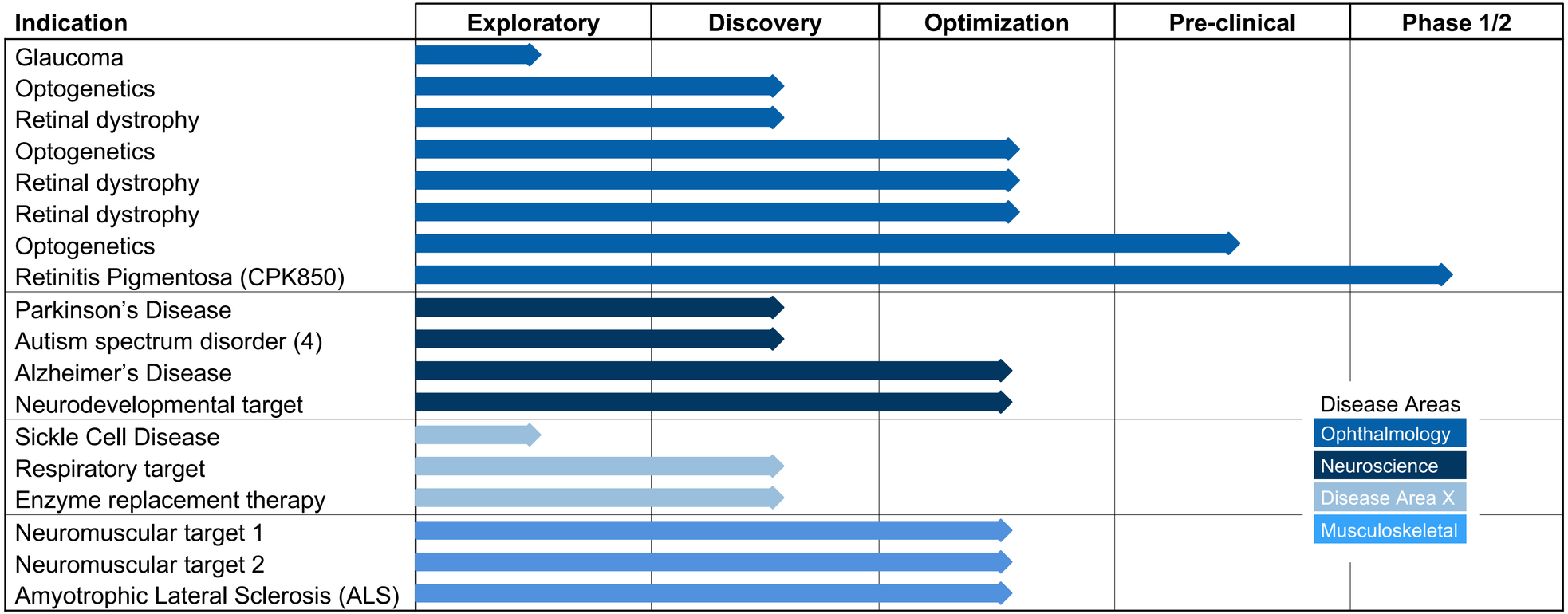
Optogenetic Gene Therapy

- Delivers a light sensitive protein to surviving cells of a degenerating retina
- Treats Inherited Retinal Dystrophy (IRD) patients agnostic of the genetic cause of disease (may be caused by mutations in over 200 different genes)
- May benefit macular degeneration patients with geographic regions of atrophy and surviving inner retinal cells
- Recent acquisitions position Novartis for leadership in the optogenetics space

vedere™ ARCTOS medical

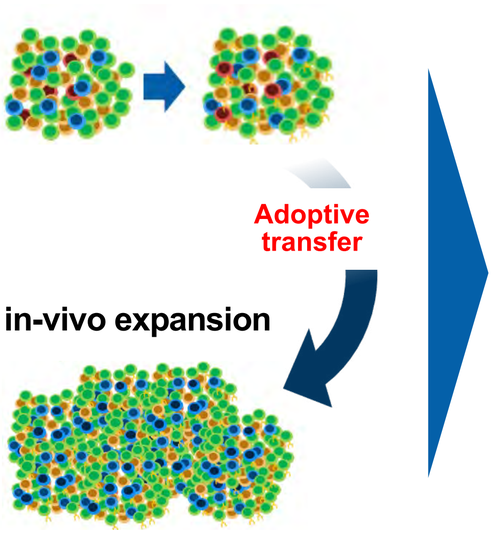


Novartis gene therapy research pipeline covers multiple disease areas and indications



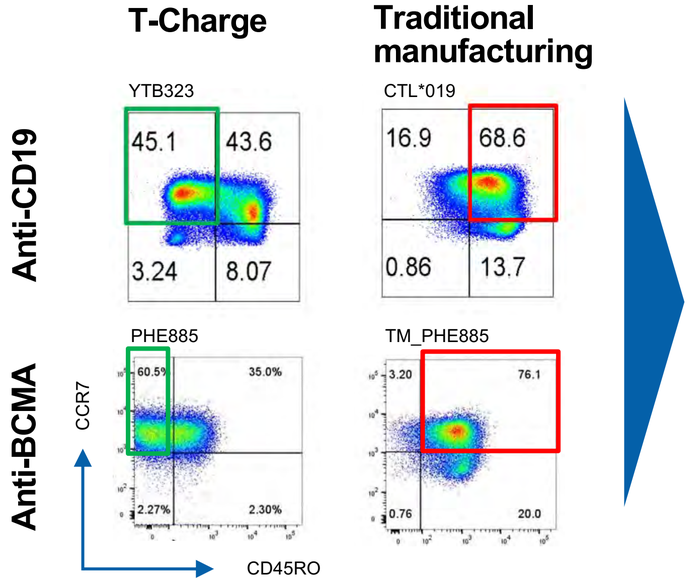
T-Charge™: A redesigned internal CAR-T technology platform

