

# Meet Novartis Management 2020

## Agenda

**November 24, 2020**

All times in CET

14:00 – 14:45 **Novartis Group** (incl. CEO intro)

Break / 15 minutes

15:00 – 15:45 **Pipeline / R&D**

Break / 60 minutes

16:45 – 17:30 **Pharmaceuticals**

Break / 15 minutes

17:45 – 18:30 **Oncology**

Break / 15 minutes

18:45 – 19:30 **Sandoz**



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## Welcome to the Meet Novartis Management 2020 interactive guide, which accompanies our investor day.

Use the navigation tabs above to go to any of the main sections in this document: Group, Key Assets, Sandoz and Appendix. And use the tabs within each of those sections to navigate further to our franchises and products featured here.

The   buttons top right allow you move through the section content. The  button will bring you back to this page to see the overview of all content below.

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Piqray®  
Tabrecta™  
Canakinumab  
<sup>177</sup>Lu-PSMA-617  
TNO155  
LXH254

**Oncology: Hematology**  
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## Sandoz

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Where we are today

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# Group

Where we are today

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Click to view  
**MNM Agenda**



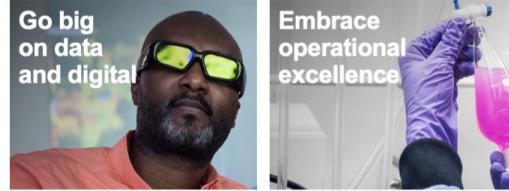
# In 2018, we set out a clear strategy that we are executing

## Strategy set out in 2018...

### Our focus



### Our five priorities



## ...is delivering...

- ✓ Consistent top-line growth
- ✓ Sustained bottom-line expansion

## ...while positioning Novartis for the long-term

- ✓ 100% focused as a medicines company
- ✓ Record-high engagement score
- ✓ Leading pipeline, with 4 advanced therapy platforms
- ✓ USD 2bn cost savings achieved over 2017-2020
- ✓ Building a leading digital and data science platform
- ✓ Improving ESG scores, industry leader across 3 key indices

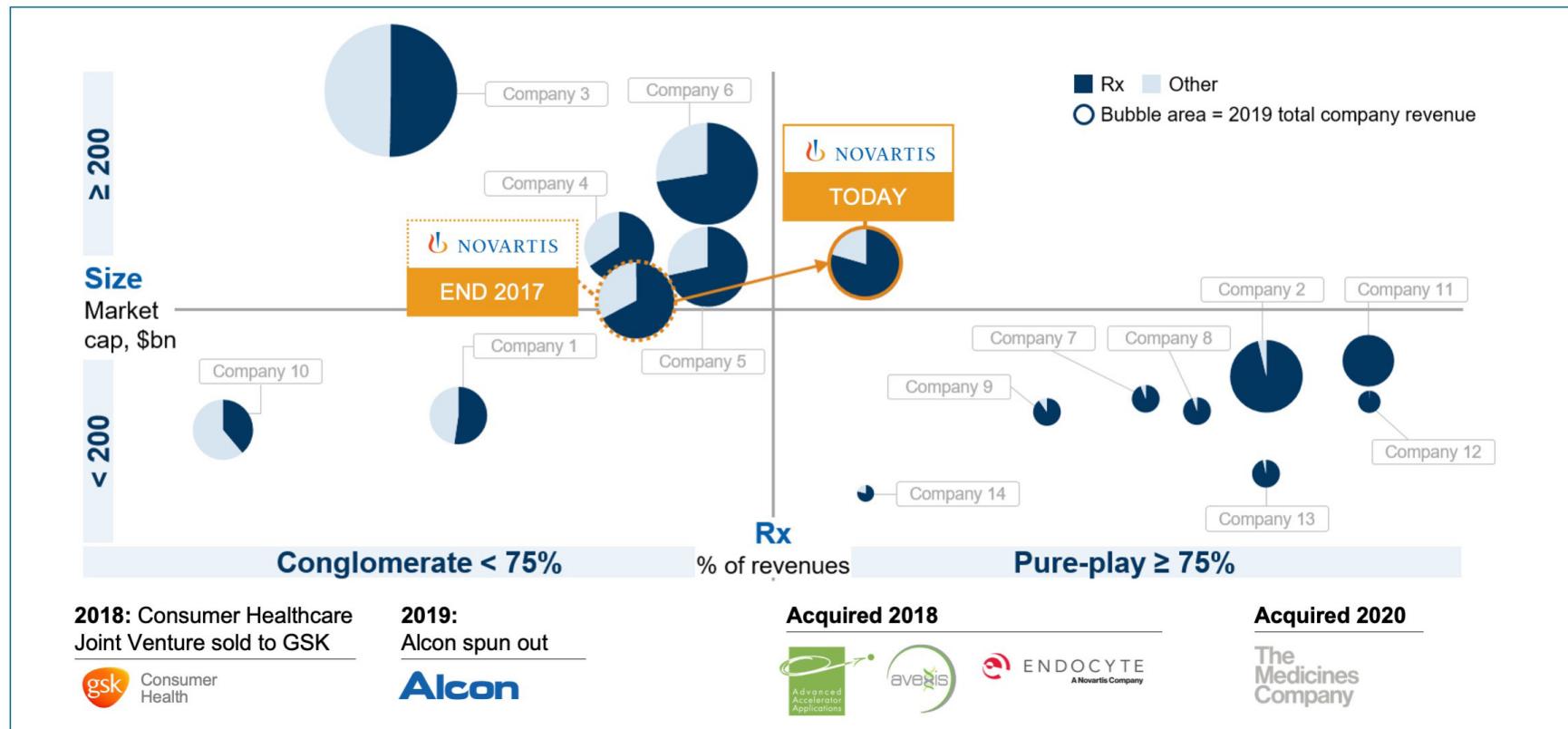
## Strong operational performance over the past three years

Continuing operations <sup>1</sup>	2017	% 2018 growth (cc)	2018	% 2019 growth (cc)	2019	% 9M 2020 growth (cc)	9M 2020	FY guidance <sup>3</sup>
<b>Net sales</b> USD bn, growth cc <sup>2</sup>	42.3	+5%	44.8	+9%	47.4	+4%	35.9	To grow mid single digit
<b>Core<sup>2</sup> OpInc</b> USD bn, growth cc <sup>2</sup>	11.7	+7%	12.6	+17%	14.1	+16%	11.9	To grow low double digit to mid teens
<b>Innovative Medicines</b> <b>Core<sup>2</sup> margin</b> %, growth cc <sup>2</sup>	31.0%	+1.0% pts	32.0%	+1.8% pts	33.5%	+2.7% pts	36.3%	Mid 30s <sup>4</sup>

1. Continuing operations excludes Alcon, includes the businesses of Innovative Medicines and Sandoz as well as the continuing corporate functions. 2. Constant currencies (cc) and core results are non-IFRS measures. 3. Guidance assumes that we see a continuation of the return to normal global healthcare systems including prescription dynamics, particularly ophthalmology, in Q4 2020. In addition, we assume that no Gilenya and no Sandostatin LAR generics enter in 2020 in the US. 4. Historically Q4 margin lower due to seasonality.

# We have focused the company

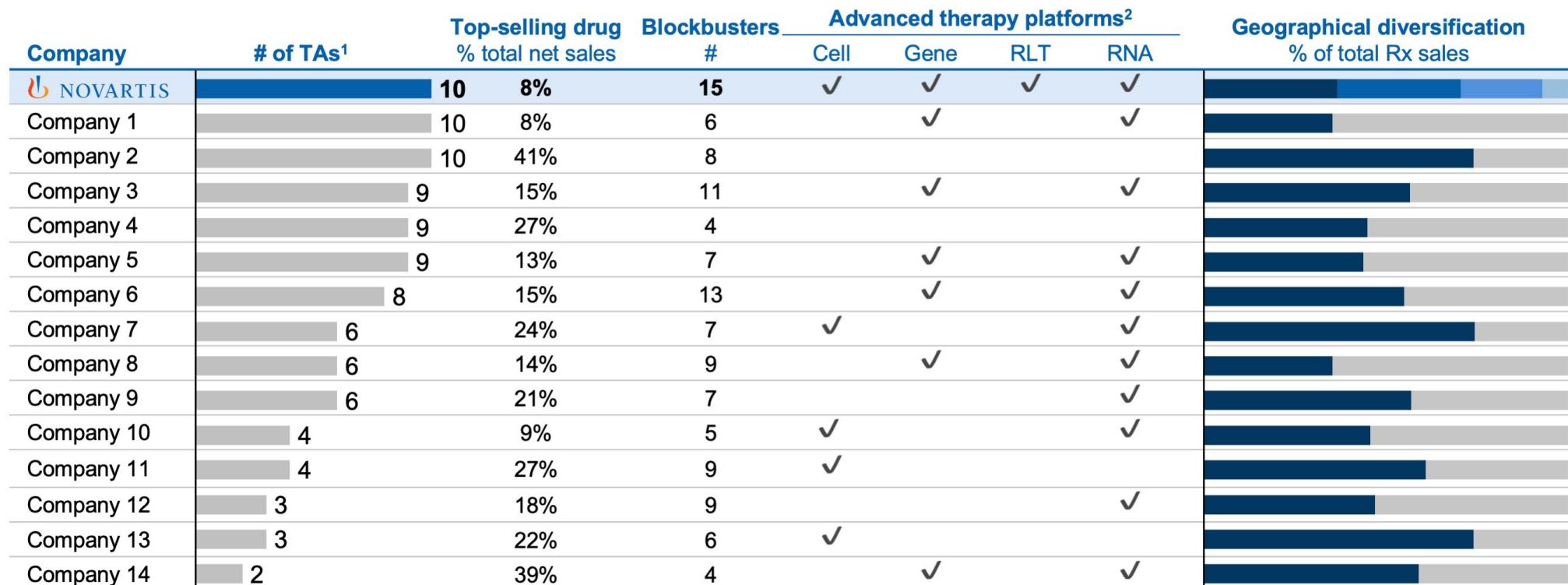
## Our focus



Note: Companies grouped by strategic archetype, not strictly to scale. Source: Evaluate Pharma, S&P Capital IQ, Annual Reports. Revenues FY 2019, Market Caps as of Jan 1, 2020 except Company 2 (May 8, 2020). Rx = Innovative medicines. Other = vaccines, animal health, generics / biosimilars, consumer health, medical devices / diagnostics, revenues not attributable to a specific segment / TA and other revenues.

# Today, we present investors a unique profile

Diversified across geographies and TAs, while providing exposure to cutting-edge platforms

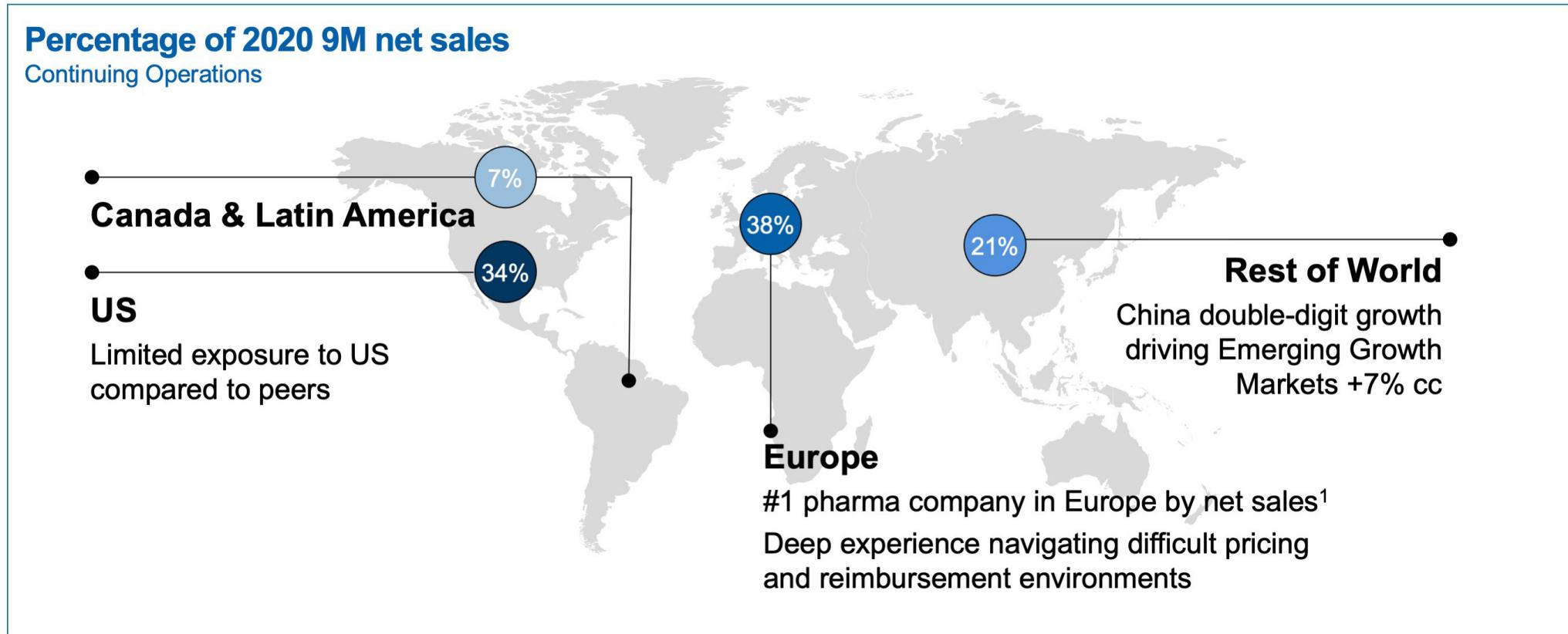


1. Only TAs (Therapeutic Areas) with annual 3<sup>rd</sup> party sales > USD 500m in 2019; TA definition as per Evaluate Pharma; manual adjustments to keep classification consistent vs. previous years. 2. Defined as net sales from one of the mentioned therapy platforms by 2025 according to Evaluate Pharma and publicly available pipeline information.

Source: Evaluate Pharma 2020

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

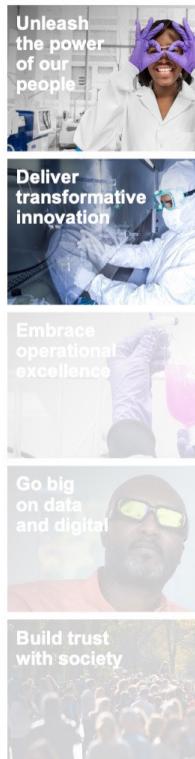
# Novartis business diversified geographically with modest US pricing exposure



1. Source Evaluate Pharma 2019 Pharmaceutical segment sales report.

# We are making progress on culture, pipeline, and launch execution...

## Our 5 priorities

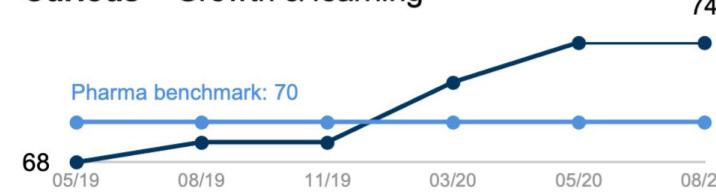


### Significant progress on our culture journey

#### Inspired – Engagement<sup>1</sup>



#### Curious – Growth & learning<sup>1</sup>



#### Unbossed – Manager effectiveness<sup>2</sup>

**82** Manager recommendation score  
+5 vs. benchmark

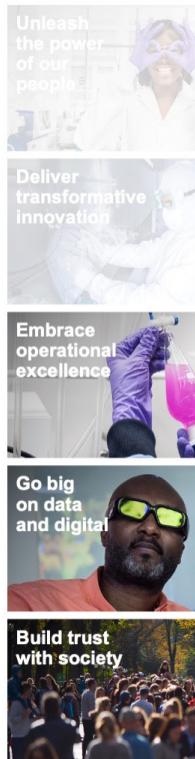
### 10 key approvals received over the past 3 years



1. Source: Quarterly Glint Engagement Survey Scores (out of 100). 2. Source: Team Perspectives, March 2020, 63k participants. 3. DLBCL. 4. nrAxSpA.

# ...as well as productivity, digitalization and ESG

## Our 5 priorities



### Advancing on NTO and NBS transformations

#### Novartis Technical Operations

Reducing asset-intensity and enhancing standardization, while investing in innovative technologies

- 14 Sites exited
- 123 Warehouses reduced
- 2 New Operation Centers
- 2 New EU sites for Kymriah
- 1m+ Square feet footprint for GTx
- \$2bn Further productivity (mid-term)

#### Novartis Business Services

Continuing on the journey to become a 4<sup>th</sup> gen enterprise transformation engine

### Building a leading digital and data science platform

#### Scaling our 12 Lighthouses

3k+ Trials ingested in Data42

750k+ Patients data ingested in Data42

#### Bold moves starting to pay off



#### Continuous investments in:

- People: DS&AI community with 800+ data scientists
- Foundations and enterprise data management

### On our way to become a trusted ESG leader

Integrating ESG across our operations, whilst strengthening KPIs and their measurements

Setting ourselves up to achieve a consistent leadership position

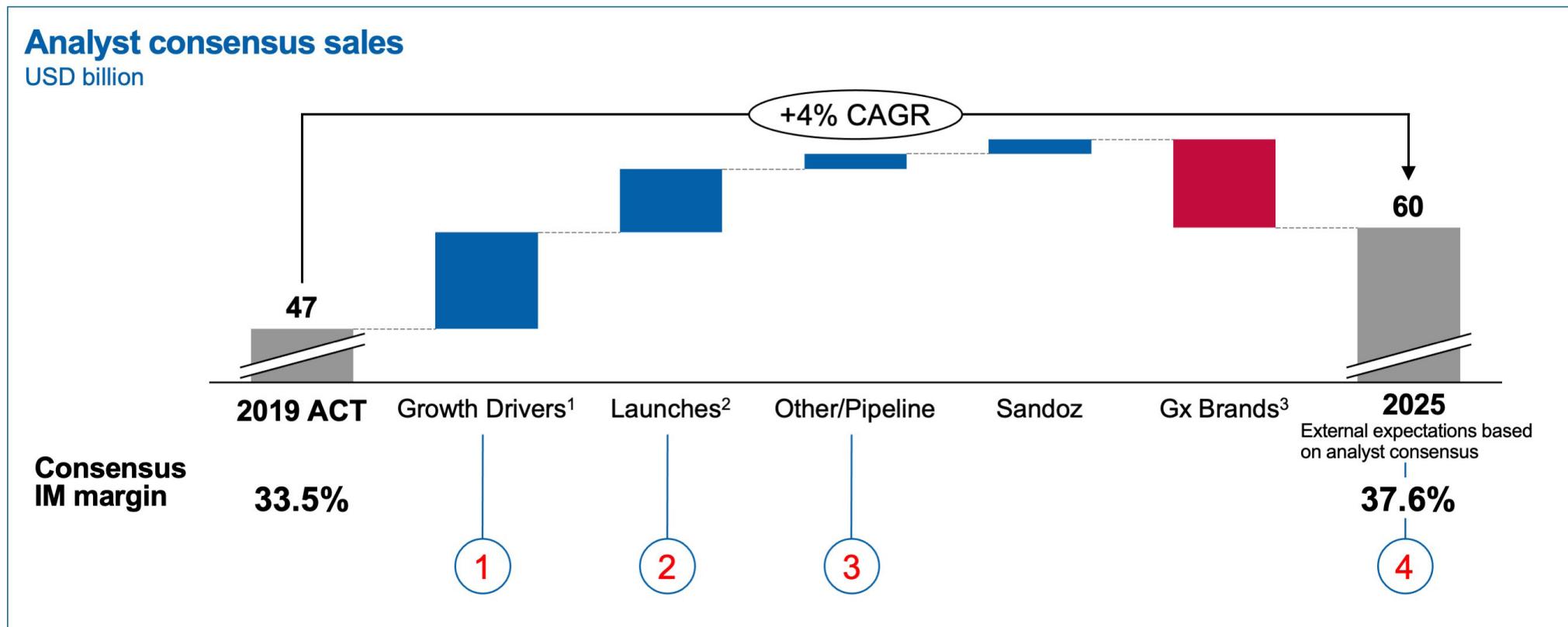
Our progress resulted in upgrades to ESG rankings

Top-tier sector-leading performance

Novartis access programs / management best-in-class

See pages 31-32 for further details

# Confident that we will grow top and bottom line every year to 2025 and meet external expectations



## 1 Growth drivers

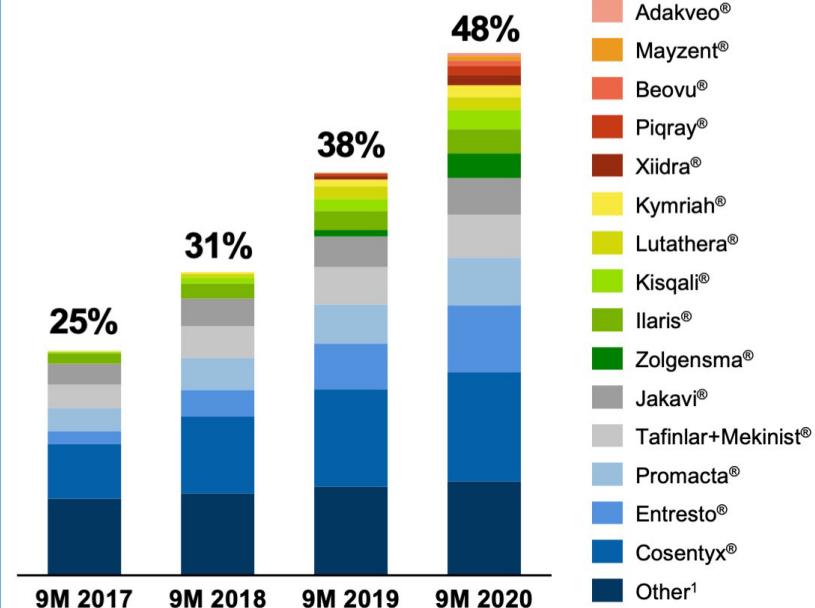
# Strong operational performance from growth drivers provides foundation for future expansion

## Key growth driver sales 9M 2020

	Sales USD Million	Growth vs. PY		Growth vs. PY cc
		USD Million	USD Million	
Entresto® sacubitinib/valsartan	1,781		573	48%
Zolgensma®	666		491	nm
Cosentyx® (secukinumab)	2,886		300	12%
PROMACTA® (eltrombopag)	1,267		231	24%
PIQRAY®	236		187	nm
KISQALI® ribociclib	503		178	59%
Xiidra®	268		166	164%
Beovu®	153		153	nm
Tafinlar® + Mekinist® (Aldesleukin)	1,134		152	17%
KYMRIAH® (tisagenlecleucel) for t-cell therapy	333		151	82%
JAKAVI® ruxolitinib	963		142	19%
ILARIS® (canakinumab) TM & © Novartis AG	633		140	30%

nm – not meaningful

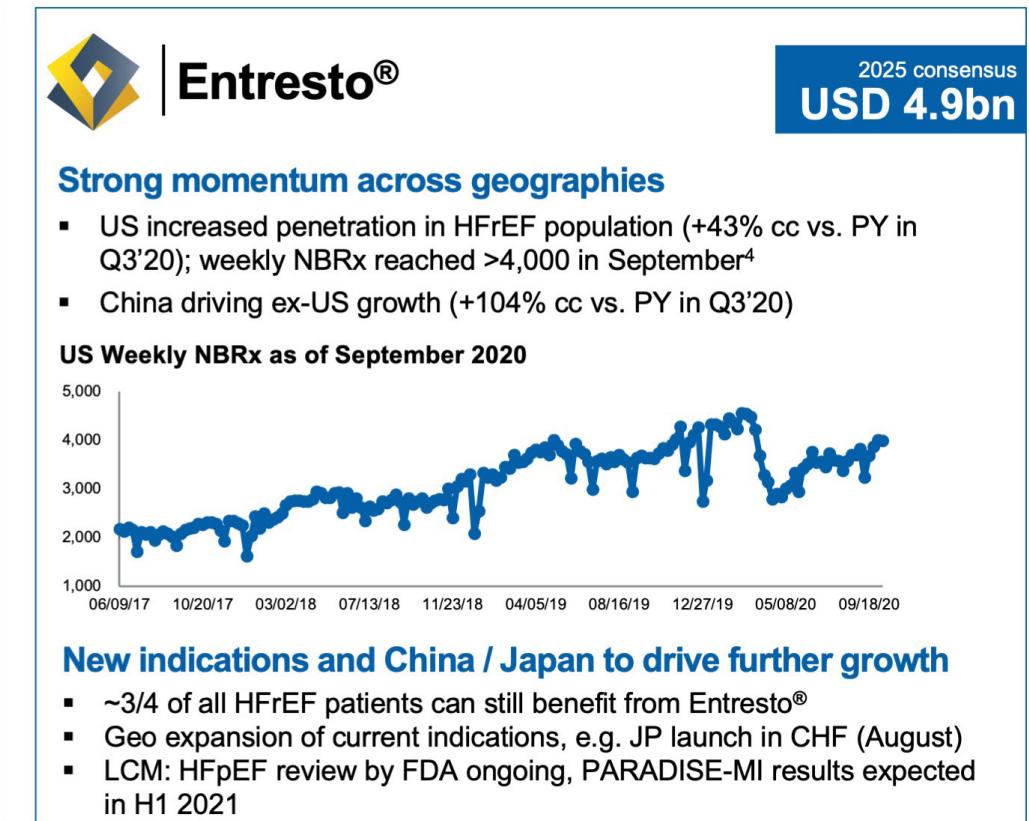
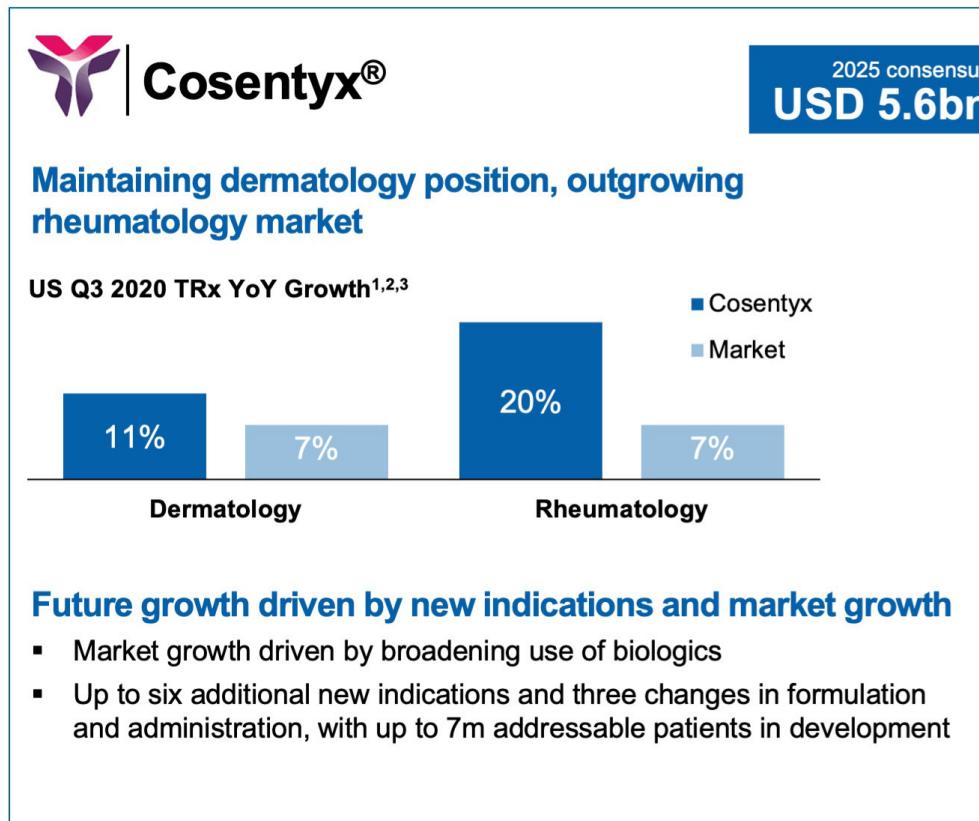
## Key growth drivers now 48% of Innovative Medicines sales



1. Includes Tasigna®, Xolair®, Aimovig®, Tabrecta™, Luxturna®, Kesimpta®, Enerzair®, Atecurta®

1 Growth drivers

# Cosentyx® delivering solid performance; strong trajectory for Entresto®, LCM plans in place to sustain growth in the long-run



Source: Novartis Investor Relations in-house consensus as of November 12, 2020. References at page 35.

## 1 Growth drivers

# Zolgensma® momentum sustained by geographical expansion, Kisqali® performing well on the back of positive data



## Strong performance driven by geographic expansion

- Expect steady sales in the US going forward
- Solid uptake in Europe; Germany ~50% of ex-US sales in Q3
- Patient mix will continue to shift over time post market launch from heavy prevalent/switch to a greater proportion of incident patients

## Expanding access in Europe and Emerging Markets to drive further growth

- Geographic expansion including Switzerland, Canada, Australia and emerging markets expected Q4 2020 / H1 2021
- Access pathways established in 9 EU countries; rapid uptake with immediate full reimbursement in Japan; approved in Brazil
- AVXS-101 IT: Working with FDA on Ph3 confirmatory trial and to lift partial clinical hold

2025 consensus  
USD 2.0bn



## Opportunity to fully realize potential of best-in-class profile

- 9M 2020 sales at USD 503m (+59%, cc) driven by consistent OS benefit from two pivotal Ph3 trials (MONALEESA-7 and -3) across all geographies, despite market slowdown during COVID-19
- Selective and preferential inhibition of CDK4 over CDK6 continues to drive differentiation within the class
- Highest rating of any CDK4/6 inhibitor on ESMO Magnitude of Clinical Benefit Scale, based on OS and Quality of Life benefits

## Adjuvant indication presents sizeable opportunity

- Additional OS results to be reported in metastatic setting, including MONALEESA-2 (event based, expected in H2 2021)
- NATALEE adjuvant study: Potential to make Kisqali® the only CDK4/6i with evidence supporting use in intermediate and high-risk populations (70% of adjuvant patients). Read-out expected in 2022

2025 consensus  
USD 1.6bn

Source: Novartis Investor Relations in-house consensus as of November 12, 2020

## 2 Launches

# Kesimpta® trending in the right direction, Leqvio® only waiting for action dates in major markets



## Kesimpta®

2025 consensus  
USD 1.8bn

### HCP engagement translating into adoption

95%+ (>6,000) of MS prescribing targets reached

95% of field force territories have adopted Kesimpta®

5.2%<sup>1</sup> NBRx share 11 weeks post launch

### Securing rapid and broad access

- Commercial bridging program
- Approximately 50% first line commercial access including CVS and Aetna commercial formularies, first Medicare win, Blue Cross Blue Shield regional accounts

### Patient initiation seen as simple, easy and fast

- Favorable feedback from HCPs and patients

## Leqvio® (inclisiran)\*

2025 consensus  
USD 1.4bn

### Significant unmet need<sup>2,3,4</sup>

>135m ASCVD patients

80% of statin-treated patients not at goal

>50% of patients not adhering to treatment

>USD 1tn Expected global cost of CVD by 2030

### 2 doses a year to reduce persistently elevated LDL-C

### Worldwide launch preparation progressing well

- EU approval expected December '20 / January '21 for all 27 member states and others including UK; FDA action date expected December '20
- Ready for launch in US and Germany; population health agreement with NHS on track

Source: Novartis Investor Relations in-house consensus as of November 12, 2020. \* Product and brand name are not FDA approved. Currently under FDA review. References at page 35.

## 2 Launches

## Recent and upcoming launches expected to fuel Oncology growth in the short- to mid-term

 <p>2025 consensus <b>USD 1.3bn</b></p>	<ul style="list-style-type: none"> <li>9M 2020 sales at USD 236m, driven by strong demand and PIK3CA testing rate uptake in US</li> <li>Global rollout continued, with &gt;50 countries now approved</li> <li>"EPIK" development program with potential opportunity to serve additional ~100k patients</li> </ul>	 <p>2025 consensus <b>USD 0.8bn</b></p>	<ul style="list-style-type: none"> <li>Strong launch execution with USD 71m net sales in the US for 9M 2020</li> <li>Approved for reduction in frequency of VOCs in SCD in 36 countries, incl. US &amp; EU countries</li> <li>Estimated 2,500 SCD patients have been treated with Adakveo since approval</li> </ul>
 <p>2025 consensus <b>USD 0.9bn</b></p>	<ul style="list-style-type: none"> <li>9M 2020 sales at USD 336m, with majority of sales still coming from US</li> <li>2-tier FF to enable E2E business model, covering nuclear medicine and community centers</li> <li>OS data H1 2021, ongoing evidence generation for re-treatment benefit after progression</li> </ul>	 <p>2025 consensus <b>USD 0.6bn</b></p>	<ul style="list-style-type: none"> <li>3-4% of NSCLC patients have METex14 mutations, associated with poor prognosis</li> <li>US launch off to an encouraging start, leveraging robust omni-channel capabilities</li> <li>Tabrecta™ LCM plan with potential opportunity to serve ~100k additional patients</li> </ul>
 <p>2025 consensus <b>USD 1.2bn</b></p>	<ul style="list-style-type: none"> <li>9M 2020 sales at USD 333m, driven by strong uptake across US, EU and Japan</li> <li>&gt;26 countries covering at least one indication and more than 260 qualified treatment centers</li> <li>Next indications to be filed in 2021: r/r FL and r/r DLBCL 1<sup>st</sup> relapse</li> </ul>	 <p>2025 consensus <b>USD 0.3bn</b></p>	<ul style="list-style-type: none"> <li>Unmet need in later lines of CML remains high, with 75% failure rate in 3L</li> <li>Asciminib has the potential to address TKI-resistance and intolerance in CML</li> <li>ASCEMPL Ph3 study met its primary endpoint, 1<sup>st</sup> submission H1 2021</li> </ul>

Source: Novartis Investor Relations in-house consensus as of November 12, 2020

## 3 Pipeline

# Leading pipeline by key measures...

## Scale

# of projects<sup>1</sup>

116

Phase 1/2

49

Phase 3/  
Registration

>65

NMEs

## Innovation

20

Advanced platform  
therapies in clinical  
development

~90%

Pipeline<sup>2</sup> potentially  
first-in-class /  
first-in-indication

~80%

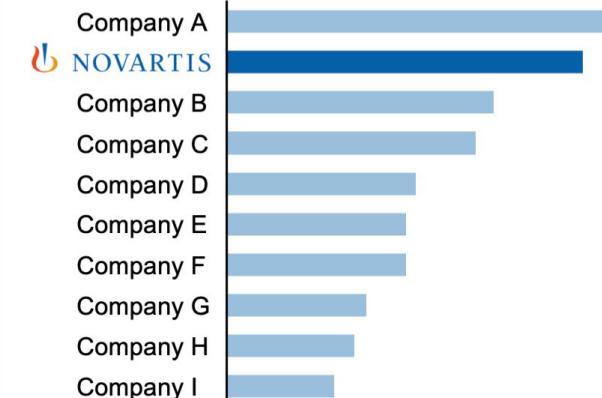
Target areas of high  
unmet need<sup>3</sup>

## Value

Estimated 2026 sales from  
products launched 2020-2026<sup>3</sup>

#2

Replacement power



1. Including Global Health, excluding Sandoz. 2. Projects in confirmatory development. 3. Innovative Medicines product sales excl. Vaccines and LCM products (e.g. new formulations, combos with off-patent molecules); compound-based analysis (Ph2 and 3) with additional indications allocated to 1<sup>st</sup> launch. Source: Novartis peer group analysis based on data from Evaluate Pharma (download from September 24, 2020).

## 3 Pipeline

# ...including strengthening our advanced therapy platforms along the value chain

Research & Development		Manufacturing		Commercialization	
Gene Therapy	Clinical programs		Pre-clinical	Internal sites	More info
	Program	Condition	Count		
Cell Therapy	4 OAV101	SMA IT	19	3 Libertyville (US) Longmont (US) Durham (US)	1m+ Square feet footprint of the internal network
	OAV201	Rett syndrome			
	ADPT03	Sickle cell anemia			
	CPK850	RP			
	8 CTL019	Multiple <sup>1</sup>	10	3 Morris Plains (US) Stein (CH) Les Ulis (FR)	4 Continents spanned by Novartis' manufacturing network
	JEZ567	AML			
	LXF821	Glioblastoma multiforme			
	MCM998	Plasma cell myeloma			
	YTB323	Hematological malignancy			
RLT	4 <sup>177</sup> Lu-NeoB	Multiple solid tumors	14	6 Millburn (US) Ivrea, Saluggia, Forli (IT) Zaragoza (ES) IDB (NL)	1 Additional site under construction in Indianapolis (US)
	<sup>177</sup> Lu-oxodotreotide	GEP-NET 1L G3			
	<sup>177</sup> Lu-PSMA-617	mCRPC			
	<sup>177</sup> Lu-PSMA-R2	Prostate cancer			

4 additional clinical programs relating to RNA (including KJX839 and TQJ230)

1. DLBCL 1<sup>st</sup> relapse, r/r follicular lymphoma, r/r DLBCL in combo with pembro, 1<sup>st</sup> line high risk pediatric and young adult ALL. 2. Both pALL and DLBCL.

## 3 Pipeline

# Moving forward promising assets to drive long-term growth (1/3)

Lifecycle management (further information in our Key Assets section)

## Selected opportunities

Asset	Next indication	FIC	FII	Peak sales (by indication)	Phase	Next milestone	Submission	Additional indications
 Entresto®	HFpEF	★	★	●●	Registration	Approval US - 2021	✓	Essential hypertension (ex US) Pediatric
	Post-AMI	★	★	●	III	FIR - H1 2021	2021	
 Cosentyx®	HS	★	★	●	III	iFIR <sup>1</sup> - H2 2021	2022	Derm: L. Planus Rheum: jPsA/ER GCA Peds PsO Lupus Nephritis
 KISQALI®	Adjuvant BC			●●●●	III	MONALEESA-2 OS FIR H2 2021 NATALEE Ph III aBC FIR 2022	2023	n/a
BYL719	PROS	★	★	●	II	Submission 2021	2021	TNBC Ovarian cancer HER2+ aBC HNSCC 2/3L
 Beovu®	DME			●●●	III	Primary FIR - Q4 2020 (2 <sup>nd</sup> pivotal study read-out)	2021	RVO Diabetic retinopathy

FIC/FII: First in class = first compound launching with a specific MoA / First in indication = expected to launch at least 6 months before first competitor with the same target/MoA in the same indication. (i) FIR: (interim) First Interpretable Results (study read-outs). 1. iFIR is the primary readout / analysis for the study.

Unprobabilized peak sales (USD): ● <500m ●● 500m-1bn ●●● 1-2bn ●●●● >2bn

## 3 Pipeline

## Moving forward promising assets to drive long-term growth (2/3)

Pharmaceuticals (further information in our Key Assets section)

### Selected opportunities

Asset	Next indication	FIC	FII	Peak sales (by indication)	Phase	Next milestone	Submission	Additional indications
<b>LNP023</b> (iptacopan) Factor B Inhibitor	IgAN	★		●●●	II	Ph III FPFV H1 2021	2023	PNH <sup>1</sup> aHUS C3G iMN
<b>CFZ533</b> (ascalimab) Anti-CD40 mAb	Sjögren's	★	★	●●●	II	iFIR <sup>2</sup> - 2022	≥ 2024	Kidney Tx Liver Tx
<b>QGE031</b> (ligelizumab) Anti-IgE mAb	CSU			●●●	III	FIR - H2 2021	2022	Pediatric CSU CINDU, food allergy
<b>TQJ230</b> (pelacarsen) Antisense oligonucleotide	CVRR-Lp(a)	★	★	●●●●	III	FIR - 2024	≥ 2024	n/a
<b>LMI070</b> (branaplam) RNA splicing modulator	Huntington disease	★	★	●●●●	I	Ph IIb FPFV H1 2021	≥ 2024	SMA

FIC/FII: First in class = first compound launching with a specific MoA / First in indication = expected to launch at least 6 months before first competitor with the same target/MoA in the same indication. (i) FIR: (interim) First Interpretable Results (study read-outs). 1. PNH indication planned to be submitted first. 2. iFIR is the primary readout / analysis for the study.