Minimal ex vivo culture to maximize in vivo expansion



- T-Charge manufacturing process time will be less than 2 days
- With T-Charge, CAR-T cells can expand within their natural environment when infused into the patient
- 10-50-fold fewer CAR-T cells infused compared to existing CAR-T therapies

T-Charge preserves T cell "stemness," an important T cell characteristic closely tied to its therapeutic potential

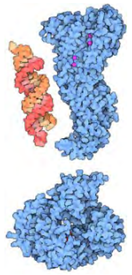


Flow cytometry shows:

- T-Charge retains naïve / Tscm cells (CD45RO-/CCR7+)
- In contrast, the traditionally generated product consists mainly of central memory T cells (Tcm) (CD45RO+/CCR7+)

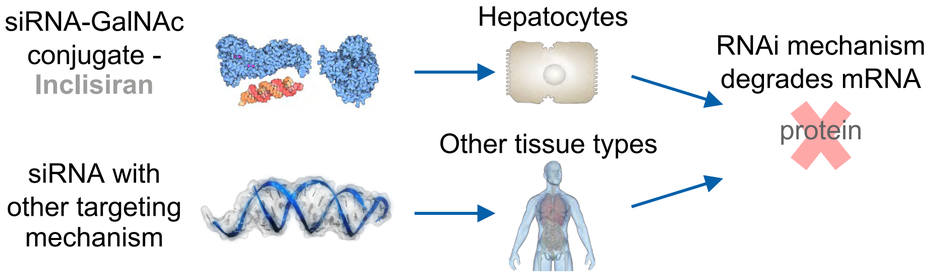
Exploring new approaches in RNA therapeutics

Small interfering RNA to inhibit translation of PCSK9 (cardiovascular disease) - Inclisiran

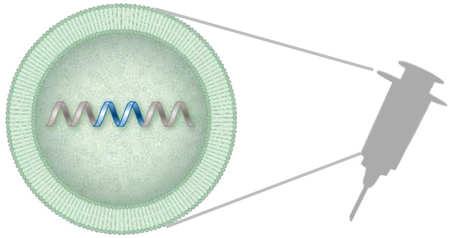


Antisense therapy to lower lipoprotein(a) (cardiovascular disease) - Pelacarsen

Tissue targeted siRNA ex-hepatocytes



mRNA cancer vaccine



Appendix

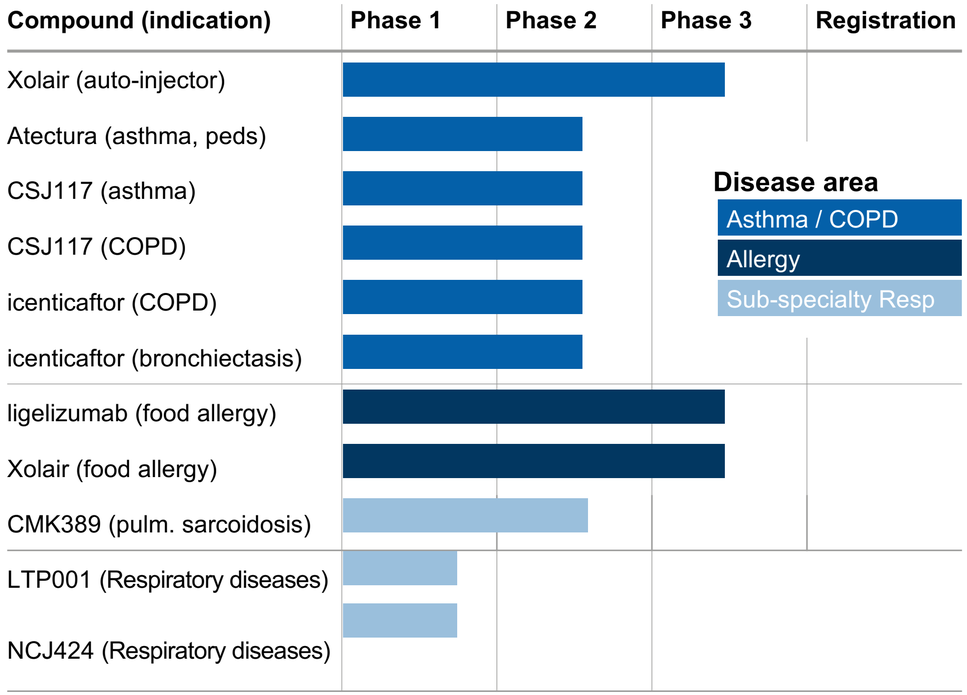
Respiratory & Allergy

Our Respiratory & Allergy strategy is focused on areas of high unmet need, with a strong mid and late-stage pipeline

Respiratory & Allergy strategy

- Drive innovation in **specialty asthma** *via* CSJ117 anti-TSLP inhaled monotherapy as potential 1st inhaled biologic
- Deliver life-altering improvements for **COPD** patients, initially with icenticaftor's CFTR potentiation, complemented by CSJ117 and early-stage assets
- Become **food allergy** leader by transforming SoC anaphylaxis avoidance to proactive treatment, enabling patients and families to live free from fear with ligelizumab and supported by pipeline/ LCM
- Address **life-threatening sub-specialty** respiratory diseases, e.g., fibrotic lung disease, capitalizing on understanding of complex pathobiology and a diverse array of assets/ MoAs

Assets highlighted today:
CSJ117, icenticaftor



Note: ligelizumab food allergy content covered in the context of the IHD presentation^ Note: bars in gantt chart indicate current phase of development.