Unprobabilized peak sales (USD): ● <500m ●● 500m-1bn ●●● 1-2bn ●●●● >2bn

## 3 Pipeline

## Moving forward promising assets to drive long-term growth (3/3)

Oncology (further information in our Key Assets section)

Selected opportunities

Asset	Next indication	FIC	FII	Peak sales (by indication)	Phase	Next milestone	Submission	Additional indications
<b>ACZ885</b> (canakinumab) Anti-IL-1 $\beta$ mAb	NSCLC 1L/2L	★	★	●●●●	III	CANOPY-1 FIR H2 2021 CANOPY-2 FIR H1 2021	2021 <sup>1</sup>	NSCLC adjuvant
<b><sup>177</sup>Lu-PSMA-617</b> Radioactive lutetium-labelled small molecule	mCRPC 3L	★		●●	III	VISION FIR H1 2021	2021	mCRPC pre-taxane
<b>MBG453</b> (sabatolimab) Anti-TIM-3 mAb	HR-MDS	★	★	●●●	III	FIR <sup>2</sup> H2 2021	2021 (US)	AML Maintenance MRD+ AML
<b>TNO155</b> Low molecular weight SHP2 inhibitor	Solid tumors	★	★	●●●●	II	Data presentation H1 2021	tbd	Multiple combinations being explored including 1L KRAS NSCLC
<b>LXH254</b> Low molecular weight B/C-RAF inhibitor	BRAF/NRASm Melanoma	★	★	●●	II	Expansion phase start H2 2021	tbd	mRAS/RAF NSCLC

FIC/FII: First in class = first compound launching with a specific MoA / First in indication = expected to launch at least 6 months before first competitor with the same target/MoA in the same indication. (i) FIR: (interim) First Interpretable Results (study read-outs). 1. Depending on timing of final read-out submission may move to early 2022. 2. FIR is for the Ph2 study (e.g. STIMULUS MDS-1).

Unprobabilized peak sales (USD): ● <500m ●● 500m-1bn ●●● 1-2bn ●●●● >2bn

## 3 Pipeline

## Wild cards: High-risk, high-reward programs

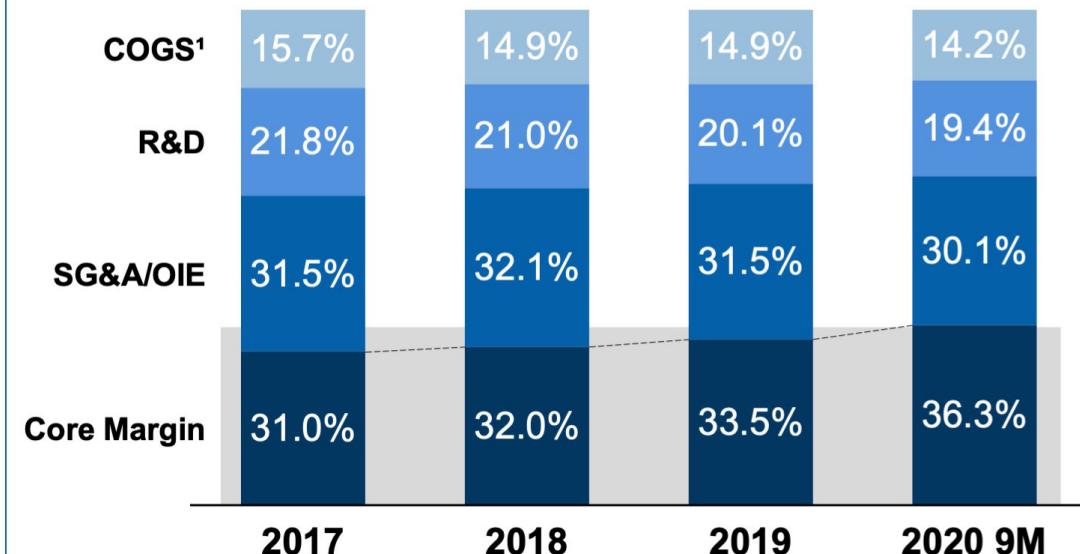
	Description	Unmet need	Status
<b>CSJ117</b> Asthma	Potent neutralizing antibody fragment directed against human TSLP, an upstream epithelial-cell-derived cytokine involved in the asthmatic airway inflammation. Delivered via dry powder inhaler directly to the lungs	Currently approved injectable biologic therapies require phenotyping and are limited to high eosinophilic disease	Recruiting Ph2b study in patients with severe uncontrolled asthma
<b>ECF834</b> Dry Eye	Recombinant human lubricin is a mucin-like glycoprotein naturally present on the ocular surface with anti-inflammatory, lubricating and anti-adhesive properties	Unmet need for fast-acting, effective, durable, tolerable pharmacological treatment for DED, particularly in moderate-to-severe cases	Ph2b readout expected H2 2021
<b>LNA043</b> Osteoarthritis	Modified human ANGPTL3 with the potential to repair damaged cartilage - the underlying cause of osteoarthritis (OA) - when administered as an intra-articular injection	OA is a degenerative, chronic, progressive joint disease with no current treatment targeting the prevention of degeneration	Projected start of Ph2b in 2021
<b>QBW251</b> COPD	Oral CFTR potentiator targeting life-altering improvements in symptoms of COPD, by enhancing mucus clearance and reducing pulmonary infections	Despite optimized inhaled therapies, most COPD patients continue to suffer debilitating symptoms that significantly impact their lives	Ph2b readout expected H2 2021
<b>NIS793</b> Solid Tumors	Fully human anti-TGFβ IgG2 monoclonal antibody designed to inhibit TGFβ pathway in tumor cells as well as modulate the tumor microenvironment, reversing both immunosuppression and fibrosis	Large unmet need in several tumor types resistant and/or refractory to current treatments	Recently achieved FPFV in Oct 2020

## 4 Margins

## Delivering on Innovative Medicines core margin of mid 30s...

### Innovative Medicines

Core margin (%)



#### Key drivers of expansion

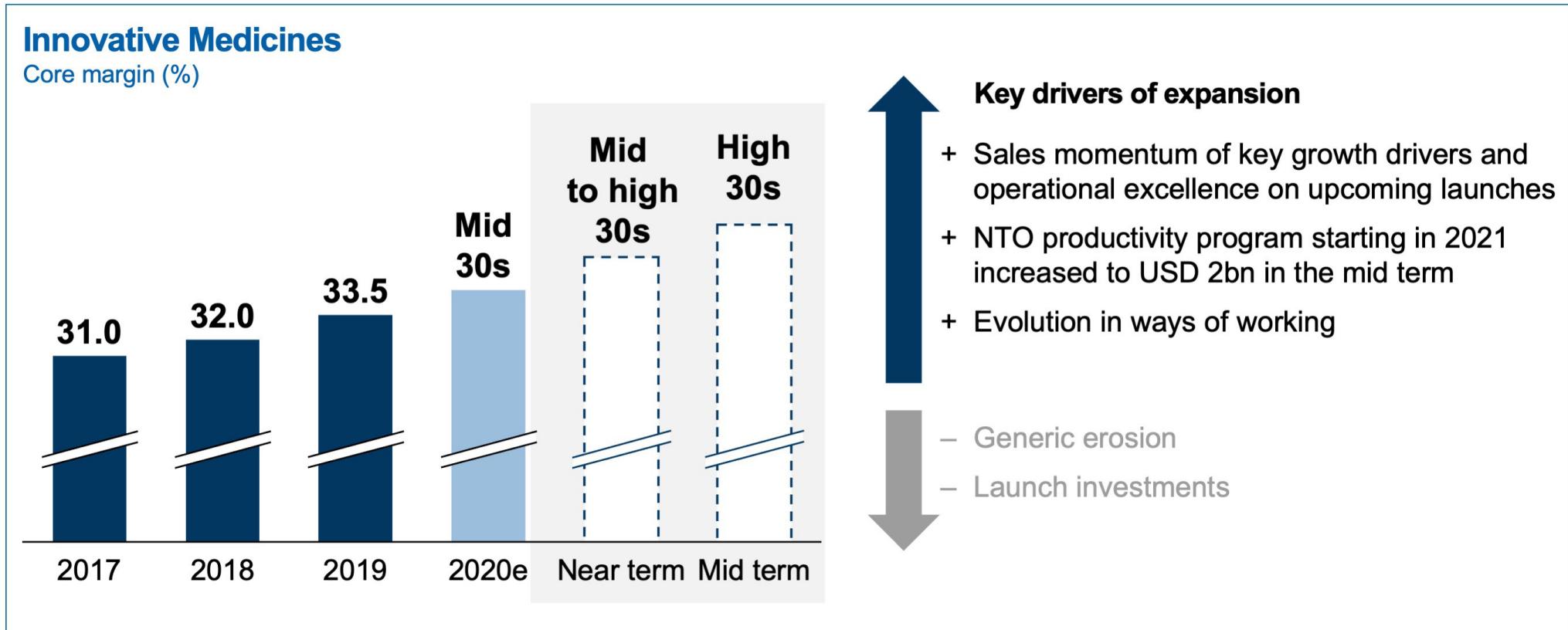
- + Manufacturing Network Transformation
- + NBS productivity programs and procurement savings
- + Resource allocation in commercial units
- + Leverage from sales momentum of key growth drivers
- Generic erosion
- Launch and growth investments

FY 2020 core margin expected below 9M actuals around mid 30s<sup>2</sup>

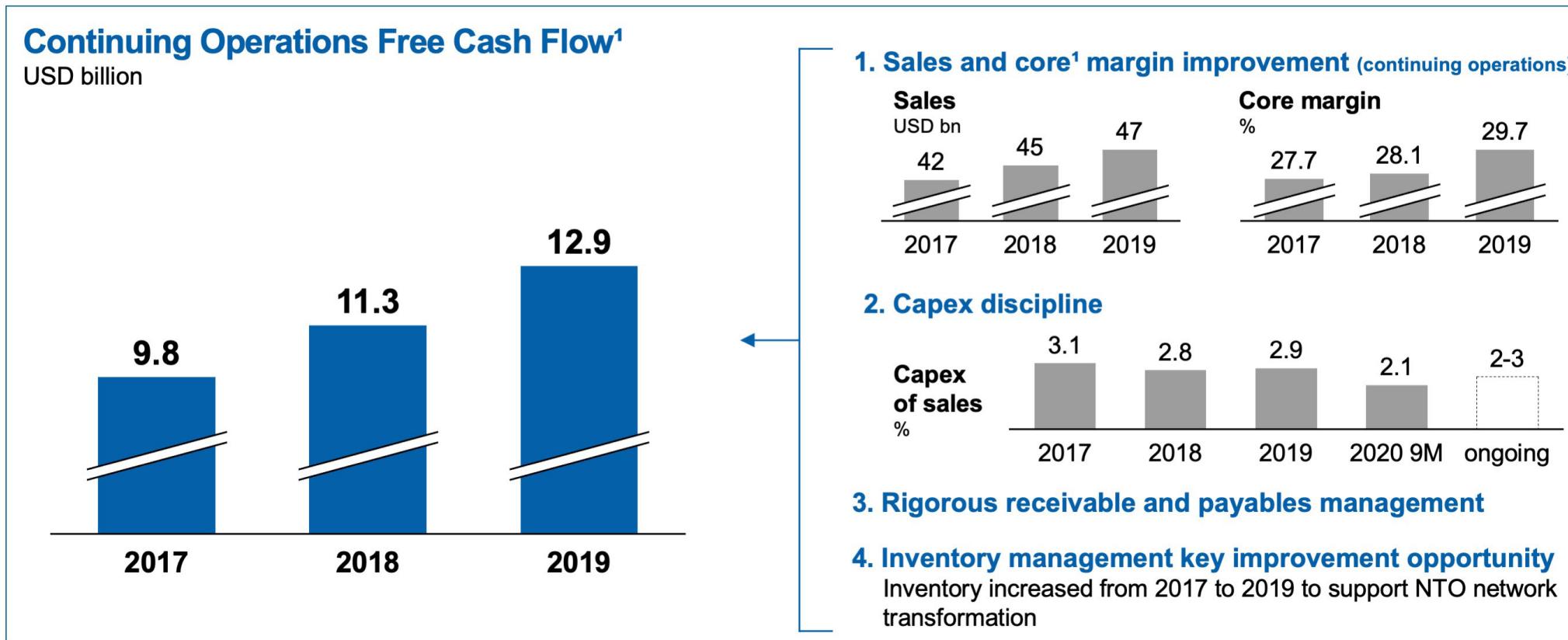
1. Includes other revenues and sales to other segments. 2. Historically Q4 margin lower due to seasonality

## 4 Margins

## ...and raising outlook to high 30s mid-term



# Strong Free Cash Flow development driven by growth, margin expansion and balance sheet discipline



1. Free cash flow and core margin are non-IFRS measures.

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

## 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 8% in CHF and 10% in USD<sup>1</sup> between 1996-2019
- 3 Value-creating bolt-ons** > Guide to spend up to ~5% of market cap per year, but only if good strategic fit, right price and value creating
- 4 Share buybacks** > Announcing immediate share buyback of up to USD 2.5bn

1. Converted at historic exchange rates at the dividend payment dates as per Bloomberg; assumes a USD/CHF exchange rate of 0.9690 as of December 31, 2019 for 2019.

# Initiating up to USD 2.5bn share buyback, highlighting confidence in top-line growth and margin expansion

## Expect growth on top and bottom line

- Growth drivers and recent / upcoming launches, foundations for future expansion
- Leading pipeline, fueling growth mid- to long-term and hedging against patent cliffs
- Committed to driving consistent margin expansion

**Up to USD 2.5bn share buyback** will be executed under the existing AGM authority

**Novartis' liquidity and strong balance sheet**, in line with our capital structure reflecting AA- (S&P) / A1 (Moody's) credit rating, supports such a share buyback

**The buyback will start immediately** and will be executed until H1 2021

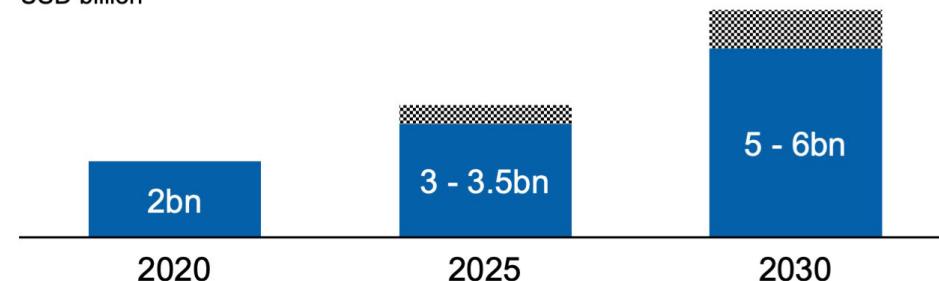
# Sandoz aims to grow low-to-mid single digit by focusing on biosimilars and selected segments of standard Gx

## Biosimilars

- The biosimilar market offers a significant and growing opportunity (market expected to grow ~80% to 2026)
- Focusing on biosimilar leadership, with 15+ molecules in our pipeline, and adding at least one new project per year

### Biosimilars revenue ambition

USD billion



## Small molecules

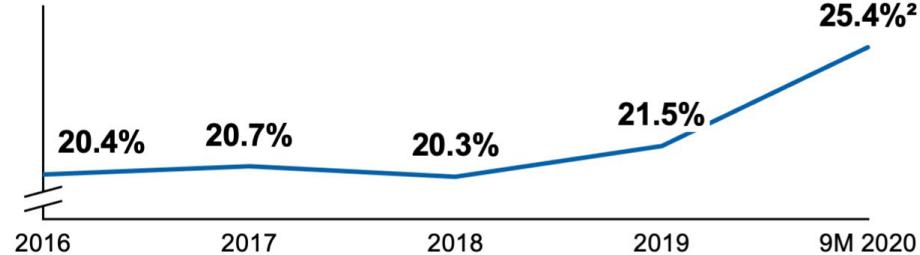
- Sandoz is on track to submit ~40 first-to-files in US until 2024
- >80% loss of exclusivity coverage (LoE) in Europe and >50% LoE coverage<sup>1</sup> in US
- Increased focus on Oncology and Respiratory
- Ambition to outgrow the global market

1. Based on current pipeline.

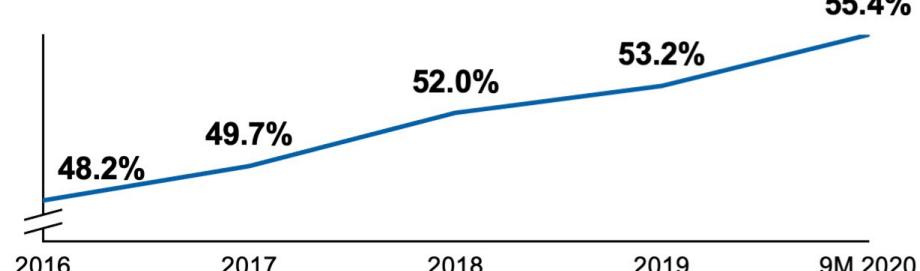
# Continue margin improvement to reach mid-to-high 20s core ROS

## Sandoz financial progress

### Core<sup>1</sup> ROS



### Core<sup>1</sup> Gross Margin



### Key drivers of margin expansion

- + Manufacturing Network Optimization
- + Shift of portfolio to more differentiated therapeutics including Biosimilars, which create a positive mix
- + Digital to transform commercial model and development
- + Core ROS to reach top quartile in industry (mid-to-high 20s in mid to long term)

1. Core figures are non-IFRS measures. 2. COVID-19 favorability included.

# ESG aspirations with clear mid- and long-term goals...

Integrating ESG across our operations, whilst strengthening KPIs and their measurements

	Ethical Standards	Pricing & Access	Global Health Challenges	Corporate Citizenship
<b>Achievements to date</b>	Resolving longstanding legal issues  Launched new Code of Ethics	100+ EMBS YTD, exceeded target of 20% patient reach in LMICs  New Sub-Saharan Africa strategy	Innovative Sustainability-Linked Bond  Expanded Africa SCD program	YTD vs. 2016: -17% carbon own operations, -3% waste, -29% water  44% female in management  Strong COVID-19 response
<b>Selected mid-term goals</b>	Third party risk assessment conducted on 100% suppliers by 2022	+200% patient reach in LMICs with SIT <sup>1</sup> 100% SIT launches w/ access strategy +500% patient reach in SSA by 2025 <sup>2</sup>	+50% patient reach with flagship programs <sup>1</sup>	Management gender balance by 2023  Carbon neutral own operations by 2025
<b>Long-term aspirations</b>	Be recognized in the healthcare sector for human rights	Full implementation of Novartis access principles, incl. clinical trial diversity	Launch novel medicines to eliminate malaria	Full carbon, plastic, water neutrality <sup>3</sup>

1. 2025 vs. 2019 baseline. 2. 2025 vs. 2020 baseline. 3. 2030 vs. 2016 baseline. EMB – Emerging Market Brands SCD – Sickle Cell Disease SIT - Strategic Innovative Therapies

## ...and improving our ESG scores across multiple rating agencies

Agency	Score	Score		Sector Ranking <sup>1</sup>	
		Current	Previous	Current	Previous
 SUSTAINALYTICS <sup>2,7</sup>	Risk score	▲ 21	30	▲ 3 / 392	14 / 165
	Controversy level	▲ 3	5	► 4 / 395	3 / 233
 ISS ESG <sup>2,8</sup>	ESG score	► B-	B-	▲ 1 / 6	6 / 6
	ESG score	▲ 4.7	4.1	▲ 2-4 / 6	8 / 11
 FTSE4Good <sup>2</sup>	WAKI	▲ 4.9	4.3	▲ 2 / 20	3 / 20
	ESG score	▲ A	BBB	▲ 3 / 15 <sup>5</sup>	4-9 / 15
	MSCI Global Compact	▲ Watchlist	Fail	► 8 / 83	8 / 61
 access to medicine index <sup>3</sup>	Ranking	▲ 3.2	2.9		
 CDP <sup>4</sup> DRIVING SUSTAINABLE ECONOMIES	Climate Water	► A- ▲ A	A- B		
 SAM <sup>6</sup> Now a Part of S&P Global	ESG score	▲ 73	70		

Top-tier sector-leading performance

Novartis access programs / management best-in-class

WAKI – Weighted-average key issue score. 1. Peer group as defined by each ESG rating agency. 2. 2020 / 2019 scores. 3. Published every 2<sup>nd</sup> year. Result shown shows 2018 / 2016 scores. 4. 2019 / 2018 scores. 5. Based on Novartis official peer group. 6. 2020 / 2019 scores. Novartis has been a member of the DJSI World and EU index since 2002. 7. Updated October 15, 2020. 8. Updated September 25, 2020.

# Concluding thoughts

## Group key messages

1

### We are executing on our strategy

- 100% focused as a medicines company
- Significant progress on each of our five strategic priorities
- Strong operational performance, with consistent top- and bottom-line expansion

2

### Looking ahead, we believe we can consistently grow both our top and bottom line

- Growth drivers and recent / upcoming launches expected to lay the foundation for future expansion
- Leading pipeline, fueling growth in the mid- to long-term and hedging against patent cliffs
- Committed to driving consistent margin expansion

3

### We provide investors with a unique profile

- TAs breadth and depth
- Exposure to cutting-edge platforms
- Diversification of revenues, both in terms of assets and geographies

# Meet Novartis Management 2020

## Participating members of the Executive Committee

**Vas Narasimhan**

CEO, Novartis

**Harry Kirsch**

CFO, Novartis

**Marie-France Tschudin**

President, Novartis Pharmaceuticals

**Susanne Schaffert**

President, Novartis Oncology

**Richard Saynor**

CEO, Sandoz

**John Tsai**

Global Head, Drug Development and CMO, Novartis

**Jay Bradner**

President, Novartis Institutes for BioMedical Research (NIBR)

**Shannon Thyme Klinger**

Chief Legal Officer, Novartis

**Steffen Lang**

Global Head, Novartis Technical Operations

# References

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**Slide 12**

1. TRx growth is calculated by comparing product volume across two time periods (YoY refers to Q3 2020 compared with Q3 2019). NBRx share calculated as product NBRx volume divided by market NBRx volume.
2. IQVIA National Prescription Audit for Dermatology through September 2020; PsO market includes Enbrel®, Humira®, Siliq®, Skyrizi™, Stelara®, Taltz®, Tremfya®. NBRx share refers to monthly data for Q3 2020 (Quarter ending September 30). Note the quarter ended mid-week.
3. IQVIA National Prescription Audit for Rheumatology through September 2020; SpA market includes Cimzia®, Enbrel®, Humira®, Simponi®, Stelara®, Taltz®. NBRx share refers to monthly data for Q3 2020 (Quarter ending September 30). Note the quarter ended mid-week.
4. IQVIA National Prescription Audit Data.

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**Slide 14**

1. IQVIA reported NBRxs through October 30, 2020.
2. Ray KK et al. N Engl J Med. 2020;382(16):1507-1519. 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-\(cvds\)](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)). Accessed May 28, 2020.
5. Bruckert E, Parhofer KG, Gonzalez-Juanatey JR, et al. Proportion of High-Risk/Very High-Risk Patients in Europe with Low-Density Lipoprotein Cholesterol at Target According to European Guidelines: A Systematic Review. Adv Ther. 2020;37(5):1724–1736.

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# Key Assets

## Overview

### Immunology, Hepatology & Dermatology

Cosentyx®  
Iscalimab  
Ligelizumab

### Cardiovascular, Renal & Metabolism

Entresto®  
Leqvio®  
Pelacarsen  
Iptacopan

### Neuroscience

Kesimpta®  
Branaplam

### Ophthalmology

Beovu®

### Oncology: Solid Tumors

Kisqali®  
Piqray®  
Tabrecta™  
Canakinumab  
<sup>177</sup>Lu-PSMA-617  
TNO155  
LXH254

### Oncology: Hematology

Asciminib  
Sabatolimab

Click to view  
**MNM Agenda**



# Building depth across our core therapeutic areas

	ONCOLOGY	PHARMACEUTICALS					BIOPHARMA
		CRM	IHD	Neuroscience	Ophthalmology	Respiratory	
<b>Select commercial assets</b>	 <b>PROMACTA</b> letrorubopag  <b>Tafinlar</b> + <b>Mekinist</b> (olaratumab) + (enzalutamide)  <b>KISQALI</b> ribociclib  <b>KYMRIAH</b> (tisagenlecleucel)  <b>JAKAVI</b> ruxolitinib  <b>TABRECTA</b>  <b>ADAKVEO</b> crizanlizumab-icma FOR IV INFUSION - 10 mg/ml  <b>PIQRAY</b> (alpelisib) tablets	 <b>Entresto</b> sacubitinil/valsartan	 <b>Cosentyx</b> secukinumab	 <b>GILENYA</b> (fingolimod) capsules  <b>MAYZENT</b> (siponimod) tablets  <b>Zolgensma</b>	 <b>Aimovig</b> (rimegepant) tablets  <b>Beovu</b> brolozumab  <b>LUCENTIS</b> ranibizumab injection	 <b>Xolair</b> Omalizumab  <b>ENERZAIR</b> Alectura	 <b>ZARXIO</b> (filgrastim-sndz)  <b>Erelzi</b> (elotuzimab)  <b>RIXATHON</b> rituximab  <b>Zessly</b> infliximab  <b>ZIEXTENZO</b> (pegfilgrastim-bmez)
<b>Select pipeline assets and opportunities</b>	 <b>Piqray®</b> New indications  <b>Kisqali®</b> Adjuvant HR+/HER2- BC  <b>Asciminib (ABL001)</b> CML 3L  <b>Canakinumab (ACZ885)</b> NSCLC 1L / 2L / Adjuvant  <b>177Lu-PSMA-617</b> mCRPC  <b>Sabatolimab (MBG453)</b> HR-MDS, unfit AML  <b>NIS793</b> Solid tumors  <b>TNO155</b> Solid tumors  <b>LXH254</b> Melanoma	* <b>Entresto®</b> HFpEF, post-MI	* <b>Cosentyx®</b> HS, GCA, LP	* <b>AVXS-101 IT</b> SMA IT	<b>Beovu®</b> DME, RVO	* <b>CSJ117</b> Asthma	<b>Trastuzumab</b> <sup>1</sup>
	 <b>Inclisiran (KJX839)</b> Hyperlipidemia, CVRR-LDLC	* <b>Inclisiran (KJX839)</b> Hyperlipidemia, CVRR-LDLC	* <b>Iscalimab (CFZ533)</b> Sjögren's / Transplant	* <b>Branaplam (LMI070)</b> SMA, HD	* <b>UNR844</b> Presbyopia	* <b>QBW251</b> COPD	<b>Insulins (3)</b> <sup>2</sup>
	 <b>Iptacopan (LNP023)</b> Renal diseases, PNH	* <b>Iptacopan (LNP023)</b> Renal diseases, PNH	* <b>Ligelizumab (QGE031)</b> CSU/CIU, food allergy, CINDU	* <b>AVXS-201</b> Rett Syndrome	<b>ECF843</b> Dry eye		 <b>Natalizumab</b> <sup>3</sup>
	 <b>Pelacarsen (TQJ230)</b> CVRR	* <b>Pelacarsen (TQJ230)</b> CVRR	* <b>Ilanalumab (VAY785)</b> Sjögren's, AIH		<b>SAF312</b> COSP		 <b>Denosumab</b>
			 <b>Remibrutinib (LOU064)</b> CSU / CIU, Sjögren's				<b>9+ biosimilars in pre-clinical development</b>
			 <b>Tropifexor (LJN452)</b> NASH				
			 <b>LNA043</b> Osteoarthritis				

★ Further detail in the Key Asset section  
(please use navigation bar at top to select)

1. Alliance program (EirGenix. 2. Alliance program (Gan&Lee). 3. Alliance program Polpharma.

# Immunology, Hepatology & Dermatology

**Cosentyx®**

**Iscalimab**

**Ligelizumab**

Click to view  
**MNM Agenda**

# Cosentyx®

## (secukinumab)

Human anti-IL17A  
monoclonal antibody  
directly inhibits IL-17A, a  
multisource cytokine that  
causes skin and enthesal  
inflammation

Marketed; LCM in Phase 2,3

### Key highlights

- Proven sustained efficacy and safety data across psoriasis (PsO), psoriatic arthritis (PsA) and ankylosing spondylitis (AS)
- USD 1bn sales delivered in Q3 2020
- Non-radiographic axial SpA (nr-axSpA) approved as 4<sup>th</sup> indication by FDA and EMA
- Pediatric psoriasis (EU), AS (China) recently approved
- Submissions for Cosentyx® 300mg AI/PFS and pediatric PsO (US)
- Robust clinical evidence with >100 studies, also in persistent manifestations of PsO, namely scalp, palms, soles, nails and joints involvement
- Recent key publications<sup>1</sup> EXCEED (PsA H2H vs. Humira), PREVENT (nr-axSpA), MEASURE (five-year data in AS)
- Expect to reach USD 5bn+ in sales with PsO, PsA, AS and nr-axSpA, maintaining share in a growing Dermatology market and accelerating growth in Rheumatology
- Reaching up to 7m additional addressable patients by expanding beyond current approved indications over the next 10 years

AS = Ankylosing Spondylitis, SpA = Spondyloarthritis, PsO = Psoriasis; PsA = Psoriatic Arthritis, RWE = Real world evidence, AI = Auto Injector, PFS = Pre-Filled Syringe; nr-axSpA - non-radiographic Axial Spondyloarthritis. 1. EXCEED: McInnes Ian B, et al. Lancet. 2020;395:1496–505, PREVENT: Deodhar A, et al. Arthritis Rheumatol 2020;10:1002/art.41477, MEASURE 2 (5 year results): Marzo-Ortega et al. Lancet Rheumatology 2020, Vol 2, Issue 6, Pages e339-e336.

# Cosentyx® poised to maintain strong position in growing dermatology market, set to accelerate in rheumatology

>400k patients reached, >5 years efficacy and safety data, strong 1<sup>st</sup>-line access

**Steady Cosentyx® sales growth over the years**  
USD billion

Year	Ex-US (USD billion)	US (USD billion)	Total (USD billion)
2015	0.3	0.3	0.6
2016	1.2	1.2	2.4
2017	2.0	2.0	4.0
2018	2.8	2.8	5.6
2019	3.5	3.5	7.0
2020 (YTD Sept)	2.9	2.9	5.8

Consensus 2020 = 3.9

Strong dermatology position, outgrowing rheumatology market in US<sup>1,2</sup>

PsO YoY: US TRx +11% vs. market +7%, maintaining strong NBRx share ~16%

SpA YoY: US TRx +20% vs. market +7%, leading NBRx share ~30%

**Strong dermatology position**

**USD 17bn market WW, double-digit growth long-term**

15% biologic penetration<sup>3,4</sup>

8/10 patients achieve clear or almost clear skin<sup>5</sup>

Dedicated studies in scalp, nails, palmoplantar<sup>6</sup>

Biologic of choice for 2/3 of patients with multiple manifestations<sup>7</sup>

**Ready to accelerate in rheumatology**

**USD 12bn market WW, double-digit growth long-term**

14% axSpA, 23% PsA biologic penetration<sup>8,9</sup>

Efficacy in joints with AS<sup>10</sup> and PsA<sup>11</sup> is increasingly supported by guidelines<sup>12-14</sup>

Ongoing, first-of-its-kind evidence generation with MAXIMISE<sup>15</sup> and ULTIMATE<sup>16</sup>

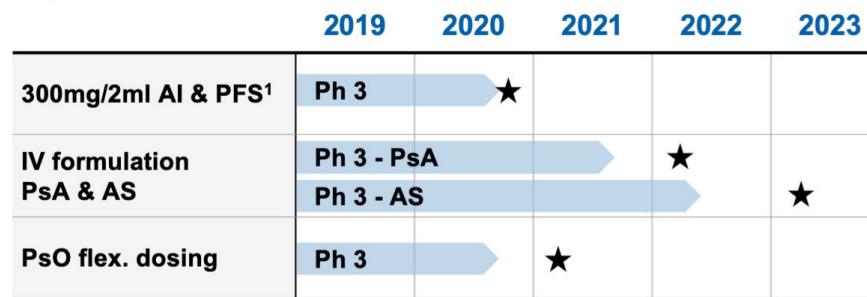
PREVENT reinforces substantial benefits across axSpA spectrum<sup>17</sup>

PsO = Psoriasis; PsA = Psoriatic Arthritis; AS = Ankylosing Spondylitis; nr-axSpA = non-radiographic axial spondyloarthritis. 1. IQVIA National Prescription Audit for Dermatology through September 2020; PsO market includes Enbrel®, Humira®, Siliq®, Skyrizi™, Stelara®, Taltz®, Tremfya®. NBRx share refers to monthly data for Q3 2020 (Quarter ending September 30th). Note the quarter ended mid-week. 2. IQVIA National Prescription Audit for Rheumatology through September 2020; SpA market includes Cimzia®, Enbrel®, Humira®, Simponi®, Stelara®, Taltz®. NBRx share refers to monthly data for Q3 2020 (Quarter ending September 30). Note the quarter ended mid-week. 3. Based on 'WW IQVIA total brand sales' and 'Indication level brand data for G6 PSO' (2019). 4. Bx treated : DRG + IQVIA patient equivalents (2019). 5. CLEAR, CLARITY. 6. SCALP, TRANSFIGURE, GESTURE. 7. Corrona LLC, data on file. Corrona Report: Real-World Data from the Corrona Psoriasis Registry®. June 15, 2018. 8. Evaluate Pharma, SpA Market – Bx & Orals (2019). 9. PsA and axial SpA: Epidemiology, diagnosed, treated and Bx pool and aligned with DRG, latest CPO inputs (internal assumption based multiple data sources) (2019). 10. MEASURE. 11. EXCEED, FUTURE. 12. Coates LC et al. Arthritis Rheumatol. 2016;68(5):1060-1071. 13. Gossec L et al. Ann Rheum Dis. 2020;79(6):700-712. 14. Ward M et al. Arthritis Rheumatol. 2019 Oct;71(10):1599-1613. 15. MAXIMISE. 16. Novartis Media & Investor Release, Nov. 5, 2020. 17. Deodhar A, et al. Arthritis Rheumatol 2020. doi:10.1002/art.41477.

Cosentyx® Iscalimab Ligelizumab

# Developing Cosentyx® across 10 indications/label expansions to address key unmet needs

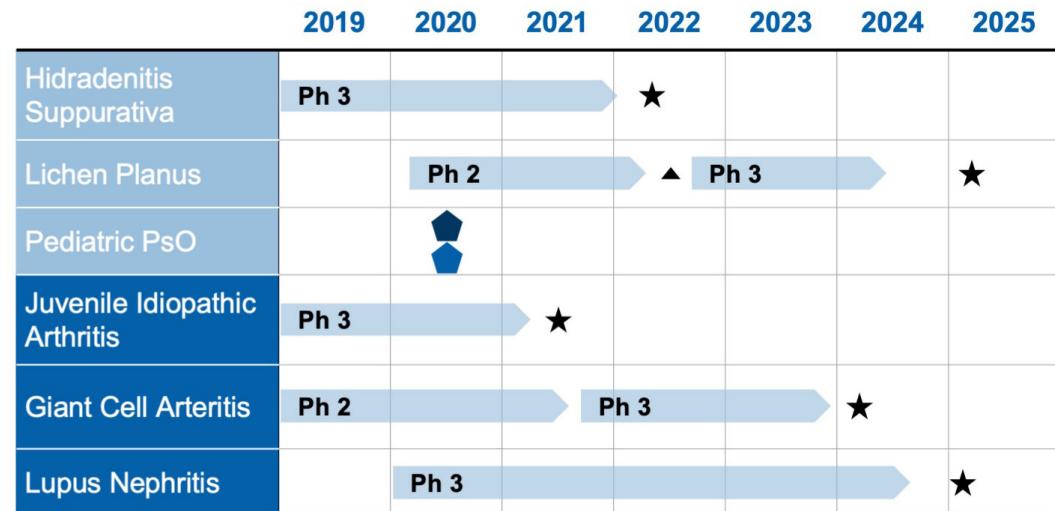
## Expansion in formulations and administration



## Addressable patients per indication (EU5 and US)

Indication	Patients	Comment
Hidradenitis Suppurativa	>400K	High unmet need and high disease burden
Lichen Planus	>2,500K	Significantly impaired quality of life and lack of approved systemic therapies
Juvenile Idiopathic Arthritis	>10K	Enhancing strong safety profile
IV formulation (PsA/AS)	>3,500K	Additional access for Medicare patients in US
Giant Cell Arteritis	380K	Amongst most common inflammatory disease in elderly
Lupus Nephritis	>140K	Major cause of morbidity and mortality in SLE patients

## New indications



Additional specialty indications under consideration

★ Estimated submission

◆ EU approval granted in H12020

▲ Potential for early submission

◆ FDA submission done in H22020

Rheumatology indications

Dermatology indications

Formulation/administration changes

1. Submitted in EU H1 2020 and in US H2 2020. Note: Pediatric PsO (Approved in EU H1 2020 and filed in US H2 2020). PsO = psoriasis; PFS = prefilled syringe.

# Hidradenitis Suppurativa

Secukinumab as a potential novel therapy to address a debilitating disease

## High unmet need in Hidradenitis Suppurativa

- Chronic, inflammatory disabling skin disease, with recurrent, painful nodules and abscesses, leading to impairing scarring and subdermal tunnels
- Impact on quality of life due to chronic pain/scarring, odor, purulent discharge and loss of function
- The global prevalence rate is estimated to be ~1%<sup>1</sup>, ~400K (200k in the US, 200k in EU5) patients suffering from moderate to severe HS.
- Largely underdiagnosed with diagnosis rate ~20%<sup>2</sup>



Images reproduced with permission from Kang et al.<sup>3</sup>

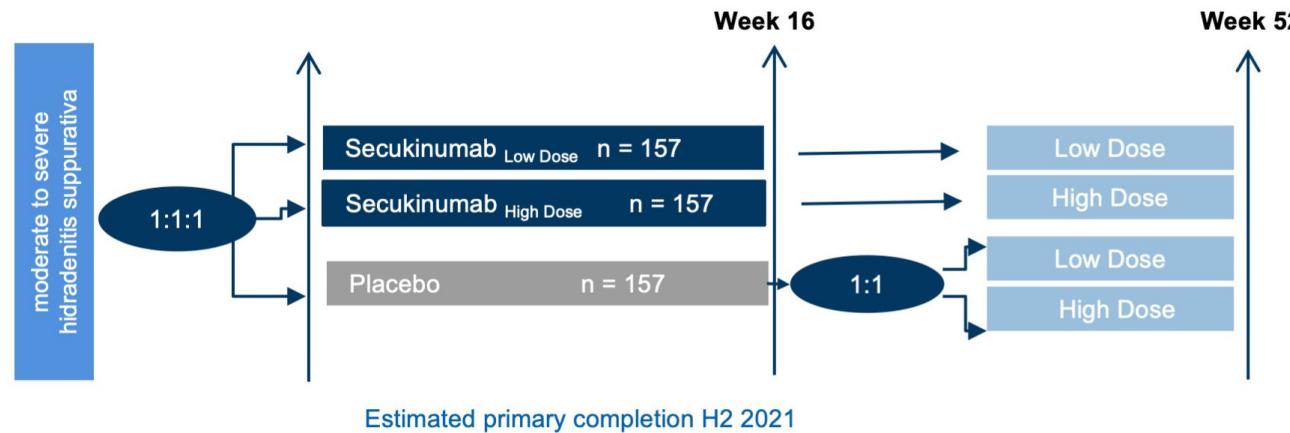
## Need for new mechanisms to control disease

- Available treatment options do not prevent disease progression nor control symptoms optimally
- A TNF inhibitor is the only biologic treatment approved for HS, with partial response achieved by 50% of the patients<sup>4</sup> that is not always durable
- IL-17 is highly expressed in the lesions. Goal of therapy is to prevent disease progression and reduce inflammation in existing lesions

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. 4. Martin-Ezquerre et al., J Eur Acad Dermatol Venereol., 2015.