CSJ117

WILD CARD

Inhaled TSLP inhibitor

Phase 2

Key highlights

- **40% of asthma patients uncontrolled** despite maximum standard of care; biologic penetration low at 4% and limited to T2-high population
- CSJ117 **binds with high affinity to human TSLP**, a key upstream cytokine in the asthma inflammatory cascade
- Potential to become the **first inhaled biologic directly targeting airways**, at the site of TSLP expression for a broad patient population in asthma
- **TSLP mechanism proven** to reduce exacerbations in T2-high and T2-low patients
- CSJ117 PoC study showed **reduction in airway inflammation**
- **Asthma Ph2b dose range** finding and safety extension studies ongoing; initiation of Ph3 program expected in 2023.
- In parallel development for **severe COPD.** Ph2 PoC study is recruiting. Readout expected in 2023
- **US/EU**: Patent on composition of matter (2036/2036)[1]

1. Patent term extensions and regulatory-based exclusivities are possible

On track to be first inhaled biologic, CSJ117 has the potential to transform severe asthma & COPD treatment paradigms

CSJ117 acts on upstream TSLP target in inflammation pathway

Potential to be first inhaled Bx directly targeting airways, at the site of TSLP expression

Convenient inhaled administration for a broad patient population (both T2-high and T2-low)

Asthma

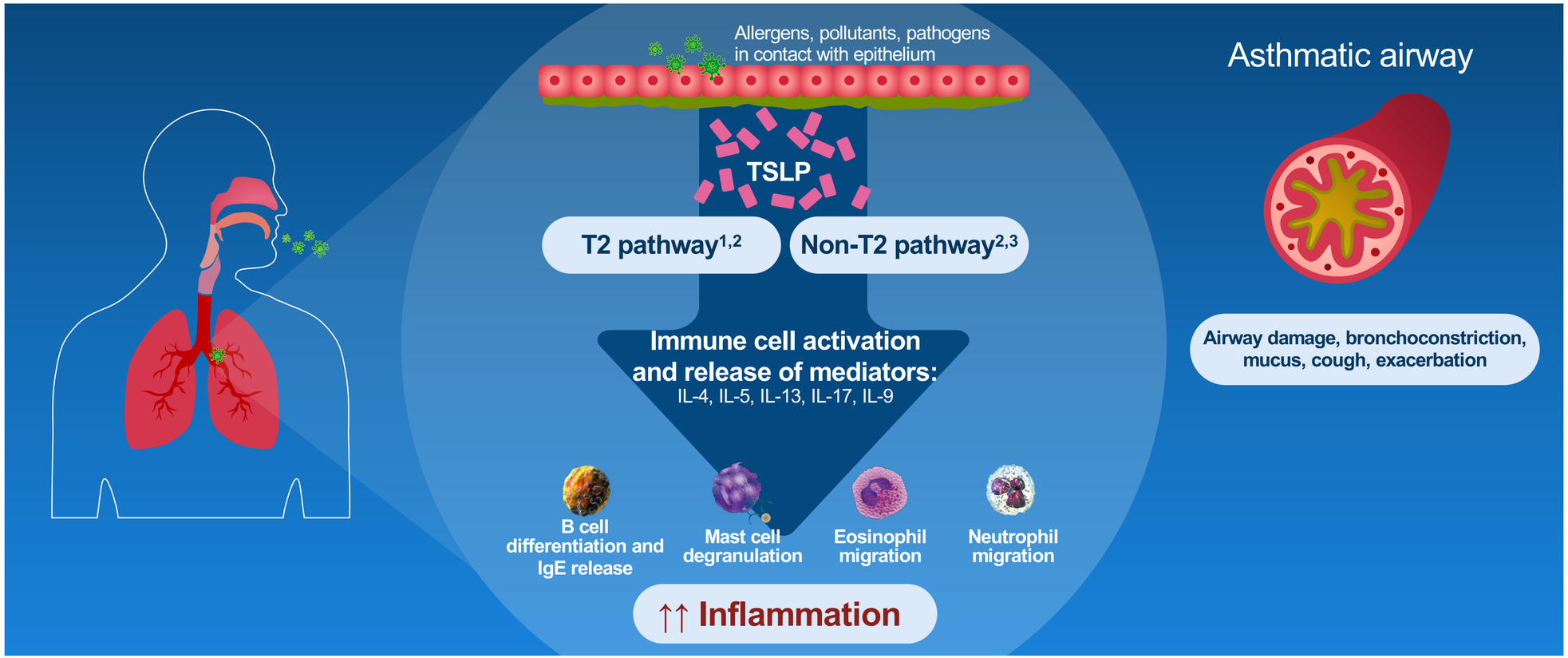
- In asthma, 40% of the >339m patients have moderate-to-severe disease and suffer daily from the impact of being uncontrolled despite maximal standard of care
- Only 4% of the severe asthma patients have access to the currently approved injectable Bx that require phenotyping and are limited to allergic and eosinophilic diseases
- No approved Bx treatment for the T2-low asthma population (up to 50% of patients)