# Phase 3 program in Hidradenitis Suppurativa

## SUNRISE & SUNSHINE<sup>1</sup>



- Two identical Phase 3, randomized, double-blind, placebo-controlled, multicenter studies to evaluate the efficacy and safety of secukinumab vs. placebo in patients with moderate to severe hidradenitis suppurativa<sup>1</sup>
- The primary endpoint is the achievement of HiSCR<sup>2</sup> at Week 16. HiSCR response is defined as at least a 50% decrease in Abscess and Inflammatory Nodule (AN) count with no increase in the number of draining fistulae.

1. ClinicalTrials.gov Identifier: NCT03713632. 2. HiSCR: Hidradenitis Suppurativa Clinical Response.

## Study attributes

- Scientific rationale based on reports suggestive of efficacy in HS patients

# Lichen Planus

Significantly impaired quality of life with currently no approved systemic therapies

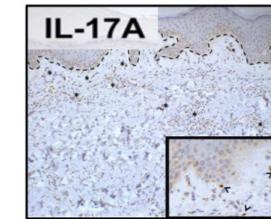
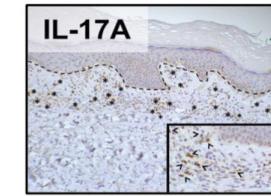
## Unmet need in Lichen Planus

- Chronic inflammatory disorder of the skin and mucosa
- Impact on patient's quality of life comparable to psoriasis
- Prevalence of 0.4% - 2.6% of the general population<sup>1</sup>
- Current standard of care topical and systemic corticosteroids
- No approved systemic treatment options available for corticosteroid refractory patients (60% of topically treated patients)

Week 0



Week 12



## Clinical and molecular response to secukinumab identifies lichen planus as a Th17-driven disorder<sup>2</sup>

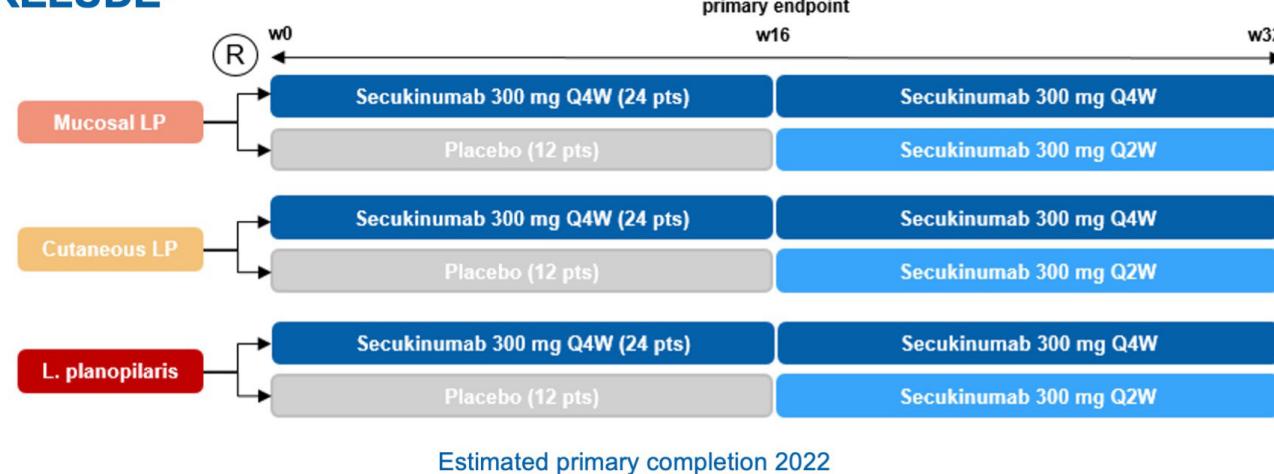
Available treatment options of local and systemic corticosteroid leave many patients refractory and are the only approved therapies

Th17 axis is essential for lichen planus pathophysiology with reported clinical and molecular response to IL-17 inhibition

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.

## Phase 2a/b in Lichen Planus

### PRELUDE<sup>1</sup>



- Innovative basket study design evaluating secukinumab in 3 subtypes of lichen planus in a single study
- Randomized, placebo-controlled, double-blind, multi-center Phase 2 trial
- Testing 2 dosing regimens
- New outcome measuring tools developed specifically for lichen planus

### Study attributes

No clinical proof of concept data

Rationale for targeting IL17A based on positive case series

1. ClinicalTrials.gov Identifier: NCT04300296.

# Lupus Nephritis

A major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients

## Unmet need in Lupus Nephritis (LN)

- Up to 50% of patients<sup>1</sup> with SLE suffer from LN
- No approved therapies currently available, steroids and off-label B-cell depleting therapy (for refractory patients) used
- ~50% of patients do not achieve remission with standard of care
- Most patients continue to have flares and suffer from toxicity during maintenance regimen; 17%-22% of LN patients progress to end-stage renal disease (ESRD) within 10 to 15 years

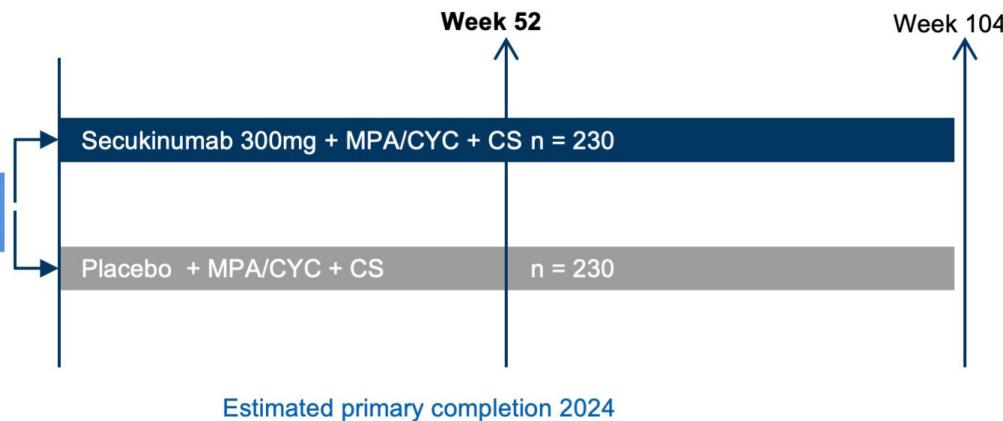
## Goal to improve therapeutic response, reduce use of steroids and prevent progression to end-stage renal disease (ESRD)

- Need for a steroid sparing regimen with an increase in complete renal response and a proven safety profile (no lab monitoring etc.)
- Secukinumab has the potential to become induction and maintenance therapy in adult patients with active lupus nephritis – assumes treating patients with LN class III/IV +/-V (approx. 72% of LN patients)

1. Hoover, P.J., et al. (2016) Kidney International.

# Phase 3 SELUNE trial in patients with Lupus Nephritis

## SELUNE<sup>1</sup>



- 2-year, Phase 3 randomized, double-blind, parallel-group, placebo-controlled trial to evaluate the safety, efficacy, and tolerability of 300mg s.c. secukinumab vs. placebo, in combination with SoC therapy, in patients with active Lupus Nephritis
- Primary end-point: proportion of patients achieving Complete Renal Response (CRR) following 52 weeks of treatment

## Study attributes

Robust scientific rationale for IL-17 inhibition and clinical evidence with case report indicating secukinumab efficacy in LN refractory to standard of care

Adaptive design trial with planned Futility Analysis when 30% pts (N=138) achieve 52 weeks of treatment (Go/No go decision)

1. ClinicalTrials.gov Identifier: NCT04181762. MPA = Mycophenolic acid. CS = Corticosteroids.

# Our continued commitment to pediatric patients

Addressing 2 sub-types of Juvenile Idiopathic Arthritis (JIA): Juvenile Psoriatic Arthritis (JPsA) and Enthesitis Related Arthritis (ERA)

## Unmet need in JIA

- JIA is the most common childhood rheumatic disease, covering six subtypes. In the US, patients with JPsA and ERA represent ~20% of the overall JIA population (~5% JPsA, ~15% ERA)<sup>1</sup>
- Across the US and EU5, approx<sup>1</sup>. 16,000 patients with diagnosed JPsA/ERA
- Due to the progressive nature of these diseases and the age of onset, need to treat patients aggressively, as lasting joint inflammation in children can lead to long-term damage
- 33% of children with ERA lack response to anti-TNF therapy and NSAIDs

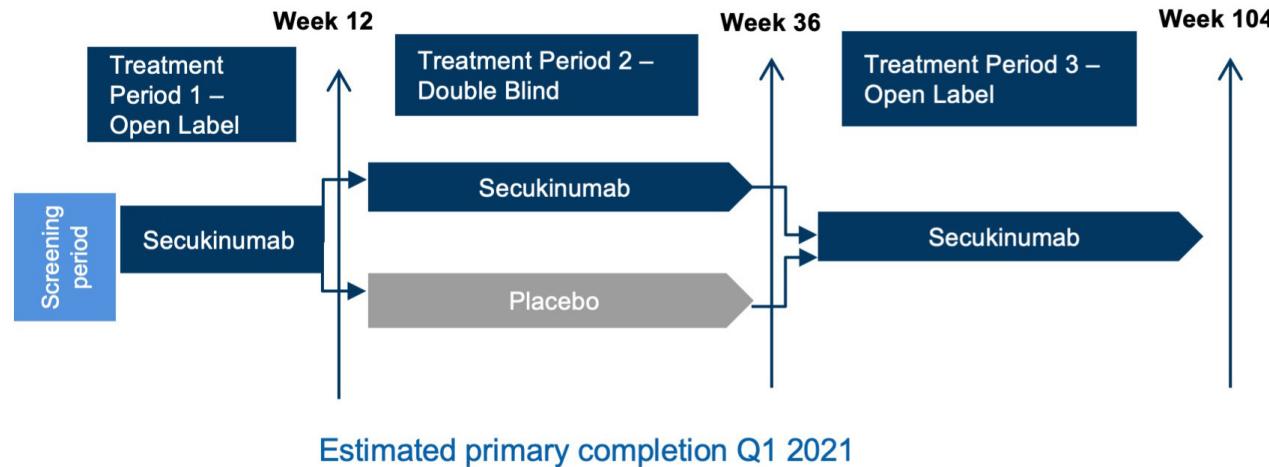
## Lack of targeted treatment options

- Current standard of care (SoC) is NSAID and/or conventional synthetic DMARDs
- Limited options for patients inadequately controlled on SoC:
  - Only 1 anti-TNF (golimumab) approved for treatment of JPsA in the US
  - No biologics approved for ERA in the EU
- Although JPsA and ERA affect a relatively small patient population, the high burden of disease and limitation in available treatment options demand for safe and new targeted therapies

1. Petty RE, Southwood TR, Manners P, et al (2004) Journal of Rheumatology.

# Phase 3 trial in patients with Juvenile Idiopathic Arthritis

## JIA study<sup>1</sup>



- Double-blind, placebo-controlled, event-driven randomized withdrawal study to investigate the efficacy and safety of secukinumab treatment in the Juvenile Idiopathic Arthritis (JIA) categories of Juvenile Psoriatic Arthritis (JPsA) and Enthesitis-related Arthritis (ERA)
- Primary endpoint: time to flare in Treatment Period 2

## Study attributes

Published case reports show efficacy of secukinumab in children and adolescents with ERA and JPsA<sup>2,3</sup>

By trial design, ACR30 responders to secukinumab in the open label TP1 period entered in the placebo-controlled TP2.

1. ClinicalTrials.gov Identifier: NCT03769168. 2. Wells LE, et al. Use of secukinumab in a pediatric patient leads to significant improvement in nail psoriasis and psoriatic arthritis. Pediatr Dermatol. 2019 Feb 27. 3. Foeldvari I, Baer J. Secukinumab Is a Promising Treatment for Patients with Juvenile Enthesitis Related Arthritis Nonresponsive to Anti-TNF Treatment [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).

# Giant Cell Arteritis (GCA)

Still unmet need despite an approved biologic therapy; Cosentyx® Ph3 program planned to start in H2 2021

## Unmet need in GCA

- Most common form of adult primary systemic vasculitis with features of cranial and/or large-vessel vasculitis; primarily affects elderly patients (mean age, 74 yrs); annual incidence up to 27 (US) - 32 (EU)/100K persons  $\geq$  50 yrs
- Substantial morbidity due to complications of irreversible vision loss and stroke<sup>1</sup> and associated toxicity of prolonged glucocorticoid treatment
- A strong unmet medical need remains for safe and effective treatments that bring an earlier and further reduction of glucocorticoids
- Efficacy: failure in achieving sustained remission and significant rates of relapse with existing treatment including glucocorticoids and anti-IL6R mAb

## Rationale for IL-17 clinical development program

- IL17A plays an important role in the pathogenesis of GCA as evidenced by polymorphisms in IL17A locus associated with GCA and  $\uparrow$ IL17A in temporal arteries and  $\uparrow$  TH17 cells in blood, with rapid decline following GC treatment predictive of sustained remission
- Cosentyx® has the potential to offer GCA patients a first in class anti-IL-17A treatment option, with a proven safety profile
- Phase 2 / PoC<sup>2</sup> study readout expected in H1 2021
- Phase 3 program design under development with
  - Randomized, double-blind, multicenter 52wk study to evaluate the efficacy and safety of secukinumab vs. placebo in patients with newly diagnosed or relapsing GCA

1. Koster M, et al.(2016) Current Treatment Options in Rheumatology. 2. ClinicalTrials.gov Identifier: NCT03765788.

# Iscalimab (CFZ533)

Fully human monoclonal antibody blocking the CD154-CD40 pathway

Phase 2

## Key highlights

- Iscalimab blocks CD154-CD40 pathway with broad potential in multiple diseases
- Positive Proof of Concept study in Sjögren's syndrome, the second most common rheumatic autoimmune disease after Rheumatoid Arthritis
- Positive Proof of Concept study in kidney transplantation, suggesting better renal function and pristine renal histology compared to current SoC
- Iscalimab has the opportunity to be first-in-class in solid organ transplantation and Sjögren's.

# Iscalimab blocks CD154-CD40 pathway with broad potential in multiple diseases

## CD40 involvement

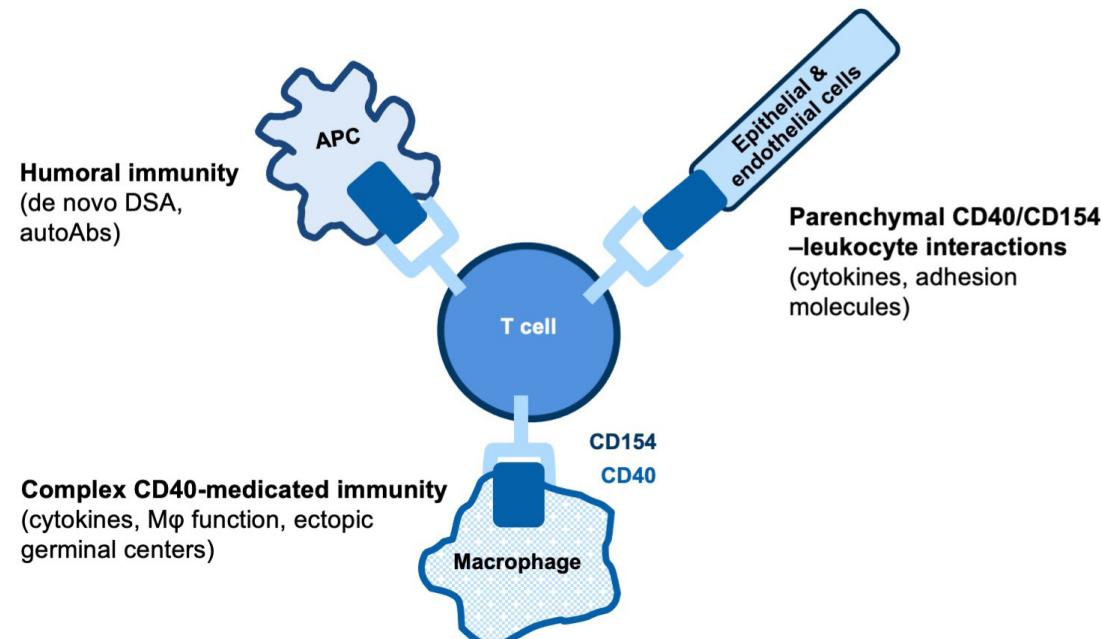


Figure adapted from Mathur RK et al. 2006<sup>1</sup>

### CD40 (48 kDa membrane bound; ~20 kDa soluble form)<sup>2</sup>

- Constitutively expressed on B cells and APCs (e.g. monocytes, macrophages, dendritic cells)
- Expressed on platelets, and under certain conditions on eosinophils and parenchymal cells

### CD154 (CD40 ligand)

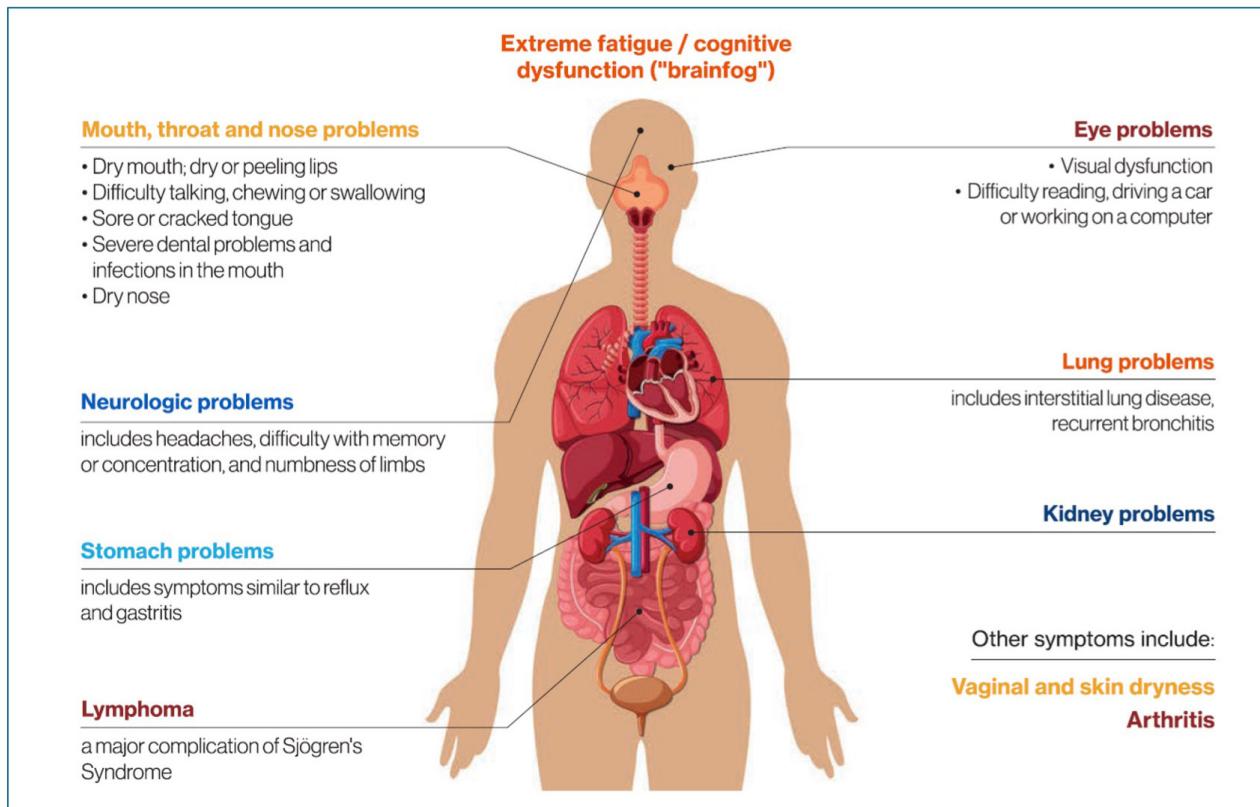
- Induced on a variety of cell types including activated T cells, platelets, and B cells

### CD40-CD154 signaling<sup>3</sup>

- Important for germinal center function, antibody production, and humoral memory
- Regulates macrophage, dendritic cell and parenchymal cell function
- Implicated in various autoimmune diseases

APC, antigen presenting cell; DSA, donor-specific antibodies. 1. Mathur RK, et al. Trends Parasitol. 2006;22(3):117-22. 2. Van Kooten C, Banchereau J. J Leukoc Biol. 2000;67(1):2-17. 3. Kawabe T, et al. Nagoya J. Med. Sci. 2011;73:69-78

# Sjögren's syndrome and rationale for CD40 as a therapeutic target



## Prevalence and treatment

- Autoimmune disease; prevalence in adult population 0.2%
- No cure or disease modifying treatment approved

## Rationale for isCALIMAB

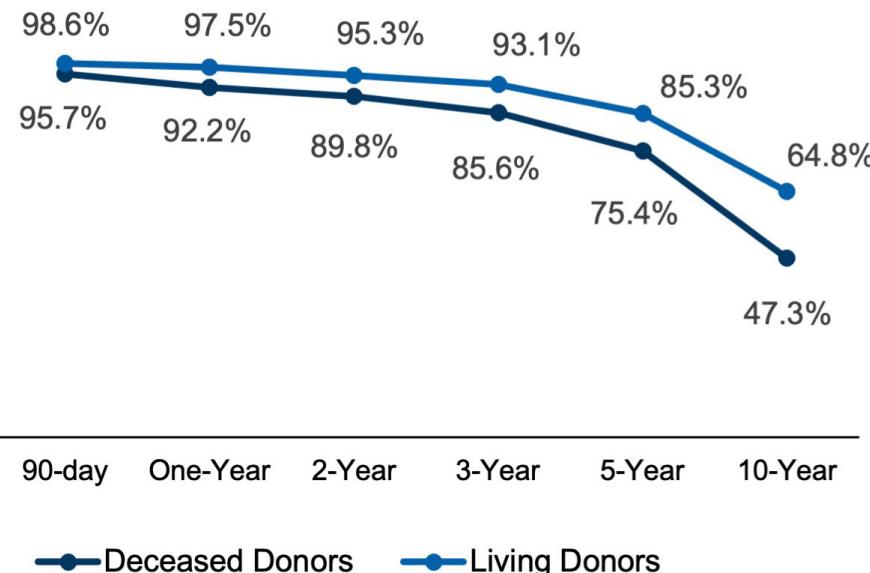
- A hallmark diagnostic feature of Sjögren's syndrome is B-cell hyperreactivity
- T-cells and B-cells infiltrate patients' salivary glands and upregulate CD40 and CD154
- Positive Proof of Concept study

Fisher et al. Abstr # 1784; Am College of Rheumatology 2017.

# Kidney and liver transplantation

Significant unmet need in transplantation to prolong graft survival and reduce side effects

## Graft survival probabilities (%)



2018 USRDS Annual Data Report Reference Tables, adjusted for age, sex, race, ethnicity, and primary cause of ESRD. Graft survival is determined as the earliest occurrence of either death with graft function or graft failure requiring dialysis or re-transplant.

## Challenges with existing standard of care, such as CNI-based therapies

### Renal toxicity

Chronic toxicity → chronic dysfunction  
→ return to dialysis

### Cardio-metabolic complications

Frequent new-onset post-transplant diabetes, hypertension, increased cardio-vascular mortality

### Insufficient graft protection

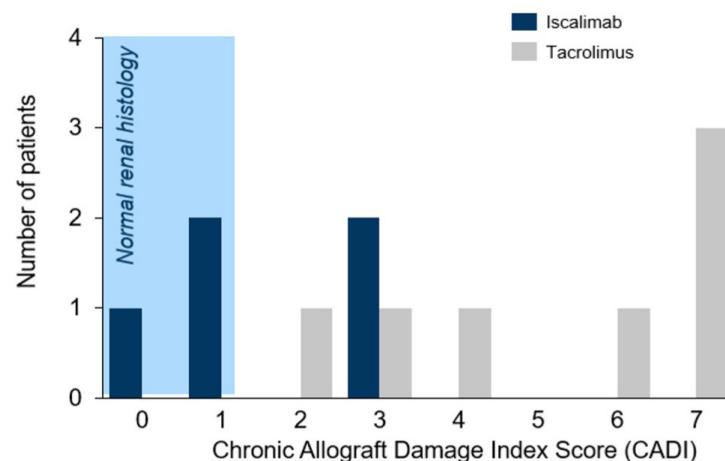
From recipient immune defense leading to progressive graft damage  
→ return to dialysis

### Cancers and infections

Cancers, bacterial and viral infections; complications due to (over-) immunosuppression

# Potential to reimagine transplant with better graft protection and less toxicity

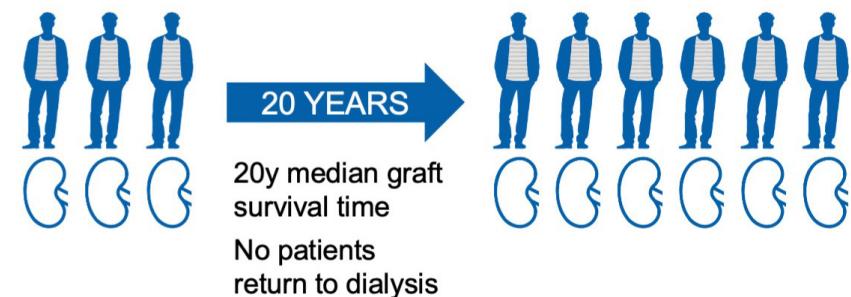
## Superior graft quality with iscalimab<sup>1</sup>



Graft loss increases with CADI; after 3 years, the graft loss is<sup>2</sup>:

- CADI 0-1: 0%
- CADI 2-4: 5%
- CADI >4: 17%

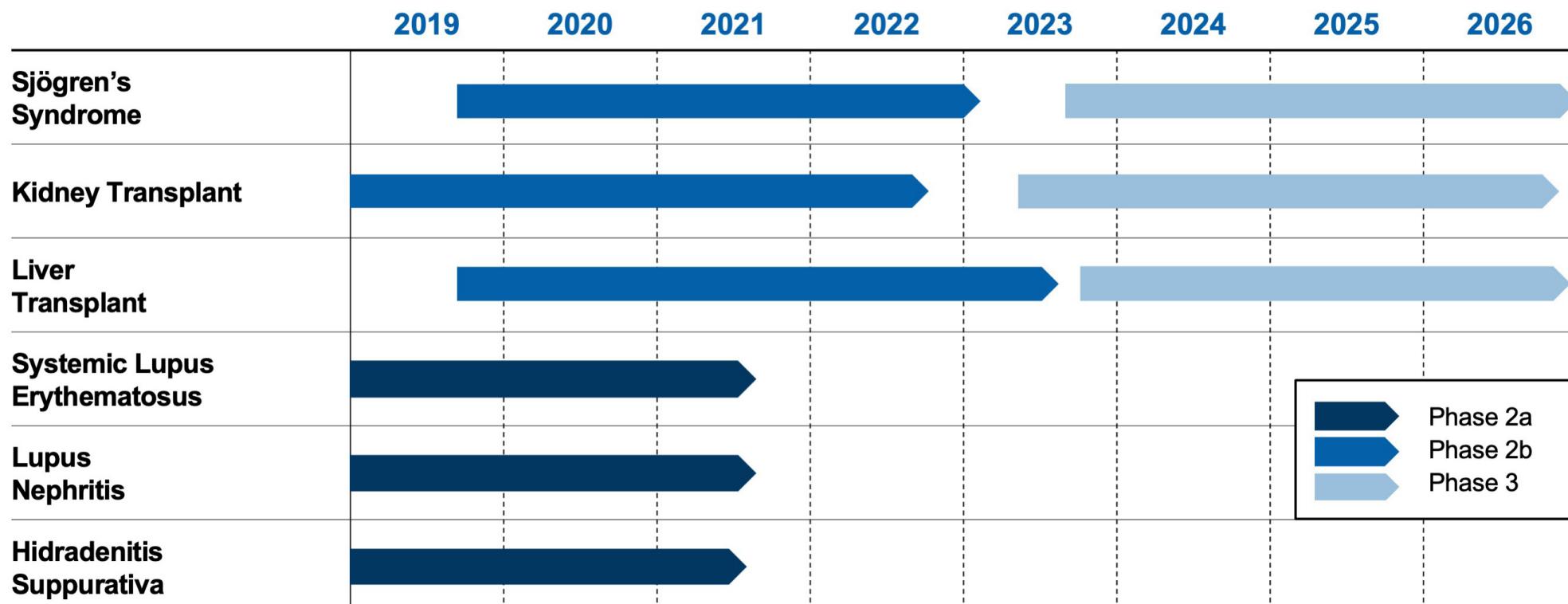
1. Farkash et al, Am Transplant Congress 2019. 2. Yilmaz et al 2003, J Am Soc Nephrol 14: 773-779.



Extending graft survival translates into:

- More organs available for more patients
- Fewer patients on dialysis
- Higher QoL and fewer patients dying

## Advancing iscalimab in a range of indications through 2020-26



Timelines are tentative assuming limited further impact of COVID-19

# Prevalent and incident patient populations

## Market potential in G7 countries

Indication	Prevalence	Incidence
Sjögren's Syndrome <sup>1</sup>	950,000+	
Kidney transplantation <sup>2</sup>	500,000+	40,000+
Liver transplantation <sup>3</sup>	300,000+	15,000+
Systemic Lupus Erythematosus <sup>4</sup>	500,000+	
Lupus Nephritis <sup>5</sup>	180,000+	
Hidradenitis Suppurativa <sup>6</sup>	~3m (150,000+ Hurley stage II and III)	

1. Data monitor Healthcare Report 2018; BMJ Best Practice, 2017; Corne & Chiche, 2015; Maciel et al., 2017; Patel & Shahane, 2014 ; Kantar Health report 2014. 2. Prevalence: Novartis internal estimate; incidence: US – unos.org, EU/global - European Commission Transplant Newsletter 2020. 3. Prevalence: Novartis internal estimate; incidence: US - unos.org, EU/global - European Commission Transplant Newsletter 2020. 4. 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). 5. DRG Lupus Nephritis Disease report, Novartis internal analysis. 6. Phan K et al. Biomedical Dermatology 2020; Primary Market Research.

# Ligelizumab

## (QGE031)

Humanized anti-IgE  
monoclonal antibody  
blocking IgE/Fc $\epsilon$ RI  
pathway

Phase 3

### Key highlights

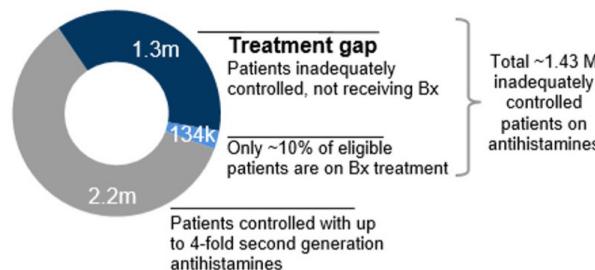
- Ligelizumab with potential to become first-line biologic after antihistamine therapy in Chronic Spontaneous Urticaria (CSU)
- Nature Communications publication demonstrates that ligelizumab shows more profound inhibition of IgE binding to Fc $\epsilon$ RI (high affinity IgE receptor)<sup>1</sup>
  - Mechanistic and functional profile of ligelizumab rationalizes Ph2b results with more patients achieving symptom control vs. Xolair®
- Currently assessing ligelizumab in other anti-IgE/Fc $\epsilon$ RI mediated diseases - Chronic Inducible Urticaria (CINDU) and Food Allergy, with combined blockbuster potential
- Ph3 CSU superiority studies vs. Xolair® (PEARL 1, 2) finished recruitment in adults; first results expected H2 2021 with submission in 2022 (COVID impact)

1. "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

# Chronic Spontaneous Urticaria

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

1.3m+ CSU patients are still inadequately controlled



- CSU diminishes quality of life with unpredictable onset of itch, hives and/or angioedema<sup>1</sup>
- Approximately 40% do not respond to up-dosed second generation antihistamines<sup>2</sup>
- Up to 30% of people with moderate to severe CSU suffer from depression or anxiety<sup>1</sup>

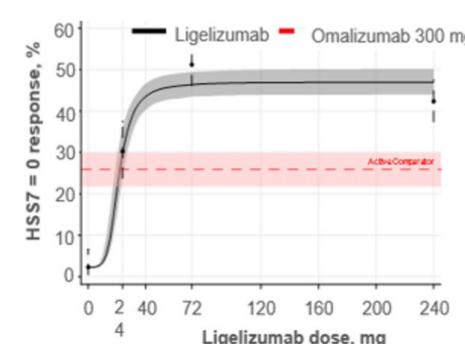
Phase 2b study with clear dose-response on complete hives control and USA7<sup>3</sup> change from baseline<sup>4</sup>



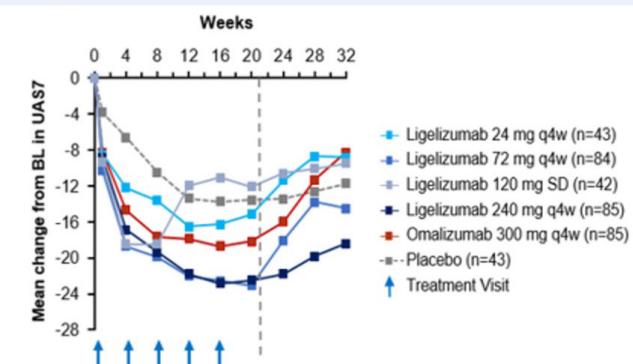
The NEW ENGLAND  
JOURNAL of MEDICINE

"Ligelizumab for chronic spontaneous urticaria"  
Primary publication of the Phase 2b study (QGE0312201)<sup>4</sup>

A. Dose-response curve



B. Change from baseline in UAS7 over time



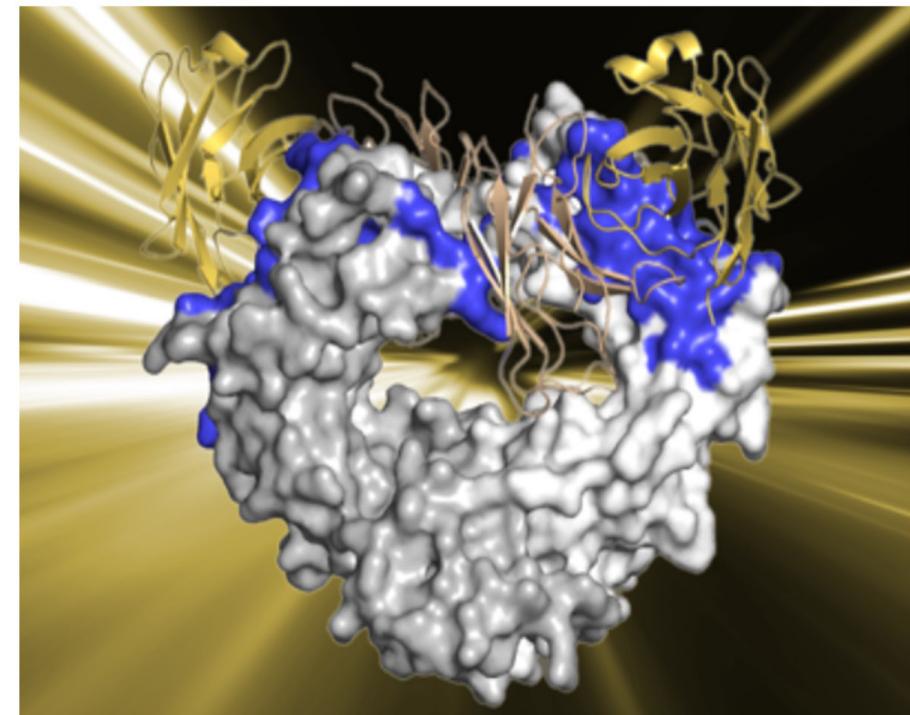
**Primary objective achieved:** Dose response relationship with respect to complete weekly hives response rate (HSS7<sup>5</sup>=0) at week 12

1. Zuberbier T et al. Allergy 2018;73:1393-1414. 2. Novartis on file market research; 2017; Allen P. Kaplan, 2012. 3. UAS7 = Urticaria Activity Score over 7 days. 4. Maurer M., et al, N Engl J Med. 2019. 381(14): 1321-32.  
5. HSS7 = Hives Severity Score over 7 days.

# Mechanistic differences between ligelizumab and omalizumab (Xolair®) provide scientific rationale for strong Ph2b results

## Ligelizumab recognizes a different epitope of the IgE molecule than Xolair®

- Higher affinity to IgE is due to formation of more stable IgE-ligelizumab complexes (slower off-rate)
- More potently inhibits IgE binding to the high affinity IgE receptor (FcεRI) on effector cells than to the low affinity receptor FcεRII (CD23)
- More potently inhibits mast cell and basophil activation and degranulation
- More potently inhibits IgE production



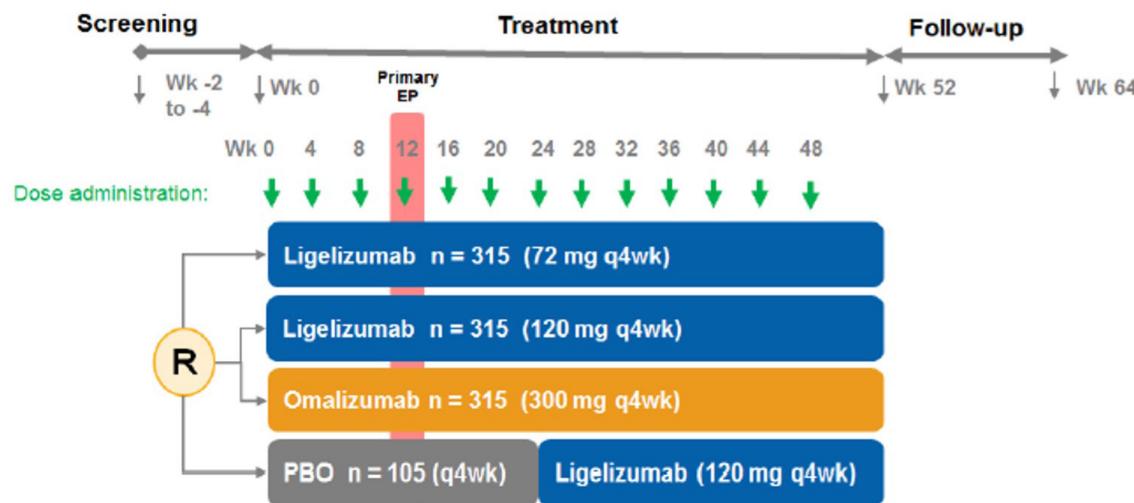
"The mechanistic and functional profile of the therapeutic anti-IgE antibody ligelizumab differs from omalizumab" Gasser P., et al. Nature Communications 2020;11(1):165.