COPD

- One of the leading causes of mortality and healthcare burden, including significant disability adjusted life-years lost
- Current therapies (inhaled bronchodilators and corticosteroids) may improve symptoms, yet many patients remain symptomatic and at risk of exacerbations
- No approved Bx treatment

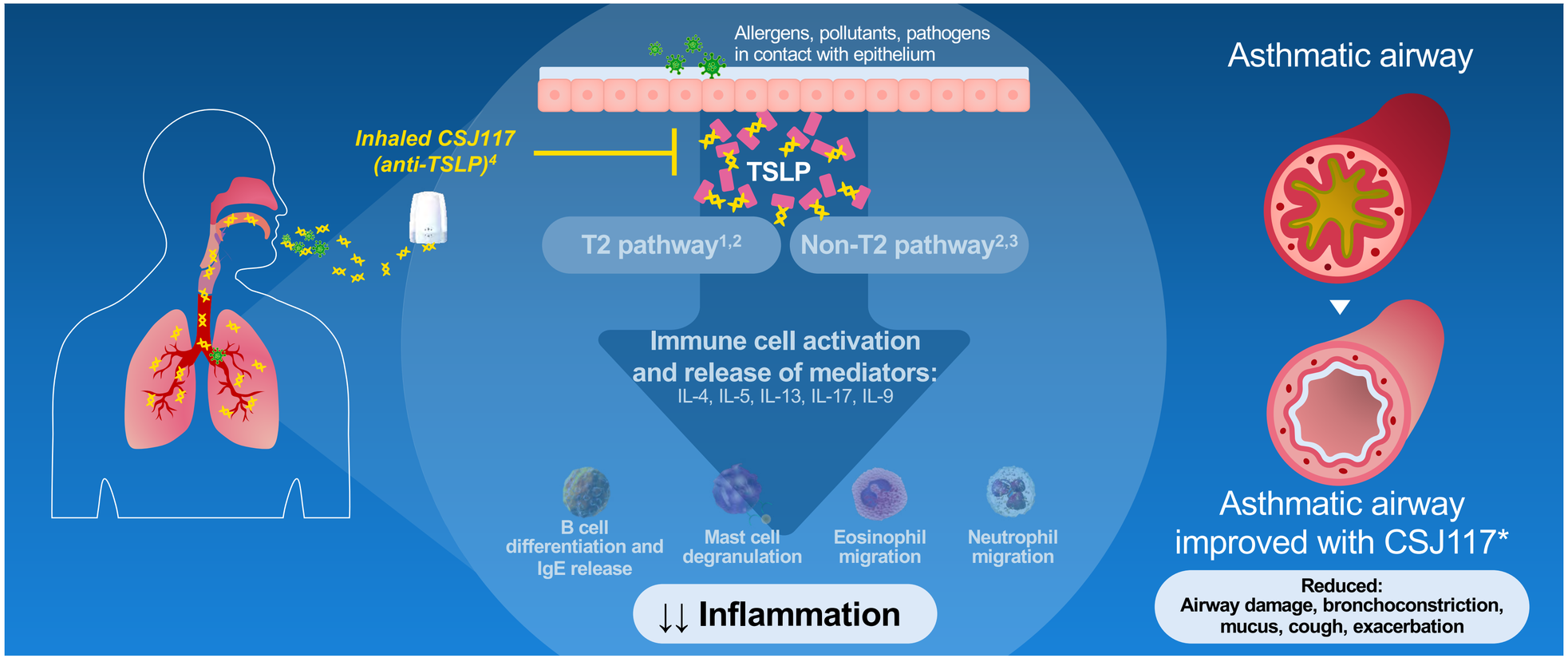
Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017; 390: 1211–59.

TSLP is an upstream mediator of asthma, triggering inflammation via T2 and non-T2 pathways



IL, interleukin; TSLP, thymic stromal lymphopoietin. 1. Nagajima S, et al. Allergol Int. 2020;69:197–203; 2. Brusselle GG, et al. Nat Med. 2013;19:977–9; 3. Gauvreau GM, et al. Expert Opin Ther Targets. 2020;1–16

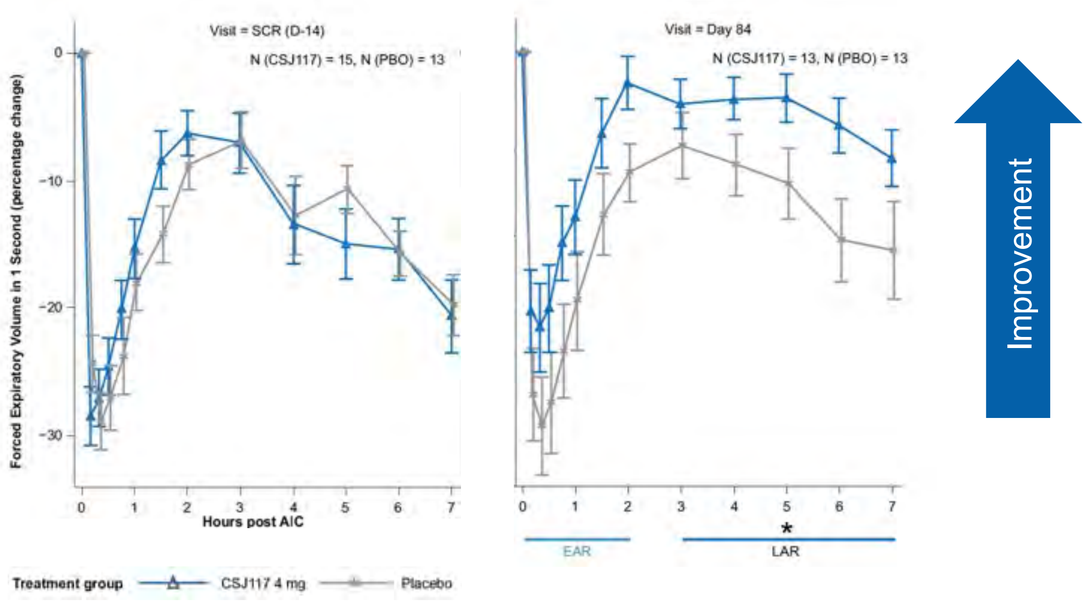
CSJ117 is an inhaled anti-TSLP antibody fragment which inhibits both T2 and non-T2 mediated inflammation