# Ligelizumab Phase 3 CSU studies

Aim to demonstrate superiority vs omalizumab

## PEARL 1 and 2 ongoing; first results expected H2 2021

2 multi-center, randomized, double-blind, active/placebo-controlled studies with 1050 patients each



1. UAS7 = Urticaria Activity Score over 7 days.

## Well powered, bold Head-to-Head comparison vs SoC

(highest approved Xolair® dose 300mg)

### 1° endpoint:

Absolute change from baseline in UAS7<sup>1</sup> at week 12

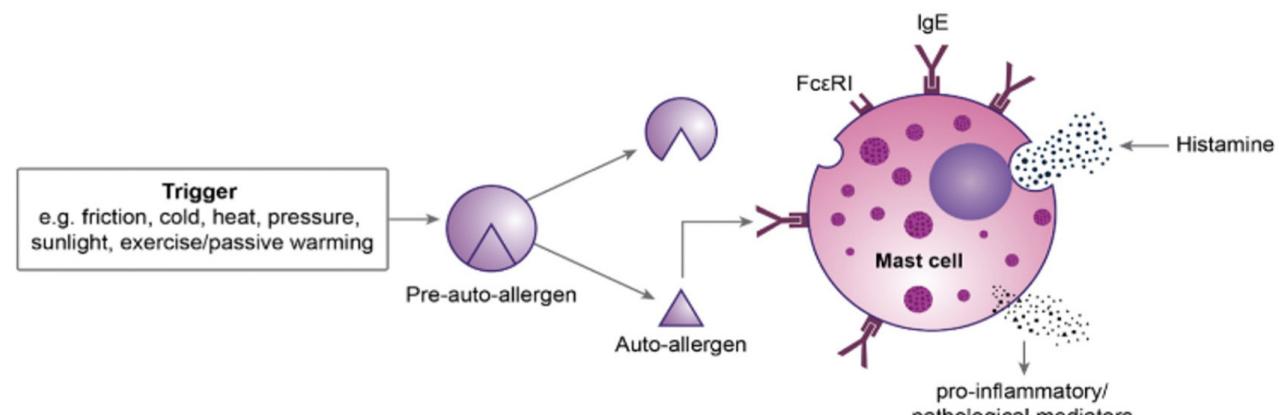
### Key 2° endpoints at week 12:

- Complete absence of hives and itch, % of subjects with no itch, no hives
- Improvement of itch severity score
- Impact on subject's quality of life
- Cumulative number of weeks without angioedema

# Exploring ligelizumab in other IgE/FcεRI inhibition mediated diseases - Chronic Inducible Urticaria (CINDU)

- Approximately 1/3 of chronic urticaria patients have CINDU<sup>1</sup>
- The current SoC is second generation antihistamines<sup>2</sup>
- While disease triggers in majority of cases are unavoidable, there are no approved therapies for uncontrolled CINDU patients<sup>2</sup>
- The therapeutic goal is to achieve complete symptom control by blocking the effects of mast cell mediators and prevention of mast cell degranulation<sup>2</sup>

## IgE/FcεRI inhibition a promising therapeutic target in CINDU<sup>2</sup>

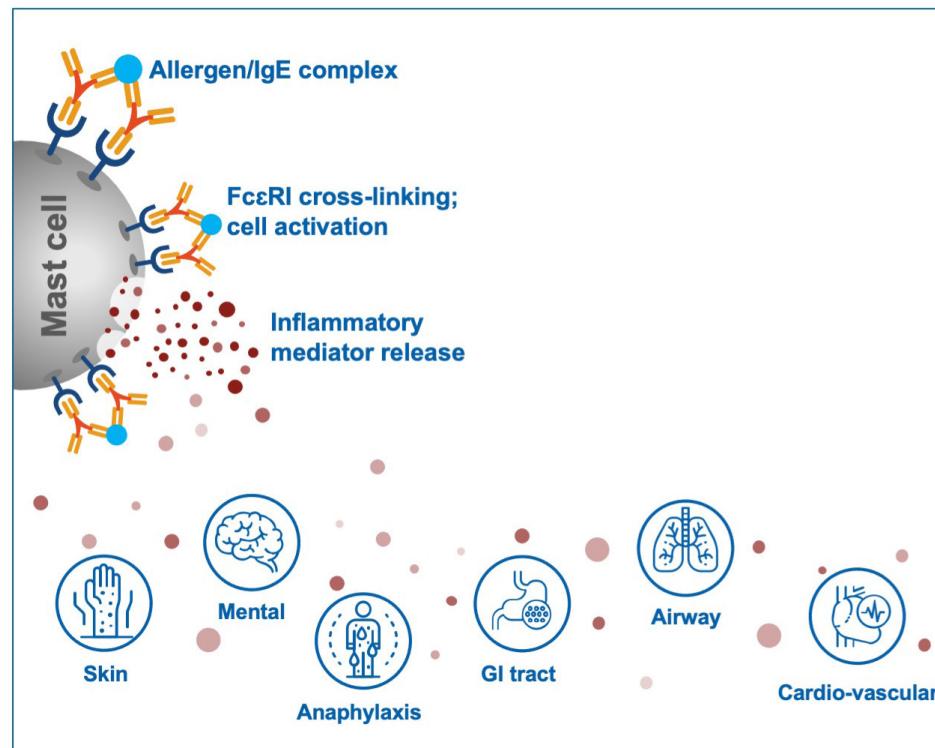


- Pathophysiology includes activation and degranulation of tissue-resident mast cells and release of pro-inflammatory mediators<sup>2</sup>
- The respective trigger may result in de novo synthesized autoantigen/ autoallergen, which is detected by IgE bound to skin mast cells<sup>2</sup>

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.

# Potential best-in-class therapy in Food Allergy

Protecting patients from allergic reactions triggered by accidental exposure



- Prevalence is 3-8% across countries; allergy to multiple foods is common<sup>1</sup>
- High unmet need for effective and safe treatments<sup>2</sup> to improve quality of life of patients and families<sup>3</sup>
- Current standard of care is avoidance of allergens and injectable epinephrine to treat reactions<sup>3</sup>.
- However:
  - 42% of children and 51% of adults have experienced at least one severe food-allergic reaction<sup>4,5</sup>
  - Reactions can be triggered by tiny exposures (e.g. fraction of a peanut<sup>6</sup>)

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](http://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.

# Currently exploring ligelizumab potential in other IgE/FcεRI inhibition mediated diseases

## Market potential

Indication	Market size (USD)	
CSU	●●●	
Food Allergy	●●●	
CINDU	●○○	
●○○ <500m	●●○ <500m – 1bn	●●● >1bn

## Upcoming milestones for development program

	2020	2021	2022	2023	2024	2025
CSU		Phase 3				
Food Allergy			Phase 3			
CINDU			Phase 3			

- CSU PEARLs readout expected H2 2021; submission 2022
- Food Allergy: Initiation of Ph3 program expected H2 2021
- CINDU: Initiation of Ph3 program expected H2 2021

# CRM

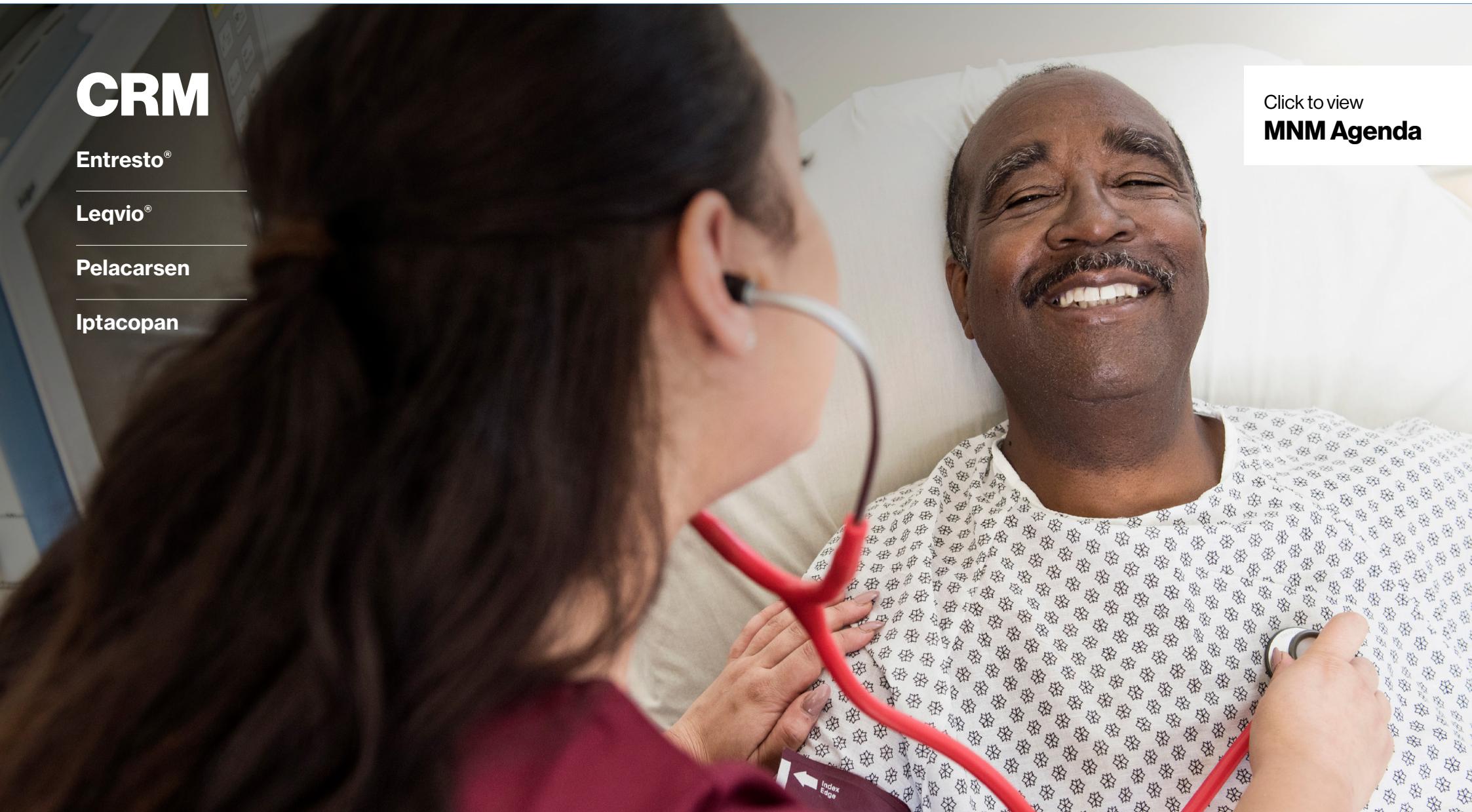
Entresto®

Leqvio®

Pelacarsen

Iptacopan

Click to view  
**MNM Agenda**



# Entresto®

Angiotensin receptor neprilysin inhibitor (ARNI) providing dual blockage of critical pathways involved in the pathogenesis of heart failure

Marketed; LCM in Phase 3

## Key highlights

- Significant growth opportunity through geographic expansion with current and LCM indications
  - ~3/4 of all HFrEF patients can still benefit from Entresto®
- Heart failure with reduced ejection fraction (HF-rEF)
  - Approved in 115 countries
  - Strong growth across all geographies
  - Extensive clinical and real-world evidence supporting use as first-line treatment
- Heart failure with preserved ejection fraction (HF-pEF)
  - FDA AdCom on December 15, FDA action date in Q1 2021
- Post acute myocardial infarction (PAMI)
  - Ph3 PARADISE-MI study ongoing with readout expected in Q2 2021
- Pediatric heart failure
  - Approved in US
  - PANORAMA-HF study ongoing with readout expected 2022

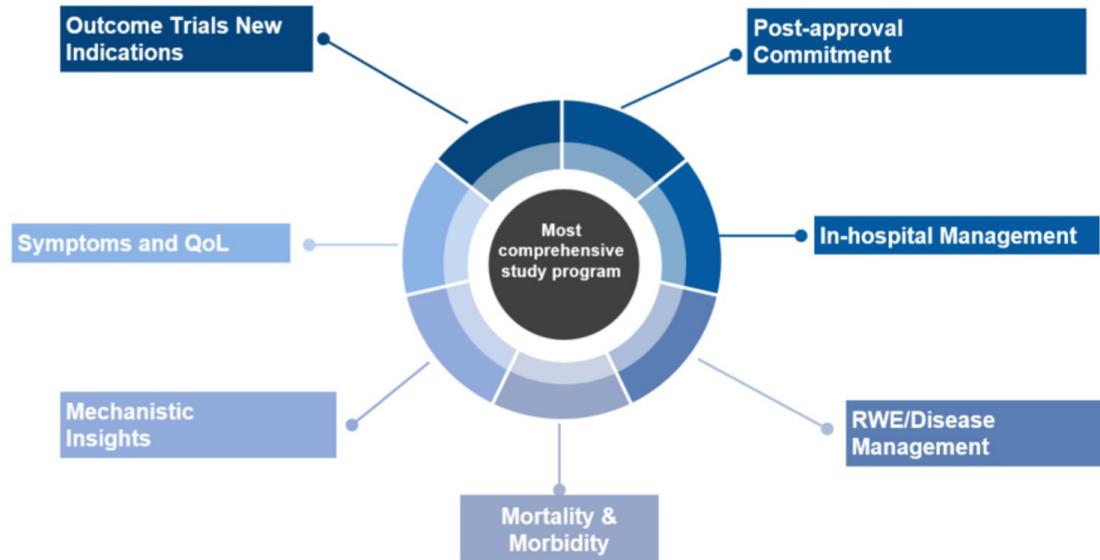
# Entresto® is the essential, first choice therapy in HFrEF

Increasing use and adoption as 1<sup>st</sup> line treatment, supported by broad evidence base

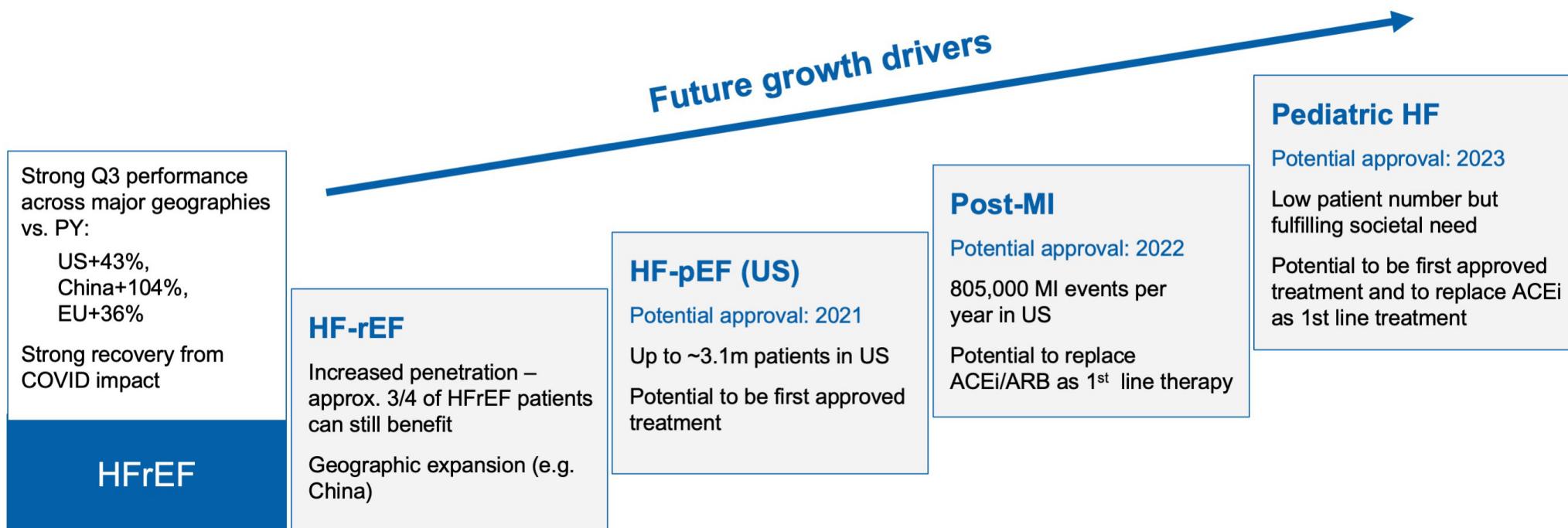
## Key characteristics supporting first line use of Entresto®

- Essential role of both neprilysin and RAAS inhibition in clinical outcomes
- Improved cardiovascular outcomes vs. conventional RAAS inhibition
- Safe and effective in broad populations including ACEi/ARB naïve patients
- Easy and safe initiation in-hospital or immediately after discharge
- Well understood reversal of cardiac remodelling based on unique MoA
- Effectiveness and safety confirmed by large body of RWE in clinical practice
- Guidelines support as SoC

Entresto® has the most comprehensive evidence of all HF therapies including >20,000 patients in clinical trials and >300,000 patients in RWE



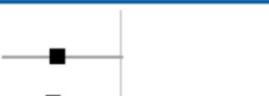
# Entresto® has significant growth opportunity through geographic expansion in HFrEF and LCM indications with high unmet need



# Entresto® could be the first approved pharmacological therapy for HF-pEF in US

Review ongoing with action date in Q1 2021

## PARAGON<sup>1</sup>

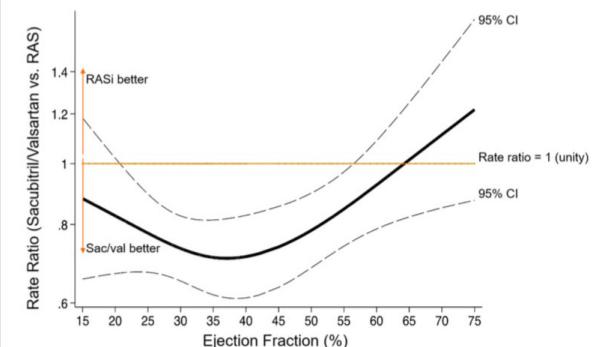
Endpoint	Sac/val N=2407	Valsartan N=2389	Rate Ratio (95% CI)	Rate Ratio (95% CI)	2-sided P-value
<b>CEC-confirmed</b>					
Primary endpoint	894	1009	0.870 (0.753, 1.005)		0.059
Expanded composite endpoint*	934	1064	0.861 (0.747, 0.993)		0.040
<b>Supportive analyses of the primary endpoint</b>					
Investigator reported primary endpoint events	1064	1241	0.843 (0.736, 0.966)		0.014

← sacubitril/valsartan better      valsartan better →

- FDA Advisory committee December 15, 2020
- Favorable safety profile in line with rEF population
- Totality of evidence including several supportive analyses demonstrates a beneficial treatment effect

## Trial profile

- Narrowly missed the primary endpoint
- The observed treatment effect was greater in patients with EF below normal<sup>2</sup>

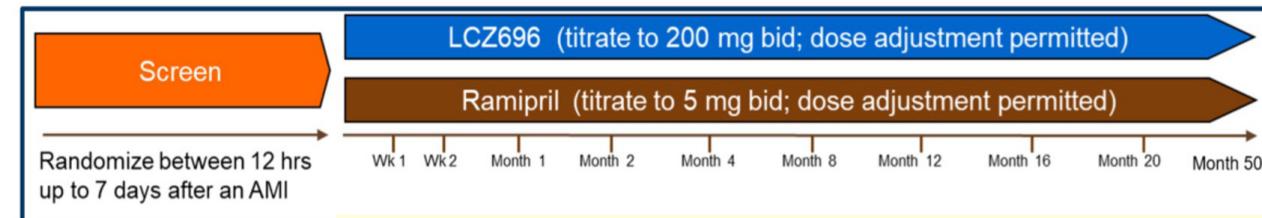


1. Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction; S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin Colet, J. Cleland, H. D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiwa, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON HF Investigators and Committees; September 1, 2019, at NEJM.org.; DOI: 10.1056/NEJMoa1908655. 2. LVEF pooled analysis PARADIGM/PARAGON. Solomon S et al. 2020 Circulation. \* HF hospitalizations, CV death and urgent HF visits.

# PARADISE-MI in patients with post acute MI is ongoing

## Results expected in Q2 2021

### Study design Ph3 PARADISE-MI study



### Trial profile

Comparison to ACE inhibitor ramipril to show superiority to current SoC

Potentially extends use to preventing the development of HF in patients post-AMI

Mitigation strategies were put into place to address potential impact of COVID-19 on trial

#### Patients

5670 patients following an acute myocardial infarction without prior history of heart failure

#### Primary objective

Demonstrate superior efficacy of Entresto® compared to standard of care (ramipril) in time to first composite event

#### Primary composite endpoint

CV death, HF hospitalizations, outpatient HF visits

# Confidence in future growth based on current and new indications

Potential to reach up to 9m patients worldwide at peak with Entresto®

## Market potential

Indication	USD
HF-rEF	●●●
HF-pEF (US)	●●○
pAMI	●●○
Pediatric HF	●○○
●○○ <100m	●●○ 100m – 2bn
	●●● >2bn

## Upcoming milestones for development program

	H2 2020	H1 2021	H2 2021	H1 2022	H2 2022	H1 2023
HF-pEF		★ (US)				
pAMI	Phase 3		★			
Peds	Phase 3			★		

★ Expected submission

★ FDA action date

# Leqvio®\*

## (inclisiran)

First and only siRNA LDL cholesterol lowering treatment

Awaiting regulatory decision

### Key highlights

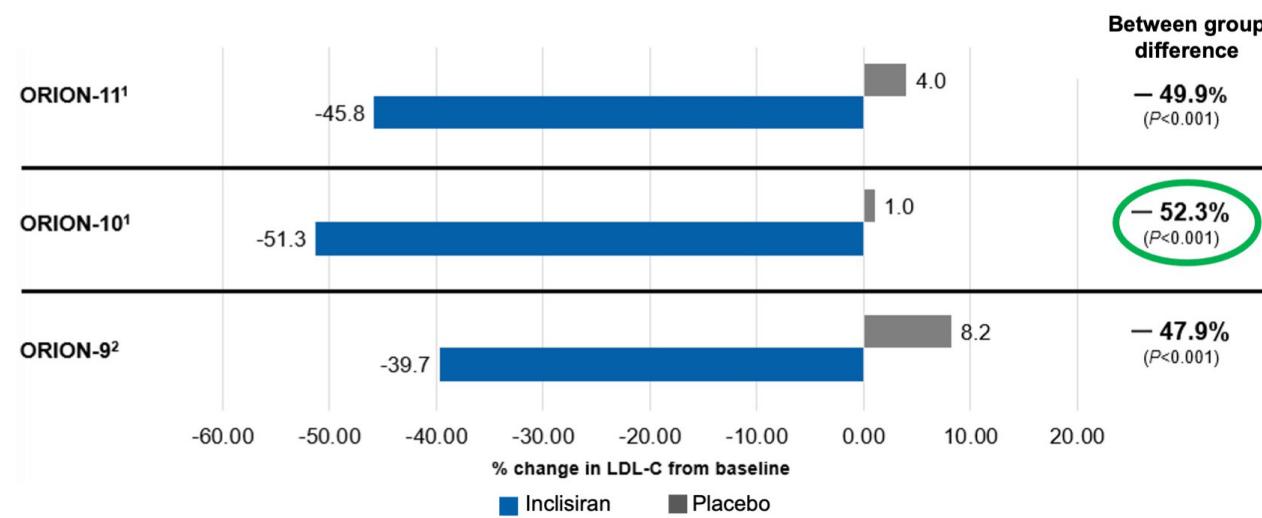
- More than 135m ASCVD patients worldwide<sup>1,2, 3</sup>
- Positive CHMP opinion received October 15, 2020:
  - European approval expected December / January in 27 EU members states plus UK, Norway
  - Launch in Germany in H1 2021, launch in UK in H2 2021
- China and Japan additional studies planned in order to pursue approval
- FDA action date December 2020; inspection of production site (Italy) pending
- Effective and sustained LDL-C reduction up to 52% with only two doses a year<sup>3†</sup>
- Safety comparable to placebo

\*Product and brand name are not FDA approved. Currently under FDA review. <sup>†</sup> Given as an initial dose, again at 3 months, and then every six months thereafter. 1. 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. 2. World Health Organization. *Cardiovascular diseases (CVDs).* [https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)). Accessed May 28, 2020. 3. Ray KK et al. *N Engl J Med.* 2020;382(16):1507-1519.

# Inclisiran delivers an effective and sustained LDL-C reduction of up to 52%<sup>1, 2</sup>

- Cardiovascular disease is the number one killer worldwide, responsible for one in every three deaths globally
- Effective and sustained LDL-C reduction remains a challenge, with 80% of people with ASCVD not achieving guideline-recommended LDL-C targets on statins alone
- Barriers include difficulties in making lifestyle changes and the inability to access some therapies or adhere to treatment
- These challenges underscore the significant unmet need for a new type of medicine

**Inclisiran effected significant reductions in LDL-C vs. placebo at Day 510, on top of SoC**  
Range, -47.9% - 52.3%



Note: ORION 9 studied patients with HeFH, ORION 10 patients with ASCVD, and ORION 11 patients with ASCVD or risk equivalent

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.

# Inclisiran is well tolerated with a safety profile comparable to placebo

- No significant safety or tolerability concerns have been identified with the long-term administration of inclisiran<sup>1,2</sup>
- Most common adverse events occurred with similar frequency in the inclisiran and placebo groups
- The only adverse reactions associated with inclisiran were at the injection site all of which were mild or moderate in severity, transient and resolved without sequelae
- The most common adverse reactions reported were diabetes mellitus, hypertension, nasopharyngitis, arthralgia, back pain, dyspnea, bronchitis and upper respiratory tract infection

ORION-9 (n=481)<sup>1</sup>ORION-10 (n=1,559)<sup>2</sup>ORION-11 (n=1,615)<sup>2</sup>

Safety population	Inclisiran n=241		Placebo n=240		Inclisiran n=781		Placebo n=778		Inclisiran n=811		Placebo n=804	
	n	%	n	%	n	%	n	%	n	%	n	%
Patients with at least one serious TEAE	18	7.5%	33	13.8%	175	22.4%	205	26.3%	181	22.3%	181	22.5%
Pre-specified exploratory CV endpoint (MedDRA basket)	10	4.2%	10	4.2%	58	7.4%	79	10.2%	63	7.8%	83	10.3%

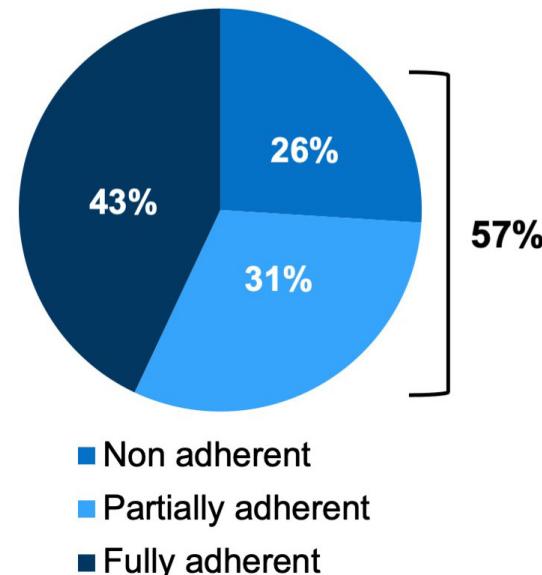
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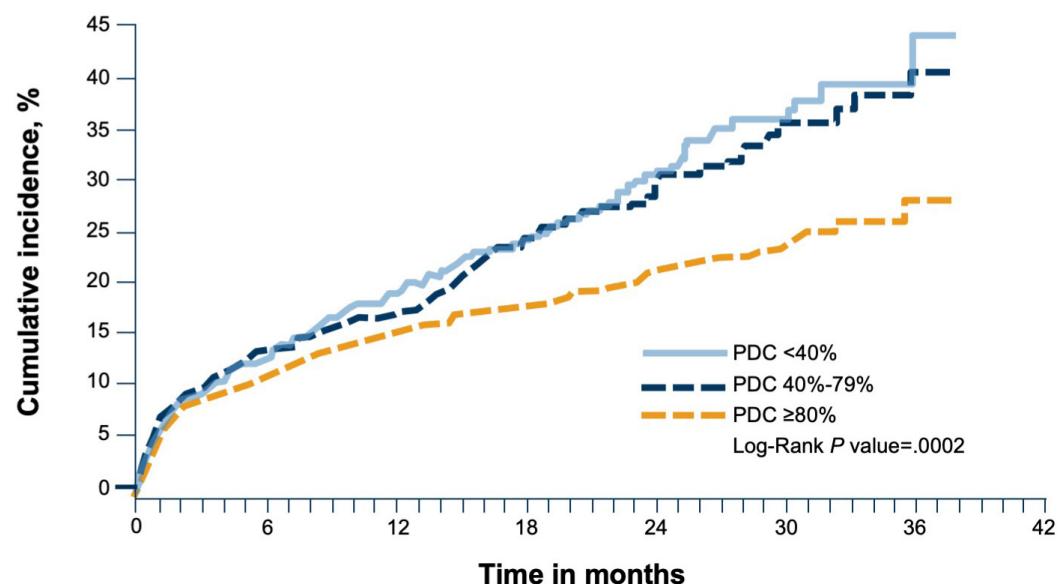
## 2 HCP-administered doses a year<sup>1†</sup> may remove adherence challenges

Commonly encountered with self-administered treatments; low adherence increases MACE

### Statin adherence in a secondary prevention cohort



### MACE according to adherence categories in a secondary prevention cohort<sup>2</sup>



MACE, major adverse cardiovascular events; MI, myocardial infarction; PDC, percent days covered.  
2. Bansilal S, et al. J Am Coll Cardiol. 2016;68:789-801.

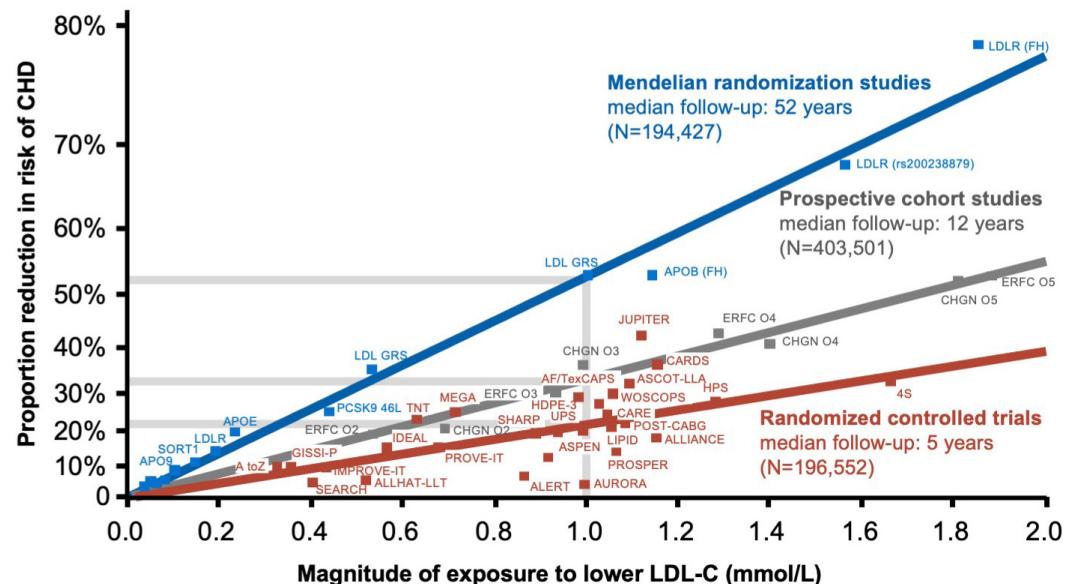
† Given as an initial dose, again at 3 months, and then every six months thereafter. 1. Ray KK et al. N Engl J Med. 2020;382(16):1507-1519.

## Reducing LDL-C improves CV outcomes

ORION-4, 15,000 patients, designed to confirm MACE and CV mortality benefit over 5 years

- Almost 1 million patient-years of clinical trial data, plus genetic and epidemiologic data, support the relationship between LDL-C and MACE<sup>3</sup>
- Each mmol/L reduction in LDL-C reduces the relative risk of ASCVD<sup>2</sup> events by 20% after 3 years and 1.5% in each subsequent year
- This relationship is reflected in international clinical treatment guidelines
- In US, the relation between LDL-C and outcomes is well established
- We continue to pursue unique access models ahead of ORION-4 outcomes data which will help physicians improve patients' outcomes
- Expected read-out in 2025

### Log-linear association per unit change in LDL-C and the risk of CV disease<sup>1</sup>



1. Figure from Ference et al Eur Heart J. 2017.

2. Atherosclerotic cardiovascular disease.

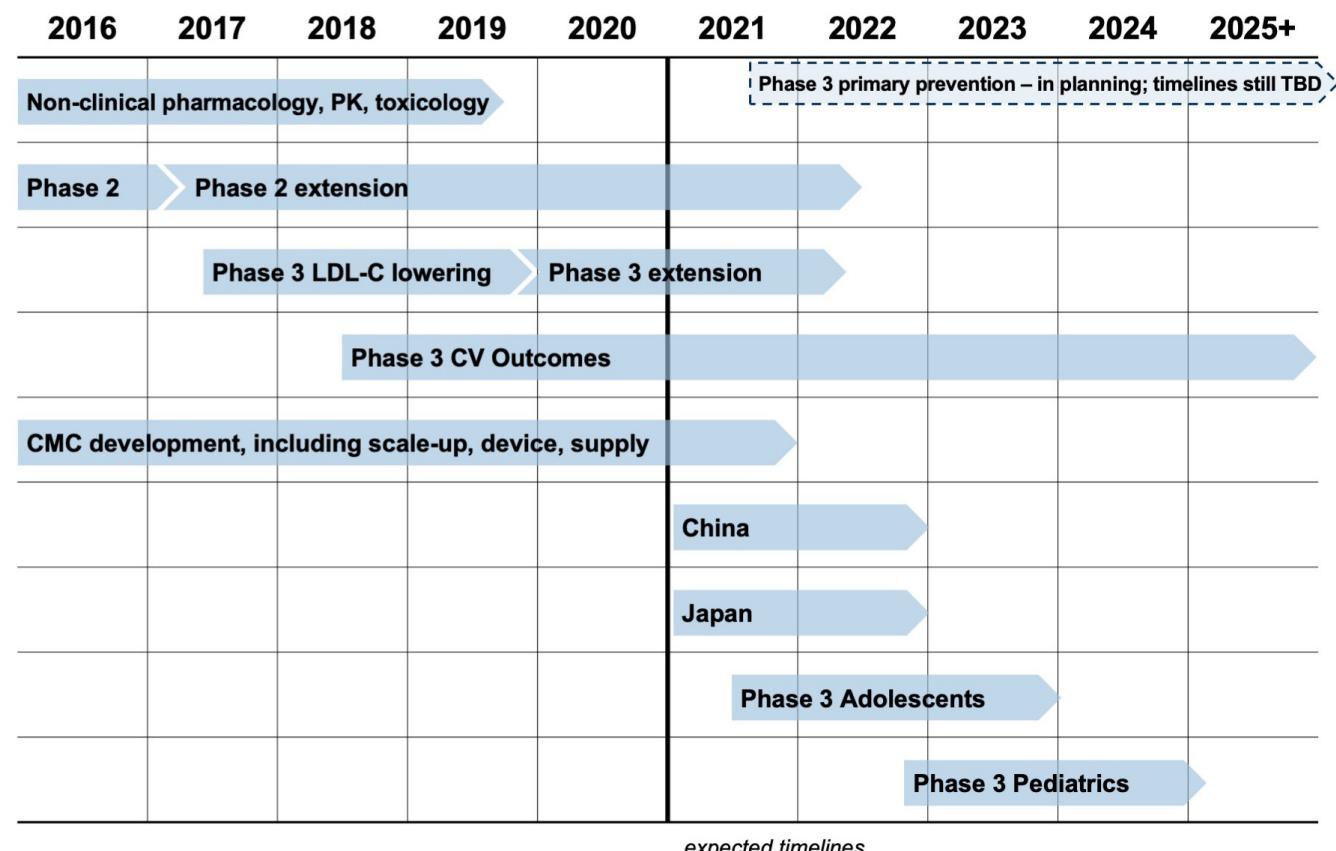
3. Major Adverse Cardiovascular Events.

# Inclisiran is supported by a robust clinical program

12 trials in 20 countries with more than 19,000 patients involved

## Phase 3 pivotal trials

- ORION-9, -10 and -11 trials are multicenter, double-blind, randomized, placebo-controlled, 18-month studies
- Primary endpoints met in all three trials
- Effective and sustained LDL-C reduction up to 52% with only two doses a year<sup>1†</sup>
- Safety comparable to placebo except for injection site reactions



<sup>†</sup> Given as an initial dose, again at 3 months, and then every six months thereafter.

1. Ray KK et al. N Engl J Med. 2020;382(16):1507-1519.

# Pelacarsen

## (TQJ230)

Antisense oligonucleotide  
for the reduction of  
lipoprotein(a)

Phase 3

### Key highlights

- Pelacarsen is an antisense oligonucleotide expected to be the first disease modifying treatment for elevated Lp(a), which is expected to reduce CV risk
- Pelacarsen addressable target population in G7<sup>1</sup> ~8m
- Ph2b data showed potent and consistent reduction of Lp(a) with a good tolerability and safety profile
- Lp(a) Heritage – prevalence trial (N ~45,000) – recruitment ongoing and readout expected in 2021
- Lp(a) Horizon - Ph3 cardiovascular outcome trial (N ~7,680; pelacarsen 80mg monthly subcutaneous injection; patient self-administered) - recruitment on track for completion in 2021. Trial readout expected 2024

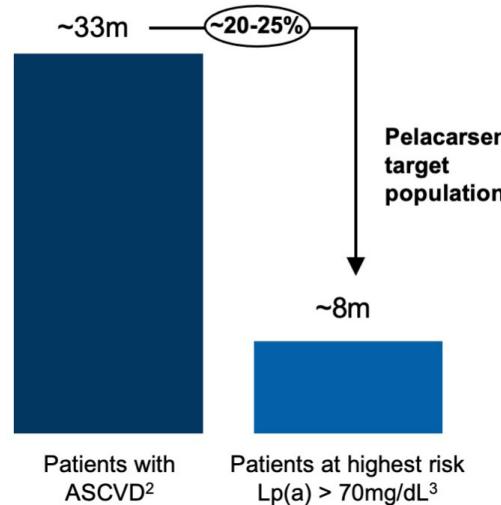
1. Potential patients defined by the population studied in Lp(a)HORIZON: patients with elevated Lp(a) and MI, stroke or PAD. Potentially eligible population dependent on trial results and label.

# Pelacarsen has blockbuster potential and would be the first treatment for high-risk patients with elevated lipoprotein(a)

## High unmet need - no treatments today

- 1 in 5 people have elevated Lp(a)<sup>4</sup>
- No approved treatment to lower Lp(a) CV risk<sup>5</sup>
- Lp(a) is inherited and cannot be addressed by diet and exercise
- Current lipid lowering therapies have limited impact on Lp(a)

## Potential eligible patients G7<sup>1</sup>



## First to market with blockbuster potential

- Pelacarsen is a novel antisense oligo therapy targeting Lp(a)
- It would be the first therapy to treat Lp(a) CV risk
- Novartis is committed to ASCVD and pioneering innovation for patients with Lp(a)

<sup>1</sup> 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. <sup>2</sup> US AHA (Heart Disease & Stroke Stats 2018 update), EU5 & JP Kantar Health EPI database, DRG Database, REACH Registry. ASCVD: Atherosclerotic cardiovascular disease. <sup>3</sup> Odyssey Outcome Trial. Estimates vary based on regional/ethnic variability. <sup>4</sup> Nordestgaard et al. Eur Heart J. 2010 Dec;31(23):2844-53. <sup>5</sup> Tsimikas S. J Am Coll Cardiol. 2017;69:692-711.