*Note: Asthma airway improvements observed in Ph2a proof-of-concept (PoC) study: NCT03138811. IL, interleukin; TSLP, thymic stromal lymphopoietin. 1. Nagajima S, et al. Allergol Int. 2020;69:197–203. 2. Brusselle GG, et al. Nat Med. 2013;19:977–9. 3. Gauvreau GM, et al. Expert Opin Ther Targets. 2020;1–16. 4. Gauvreau GM, et al. Am J Respir Crit Care Med 2020;201:A4207

In Ph2a POC study, CSJ117 improved lung function compared with placebo

Arithmetic mean (+/- SE) of % decrease in FEV[1] over a 7-hour period following AIC



Ph2a POC study data show:

- CSJ117 reduced allergen induced bronchoconstriction in adult pts with mild asthma
- Good tolerability and safety profile

Ph2b dose range finding study
is evaluating 5 doses of CSJ117 in severe asthma pts

*. p<0.05 significant difference between CSJ117 and placebo; data presented as mean ± SE. AIC, allergen inhalation challenge; AUC, area under the curve; EAR, early asthmatic response (hours 0-2); FEV1 , forced expiratory volume in 1s. LAR, late asthmatic response; PBO, placebo; SCR, screening; SE, standard error. 1. Gauvreau GM et al. 2020; poster presented at ERS International Congress 2020

Asthma Ph2b and COPD POC studies are ongoing with expected readouts in 2023

Market potential

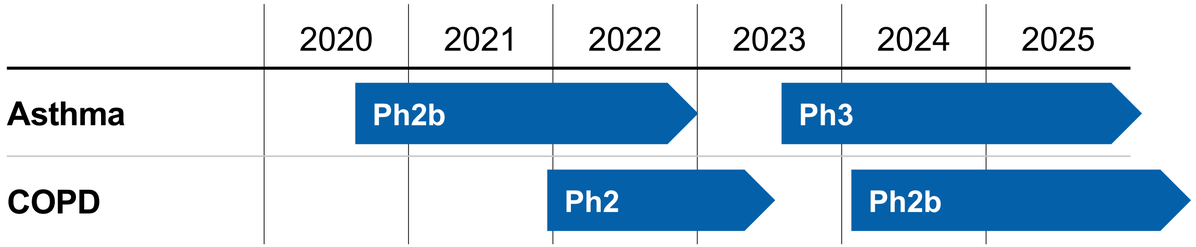
Indication	Asset potential
Asthma	●●●
COPD	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Addressable patients[1]

Indication	Patients
Asthma	850k
COPD[2]	2.4m

Upcoming milestones for development program



Asthma
Initiation of Ph3 program expected 2023

COPD
Read-out of Ph2 expected 2023

1. Approximate figures; Source: Novartis internal forecast for G7 countries 2. Total addressable population currently uncontrolled on relevant SoC.

Icenticaftor (QBW251)

Oral CFTR potentiator

Phase 2

Key highlights

- **3.8m COPD patients** in G6 with majority uncontrolled despite inhaled therapies
- **Smoking leads to CFTR dysfunction** which is associated with COPD pathology, particularly in presence of chronic bronchitis
- By potentiating CFTR ion channels across various cell types, **icenticaftor targets reductions in systemic inflammation, bacterial colonization** and **airway disease with potential for meaningful symptom improvements**
- **Icenticaftor improved CFTR function, inflammation, lung function, and bacterial colonization** in a COPD POC study[1]
- Recruitment to **Ph2b dose range finding study** has recently completed. Ph3 initiation targeted H1 2023
- Parallel **PoC study in bronchiectasis** ongoing
- **US/EU**: Patent on compound (2031/2031)[2]

COPD: Chronic Obstructive Pulmonary Disease. CFTR : Cystic Fibrosis Transmembrane Regulator. CB: Chronic bronchitis; POC: Proof Of Concept 1. Rowe SM, et al. Int J Chron Obstruct Pulmon Dis. 2020. 2. Patent term extensions and regulatory-based exclusivities are possible

Icenticaftor represents a novel approach to COPD, with potential to deliver life-altering symptom improvements

Unmet needs in COPD are large and neglected

- COPD is the 3rd leading cause of death worldwide[1]
- COPD causes high morbidity and mortality and results in significant healthcare costs[2-5]
- Many COPD patients with CB remain symptomatic and have exacerbations despite inhaled therapies[6]
- Cough, sputum and shortness of breath are the most common/persistent symptoms affecting quality of life[7,8]