# Pelacarsen: An innovative approach to reducing Lipoprotein(a)

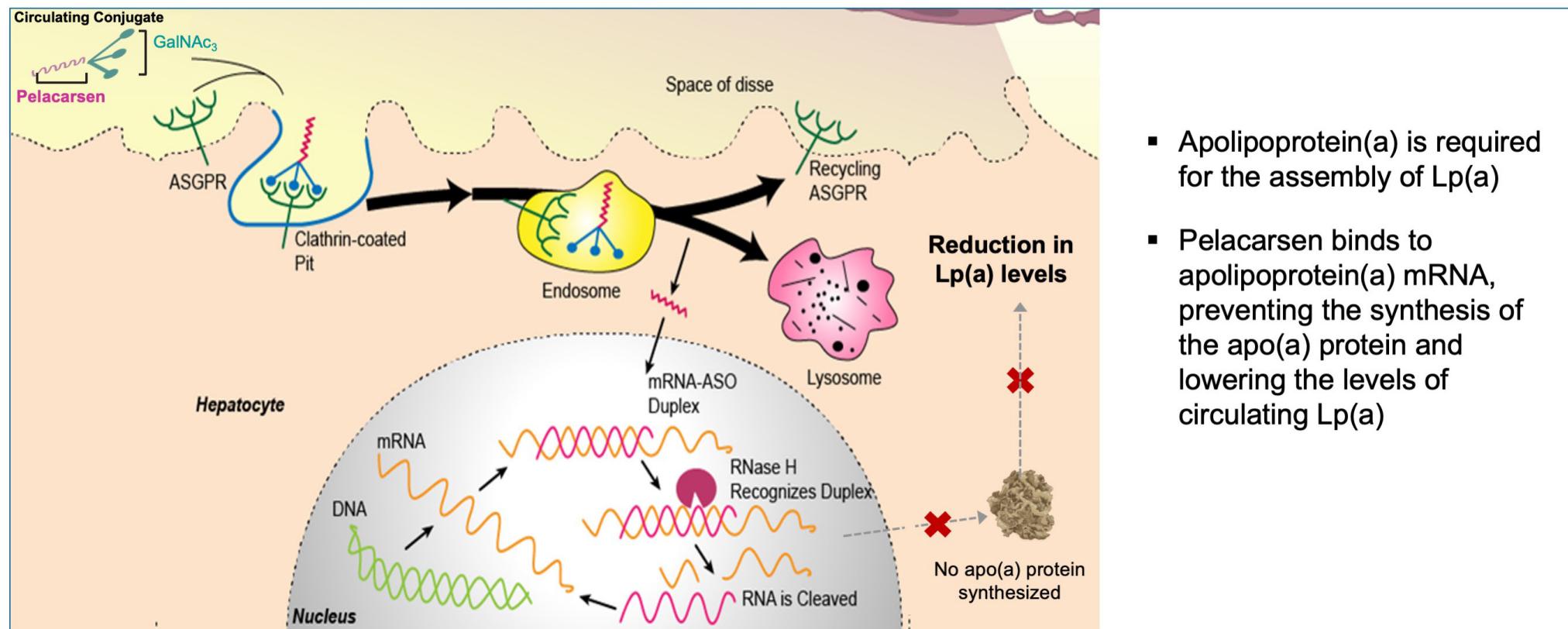
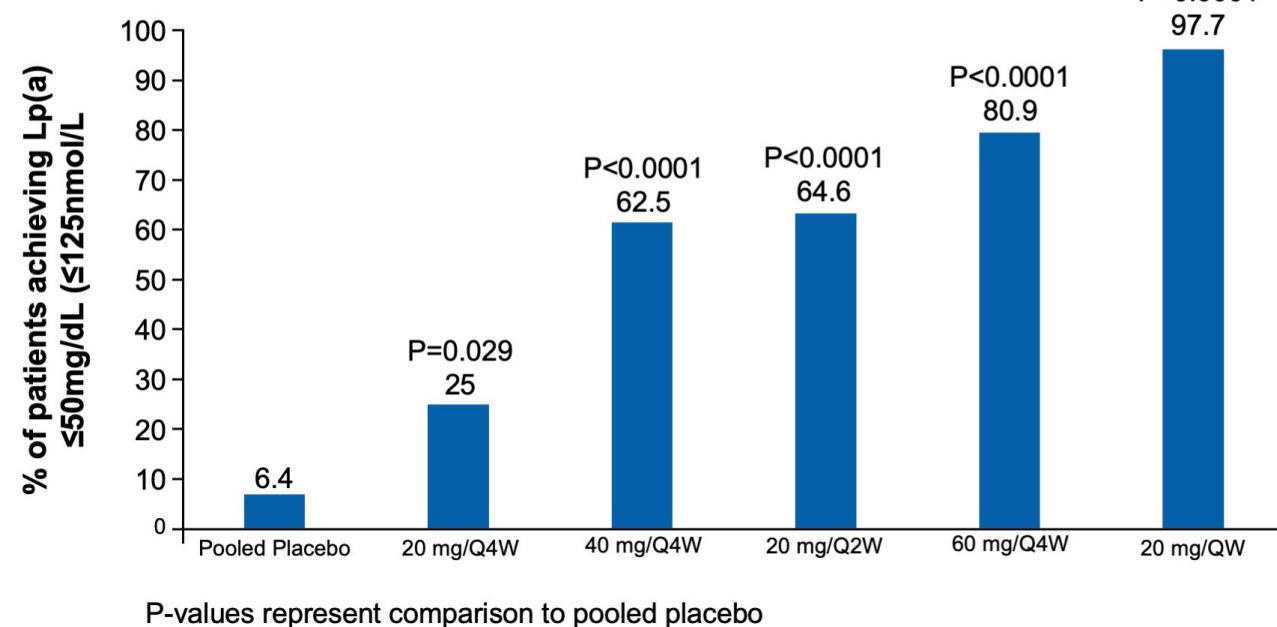


Illustration of Pelacarsen mechanism of action.

# In Phase 2b, pelacarsen significantly reduced Lp(a) in CVD patients<sup>1</sup>

## Ph2b results – pelacarsen vs. placebo

NEJM Tsimikas, et al. 2020



Ph2b data showed<sup>1</sup>:

- 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

CVD, cardiovascular disease; Lp(a), lipoprotein (a); QW, once a week. 1. Tsimikas, et al. N Engl J Med. 2020;382(3):244-255.

# Prevalence study and Ph3 outcome study ongoing with expected readouts in 2021 and 2024

## Prevalence study



- Study to evaluate prevalence of elevated Lp(a) levels in patients with established CVD
- ~45,000 patients, > 900 sites in 48 countries
- Study initiated April 2019
- Study results expected 2021

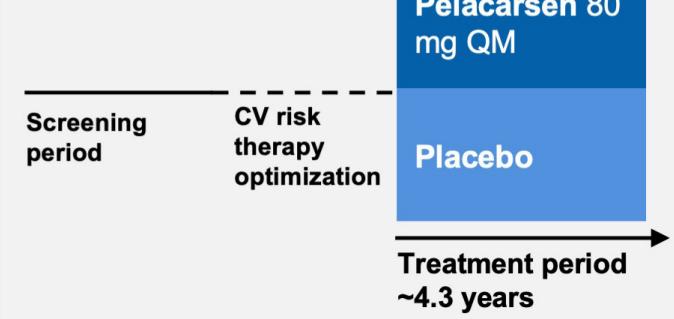
## Phase 3 outcome study



- CV outcome trial to assess effect of pelacarsen on MACE in patients with established CV disease and elevated Lp(a) on optimal therapy for other risk factors<sup>1</sup>
- Pioneering trial to evaluate impact of Lp(a) lowering on CV outcomes
- Study initiated December 2019
- Primary outcome: 2024

## Trial Design

Target N: 7680



CV, cardiovascular; MACE, major adverse CV events; Lp(a), lipoprotein (a). 1. <https://clinicaltrials.gov/ct2/show/NCT04023552>.

# Iptacopan (LNP023)

Low molecular weight  
Factor B inhibitor targeting  
the alternative complement  
pathway

Phase 2

## Key highlights

- In parallel development for five rare diseases including four in nephrology and one in hematology
- Positive Ph2 results presented at EBMT<sup>1</sup> for paroxysmal nocturnal hemoglobinuria (PNH) and at ASN<sup>2</sup> for C3 glomerulopathy (C3G)
- PRIME designation for C3G and five orphan drug designations granted
- First Ph3 planned to start December 2020 (investigated as monotherapy in PNH) followed by others in H1 2021
- First filings expected 2023 to support outlook with multi-billion potential
- Differentiated profile as potential first effective and safe anti-complement therapy with a convenient oral delivery

1. EBMT = Annual Meeting of European Society for Blood and Marrow Transplantation. 2. ASN = American Society of Nephrology Annual Meeting.

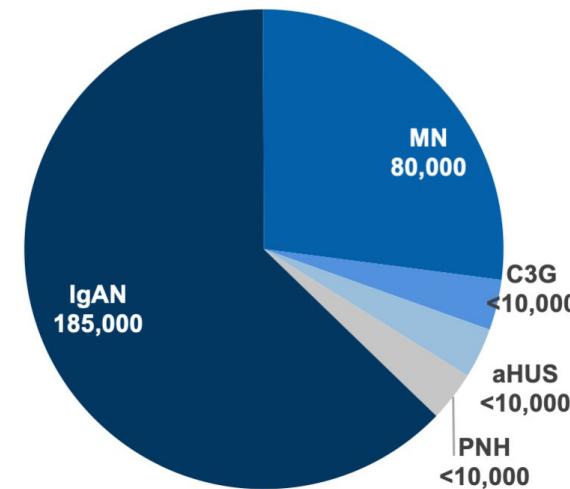
# Iptacopan: First-in-class factor B alternative pathway inhibitor

In parallel targeted development for four complement driven rare renal diseases and PNH

## High unmet need - limited treatment options

- Complement driven renal diseases (CDRD) mostly affect young adults
- Current SoC: Non-specific immuno-suppressants with limited clinical evidence and significant side effects
- 20-50% of patients progress to ESRD<sup>1</sup> within 10-20 years
- IgAN: leading cause of ESRD (dialysis/transplant) in young adults
- PNH: Many patients suffer from anemia and remain transfusion dependent despite anti-C5 therapy

## Number of patients with Targeted CDRD<sup>2</sup> in the US



## First-in-class blockbuster potential

- Iptacopan is a first in class factor B inhibitor of the alternative complement pathway
- Poised to slow progression to ESRD in complement driven renal diseases
- Positive Ph2 results in C3G, PNH
- Targeted approach in high risk IgAN patients with persistent proteinuria ≥1g/day
- Part of Novartis commitment to deliver transformative therapies to patients with renal diseases

1. End-stage Renal Disease (ESRD). 2. IgA Nephropathy (IgAN), C3 Glomerulopathy (C3G), atypical Hemolytic Uremic Syndrome (aHUS), Membranous Nephropathy (MN) and Paroxysmal Nocturnal Hemoglobinuria (PNH).

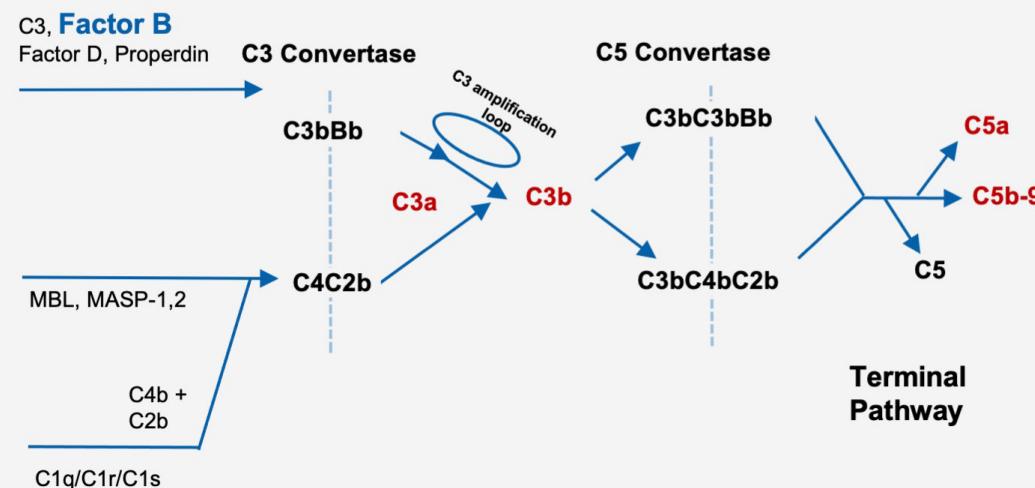
# Factor B inhibition in complement driven renal diseases

## A targeted approach to reduce injury in inflammatory renal diseases

### Complement Cascade in Renal Diseases

#### Alternative Pathway

- Atypical HUS
- C3 Glomerulopathy
- IgA Nephropathy



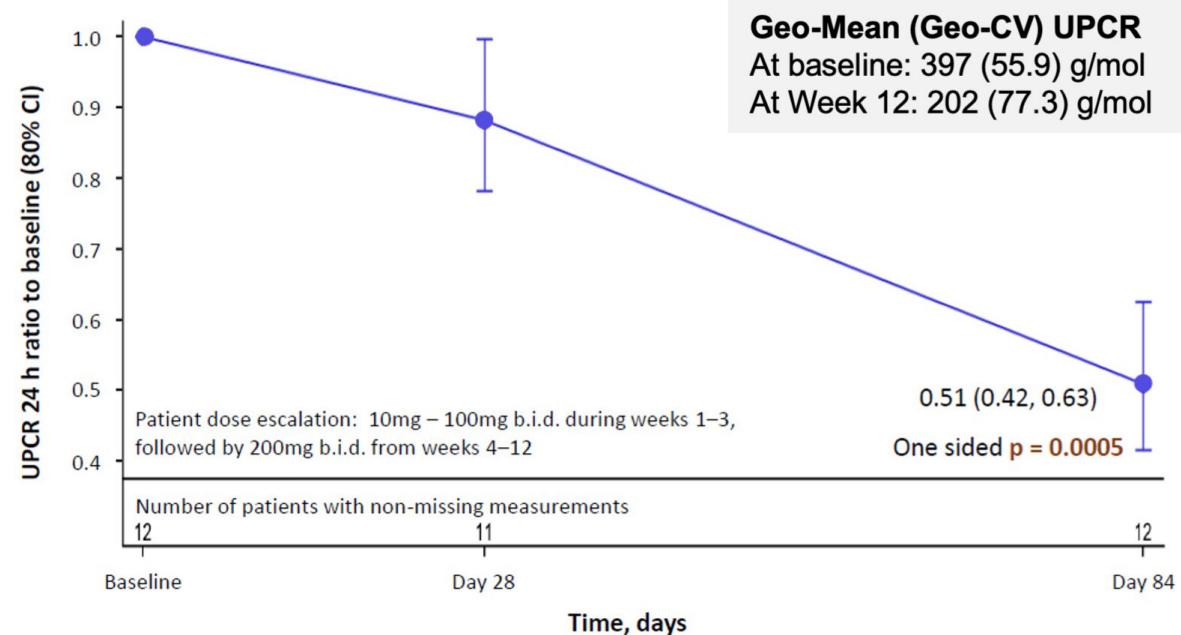
- The complement system is a critical part of the innate immune response
- Complement dysregulation can cause kidney injury
- Dysregulation of alternative complement pathway is associated with a range of glomerular diseases including IgAN, C3G and aHUS

Joshua M. Thurman, and Carla M. Nester, CJASN 2016;11:1856-1866.

# Iptacopan in C3 glomerulopathy (C3G)

Promising efficacy and favorable safety and tolerability profile seen in Ph2

## UPCR (24h urine collection) vs. baseline over time

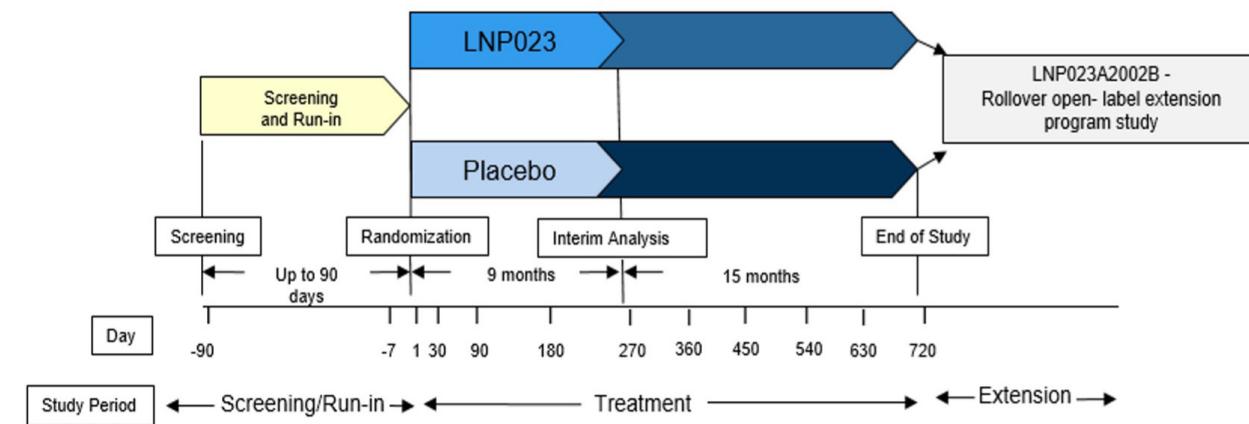


- Iptacopan reduces complement alternative pathway activity
- 49% reduction in UPCR from baseline as well as stabilization of eGFR at 3 months
- Well tolerated with no unexpected or new safety findings

# Iptacopan in IgA Nephropathy (IgAN)

Potential to slow progression to dialysis and renal transplant

## Phase 3 design (n=450)



- Adult IgAN patients with UPCR  $\geq 1\text{g/g/day}$  despite optimal RAAS blockade
- Primary Endpoint: Proteinuria reduction from baseline at 9 months (IA); Annualized eGFR slope over 2-year follow-up (EoS)

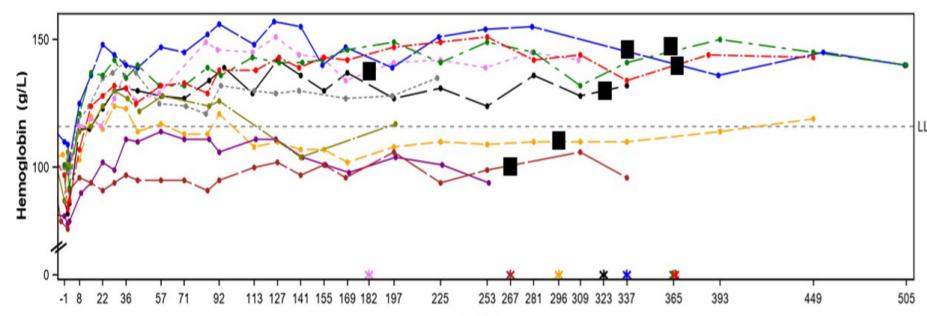
- Blinded IgAN Ph2 interim results passed futility, full primary endpoint results available Q1 2021
- FDA and EMA recognize proteinuria at 9 months as surrogate marker for accelerated/ conditional approval
- Initiation of Ph3 planned for Q1 2021

# Iptacopan in Paroxysmal Nocturnal Hemoglobinuria (PNH)

Superior efficacy and oral RoA; alternative treatment choice to current/future SoC

## PNH Ph2 Transfusion-free Hb increase<sup>1</sup>

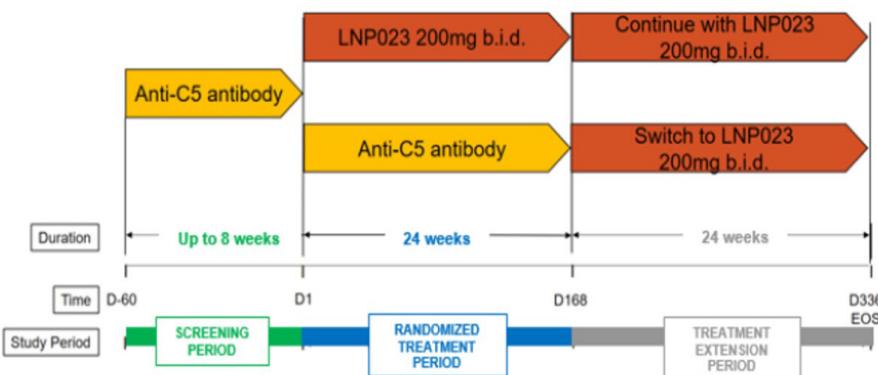
### Individual time profiles of hemoglobin (g/L)



■ Represents the last dose of eculizumab

- Add-on: improved hematological response (Hb ↑); maintained on monotherapy
- Monotherapy (in anti-C5 naive patients; not shown): >60% LDH reduction in all patients
- Lab parameter normalization indicates control of intra- and extravascular hemolysis

## PNH Ph3 design (LNP023 studied as monotherapy)



Adult PNH patients with residual anemia (Hgb <10g/dL) despite stable anti-C5 therapy in last six months

### Primary Endpoints:

- % of patients achieving increase in Hgb  $\geq 2$ g/dL from baseline in the absence of RBC transfusion
- % of patients achieving Hgb  $\geq 12$ g/dL in the absence of RBC transfusion

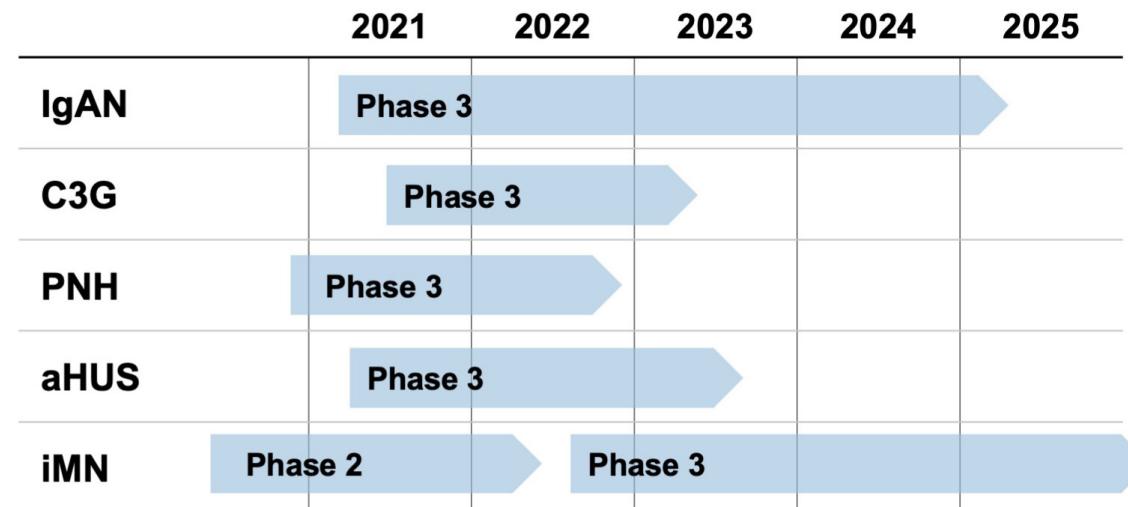
1. Colored lines represent single individuals; colored asterisks the last dose of eculizumab. The lower panel shows hemoglobin levels during combination – and LNP023 monotherapy after withdrawal of eculizumab. LLN – lower limit of normal.

# Iptacopan (LNP023) development program

First-in-class potential across a range of complement driven diseases

## Market potential

Indication	US prevalence thousands
<b>Nephrology</b>	
IgAN	~185
MN	~80
C3G	<10
aHUS	<10
<b>Hematology</b>	
PNH	<10



- Ph3 studies in four indications projected to start between December 2020 (PNH) and mid-2021
- IgAN and PNH Ph3 study designs agreed with HAs; C3G and aHUS Ph3 studies under discussion with HAs
- IA in IgAN Ph3 study potentially supports filing for accelerated / conditional approvals based on proteinuria reduction
- Anticipated worldwide filings as of 2023 with projected blockbuster sales potential
- Additional specialty indications under consideration

IgA Nephropathy (IgAN), Membranous Nephropathy (MN), C3 Glomerulopathy (C3G), atypical Hemolytic Uremic Syndrome (aHUS), and Paroxysmal Nocturnal Hemoglobinuria (PNH).

# Neuroscience

**Kesimpta®**

**Branaplam**



Click to view  
**MNM Agenda**

## Kesimpta® (ofatumumab)

Anti CD20 monoclonal antibody targeting B-Cells with a monthly 20mg sc dosing

Marketed in US

### Key highlights

- Kesimpta® demonstrated high efficacy in both Ph3 trials ASCLEPIOS I and II:
  - Patients treated with Kesimpta® experienced on average only 1 relapse every 10 patient-years<sup>4</sup>
  - 9/10 patients had no evidence of disease activity (NEDA-3) in year 2 in post hoc analysis<sup>5</sup>
- Kesimpta® is approved in the US for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Over 700k people living with RMS in major markets with over 300k in the US alone<sup>1</sup>
- The US MS market has grown to USD 15bn<sup>2</sup> in 2019
- B-cell therapies expected to account for 34% share in key markets by 2025<sup>3</sup>
- Ongoing regulatory activities in major regions and countries (EU, Japan and China)
- Ongoing long-term safety and efficacy extension study as well as a broad medical affairs and pediatric program to supplement current data for Kesimpta® over the next 5 - 10 years

Sources: 1. Calculated based on actual IQVIA SU data validated through DRG Epi database and secondary research. RMS includes CIS, RRMS, aSPMS. 2. Evaluate Pharma, net sales. 3. DRG Disease Landscape & Forecast | Market Forecast Dashboard 2018 | Key markets: US, Germany, France, Italy, Spain, UK, and Japan. 4. Assumes EDSS-confirmed relapses, based on ASCLEPIOS I & II studies. 5. Hauser S.L. et al. Ofatumumab vs Teriflunomide in Relapsing Multiple Sclerosis Analysis of No Evidence of Disease Activity (NEDA-3) from ASCLEPIOS I and II Trials. Poster presented at EAN, 23-26 May 2020 LB62. Class definition: Orals – (S1P, Tecfidera, Vumerity, Mavenclad, BTK inhibitors, Ibdilast), BRACE (Recombinant interferon-betas, Polypeptides), B-cell (Anti-CD20 monoclonal antibodies), Other mAbs (Tysabri, Lemtrada). Future launches in DRG forecast: BTK inhibitors (2025), Ibdilast (2026).

## Kesimpta® early US launch indicators are positive

Potential to become a 1<sup>st</sup> choice high efficacy DMT for patients, physicians and payers

### HCP engagement translating into adoption

**95%+**

(~6,000) of MS prescribing targets reached

**95%**

of field force territories have adopted Kesimpta®

**5.2%<sup>1</sup>**

NBRx share just 10 weeks post launch

### Securing rapid and broad access

- Commercial bridging program
- Engagement plans ongoing and on-track
- 44% (~90M) of total US commercial lives coverage
- CVS Caremark & Aetna, ESI, and Anthem commercial formularies
- Early Medicare wins in plans such as BCBS of MA

### Patient initiation seen as simple, easy and fast

- Favorable customer feedback from HCPs and patients

**2020**

**Focus on demand and patient initiations**

**Free goods** enabling rapid initiation and account for majority of initial demand

**NBRx uptake and early payor access** key lead indicators

1. IQVIA reported NBRx week ending October 30, 2020.

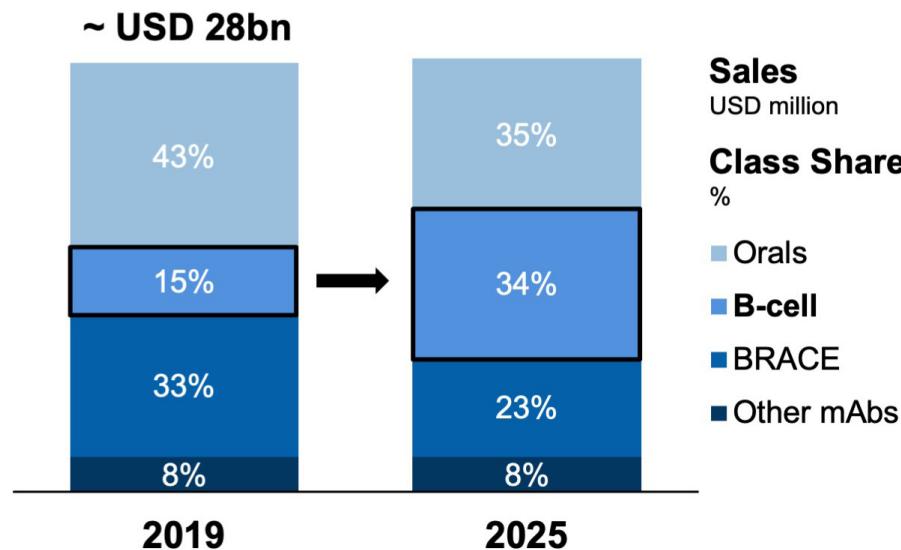
## B-cell share of MS market expected to double within the next five years

Over 700k<sup>1</sup> people living with RMS in major markets (2019) with frequent switching among classes and brands

 **US** 317k RMS diagnosed

 **EU5** 420k RMS diagnosed

WW MS market expected to remain flat; B-cell share expected to double by 2025

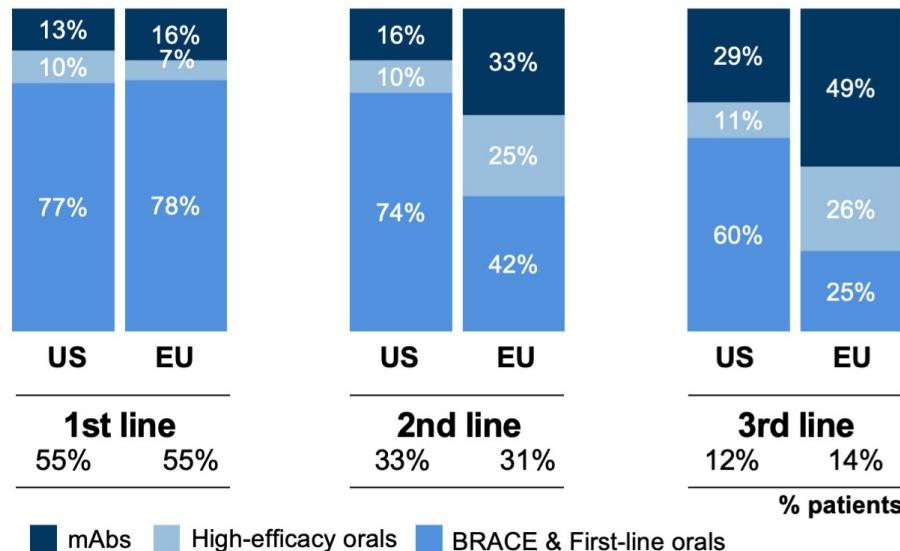


1. Calculated based on actual IQVIA SU data validated through DRG Epi database and secondary research. RMS includes CIS, RRMS, aSPMS. DRG Disease Landscape & Forecast. Analysis includes Key markets: US, Germany, France, Italy, Spain, UK, and Japan. Future launches in DRG forecast: BTK inhibitors (2025), Ibdilast (2026). 2. Class definition: Orals – (S1P, Tecfidera, Vumerity, Mavenclad, BTK inhibitors, Ibdilast), BRACE (Recombinant interferon-betas, Polypeptides), B-cell (Anti-CD20 monoclonal antibodies), Other mAbs (Tysabri, Lemtrada).

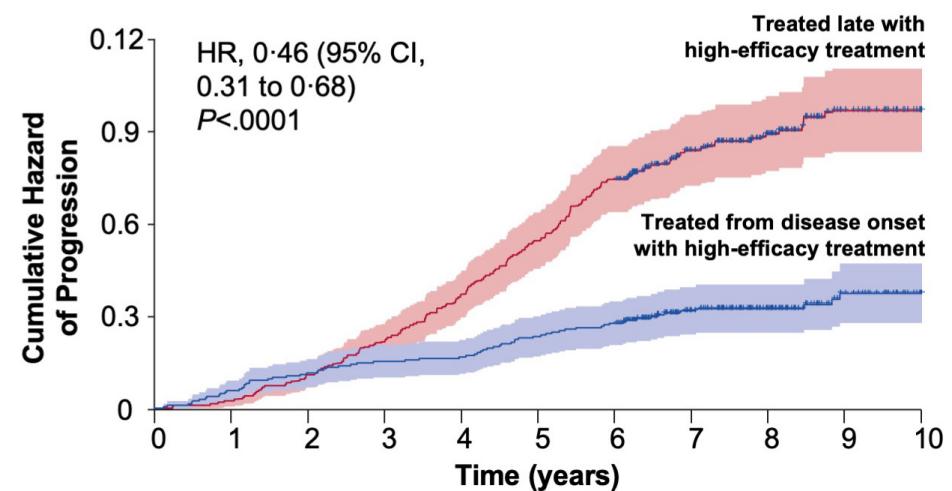
## BRACE and first-line orals commonly used in early stages

Despite data showing high-efficacy treatments started early result in better outcomes

### Use of disease-modifying treatments in MS<sup>1</sup>



### Cumulative hazard of CDP in patients with RRMS treated from disease onset versus late with high-efficacy treatment<sup>2</sup>



**MAbs:** Ocrevus®, Lemtrada®, Tysabri®; **High-efficacy orals:** Gilenya®, Mayzent®, Mavenclad®; **BRACE & First-line orals:** Interferons, Copaxone®, GA Gx; Tecfidera®, Aubagio® \*High efficacy DMTs may include orals and MAbs  
1. Symphony APLD (Sep 2018-Aug 2019). , EU5 IPSOS Monitor 2019. 2. He A et al. Lancet Neurol. 2020;19(4):307-316. Retrospective analysis, measured from disease onset. Bold lines are cumulative hazard estimates and shaded areas are 95% CIs. CDP, confirmed disability progression; CI, confidence interval; HR, hazard ratio; RMS, relapsing multiple sclerosis.

## Patients value high efficacy treatments that balance safety, convenience and have easier access

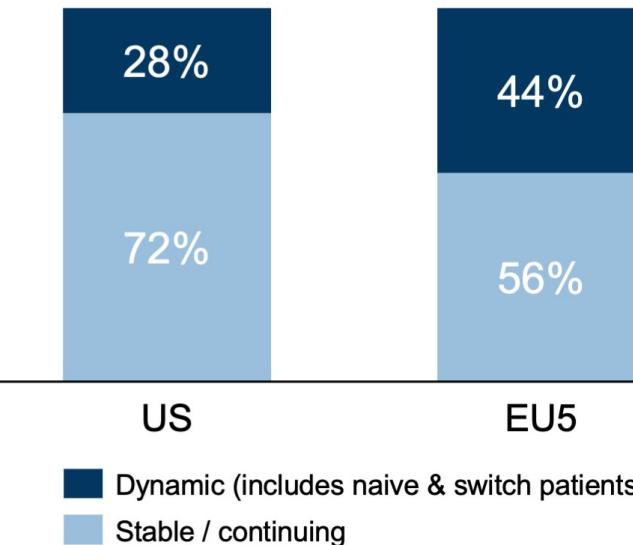
**44% of people with MS aren't satisfied with today's treatments<sup>1,2,3</sup>**

**44%**  
not satisfied

**Due to:**

- Lack of efficacy**
- Side-effects/ tolerability issues
- Treatment burden
- Direct costs of treatments and testing
- Indirect costs of time commitments

**Resulting in frequent switching (2019)<sup>1,4</sup>**



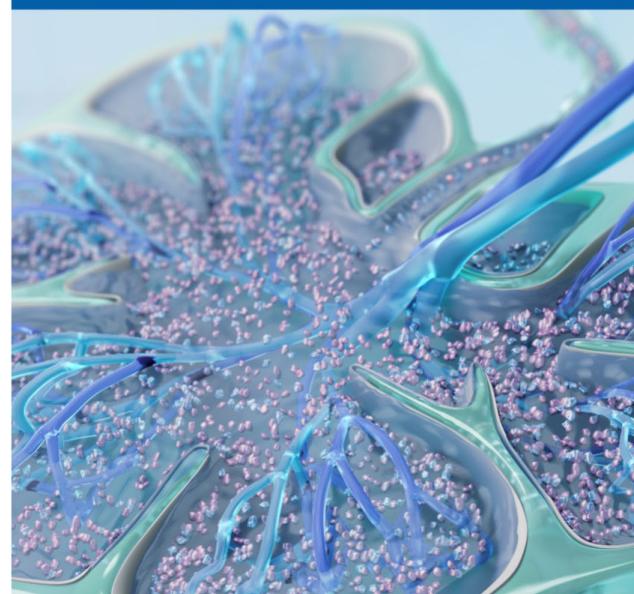
1. EU5 IPSOS Monitor Q4 2019 (Patients dissatisfied with current Oral, Injectables, and IV medications). 2. Ipsos Patient Panel: treatment experience and satisfaction 2019. 3. MS Patient Journey research 2019. 4. US Symphony APLD data 2019.

# Kesimpta® was designed to address the needs of treating physicians and people living with MS

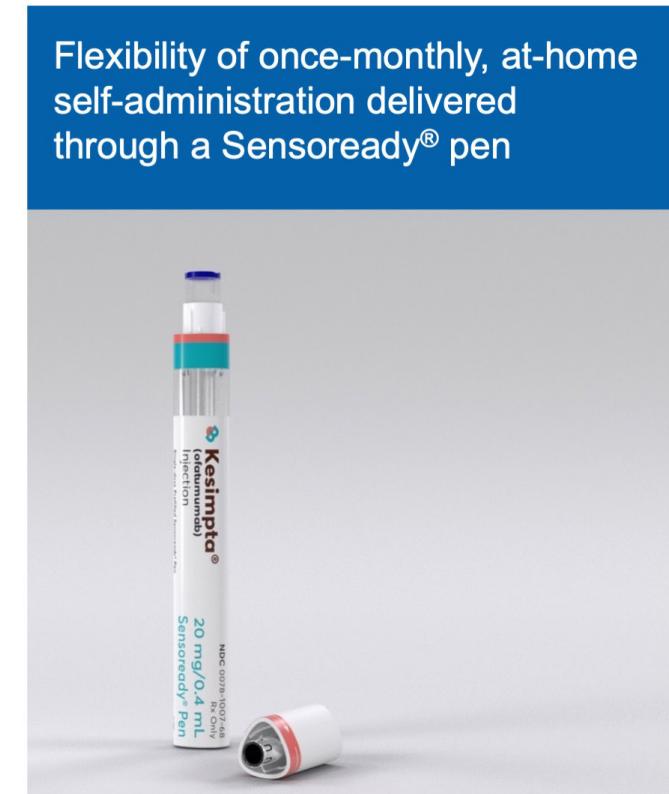
Unique mode of binding and s.c. dosing delivering high efficacy



Precise B-cell depletion in the lymph nodes, sparing the spleen, helps maintain immune function



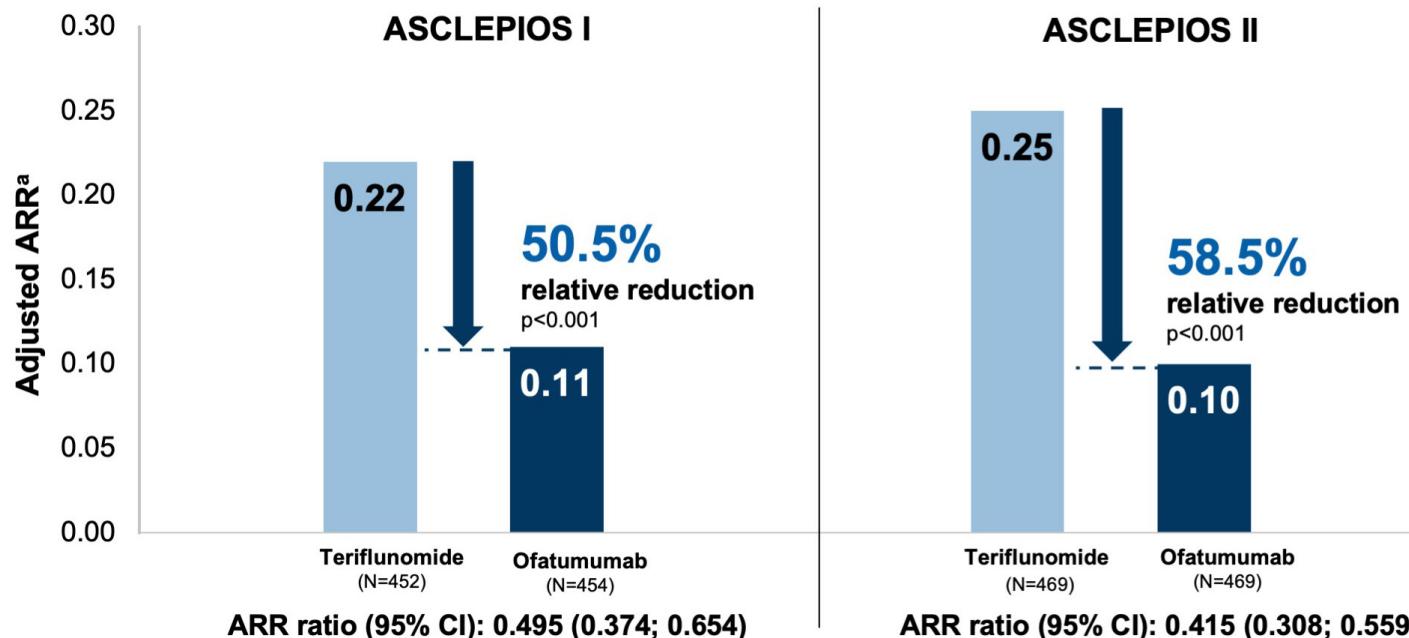
Flexibility of once-monthly, at-home self-administration delivered through a Sensoready® pen



1. Assumes EDSS-confirmed relapses, based on ASCLEPIOS I & II studies.

2. Hauser S.L. et al. Ofatumumab vs Teriflunomide in Relapsing Multiple Sclerosis Analysis of No Evidence of Disease Activity (NEDA-3) from ASCLEPIOS I and II Trials. Poster presented at EAN, 23-26 May 2020 LB62.

# Kesimpta® demonstrated up to nearly 60% reduction in relapses (ARR) vs. teriflunomide



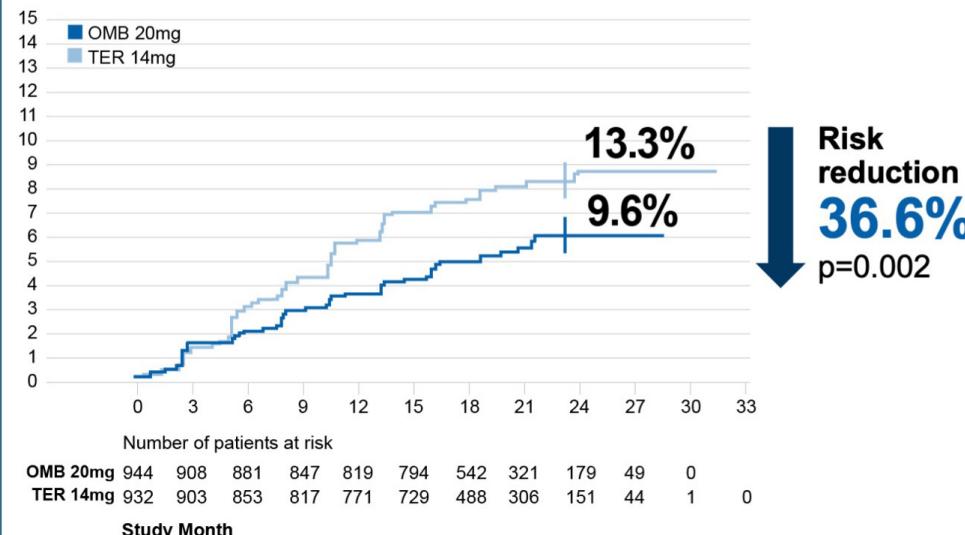
**Patients treated with Kesimpta® (ofatumumab)**  
experienced on average only 1 relapse every 10 patient-years<sup>1</sup>

**9/10 patients on Kesimpta®**  
had no evidence of disease activity (NEDA-3) in year 2 in post hoc analysis<sup>2</sup>

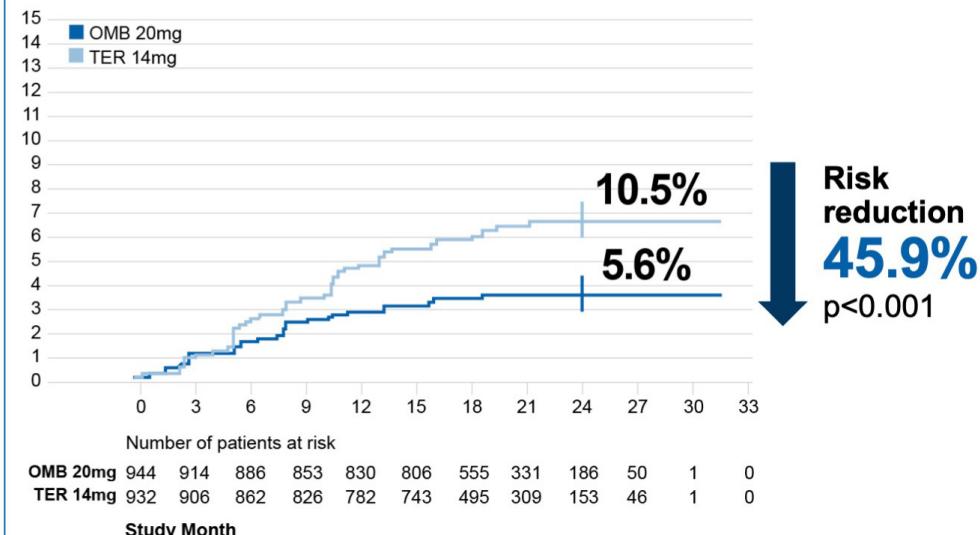
Full analysis set. Primary endpoint. <sup>a</sup>Negative binomial regression model. N, Total number of patients included in the analysis. ARR, annualised relapse rate; CI, confidence interval. Source: Kappos et al., AAN 2020, Versus Teriflunomide in Patients with Relapsing Multiple Sclerosis: Phase 3 ASCLEPIOS I and II Trials. 1. Assumes EDSS-confirmed relapses, based on ASCLEPIOS I & II studies. 2. Hauser S.L. et al. Ofatumumab vs Teriflunomide in Relapsing Multiple Sclerosis Analysis of No Evidence of Disease Activity (NEDA-3) from ASCLEPIOS I and II Trials. Poster presented at EAN, 23-26 May 2020 LB62.

# Kesimpta® showed 37% and 46% reductions in 12 and 24-week CDW1 vs. teriflunomide

## 12-week CDW2



## 24-week CDW2



Hazard ratio (95% CI): 0.634 (0.472; 0.851)

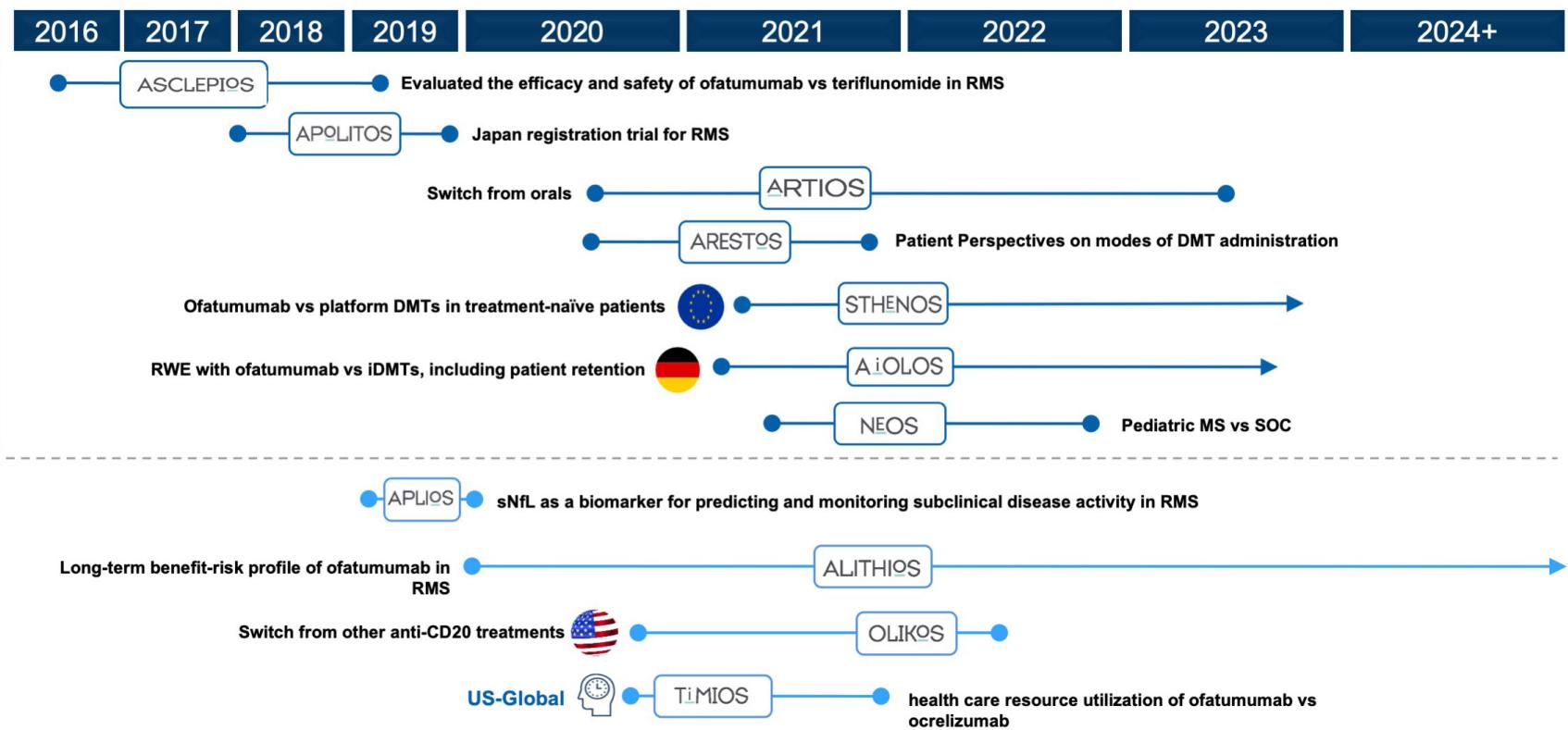
Hazard ratio (95% CI): 0.541 (0.381; 0.768)

1. CDW = Confirmed Disability Worsening. 2. Post-hoc analysis with revised definition, adapted from the OPERA trials, Hauser et al. 2017. A disability "progression" was defined as an increase from the baseline EDSS score of at least 1.0 point (or 0.5 points if the baseline EDSS score was >5.5) that was sustained for at least 12 (24) weeks.

# The AXIOS program<sup>1</sup> can further establish Kesimpta® as a first-choice high efficacy DMT for patients, physicians and payers

Support broad access and outcomes for treating physicians and MS patients

Supporting payers and efficiency in healthcare systems



1. The overall program and individual trials have been given Greek names, establishing a link to the pivotal trial, ASCLEPIOS. Note that every name ends with OS, which stands for 'Ofatumumab subcutaneous'. DMTs, Disease-modifying therapies; RMS, relapsing multiple sclerosis; s.c., subcutaneous; sNFL, serum neurofilament light chain; SOC, standard of care, iDMTs: injectable Disease-modifying therapies.

# Kesimpta® has the potential to become a 1<sup>st</sup> choice, high efficacy DMT for patients, physicians and payers

## For patients who want ...

### High efficacy

without treatment burden impacting their lives

Flexibility of at-home self-administration



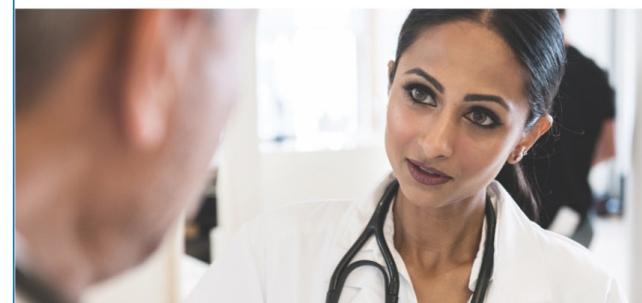
## For physicians who want...

### High efficacy

that balances safety

An easily administered, subcutaneous solution requiring no premedication

To avoid reliance on infusion infrastructure



## For payers who want...

### High efficacy

that is competitively priced to reflect its unique value and ensure broad access

An at-home treatment with no added medical costs



# Branaplam

## (LMI070)

Orally administered, small molecule RNA splicing modulator

Phase 1

### Key highlights

- In development for Huntington's disease (HD) and Spinal Muscular Atrophy (SMA), two devastating rare neurodegenerative diseases
- Multiple data readouts and next steps in H1 2021:
  1. Readout of ongoing Ph1 single-ascending dose study in adult healthy volunteers to inform Huntington's disease program
  2. Start of Ph2b dose range finding study in Huntington's disease
    - Goal: Identify dose which reduces mHTT sufficiently to provide clinical benefit while maintaining adequate levels of HTT for normal function
  3. Publication of results from ongoing Ph1/2 study in SMA

# 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 disease
- Patients typically diagnosed between 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

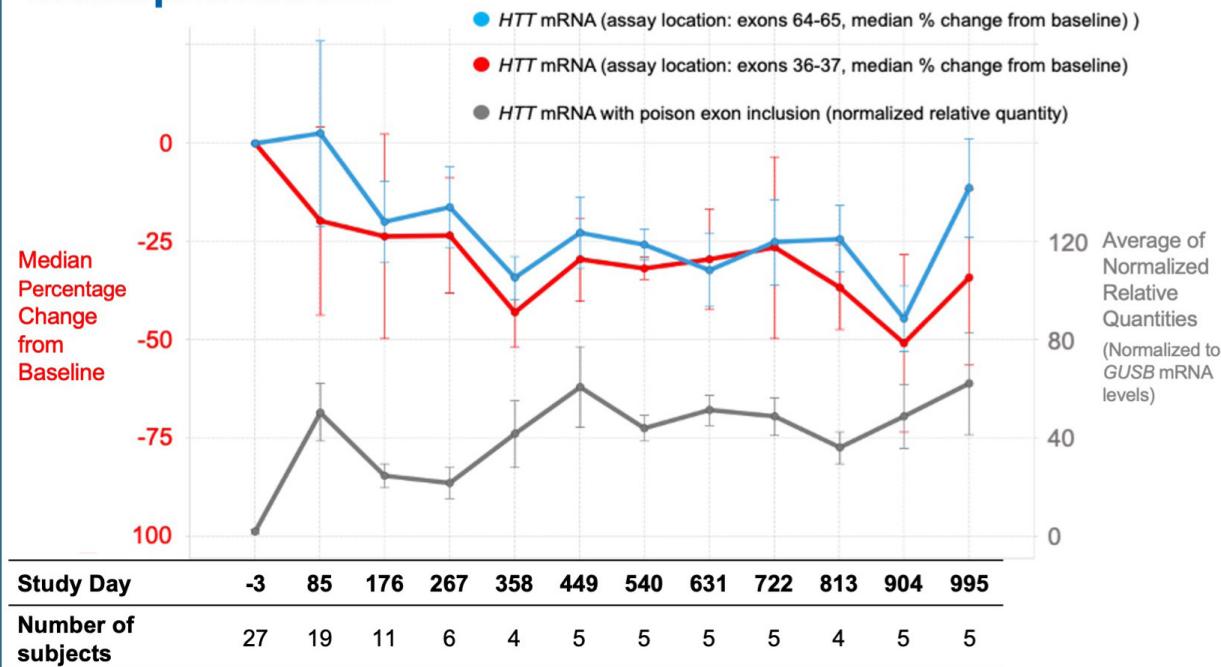
### Branaplam

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

## Ph2b in Huntington's Disease to begin in 2021

Ongoing Ph1 will readout in H1 2021 and inform development program

### Branaplam lowering of HTT mRNA in SMA patients led to development in HD



### Early stage program of novel MoA

Preclinical and clinical data provide proof of concept in HD

Branaplam lowers:

- HTT transcript and protein in vitro
- HTT transcript and mutant HTT protein levels in BacHD mice<sup>1</sup>
- HTT mRNA in SMA patients

### Market potential

Indication

Huntington's Disease

Market size (USD)



●○○ <500m

●●○ <500m – 1bn

●●● >1bn

1. Branaplam does not affect endogenous mouse HTT, the effect is specific to human HTT.

# Readout of Ph1/2 study in Spinal Muscular Atrophy in H1 2021

Preliminary data from ongoing study support continued development

## Ongoing Ph1/2 LMI070X2201 study in T1 SMA

	Part 1 <b>Dose finding and safety</b>	Part 2 <b>Safety and efficacy</b>	Part 3 <b>Long-term follow-up</b>
	COMPLETE	COMPLETE	ONGOING
<b>Objectives</b>	Safety, tolerability, PK, PD after 13 weeks of multiple oral doses of branaplam  Safety and efficacy follow-up	Safety, tolerability, growth and efficacy of two doses of branaplam over 52 weeks	Long-term safety and efficacy follow-up in patients from Parts 1 and 2
<b>Patients</b>	13 infants	25 infants	29 patients rolled over 27 currently treated

Preliminary data from Parts 1 and 2 suggest positive benefit:risk in SMA

Maximum exposure > 60 months

Effects on safety, tolerability, growth, motor function support continued study

Weekly oral doses are well-tolerated

Adverse events are mild to moderate, reversible and manageable and consistent with underlying disease

Development options being considered to improve outcomes in SMA

# Ophthalmology

Beovu®

Click to view  
**MNM Agenda**



# Beovu®

## (brolucizumab, RTH258)

Humanized single-chain  
Fv antibody fragment  
inhibitor of VEGF

Marketed; LCM in Phase 3

### Key highlights

#### Launch progressing in wAMD

- Approved in >50 countries incl. top 10 markets and 10 Emerging Markets
- Label updates received in 45 countries
- Reimbursement in US, DE, JP; these markets are ~65% of total global aVEGF market today<sup>7</sup>
- US demand recovered vs. Q2, stabilized ~1,2k vials /week
- Good launch uptake in DE-JP: ~6-8% wAMD market share achieved in the first 6 months from launch<sup>5</sup>

#### Strengthening both our efficacy and safety narrative

- Correlation between fluid and vision in wAMD demonstrated in 3 brand agnostic post-hoc analyses<sup>2,3,4</sup>
  - In two H2H studies Beovu® outperformed aflibercept in achieving superior fluid resolution (IRF and/or SRF)<sup>1</sup>
- Good progress on short-term insights and potential measures that could help reduce overall risk of AEs (patient characteristics, patient monitoring, treatment)

#### Progressing clinical development in new indications

- KITE pivotal DME study reported positive top line results<sup>6</sup>
- Progressing clinical development in DME, RVO and PDR

1. Dugel P, Koh A, Ogura Y, et al; HAWK and HARRIER Study Investigators. HAWK and HARRIER: Phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology.

2. Ursula Schmidt-Erfurth et al. Presented at The Association for Research and Vision (Virtual) May 2020. 3. Jhaveri C, et al. The Retina Society 53rd Annual Scientific Meeting (Virtual) 26–29 August 2020. 4. Singh R. Presented at the European Society of Retina Specialists Meeting 2-4 (Virtual) October 2020. 5. DE 4% market Share in total/licensed anti-VEGF market. Wet AMD estimated at ~70% of the total A-VEGF market. IQVIA PADDS and DE Pharmacy unit sales – Sep 2020, Gesundheitsforen Leipzig, 2015-2018 JP 3% market Share in total/licensed anti-VEGF market. Wet AMD estimated at ~40% of the total A-VEGF market. IQVIA PADDS unit sales, NVS JP Market research 2020.

6. <https://www.novartis.com/news/media-releases/novartis-reports-positive-topline-results-from-first-phase-iii-trial-beovu-versus-aflibercept-patients-diabetic-macular-edema-dme>. 7. Internal estimates basis 2019 sales in Evaluate Pharma & IQVIA.

# In two H2H studies in wAMD, Beovu® outperformed aflibercept in achieving superior fluid resolution (IRF and/or SRF)

AMD is a leading cause of severe and irreversible vision loss worldwide<sup>1,2</sup>

Affects 10–13% of adults aged >65 years with estimated 196M cases by 2020<sup>2</sup>

A large unmet need still exists:

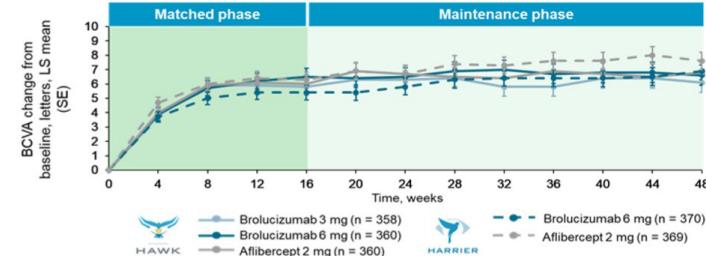
- >50% of patients have unresolved fluid<sup>3</sup>
- >50% are on less than every 8 weeks (q8w) injection intervals<sup>4</sup>

In H&H Beovu<sup>®5</sup>:

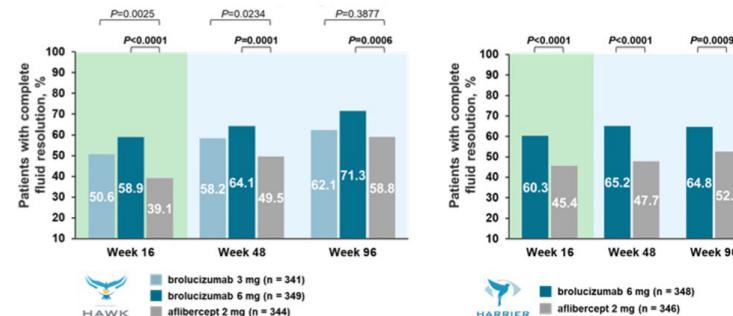
- Achieved robust vision gains
- Outperformed aflibercept in achieving superior fluid resolution (IRF and/or SRF)
- Maintained majority of patients on 12- week intervals immediately after loading through year 1

TALON and MERLIN to address new dosing regimens

## Beovu® demonstrated noninferiority to aflibercept in BCVA change from baseline at Week 48

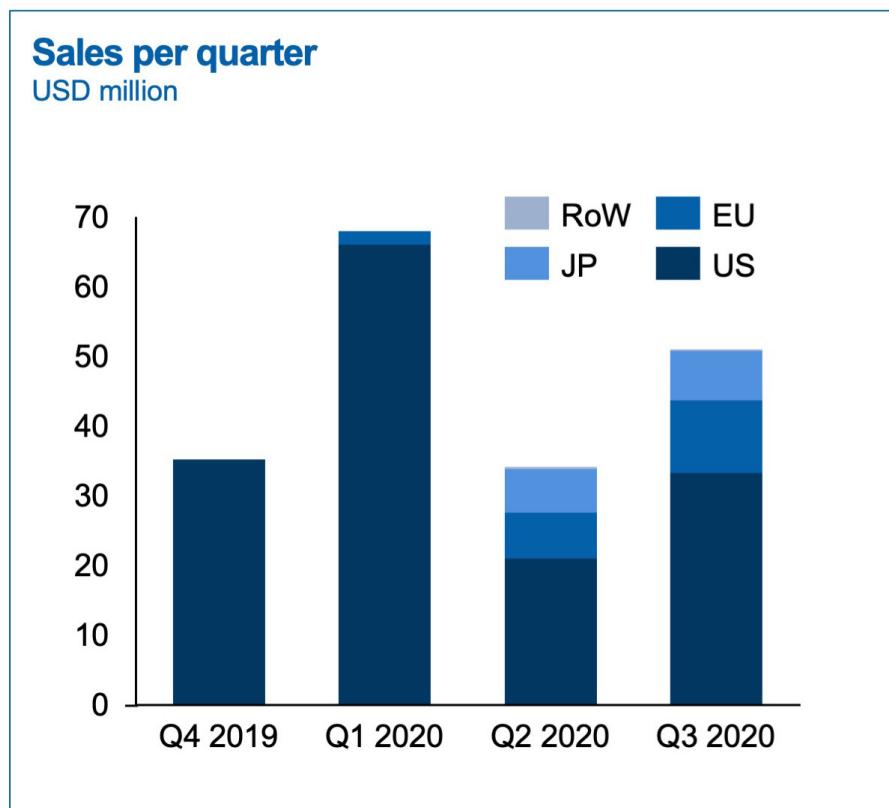


## Percentage of patients with complete fluid resolution was greater with Beovu®



AMD, age-related macular degeneration; nAMD, neovascular AMD; VEGF, vascular endothelial growth factor. 1. Schmidt-Erfurth U, et al. *Br J Ophthalmol*. 2014;98:1144-67. 2. Wong WL, et al. *Lancet Glob Health*. 2014;2:e106-e116. 3. Singer ASRS 2020. 4. MacCumber Retina Today 2020. 5. Dugel P, Koh A, Ogura Y, et al; HAWK and HARRIER Study Investigators. HAWK and HARRIER: Phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. *Ophthalmology*.

# Beovu® performance recovering after safety signal and COVID-19



## Approvals and label updates and reimbursement

- >50 MAAs received in 2020
- Safety label updates in all major geographies (45+)
- Reimbursement discussions mostly in line with expectations with some COVID delays (UK, FR)

## Markets that launched after US see good uptake

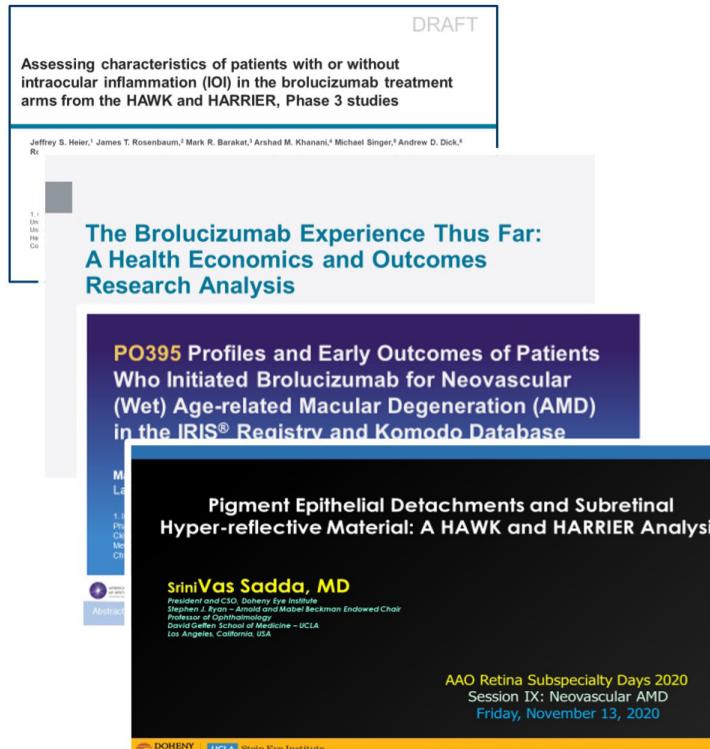
- ~6-8% wAMD market share achieved in DE-JP in the first 6 months from launch
- 20-40% share of business from naive patients<sup>1</sup>

## Further growth expected through

- Increased market penetration and geographic expansions in wAMD
- Subject to approval of additional indications (DME submission planned for Q2 2021)

1. DE: Insight Health, PIA Tool - bevacizumab data not available. JP: Based on responses of physicians in a JP monthly tracking study with limited respondent size. US: IQVIA Claims monthly data.

# New data presented at AAO (2020) for brolucizumab



- Ongoing investigations from real world data showed that patients with prior IOI and/or prior RO had highest observed risk rate for an event of IOI (including RV) and / or RO<sup>1</sup>. Similar results were seen in the RV and / or RO subgroup
- Treatment emergent ADAs (boosted and induced), but not pre-existing, may be associated with an increased incidence of RV/RO by using the conservative definition of the association<sup>2</sup>
- Additional analysis from ongoing studies are warranted to further assess findings
- In post-hoc analysis, brolucizumab 6mg is associated with greater and sustained reduction in Pigment Epithelial Detachments and Subretinal Hyper-reflective Material compared with aflibercept<sup>3</sup>
- Novartis and the Coalition are fully committed to transparently communicating all facts and findings to ensure that ECPs have the latest data
- Beovu® continues to represent an important treatment option for patients with wet AMD, with an overall favorable benefit-risk profile

1. Ip M, et al. The Brolucizumab Experience Thus Far: A Health Economics and Outcomes Research Analysis. Presented at: American Academy of Ophthalmology 2020 Virtual Congress. November 2020. 2. Heier JS, et al. Assessing characteristics of patients with or without intraocular inflammation (IOI) in the brolucizumab treatment arms from the HAWK and HARRIER, Phase 3 studies. Presented at: American Academy of Ophthalmology 2020 Virtual Congress. November 2020. 3. Sadda S, et al. Pigment Epithelial Detachments and Subretinal Hyper-reflective Material: A HAWK and HARRIER Analysis. Presented at: American Academy of Ophthalmology 2020 Virtual Congress. November 2020.

# Strong LCM plan to expand in additional indications

Addressable population expected to double with indications beyond wAMD

- Approved in >50 countries, label updates received in >45 countries
- ~1.5m treated wAMD patients in G7<sup>1</sup>; significant unmet need exists
- Post marketing safety events (RV/RVO) addressed in worldwide label updates
- Beovu® US demand recovered vs. Q2 and stabilized at ~1200 vials/week<sup>2</sup>
- Strong ex-US uptake despite context; wAMD share in DE and JP ~6-8% today<sup>3</sup>
- Market is recognizing superior drying of Beovu® and usage is expected to grow<sup>4</sup>

**wet AMD**  
(Already approved indication)

## DME

Affects **5.5m<sup>1</sup>** people in G8 countries alone

High unmet need for a new treatment option that improves patient outcomes & reduce treatment burden<sup>5,6</sup>

Low diagnosis rate **54%**<sup>8</sup>, treatment rate **~40%**<sup>8</sup>

Growing at **6% CAGR<sup>8</sup>**

2021

## RVO

Affects **2.3m<sup>1</sup>** people in G8 countries alone

High unmet need for a new treatment option that improves patients outcomes, reduce treatment burden and resolves Ischemia<sup>6</sup>

Low diagnosis rate **~63%**<sup>8</sup>, treatment rate **~58%**<sup>8</sup>

2022

## PDR

Affects **2.3m<sup>1</sup>** people in G8 countries alone

High unmet need for a new treatment option that reverse underlying severity and limit progression<sup>6</sup>

Growing at **5% CAGR<sup>8</sup>**

2023

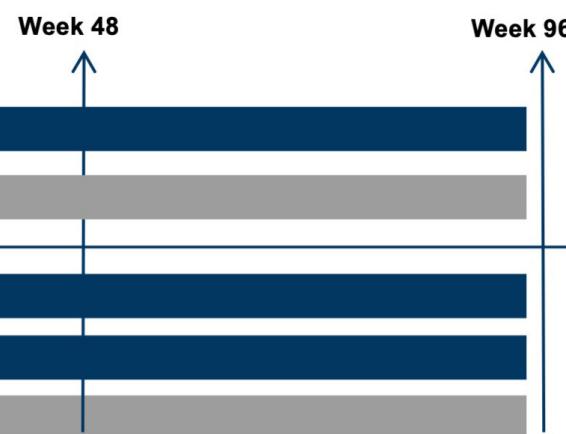
UPCOMING INDICATIONS

RV: Retinal Vasculitis. RVO: Retinal Vascular Occlusion. PDR: Proliferative Diabetic Retinopathy. Source: 1. DRG wet AMD Disease Landscape & forecast report May 2020 & Internal NVS estimates. 2. Internal NVS Sales data. 3. DE 4% market Share in total/licensed anti-VEGF market. Wet AMD estimated at ~70% of the total A-VEGF market. IQVIA PADDS and DE Pharmacy unit sales – Sep 2020, Gesundheitsforen Leipzig, 2015-2018. JP 3% market Share in total/licensed anti-VEGF market. Wet AMD estimated at ~40% of the total A-VEGF market. IQVIA PADDS unit sales, NVS JP Market research 2020. 4. ECP feedback from two independent market research conducted in US (n=150) & in DE, JP, CA, CH (n=87) during Aug-Sep 2020. 5. DRG DME & DR landscape & forecast report Sep 2020 & Internal NVS estimates. 6. Internal NVS Primary market research 2019-20. 7. DRG RVO Epidemiology report 2018 & NVS internal estimates. 8. DRG estimates + country inputs.

# KITE pivotal DME study reported positive topline results<sup>1</sup>

Progressing clinical development in DME: KITE & KESTREL

## KITE<sup>1</sup> and KESTREL<sup>2</sup>



- Two two-year, two-arm (KITE)/three-arm (KESTREL), randomized, double-masked, multicenter, Ph3 studies assessing the efficacy and safety of brolucizumab vs. aflibercept in adult patients with visual impairment due to DME
- Primary objective: Non-inferiority of brolucizumab to aflibercept with respect to the change in BCVA from baseline up to Week 52

## Comments

**KITE** pivotal DME study reported positive topline results<sup>1</sup>

- Non inferiority to aflibercept on BCVA at year 1
- Superior CST improvement versus aflibercept in a secondary endpoint over week 40-52
- >50% of Beovu® patients maintained on 3-month dosing interval through year 1, following the loading phase

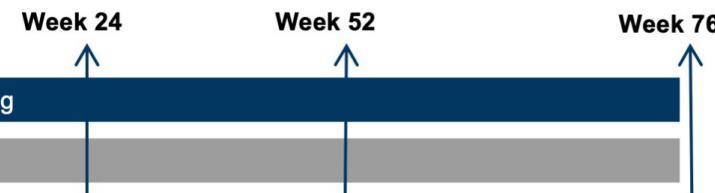
## KESTREL

Expected primary readout: December 2020

1. <https://www.novartis.com/news/media-releases/novartis-reports-positive-topline-results-from-first-phase-iii-trial-beovu-versus-aflibercept-patients-diabetic-macular-edema-dme>. 2. ClinicalTrials.gov. Study of Efficacy and Safety of Brolucizumab vs. Aflibercept in Patients With Visual Impairment Due to Diabetic Macular Edema (KESTREL). <https://clinicaltrials.gov/ct2/show/NCT03481634>. Accessed September 2020.

# Phase 3 programs in BRVO/CRVO and PDR with expected readouts in 2023 (RAPTOR, RAVEN) and 2024 (CONDOR)

## RAPTOR<sup>1</sup> and RAVEN<sup>2</sup>



- Two eighteen-month, two-arm, randomized, double-masked, multi-center, Ph3 studies assessing the efficacy and safety of brolucizumab vs aflibercept in adult patients with visual impairment due to macular edema secondary to BRVO (RAPTOR) or CRVO (RAVEN)
- Primary objective: Non-inferiority of brolucizumab to aflibercept with respect to the change in BCVA from baseline up to Week 52

## CONDOR<sup>3</sup>

- A 96-week, two-arm, randomized, single-masked, multi-center, Ph3 study assessing the efficacy and safety of brolucizumab 6mg compared to panretinal photocoagulation laser in patients with proliferative diabetic retinopathy
- Primary objective: Non-inferiority of brolucizumab to PRP with respect to the change in BCVA from baseline up to Week 54

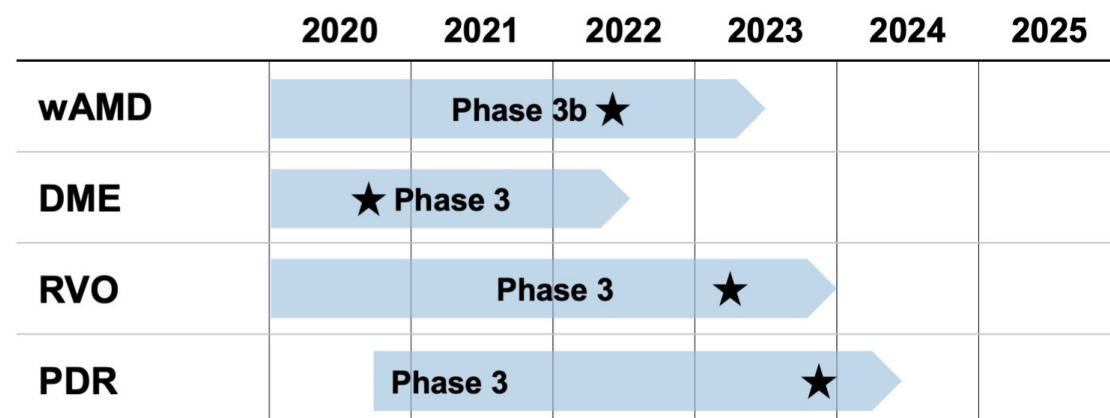
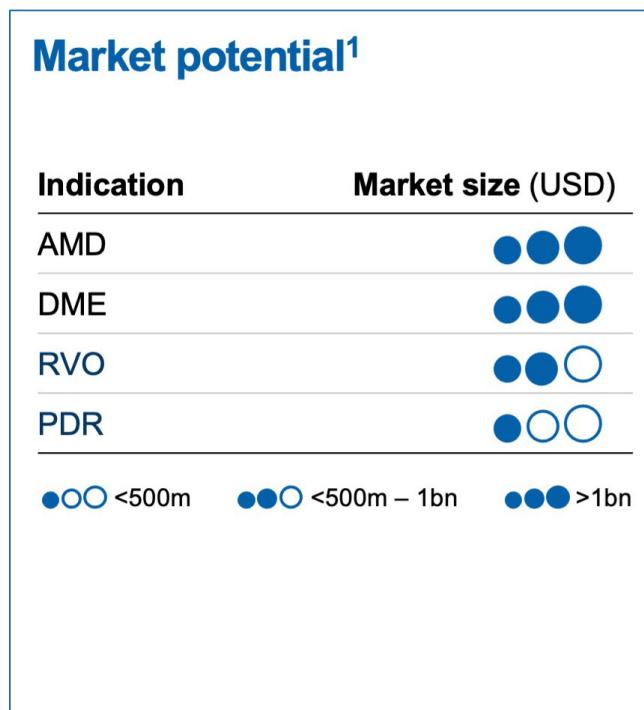
## Comments

- Anti-VEGF therapy has demonstrated efficacy in RVO and PDR patients with ranibizumab and aflibercept
- Phase 3 trials have matched dosing and observation periods vs aflibercept
- Single Phase 3 study in PDR will be used in combination with KITE and KESTREL for seeking approval

BCVA, best corrected visual acuity; PDR, proliferative diabetic retinopathy. PRP, panretinal photocoagulation. 1. <https://clinicaltrials.gov/ct2/show/NCT03802630?term=raptor&draw=2&rank=4>.  
 2. <https://clinicaltrials.gov/ct2/show/NCT03810313?term=raven&draw=2&rank=4>. 3. <https://clinicaltrials.gov/ct2/show/NCT04278417?term=brolucizumab&draw=2&rank=4>.

# Beovu® market potential and upcoming new indication milestones

Overall value driven by 4 indications



- Interim analyses (1-year data;★) may enable registration in DME and RVO indications
- Single pivotal study approach for PDR (based on regulatory precedence in Anti VEGF drug class)
- Additional specialty indications under consideration

AMD – Age-related Macular Degeneration. DME – Diabetic Macular Edema. RVO – Retinal Vein Occlusion. PDR – Proliferative Diabetic Retinopathy. 1. DRG Dry and wet AMD Disease landscape and forecast report May 2020, DRG DME/DR Disease Landscape and forecast report Sep 2020.