Potential first to market blockbuster

- Only one new drug class has been approved to treat COPD in the last decades and few new entrants are anticipated beyond repurposed asthma biologics
- Ph2b dose range finding study has completed enrolment with results expected in H1 2022[9]
- Given the multi-system efficacy of CFTR potentiation in CF[10], multiple lifecycle opportunities are in scope
- A parallel PoC study in bronchiectasis is ongoing[11]

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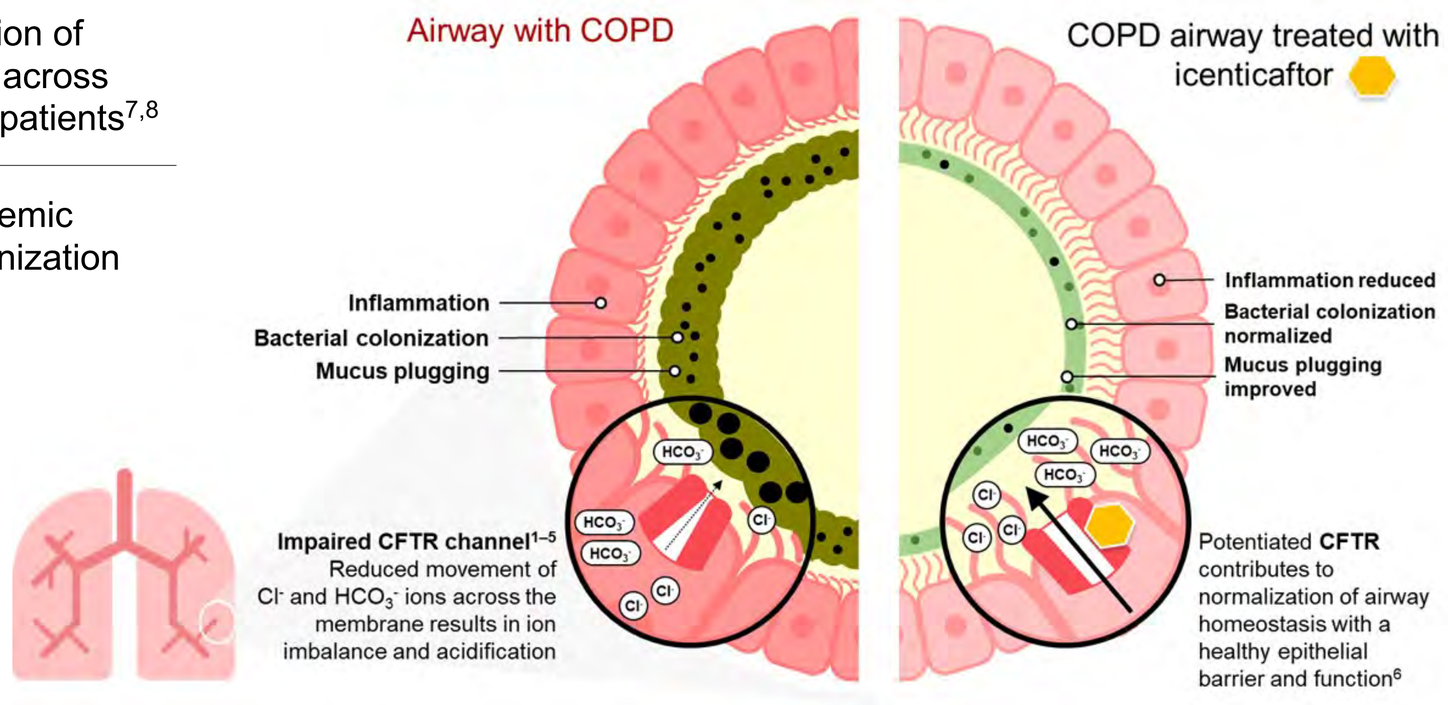
Icenticaftor, an oral CFTR potentiator, targets reductions in systemic inflammation, bacterial colonization & airway disease

CFTR potentiation: correction of acquired CFTR impairment across various cell types in COPD patients[7,8]

Targeting reductions in systemic inflammation, bacterial colonization and airway disease[6]



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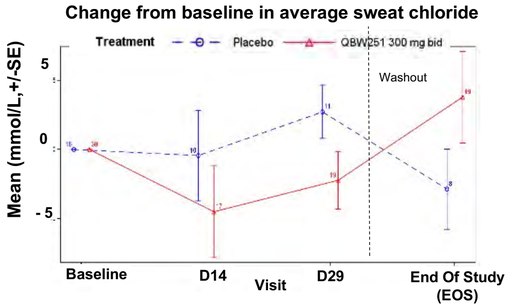
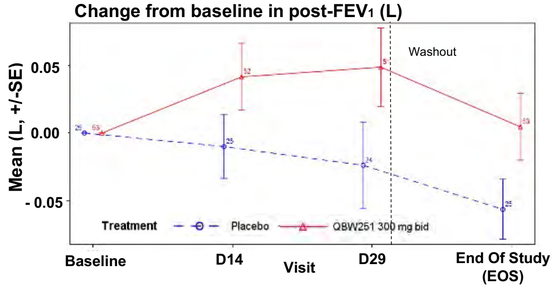
Icenticaftor improved CFTR function, inflammation, lung function, and bacterial colonization in COPD PoC study[1]

Systemic CFTR function (sweat chloride)



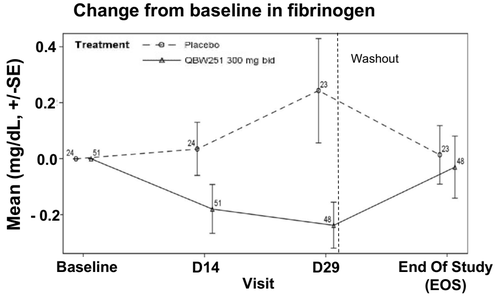
Improvement

Lung function (FEV[1])



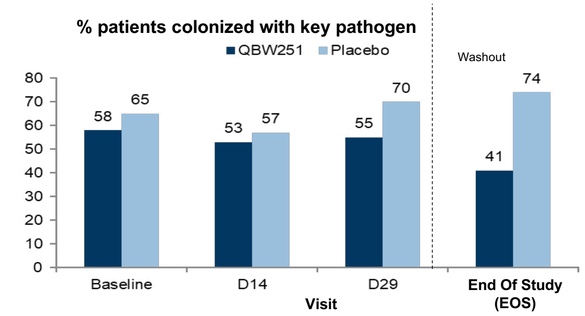
Improvement

Systemic inflammation (reduced fibrinogen)



Improvement

Bacterial colonization



Improvement

1. Rowe SM, et al. Int J Chron Obstruct Pulmon Dis. 2020. NCT02449018: Icenticaftor was well-tolerated with a similar overall incidence of AEs vs the placebo group. POC: Proof Of Concept; FEV1: Forced Expiratory Volume in 1 sec.

Icenticaftor, a novel oral CFTR potentiator, represents a potentially transformational approach to COPD

Cell health

CFTR function is disrupted in COPD

Icenticaftor potentiates CFTR in various cell types[1,2]

Lung health

By potentiating CFTR ion channels across various cell types, icenticaftor targets reductions in systemic inflammation, bacterial colonization and airway disease

Patient health

Icenticaftor aims to deliver life-altering symptom improvements in COPD patients with chronic bronchitis

1. Rowe SM, et al. Int J Chron Obstruct Pulmon Dis. 2020;15:2399-2409; 2. Liu F, et al. Science 2019; 364:1184–8

Icenticaftor targets COPD and bronchiectasis indications with large market potential

Market potential

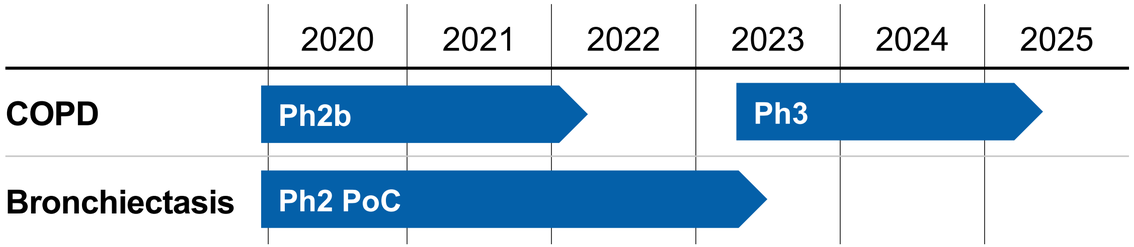
Indication	Asset potential
COPD	●●●
Bronchiectasis	

●○○ <USD 1bn ●●○ USD 1-2bn ●●● >USD 2bn

Addressable patients[1]

Indication	Patients
COPD[2]	3.8m
Bronchiectasis	650k

Upcoming milestones for development program



COPD
Ph2b dose range finding study has completed enrolment with results expected in H1 2022. Ph3 program initiation targeted H1 2023

Bronchiectasis
PoC Study ongoing

COPD: Chronic Obstructive Pulmonary Disease ; PoC: Proof of Concept 1Approximate figures; Source: Novartis internal forecast for G6 countries. 2. Total addressable population currently uncontrolled on relevant SoC.

Novartis submission schedule

New Molecular Entities: Lead and supplementary indications

LEAD INDICATIONS

2022

- **ligelizumab** — Lead
  QGE031
  CSU
- **sabatolimab**[1] — Lead
  MBG453
  HR-MDS

2023

- **iptacopan** — Lead
  LNP023
  PNH

2024

- **JDQ443** — Lead
  JDQ443
  2/3L NSCLC (mono)
- **remibrutinib** — Lead
  LOU064
  CSU
- **UNR844** — Lead
  Presbyopia
- **YTB323** — Lead
  2L r/r Diffuse large B-cell lymphoma

2025

- **icenticaftor** — Lead
  QBW251
  COPD
- **NIS793** — Lead
  1L Pancreatic cancer
- **pelacarsen** — Lead
  TQJ230
  CVRR-Lp(a)

≥2026

- **^{177}Lu-NeoB** — Lead
  AAA603
  Multiple Solid Tumors
- **branaplam** — Lead
  LMI070
  Huntington's disease
- **CEE321** — Lead
  Atopic Dermatitis
- **cipargamin** — Lead
  KAE609
  Malaria severe
- **CPK850** — Lead
  RP
- **CSJ117** — Lead
  Asthma
- **gevokizumab** — Lead
  VPM087
  1st line CRC / 1st line RCC
- **ganaplacide** — Lead
  KAF156
  Malaria uncomplicated
- **iscalimab** — Lead
  CFZ533
  Sjögren's syndrome
- **ianalumab** — Lead
  VAY736
  Sjögren's syndrome
- **libvatrep** — Lead
  SAF312
  COSP
- **LNA043** — Lead
  Knee osteoarthritis
- **LXE408** — Lead
  Visceral leishmaniasis
- **LXH254** — Lead
  Solid tumors (combos)
- **MIJ821** — Lead
  Depression
- **spartalizumab** — Lead
  PDR001
  Metastatic melanoma (combo)
- **TNO155** — Lead
  Solid tumors
- **tropifexor&licoglifloz** — Lead
  LJN452
  NASH (combos)