Kisqali®

Piqray®

Tabrecta™

Canakinumab

<sup>177</sup>Lu-PSMA-617

TNO155

LXH254

# Oncology: Solid Tumors

**Kisqali®****Piqray®****Tabrecta™****Canakinumab****<sup>177</sup>Lu-PSMA-617****TNO155****LXH254**

# Kisqali®

## Cyclin-Dependent Kinase 4/6 Inhibitor

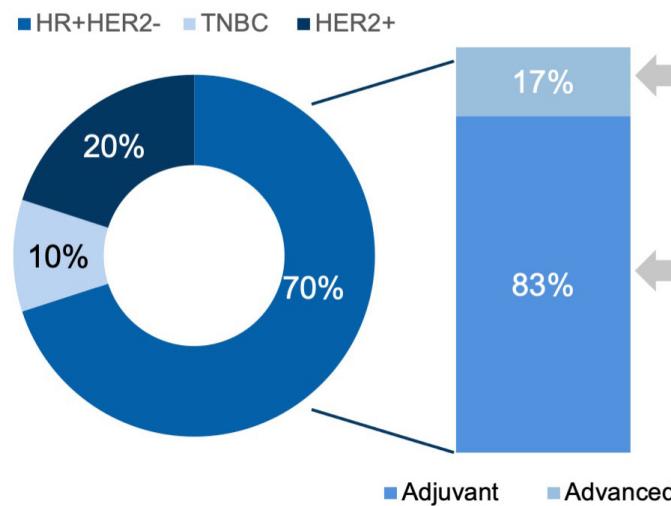
Marketed; LCM in Phase 3

### Key highlights

- Kisqali® is the only CDK4/6 inhibitor to demonstrate consistently superior Overall Survival (OS) in two large Ph3 trials, regardless of metastatic sites, endocrine treatment (ET) resistance, ET partner, treatment line or menopausal status, while maintaining Quality of Life (QoL)
- Kisqali® received the highest rating of any CDK4/6i on the ESMO Magnitude of Clinical Benefit Scale, based on OS and QoL benefits
- OS data and emerging evidence suggests that preferential and selective inhibition of CDK4 (such as that demonstrated by Kisqali®) may be relevant in both the advanced and early breast cancer settings
- **Additional OS results to be reported in metastatic setting, including MONALEESA-2 data, expected in H2 2021 (event-driven)**
- **Kisqali® is being investigated in early breast cancer in the Ph3 NATALEE study, if successful, Kisqali® will be the only CDK4/6i with evidence supporting use in the large intermediate and high-risk populations; expected readout in 2022**

# High unmet need remains in HR+/HER2- BC

## 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

- Improving OS while maintaining QoL is the #1 treatment goal
- Kisqali® stands apart as the only CDK 4/6 inhibitor that significantly improves Overall Survival in two Ph3 trials, across patient subgroups, with the QoL benefits

### Early Breast Cancer (EBC)

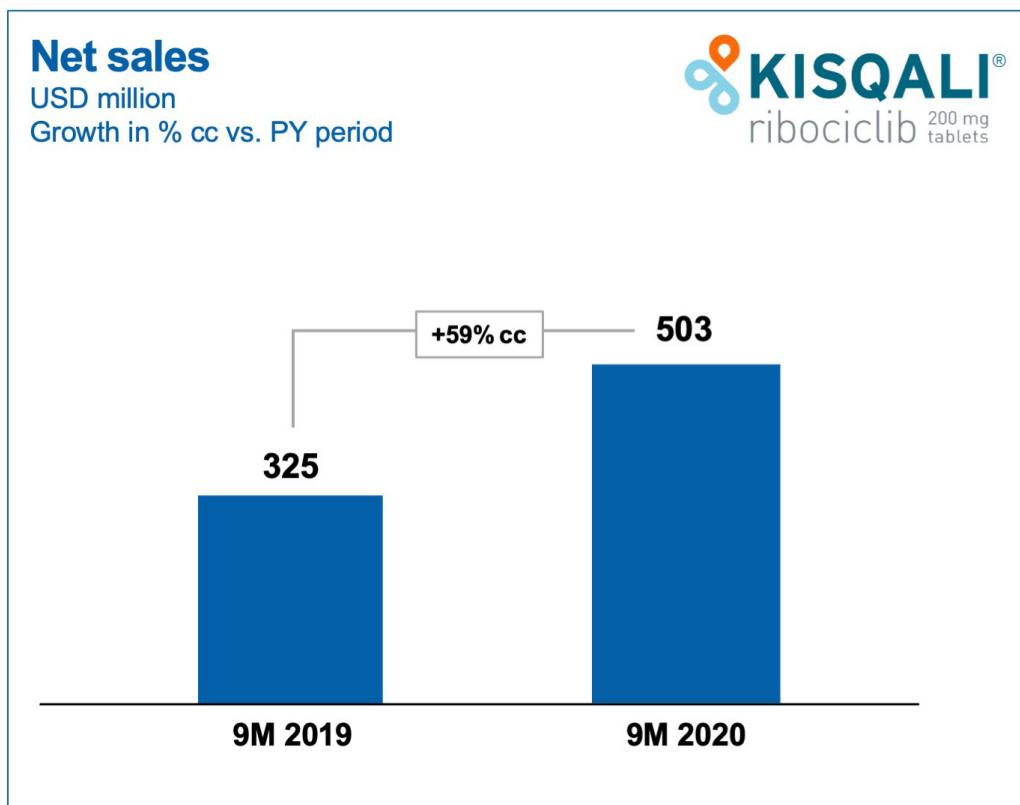
- 83% of breast cancers are diagnosed as EBC
- The objective of EBC treatment is to cure the patient by preventing disease recurrence while maintaining QoL
- Kisqali® is being investigated in EBC in the Ph3 NATALEE study with the expected readout in 2022
- If successful, Kisqali® will be the only CDK 4/6 inhibitor with evidence supporting use in the large intermediate and high-risk populations

>3x

More intermediate risk patients diagnosed vs. high risk

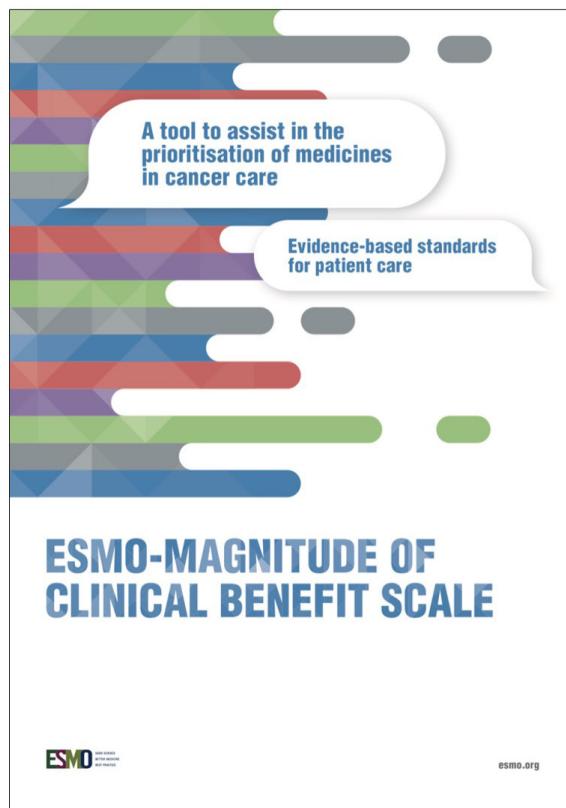
Data Source: Kantar Health – US/ EU5 Patient Metrics 2020.

# Kisqali®: Only CDK4/6i proven to extend the lives of patients in two Ph3 trials



- 9M 2020 sales up +59% cc, as only CDK4/6 with consistent OS benefit from two pivotal Ph3 trials (MONALEESA-7 and -3)
- Current and future growth in the metastatic setting driven by increasing number of top medical experts preferring Kisqali® as drug of choice over other CDK4/6 inhibitors based on the strength of OS benefit
- Kisqali® is the only CDK4/6i with the opportunity to demonstrate benefit in a broad patient population with high unmet need
- Future Kisqali® growth expected to be fueled by the expansion to the adjuvant BC setting with the NATALEE study

# Kisqali® received the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale

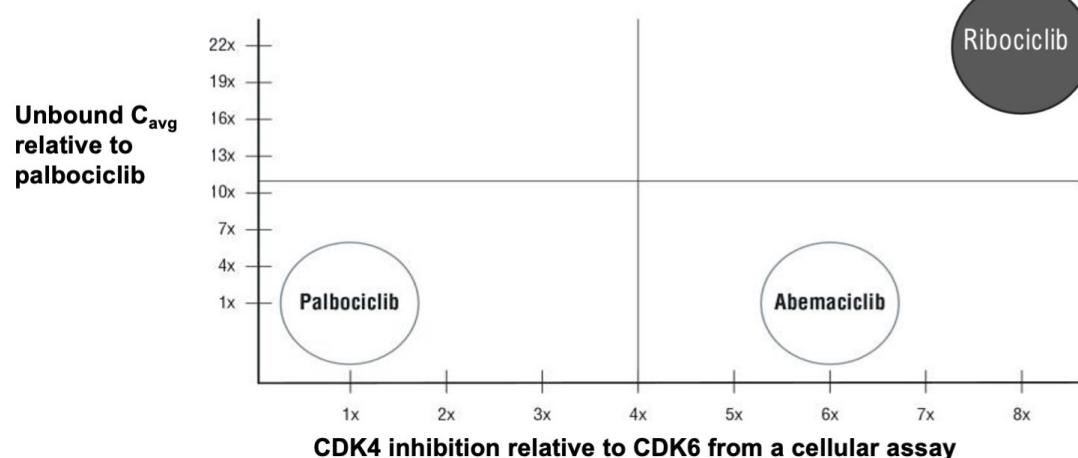


- Kisqali® has achieved the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale
  - 5 out of 5 in 1L pre-menopausal patients based on significant OS benefit and improved QoL in MONALEESA-7<sup>1</sup>
  - 4 out of 5 in 1L post-menopausal patients based on significant OS benefit and maintained QoL in MONALEESA-3<sup>1</sup>
- Additional data supporting clinical differences of Kisqali®, as well as consistent OS benefit submitted to SABCS

1. ESMO-MCBS v1.1; Scorecard version:1.

# Evidence suggests differences among CDK4/6 inhibitors

## Selected differences among CDK4/6 inhibitors<sup>3-7</sup>

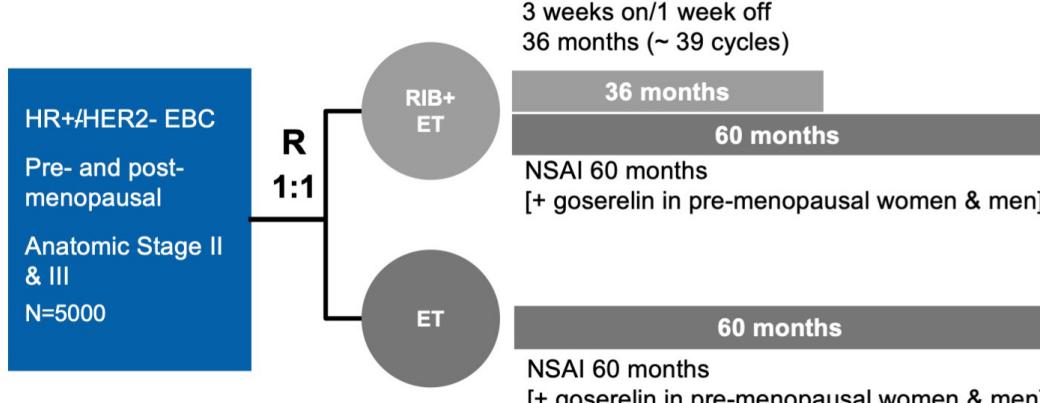


- CDK4 is a critical driver of HR+/HER2- advanced breast cancer, while CDK6 drives hematological toxicities<sup>1,2</sup>
- Kisqali® inhibits CDK4 8x more than CDK6 in vitro<sup>3,4</sup>
- Higher unbound C<sub>avg</sub> (average free drug concentration at steady state) means more drug is available to act on tumor cells<sup>4-7</sup>
- At clinically relevant doses and adjusting for differences in potency against CDK4/6 and protein binding, Kisqali® should provide greater CDK4 inhibition in vivo than competitors

1. Yu Q, et al. Cancer Cell. 2006;9(1):23-32. 2. An H-X, et al. Am J Pathol. 1999;154(1):113-118. 3. Kim S, et al. Oncotarget. 2018;9(81):35226-35240. 4. Chen P, et al. Mol Cancer Ther. 2016;15(10):2273-2281. 5. Infante JR, et al. Clin Cancer Res. 2016;22(23):5696-5705. 6. Flaherty KT, et al. Clin Cancer Res. 2012;18(2):568-576. 7. Patnaik A, et al. Cancer Discov. 2016;6(7):740-753.

# NATALEE: Pivotal Ph3 study in adjuvant setting on track for readout in 2022

## NATALEE study design



## What makes NATALEE unique?

- Includes patients with high and intermediate risk of recurrence based on AJCC prognostic staging
- Longer treatment duration: 3 vs. 2 years
- Lower dose compared to metastatic setting (400 vs. 600mg) may improve overall tolerability

## Study status

- Sample size increased from initially planned 4,000 to 5,000 patients to allow more robust assessment of the treatment effect
- Enrollment remains strong and is expected to complete by Q2 2021
- Targeting global submission in 2023 based on the final analysis
- Discontinuation rate remains below expected rate based on current aggregate data

## Indication

## Market size

Early breast cancer



●○○ <USD 500m

●●○ USD 500m – 1bn

●●● >USD 1bn

# Piqray®

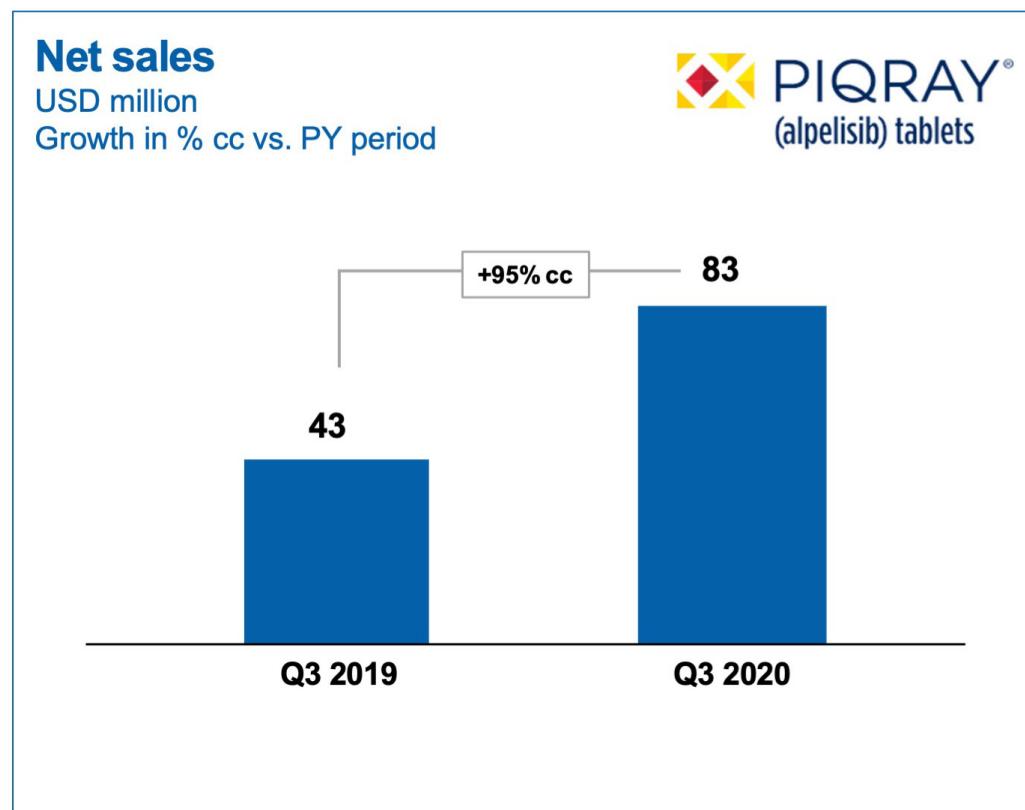
Alpha-specific PI3K  
Inhibitor

Marketed; LCM in Phase 3

## Key highlights

- Piqray® is the first and only targeted therapy for HR+/HER2- advanced breast cancer patients with a PIK3CA mutation following progression on or after an endocrine-based regimen
- Approximately 40% of patients living with HR+/HER2- advanced breast cancer have a PIK3CA mutation and face a worse prognosis
- Piqray® + fulvestrant nearly doubled mPFS in patients with a PIK3CA mutation in the pivotal SOLAR-1 study
- Piqray® listed as Category 1 preferred option for patients with a PIK3CA mutation in the NCCN guidelines
- Growing geographical footprint with regulatory approvals in >50 markets, including US and Europe; submissions under review in 48 additional markets
- Piqray® is being investigated across multiple indications in the EPIK program

# Strong uptake addressing an unmet need in HR+/HER2- advanced BC with PIK3CA mutations

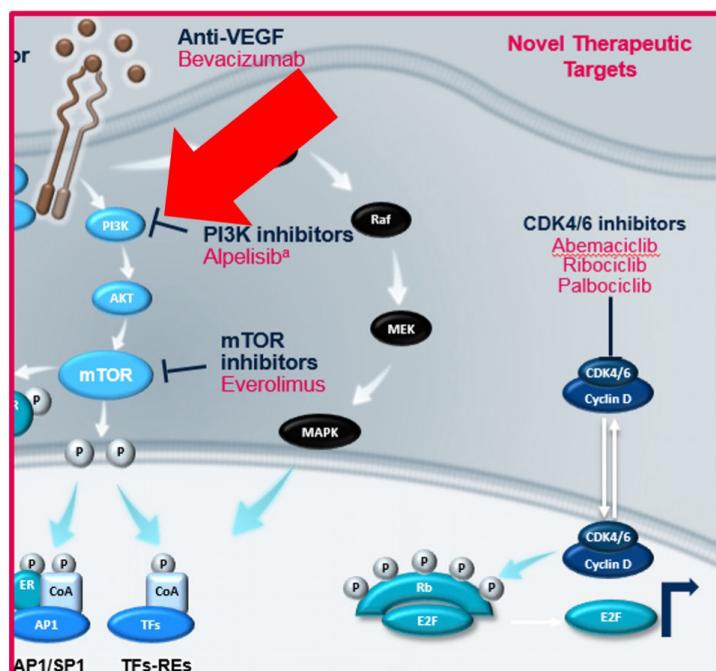


- Q3 2020 vs. PY sales up +95%, driven by strong uptake and clear unmet need in this population
- Continued growth in testing rates for PIK3CA mutation, changing the paradigm of treatment
- Approved testing modalities encompass liquid and tissue biopsies via NGS and PCR platforms, offering a wide clinical choice
- Expanding commercial footprint with European Commission approval in Q3 2020
- Robust EPIK lifecycle development programs: study initiations occurred for TNBC and HER2+ BC; ovarian & HNSCC to start in 2021<sup>1</sup>

1. RWE study for PROS also underway, submission expected 2021.

# PI3K signalling is frequently dysregulated; PI3K inhibition augments ER function and dependence in HR+ BC

## Novel therapeutic targets

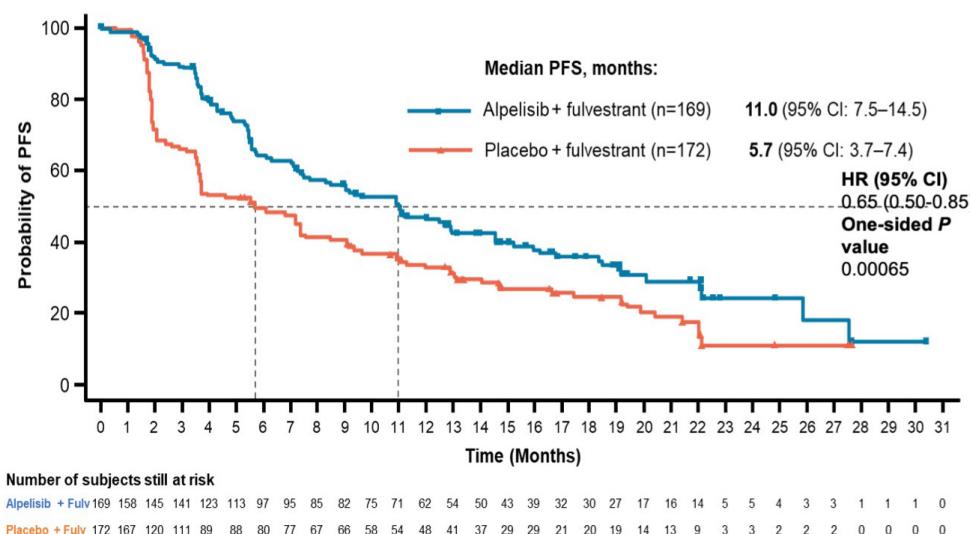


- PI3K signalling is involved in tumor growth, proliferation, and survival, and is frequently active in solid tumors<sup>1</sup>
- The PI3K pathway may be activated by gain of function mutations and/or amplification of the PIK3CA gene<sup>1, 2-5</sup>
- Mutations in PIK3CA are detected in ~40% of HR+/HER2- breast cancer<sup>6</sup>
- Tumor biology of HR+/HER2- aBC with ET and/or CDK 4/6i use, combined with the MoA of alpelisib, shows no evidence of cross-resistance with prior CDK 4/6i use that would modify the clinical effect of alpelisib<sup>1-3</sup>

1. Fruman DA, et al. Cell 2017; 170:605-635. 2. Samuels Y, et al. Science 2004; 304:554. 3. Zhang Y, et al. Cancer Cell 2017; 31:820-832. 4. Zehir A, et al. Nat Med 2017; 23:703-713. 5. Janku F, et al. Rev Clin Oncol 2018; Epub ahead of print. 6. Arthur LM, et al. Breast Cancer Res Treat 2014; 147:211-219.

# Piqray®: Improving outcomes for patients with PIK3CA mutations

## Locally assessed PFS in patients with a PIK3CA mutation (SOLAR-1)<sup>1</sup>

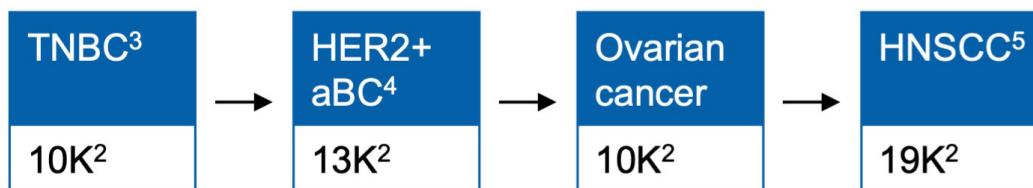


- Patients with a PIK3CA mutation face a poor prognosis
- Piqray® + fulvestrant nearly doubled mPFS in patients with a PIK3CA mutation in pivotal SOLAR-1 study
- 52% of patients in the SOLAR-1 trial received Piqray® as their first line of treatment and most of these patients were endocrine resistant<sup>1</sup>
- Piqray® demonstrated OS improvement of >1 yr (14 months) in patients with lung or liver metastases, which were observed in 41% of patients<sup>2</sup>
- BYLieve study reinforces efficacy of Piqray® use in post CDK4/6 setting, with manageable side effects

1. Andre, F. et al. N Engl J Med 2019;380:1929-40. 2. Andre, F. et al. Annals of Oncology (2020) 31 (suppl\_4): S1142-S1215.

# PI3K pathway is commonly dysregulated in cancer; addressing medical need across multiple tumor types

## EPIK Development Program<sup>1</sup>



### Indication

TNBC



HER2+ aBC



Ovarian cancer



HNSCC (2/3L)



●○○ <USD 500m

●●○ USD 500m – 1bn

●●● >USD 1bn

- PI3K pathway dysregulation is common in cancer
- EPIK program initiated with patients enrolling into TNBC and HER2+ BC trials; ovarian & HNSCC to start in 2021; filings planned in 2023+
- PIK3CA mutations are present in ~25% in HER2+ aBC and ~15% in advanced TNBC, and ~30% of TNBC have PTEN loss
- In ovarian cancer high unmet need in 2L/3L settings, particularly for BRCAwt<sup>6</sup> patients, whose tumors are platinum resistant or refractory
- PI3K pathway is a promising therapeutic target in HNSCC based on pre-clinical data

1. RWE study for PROS also underway, submission expected 2021 2. Annual incidence in the U.S. Source: Kantar Health. 3. TNBC – Triple Negative Breast Cancer. 4. aBC – advanced breast cancer. 5. HNSCC – head and neck squamous cell carcinoma. 6. BRCA wild-type.

# Tabrecta™

MET inhibitor

Marketed; LCM in Phase 3

## Key highlights

- Lung cancer affects 2m patients a year; 3-4% of NSCLC patients have METex14 mutations, associated with a poor prognosis
- Tabrecta™ is the first and only therapy approved by the FDA to specifically target METex14 mutated metastatic NSCLC; Tabrecta™ was approved in Japan in June 2020, and additional regulatory filings continue around the world
- Omni-channel launch underway, leveraging robust digital capabilities to accelerate patient access amid pandemic conditions
- Tabrecta™ has potential to expand into multiple indications in NSCLC and beyond-as a monotherapy and in combinations
- Tabrecta™ is approved with FoundationOne™, the first and only FDA approved diagnostic for METex14; **liquid biopsy diagnostic approval anticipated Q1 2021**

# Patients with METex14 mutation face poor prognosis

## Unique patient population



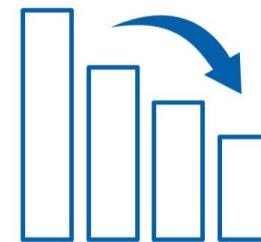
Patients with METex14 mutation are older, with a median age of 71 years and are predominately female; approximately 40% have never smoked<sup>1</sup>

## Aggressive disease



Patients with METex14 mutation have a high incidence of multi-focal disease and often have brain, bone, and liver metastases<sup>2</sup>

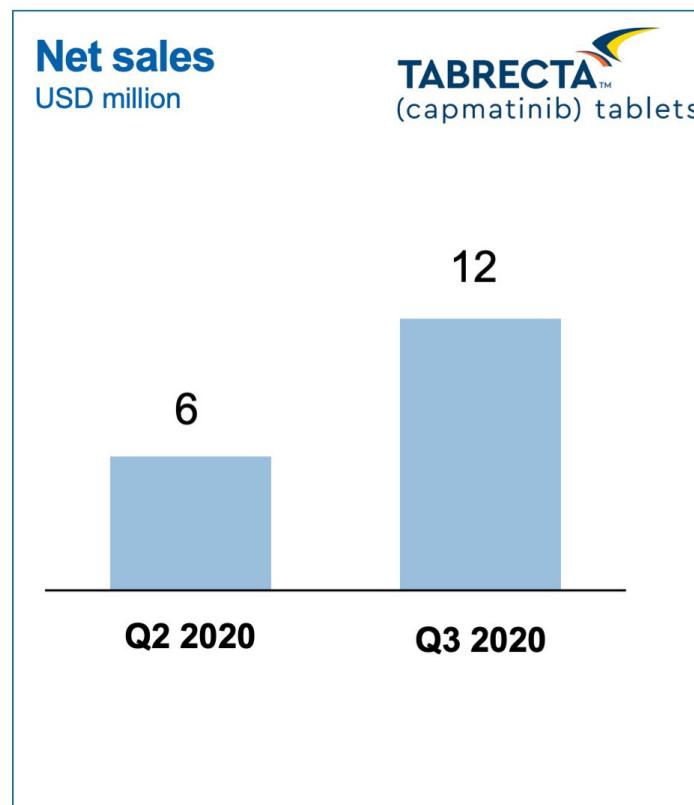
## Limited survival benefit



METex14 mutation was found to be an independent prognostic factor that predicted worse survival compared with patients without MET alteration<sup>3,4,5</sup>

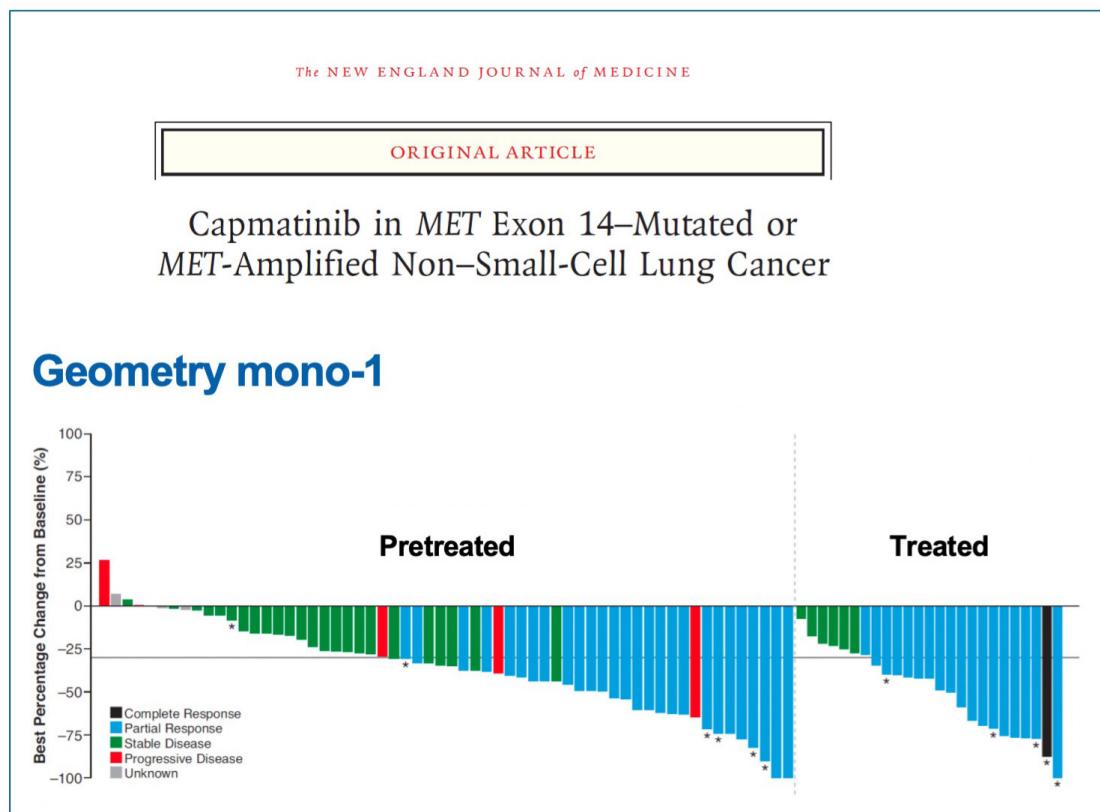
1. Ali A, et al. Curr Oncol. 2013;20(4):e300-306. 2. Subba R, Digumarthy, Dexter P, Mendoza, Eric W, Zhang, Jochen K, Lennerz, and Rebecca S. Heist. Clinicopathologic and Imaging Features of Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. Cancers. 2019 Dec; 11(12): 2033. 3. Tong JH, Yeung SF, Chan AWH, et al. Clin Cancer Res. 2016;22(12):3048-3056. 4. Yeung SF, Tong JHM, Law PPW, et al. J Thorac Oncol. 2015;10(9):1292-1300. 5. Katalinic D, Aleric I, Vcev A. MET exon 14 splicing mutation and its correlation with clinicopathological features in subjects with non-small cell lung cancer. Poster presented at: ESMO 2018 Congress; October 20, 2018; Munich, Germany.

# Strong launch as first and only approved METex14 inhibitor in the US

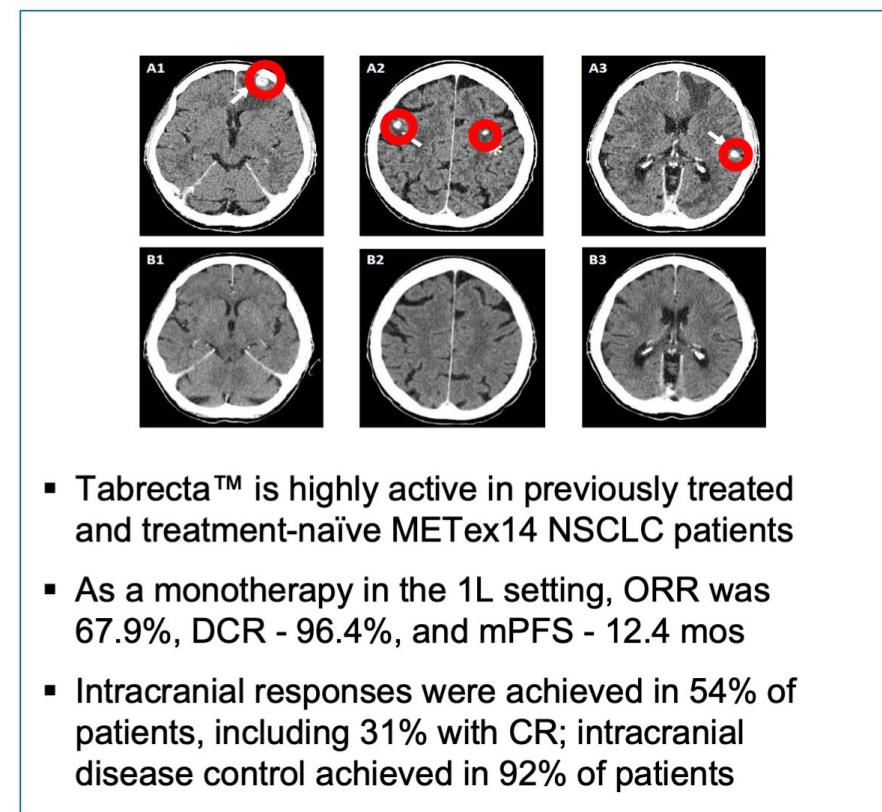


- HCPs have expressed high excitement for Tabrecta™ for METex14 mNSCLC patients
- Rapid uptake driven by significant unmet need, expanded coverage and strong Rx momentum
- Continued focus on improving the use of comprehensive genomic testing before 1L therapeutic choice, currently the case for only 30-35% of patients in US
- Anticipating addition of liquid biopsy CDx in early 2021
- Expanding to other geographies
  - Japan approval on June 29, 2020
  - Confirmatory Ph3 study started in EU
  - Regulatory filings continue in other geographies

# Strong response rates in 1L METex14 NSCLC; intracranial responses in patients with brain metastases

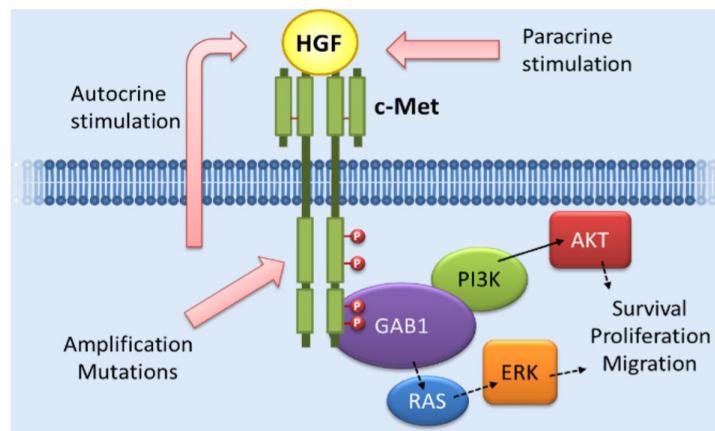


LEFT: Wolf et al. NEJM 2020; 383:944-957. RIGHT: Garon et al. Annual Meeting of the AACR; 2020 Jun 23-24; CT082.