NEW INDICATIONS

2022

- **tislelizumab** — LCM
  VDT482
  1L Nasopharyngeal Carcinoma
- **tislelizumab** — LCM
  VDT482
  NSCLC

2023

- **177Lu-PSMA-617** — LCM
  AAA617
  Pre-taxane
- **iptacopan** — LCM
  LNP023
  C3G
- **iptacopan** — LCM
  LNP023
  IgAN
- **tislelizumab** — LCM
  VDT482
  1L Gastric Cancer
- **tislelizumab** — LCM
  VDT482
  1L ESCC
- **tislelizumab** — LCM
  VDT482
  Localized ESCC
- **tislelizumab** — LCM
  VDT482
  1L Hepatocellular Carcinoma

2024

- **177Lu-PSMA-617** — LCM
  AAA617
  mHSPC
- **sabatolimab** — LCM
  MBG453
  Unfit AML
- **tislelizumab** — LCM
  VDT482
  1L Small Cell Lung Cancer
- **tislelizumab** — LCM
  VDT482
  1L Bladder Urothelial Cell Carcinoma

2025

- **asciminib** — LCM
  ABL001
  CML 1L
- **iptacopan** — LCM
  LNP023
  aHUS
- **ligelizumab** — LCM
  QGE031
  Food allergy
- **ligelizumab** — LCM
  QGE031
  CINDU
- **remibrutinib** — LCM
  LOU064
  Multiple sclerosis

≥2026

- **asciminib** — LCM
  ABL001
  CML, 2L, pediatrics
- **cipargamin** — LCM
  KAE609
  Malaria uncomplicated
- **ianalumab** — LCM
  VAY736
  AIH
- **iptacopan** — LCM
  LNP023
  iMN
- **iscalimab** — LCM
  CFZ533
  Liver Tx
- **remibrutinib** — LCM
  LOU064
  Sjögren's syndrome

1. Filing opportunity in 2022 / 2023, based on PFS and/or OS outcomes from a dual approach based on parallel Phase 2 and Phase 3 trials.

Novartis submission schedule

Supplementary indications for existing brands

2022

Cosentyx LCM
secukinumab, AIN457
PsA IVIV

Cosentyx LCM
secukinumab, AIN457
AS H2H

Cosentyx LCM
secukinumab, AIN457
Hidradenitis suppurativa

Entresto EU[1] LCM
sacubitril/valsartan, LCZ696
Pediatric CHF

Tafinlar + Mekinist LCM
dabrafenib + trametinib, DRB436
HGG/LGG - Pediatrics

Xolair LCM
omalizumab, IGE025
Auto-injector

2023

canakinumab LCM
ACZ885
Adjuvant NSCLC

Cosentyx LCM
secukinumab, AIN457
AS IVIV

denosumab BioS
GP2411
anti RANKL mAb

Kisqali LCM
ribociclib, LEE011
HR+/HER2- BC (adj)

Lutathera LCM
^{177}Lu-oxodotreotide[2]
GEP-NET 1L G3

Piqray LCM
alpelisib, BYL719
TNBC

Piqray LCM
alpelisib, BYL719
Ovarian cancer

Promacta LCM
eltrombopag, ETB115
r/r severe aplastic anemia

Xolair LCM
omalizumab, IGE025
Food allergy

2024

Adakveo LCM
SEG101
Sickle cell anaemia with crisis ped

Coartem LCM
artemether + lumefantrine, COA566
Malaria uncompl., formula for <5kg

Cosentyx LCM
secukinumab, AIN457
GCA

Jakavi LCM
ruxolitinib, INC424
Pediatrics Acute GVHD

Jakavi LCM
ruxolitinib, INC424
Pediatrics Chronic GVHD

Leqvio LCM
KJX839
Ped Hyoerlipidemia

Tafinlar + Mekinist LCM
dabrafenib + trametinib, DRB436
Thyroid cancer

2025

aflibercept BioS
SOK583
Neovascular age-related macular degeneration

Beovu LCM
brolucizumab, RTH258
Diabetic retinopathy

Cosentyx LCM
secukinumab, AIN457
Lichen Planus

Piqray LCM
alpelisib, BYL719
HER2+ adv BC

Zolgensma LCM
AVXS-101 OAV101
SMA IT

≥2026

Atectura LCM
indacaterol + mometasone, QMF149
Asthma, pediatrics

Aimovig LCM
erenumab, AMG334
Pediatric Migraine

Cosentyx LCM
secukinumab, AIN457
Lupus Nephritis

Jakavi LCM
ruxolitinib, INC424
Myelofibrosis (combination)

Kesimpta[3] LCM
ofatumumab
Multiple sclerosis, pediatrics

Kymriah LCM
tisagenlecleucel, CTL019
1L high risk ALL, pediatrics & young adults

Leqvio LCM
KJX839
CVRR-LDLC

Mayzent[4] LCM
siponimod, BAF312
Multiple sclerosis, pediatrics

Rydapt LCM
midostaurin, PKC412
Acute myeloid leukemia, pediatrics

1. Approved in US. 2. 177Lu-dotatate in US. 3. Kesimpta and Mayzent: pediatric study in multiple sclerosis run in conjunction (NEOS)

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References

Immunology, Hepatology & Dermatology | Slide 4

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