# Expanding Tabrecta™ beyond METex14 NSCLC

## Exploring combination with anti-PD-1 in NSCLC, irrespective of MET status



- MET also plays a role in immuno-modulation in the following populations of the tumor microenvironment:
  - Neutrophils
  - Dendritic cells
  - T cells
- Combination of capmatinib with anti-PD-1 enhances antitumor immunity irrespective of MET status

### Opportunity

Chemo-free alternative for ~30% of NSCLC patients with high PD-L1 expression

### Population

1L locally advanced or metastatic NSCLC with PD-L1 $\geq$  50% (est. population ~90K; G7)

### Study design

A randomized, Ph2 proof-of-concept study evaluating the efficacy and safety of Tabrecta™ plus pembrolizumab vs. pembrolizumab alone

### Primary Objective

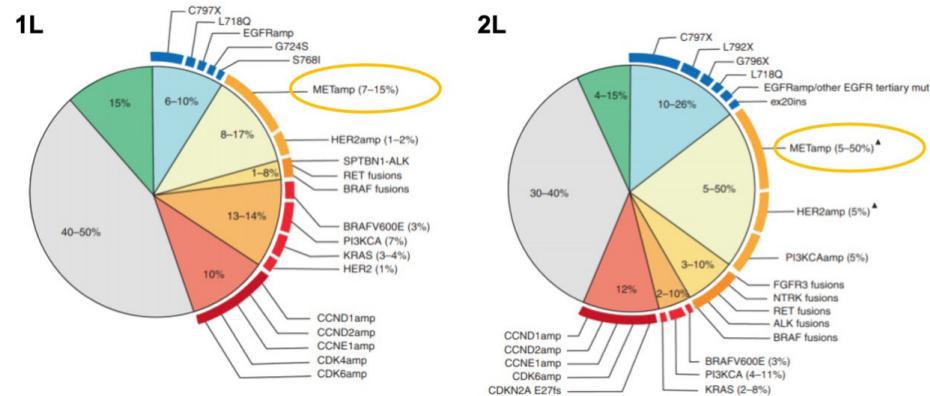
To assess efficacy of Tabrecta™ and pembrolizumab combination vs. pembrolizumab monotherapy

**Estimated completion:** H2 2021

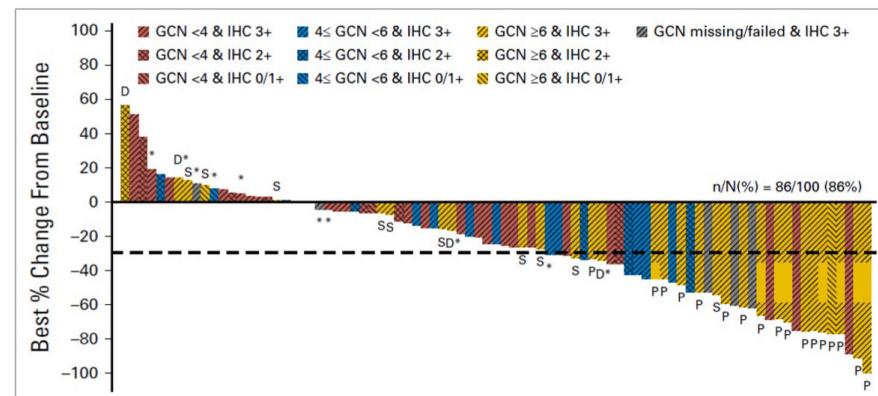
# Expanding Tabrecta™ beyond METex14 NSCLC

## Tabrecta™ to be studied in acquired resistance to EGFR inhibitors

### MET amplification is a common mechanism of resistance in 1L and 2L osimertinib failures



### MET amplification<sup>1</sup> after EGFR TKI progression enriches for response to Tabrecta™ and gefitinib



EGFR activating mutations are common in NSCLC, identified in ~10-20% of patients in US/EU and ~25-45% of patients in Asia

MET amplification is a driver of resistance; can be detected in ~5-20% of patients who have progressed after EGFR TKIs such as gefitinib, erlotinib, osimertinib (est. population ~20K; G7)

Tabrecta™ can be safely combined with EGFR TKIs; studies of Tabrecta™ with gefitinib and EGF816 in patients who progressed on 1<sup>st</sup> / 2<sup>nd</sup> generation TKIs showed that responses were enhanced in patients with MET alterations

Initiating a Ph3 study of Tabrecta™ in combination with an EGFRi in patients with EGFRmut+ NSCLC who have progressed on EGFR therapy and have MET amplification

Leonetti 2019 British Journal of Cancer 121:725. Yi-Long Wu et al. 2018 JCO 31: 3101. Ann. Oncol., 24 (2013), pp. 2371-2376 1. Yellow bars represent patients with highest gene copy number (GCN) elevation with MET amplification

# Canakinumab (ACZ885)

Anti-IL-1 $\beta$  monoclonal antibody

Phase 3

## Key highlights

- **High unmet need for new treatments:** Lung cancer affects over 2m patients a year and is a leading cause of cancer related deaths worldwide; despite treatment advances in the last five years, long-term outcomes in advanced disease remain poor
- **Pro-Tumor Inflammation and IL-1 $\beta$ :** Pre-clinical data support the role of IL-1 $\beta$  as a facilitator of Pro-Tumor Inflammation (PTI), promoting tumor processes such as angiogenesis and invasion and inhibiting anti-tumor immune responses
- **Canakinumab in lung cancer:** Canakinumab is a monoclonal antibody that targets IL-1 $\beta$ ; several lines of evidence suggest potential benefit of canakinumab in addition to current standard of care medicines in lung cancer
- **CANOPY program:** Three Ph3 registrational studies in (NSCLC) are ongoing; >1500 patients enrolled to date; extensive safety data in combination with standard chemotherapies across treatment lines; pathway inhibition confirmed in safety run-in
- **Ph3 data expected in 2021:** CANOPY-1 & 2 anticipated to readout in 2021

# Lung cancer is the leading cause of cancer-related deaths worldwide with remaining high unmet need

## #1 killer among cancers

### Deaths per incident case<sup>1</sup>

84%  Lung

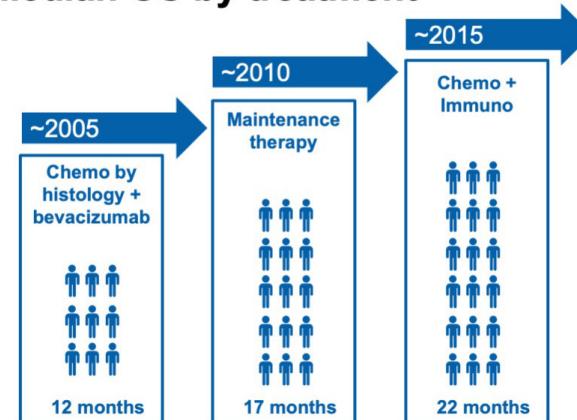
48%  Colorectal

30%  Breast

~1.8 million deaths from Lung Cancer in 2018

## Even with recent treatment advances

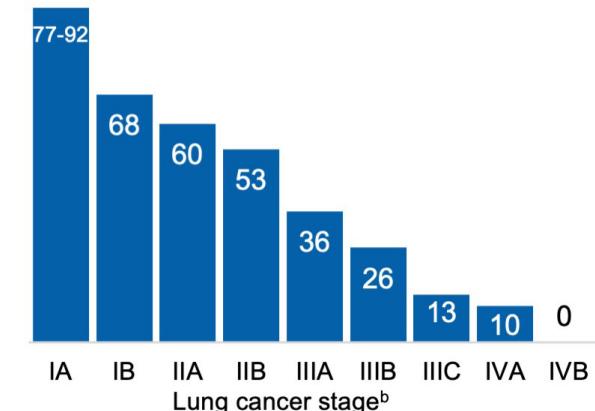
### Median OS by treatment



Treatment options are limited upon failure of platinum chemo and IO

## Long-term outcomes remain poor

### 5-year OS by stage, %<sup>4</sup>

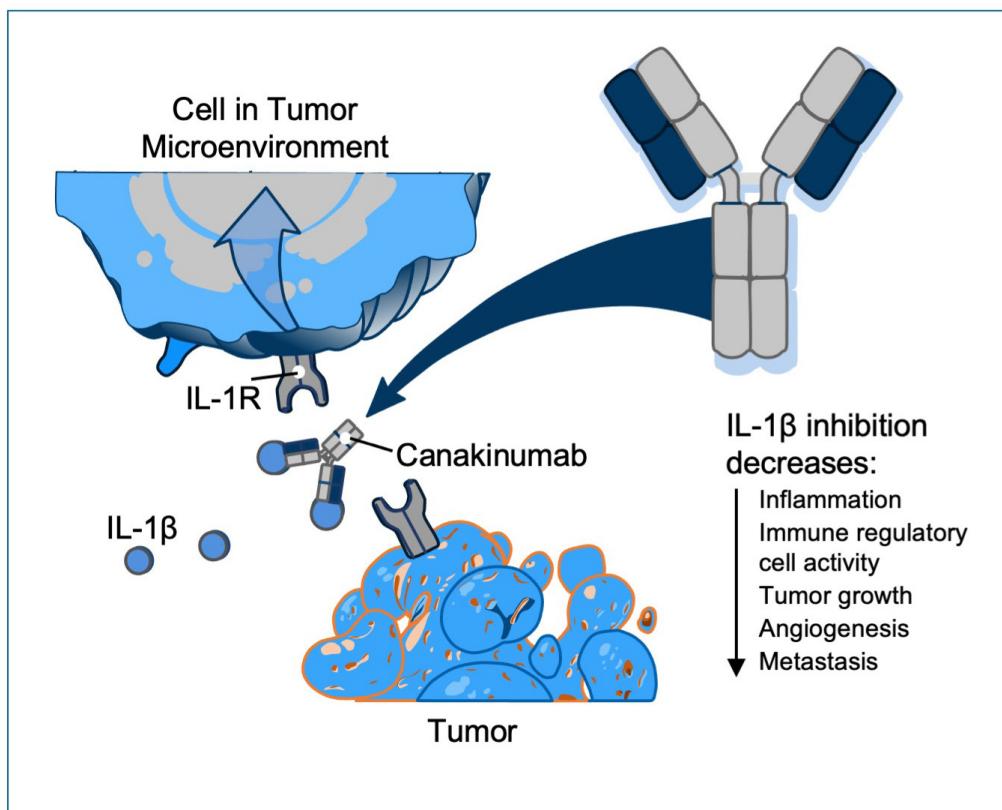


Most patients are diagnosed with advanced disease; outcomes worse in patients with high levels of CRP

a. Both sexes and all ages. b. According to AJCC/UICC v8. 1. Bray F, et al. CA Cancer J Clin. 2018;68:394-424. 2. Siegel RL, et al. CA Cancer J Clin. 2020;70(1):7-30. 3. Mascaux C, et al. Eur Respir Rev. 2017;26:170066.

4. Rami-Porta R, et al. CA Cancer J Clin. 2017;67:138. 5. GLOBOCAN 2018. Cancer Tomorrow. Reference 5 details in slide notes.

# Canakinumab is a monoclonal antibody that targets IL-1 $\beta$ , one of key drivers of PTI

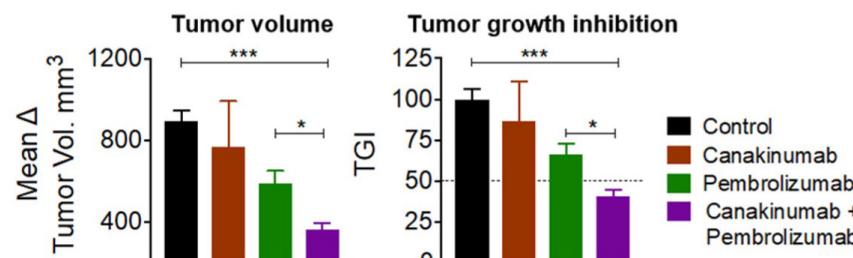


- Canakinumab is a human IgG1 monoclonal antibody with high affinity and specificity for IL-1 $\beta$
- Canakinumab binds to human IL-1 $\beta$  and neutralizes its activity by blocking its interaction with IL-1 receptors
- CANTOS study demonstrated statistically significant dose-dependent effect risk reduction in lung cancer incidence and mortality
- Pre-clinical data support the role of IL-1 $\beta$  as a facilitator of Pro-Tumor Inflammation (PTI)
- PTI enables tumor development in two key ways:
  - Drives oncogenic processes such as proliferation and survival, angiogenesis and invasion
  - Suppress anti-tumor immune response, in part, by increasing influx of immunosuppressive cells into the tumor microenvironment (TME)

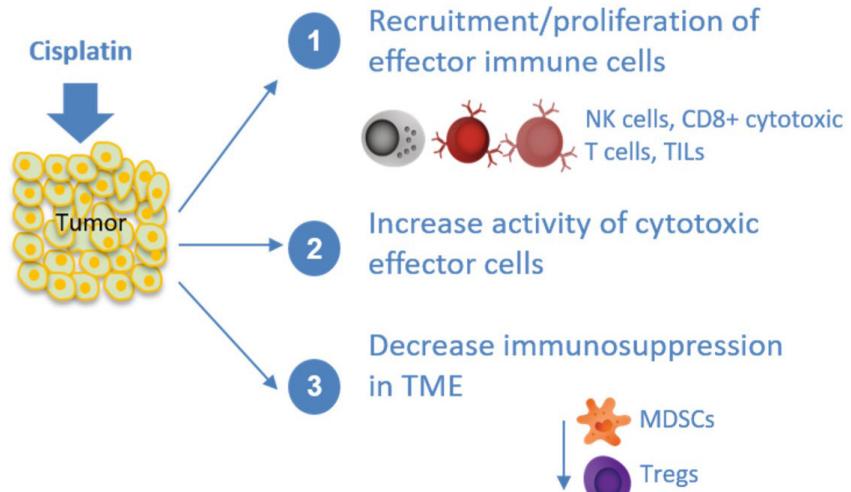
ILARIS [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2016; Alten R, et al. Arthritis Res Ther. 2008;10:R67; Rondeau JM, et al. MAbs. 2015;7:1151-1160; Voronov E, Apte RN. Curr Pharm Des. 2017;23:4893-4905; Carmi Y, et al. J Immunol. 2013;190:3500-3509.

# Scientific rationale for canakinumab combination with pembrolizumab + chemotherapy

- High levels of IL-6 and C-reactive protein (CRP) – downstream effectors of IL-1 $\beta$  – correlate with poor outcomes in NSCLC patients treated with PD-(L)1 inhibitors<sup>1-6</sup>
  - Decreasing IL-6 and CRP with canakinumab may enhance the response to PD-(L)1 inhibitors
- In a humanized lung cancer mouse model, canakinumab + pembrolizumab delayed tumor growth more than monotherapies<sup>7</sup>



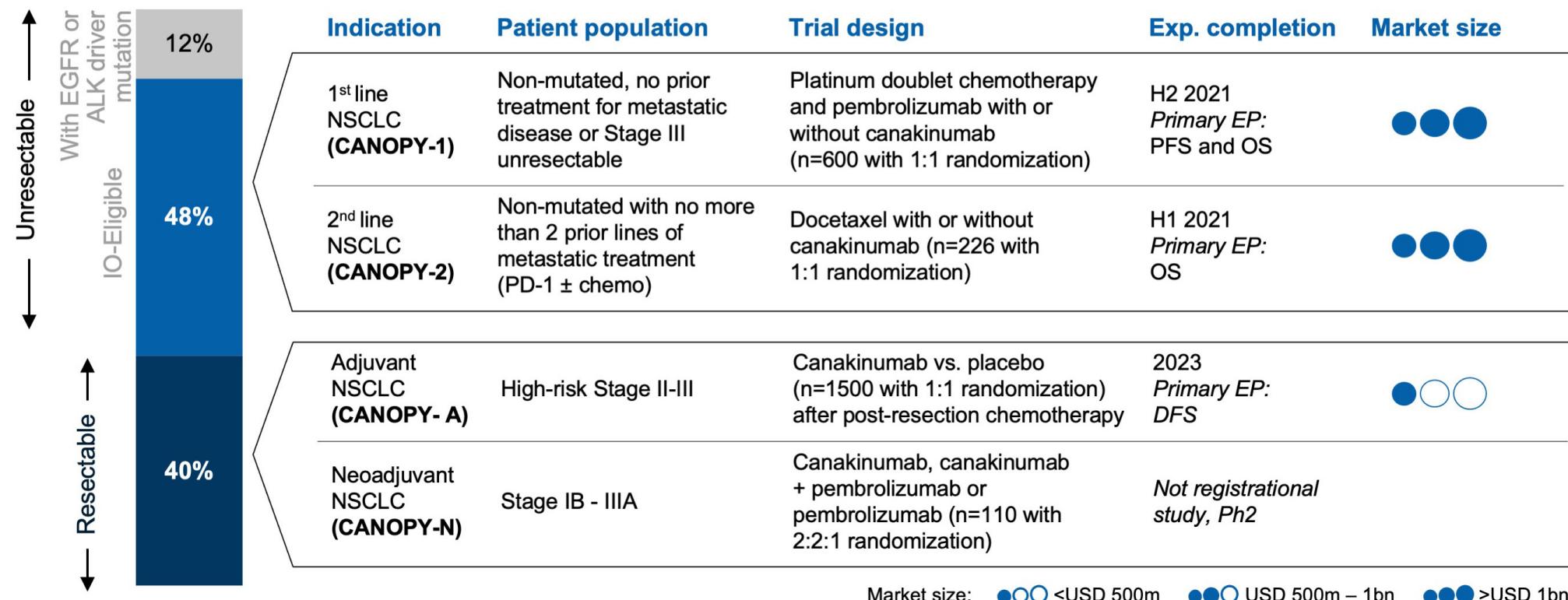
- Chemotherapy triggers immunogenic cell death, stimulating anti-tumor immune responses, which may improve response to PD-(L)1 inhibitors<sup>8,9</sup>



IL, interleukin. MDSC, myeloid-derived suppressor cell. NK, natural killer. PD-(L)1, programmed death (ligand) 1. TIL, tumor-infiltrating T cell. TME, tumor microenvironment. Treg, regulatory T cell. Naqash AR, et al. Acta Oncol. 2017;57:867-872; Oya Y, et al. Oncotarget. 2017;8:103117-103128; Iivanainen S, et al. ESMO Open. 2019;4:e00053; Patil N, et al. AACR 2018; Abstract 5707; Adachi Y, et al. Cancer Med. 2020;9:1383-1391; Matsuzawa R, et al. WCLC 2019; Abstract P2.04-21; Jayaraman P, et al. Mol Cancer Ther. 2019;18(12 Suppl):abstract C103. Zheng H, et al. Immunotherapy. 2017;9:913-927; De Biasi AR, et al. Clin Cancer Res. 2014;20:5384-5391.

# CANOPY registrational program evaluates canakinumab across a large proportion of NSCLC

## Incident + newly recurrent NSCLC



## 177Lu-PSMA-617

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

Phase 3

### Key highlights

- Targeted delivery of radiation to cancer cells has already demonstrated favorable efficacy (HR for PFS = 0.21; 95% CI, 0.13 to 0.33; P<0.001) and safety in neuroendocrine tumors (Lutathera NETTER-1 trial<sup>1</sup>)
- 177Lu-PSMA-617 is expected to be the first to market targeted radioligand therapy (RLT) addressing >80% patients with prostate cancer who express PSMA
- First independent randomized Ph2 trial TheraP<sup>2</sup> with 177Lu-PSMA-617 (initiated and sponsored by ANZUP<sup>1</sup> Cancer Trials Group) suggests a promising clinical profile in metastatic castration resistant prostate cancer (mCRPC)
- **VISION Ph3 trial in mCRPC ongoing, with radiographic progression-free survival (rPFS) readout expected H1 2021**
- Plans to expand 177Lu-PSMA-617 in earlier lines of advanced prostate cancer (APC) treatment are underway

1. Strosberg et al. NEJM. 2017; 376: 125-35. Australian and New Zealand Urogenital and Prostate Cancer Trials Group; ANZUP study ANZUP 1603.

# Despite advances in treatments, prognosis remains poor for patients with mCRPC

2<sup>nd</sup>

most diagnosed cancer  
in men

>80%

patients metastatic at  
the time of CRPC<sup>1</sup>  
diagnosis

>30%

5-year survival  
prognosis for mCRPC<sup>2</sup>  
patients

~10

months median OS<sup>3</sup>

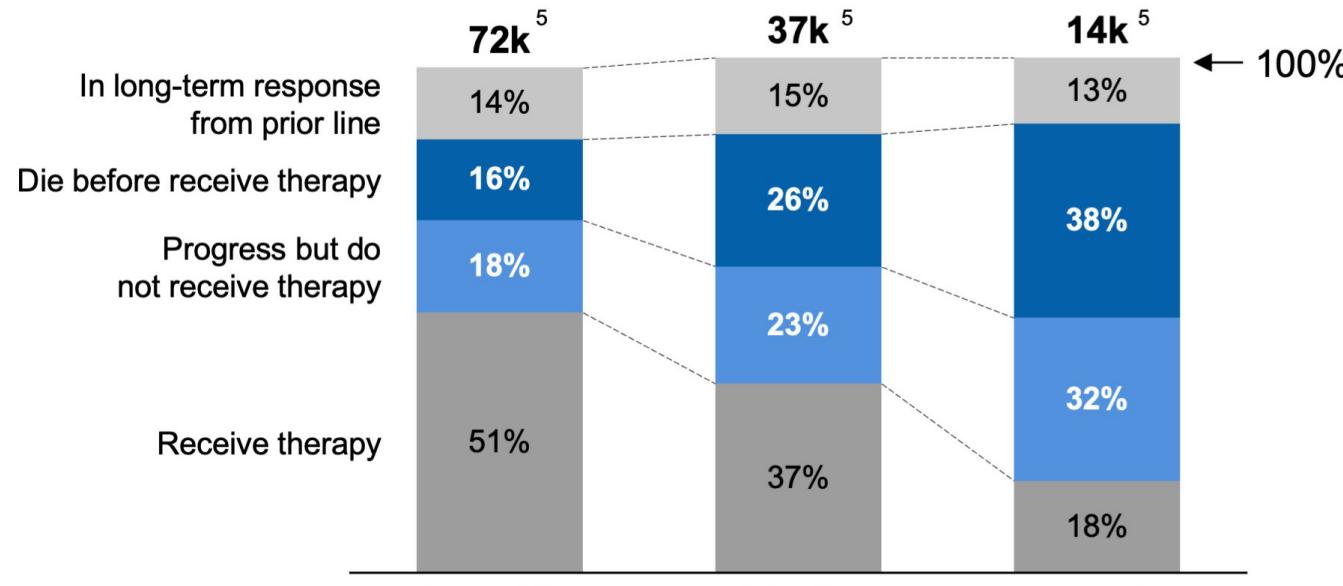


1. Castration resistant prostate cancer. 2. Metastatic castration resistant prostate cancer. 3. Antonarakis, Emmanuel – Current Understanding of Resistance to Abiraterone and Enzalutamide in Advanced Prostate Cancer; Clinical Advances in Hematology & Oncology (2016, Vol. 14, Issue 5).

# Treatments with new mechanisms of action are needed to improve outcomes beyond second line

## Patients with mCRPC<sup>1</sup>

US, EU5, Japan



Note: percentages do not add to 100% due to rounding

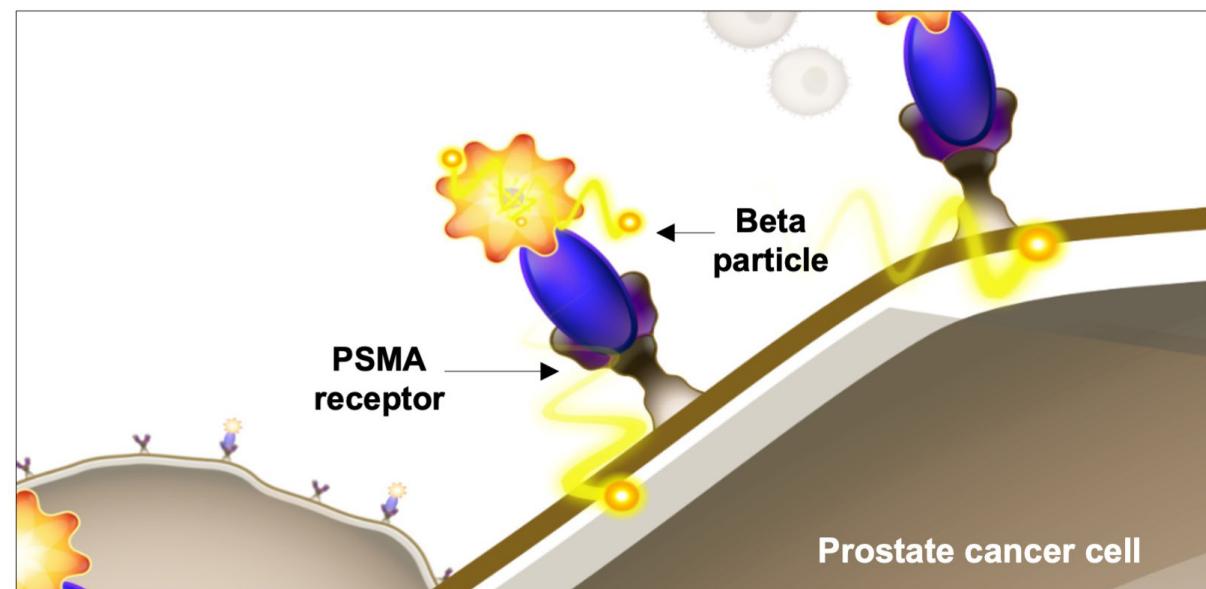
- Very limited set of treatment mechanisms available across lines in mCRPC: ARDTs<sup>2</sup>, ADT<sup>3</sup> and taxane
- Fewer patients receive each subsequent line of therapy, with no clear standard of care in late lines
- High unmet need for new MoAs<sup>4</sup>, offering a new and potentially better option for patients in second line and beyond

1. Metastatic castration resistant prostate cancer. 2. Androgen receptor-directed therapy. 3. Androgen deprivation therapy. 4. Mechanism of action. 5. Number of patients and line outcome rates based on Kantar Health CancerMPact Treatment Architecture US, EU5, JP as of 2020 (report date Dec. 2019). Patient progression rates averaged between across geographies US, EU5, JP.

# 177Lu-PSMA-617 RLT<sup>1</sup> enables targeted delivery of radiation to tumor while minimizing damage to surrounding normal tissues

## What makes PSMA<sup>2</sup> RLT unique?

- Binds to PSMA, expressed on >80% advanced prostate cancer cells<sup>3,4</sup>
- Once bound, the <sup>177</sup>Lu<sup>5</sup> atom releases an energetic beta particle resulting in lethal radiation, which
- Kills the cancer cell<sup>3</sup>, through single- and/or double-stranded DNA breaks
- Potentially minimizes damage to surrounding normal tissues<sup>3,4</sup>
- <sup>177</sup>Lu half-life is approximately 7 days

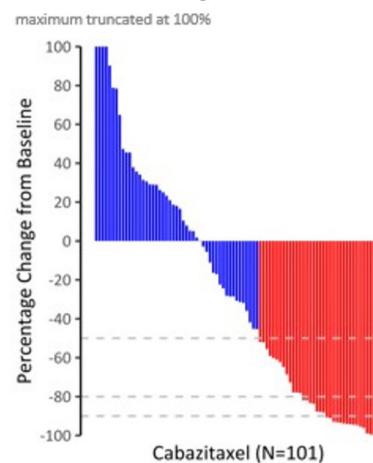


1. Radioligand therapy. 2. Prostate specific membrane antigen. 3. Ferdinandus J, et al. Curr Opin Urol. 2018;28(2):197–204. 4. Fendler WP, et al. J Nucl Med. 2017;58(11):1786–1792. 5. Lutetium.

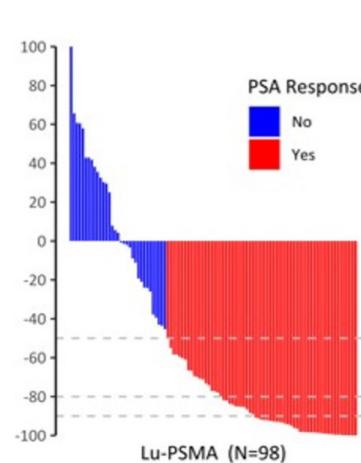
# 177Lu-PSMA-617 has shown early promising signals of efficacy and safety in TheraP, an independent randomized Ph2 trial

## Primary endpoint: PSA<sup>1</sup> ≥ 50% response (PSA50-RR<sup>2</sup>)

### Best PSA Response



**PSA50-RR** **37%**  
(95%CI) (27-46%)



**66%**  
(56-75%)

177Lu-PSMA-617 had **29% absolute** (95% CI 16%-42%; p>0.0001) greater PSA ≥ 50% response rate compared to cabazitaxel

Relatively fewer Grade 3-4 AEs<sup>3</sup> for 177Lu-PSMA-617 vs. cabazitaxel

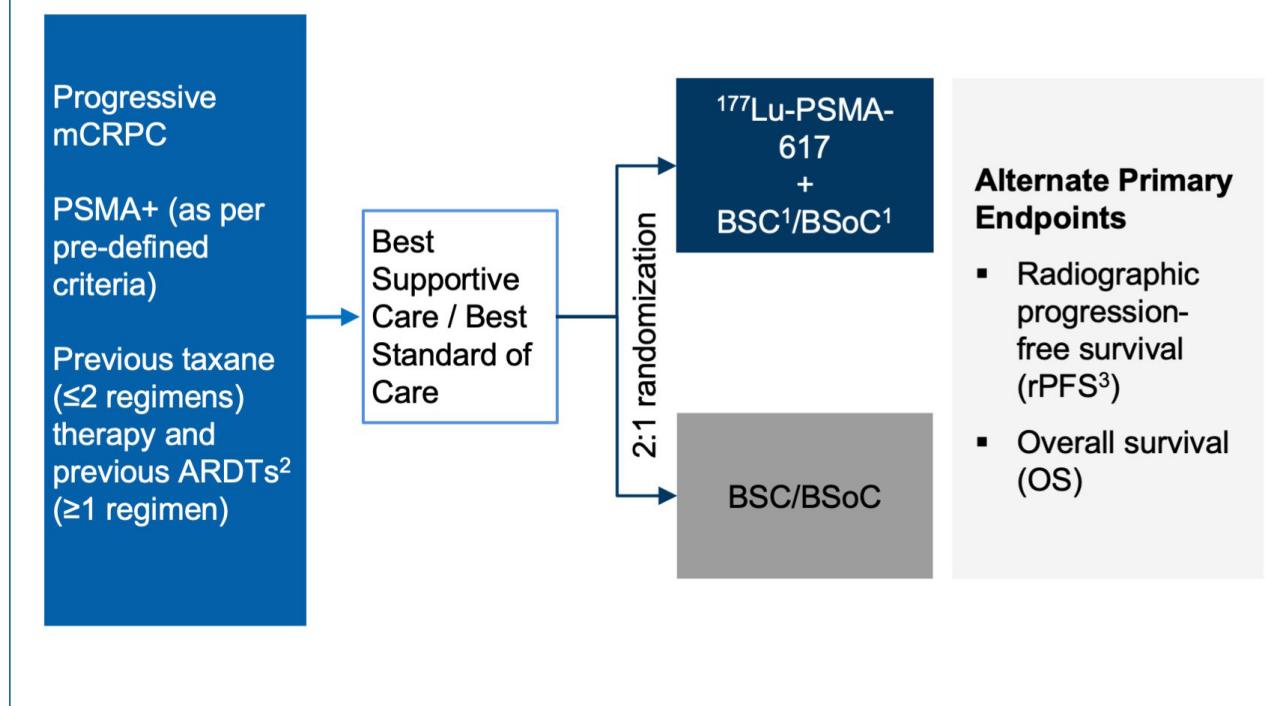


- 200 mCRPC men post docetaxel with high PSMA expression and PSA>20 ng/mL, suitable for cabazitaxel, randomized 1:1 177Lu-PSMA-617 or cabazitaxel
- Promising PSA response rate, awaiting radiographic endpoint
- Results highlight potential clinical activity of 177Lu-PSMA-617

TheraP is an independent investigator-initiated trial (IIT) sponsored by ANZUP: Australian & New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group. <https://clinicaltrials.gov/ct2/show/NCT03392428>. All data are taken from the ANZUP presentation at the 2020 ASCO Annual Meeting by Michael Hofman, MBBS. TheraP is different from VISION; Novartis awaits the VISION study readout in H1 2021. 1. Prostate-Specific Antigen. 2. Response rate. 3. Adverse events.

# VISION is the first Ph3 RLT trial in prostate cancer, with rPFS readout expected in H1 2021

## VISION study design



- Ambition to be SoC for mCRPC patients progressing after first taxane/ARDTs
- Event-driven endpoint makes it difficult to predict data cut-off
  - Primary analysis with final rPFS<sup>3</sup> endpoint and interim OS<sup>4</sup> analysis - expected in H1 2021
  - Final analysis with OS data expected in H2 2021
- US / EU submissions expected in Q4 2021

1. Best standard of care / best supportive care: broad range of active treatment options, excluding investigational agents and chemotherapy. 2. ARDT = Androgen receptor-directed therapy. 3. Radiographic progression-free survival. 4. Overall survival.

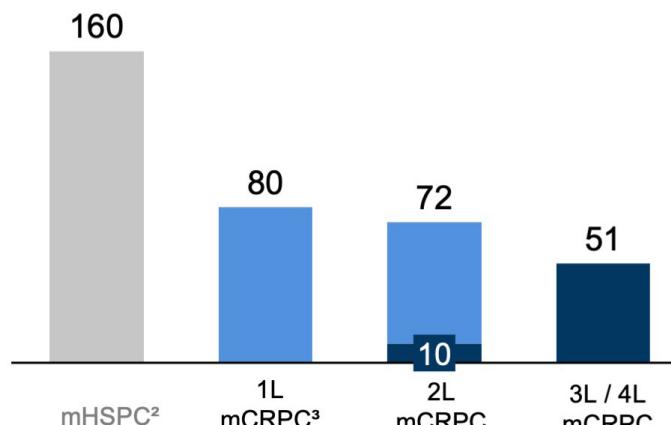
# Plans to take **177Lu-PSMA-617** into earlier lines, creating robust asset value

## Patients with metastatic PC

US, EU5, JP<sup>1</sup> ('000)

>80% of patients express PSMA<sup>5</sup>

■ mHSPC ■ mCRPC pre-taxane ■ mCRPC post-taxane



## Aim to expand into earlier lines of advanced PC treatment

### mCRPC post-taxane

Ongoing studies

Ph3 VISION;  
Expected submission 2021

Planned studies

### mCRPC pre-taxane

With further studies under evaluation

Ph3, expected FPFV<sup>4</sup> 2021

Opportunity<sup>6</sup>



Market size:  <USD 500m  USD 500m – 1bn  >USD 1bn

1. Based on Kantar Health CancerMPact Treatment Architecture US, EU5, JP (Dec. 2019). Patient numbers incl. patients in long-term response from prior line, who die before receiving therapy, progress but do not receive therapy, and receive systemic therapy (per slide 3). 2. Metastatic hormonal sensitive prostate cancer. 3. metastatic castration resistant prostate cancer. 4. First patient first visit. 5. Prostate specific membrane antigen. 6. NVS estimation based on current treatment rates with 15% of 2L patients assumed to have progressed on both a first ARDT and taxane treatment.

# TNO155

Low molecular weight  
SHP2 inhibitor

Phase 2

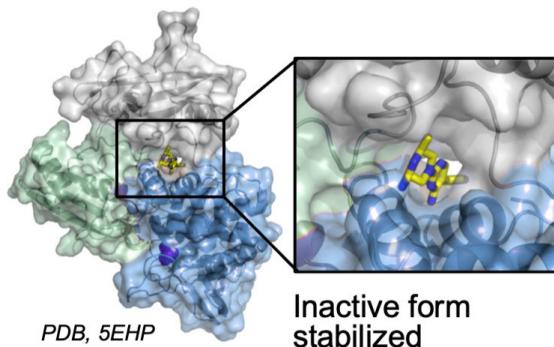
## Key highlights

- 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<sup>G12C</sup> inhibitors, and we have adopted a broad clinical combination strategy to blanket the MAPK pathway with **5 ongoing or planned combination trials in solid tumors**
- TNO155 is the first SHP2 inhibitor to enter the clinic, and has shown promising, yet very preliminary, early clinical data in MRTX849 combination trial for KRAS<sup>G12C</sup> mutant NSCLC

# TNO155: A first-in-class inhibitor of SHP2

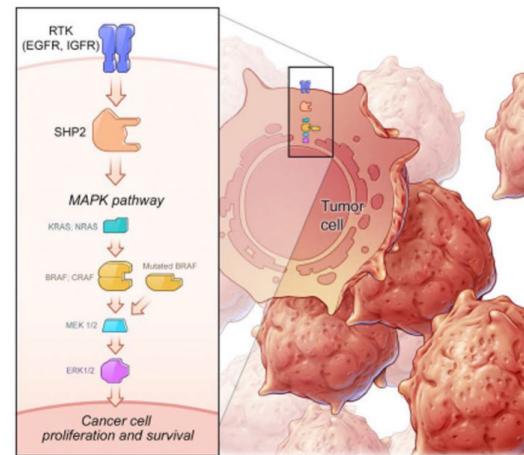
**AACR** American Association for Cancer Research®

## First SHP2i to enter the clinic



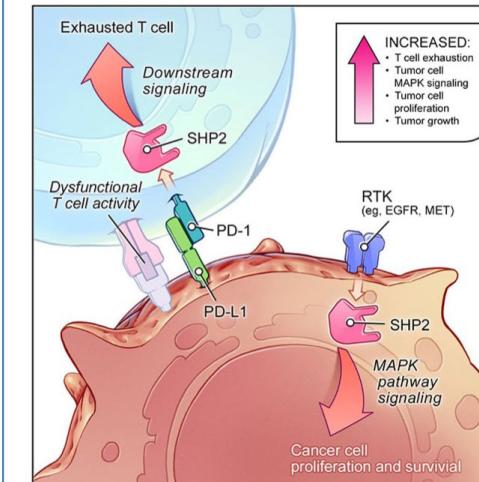
Ideal drug-like properties (e.g. high permeability, solubility, no CYP450 inhibition, ideal preclinical PK profile)

## Required for RTK signaling



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

## Downstream transducer of PD-1



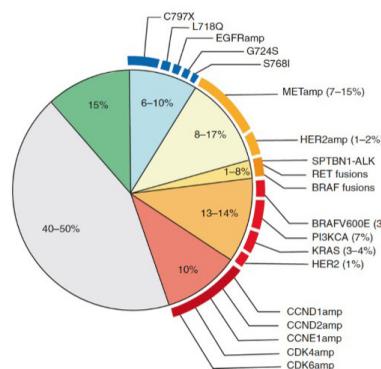
SHP2 is a downstream transducer of PD-1 signaling, a critical immune checkpoint in human malignancies

# Almost all patients develop resistance to targeted therapies

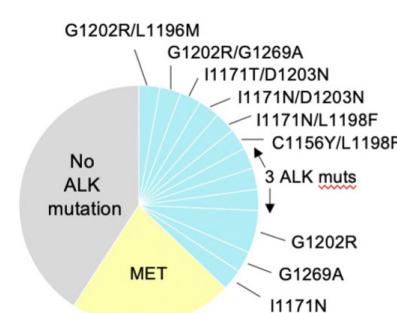
## Role of SHP2 phosphatase

### Multiple resistance mechanisms arise during targeted therapy treatment

#### 1L Tagrisso® in EGFR<sup>1</sup>



#### 2L+ Lorbrena® in ALK<sup>2</sup>



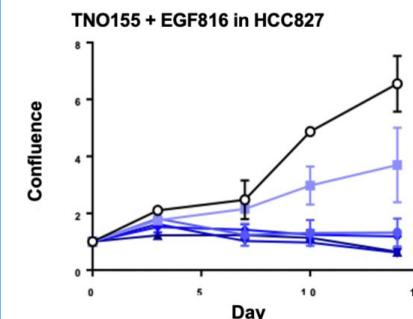
Multiple and diverse resistance mechanisms can develop in patients treated with targeted therapies, leading to clinical relapse

For highly selective, next-generation targeted agents, resistance is often mediated by off-target mechanisms that lead to MAPK re-activation

Combination strategies that target both the oncogenic driver and downstream signaling pathways are urgently needed

### SHP2 inhibition overcomes resistance mechanisms in pre-clinical models

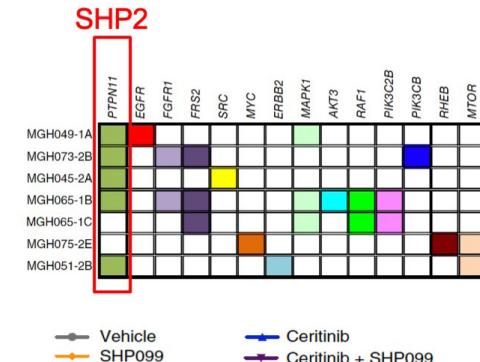
#### EGFR mutant NSCLC



#### EGF816

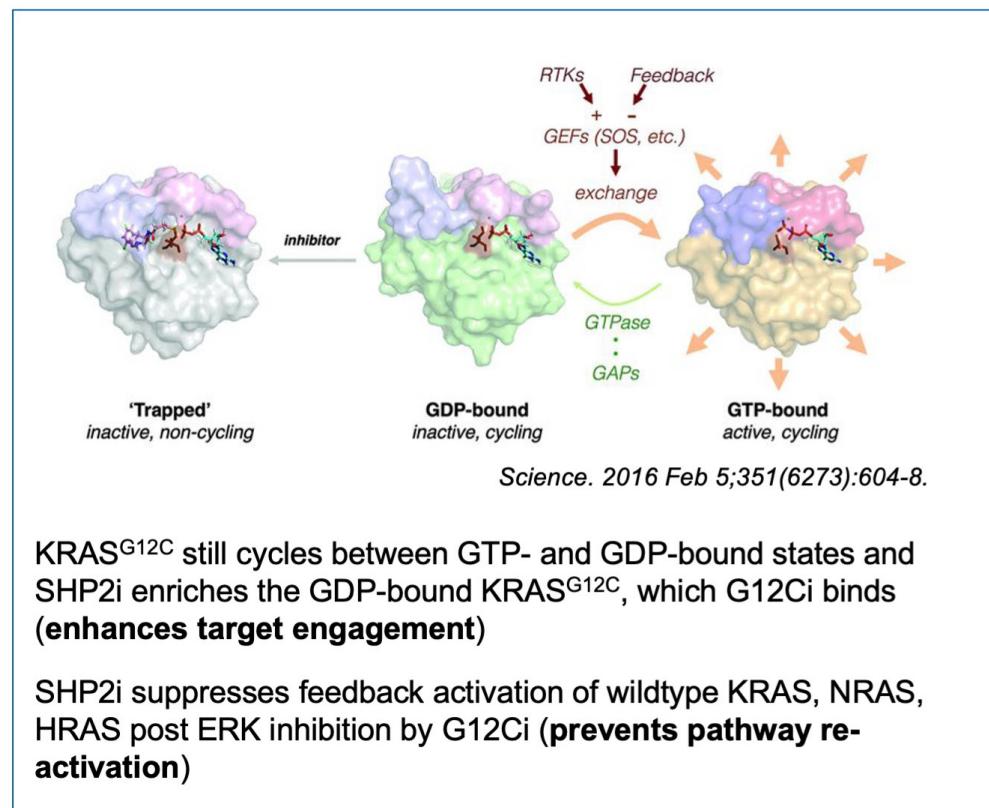
- EGF816 + TNO155 dose 1
- EGF816 + TNO155 dose 2
- EGF816 + TNO155 dose 3
- EGF816 + TNO155 dose 4
- EGF816 + TNO155 dose 5

#### ALK+ NSCLC<sup>3</sup>

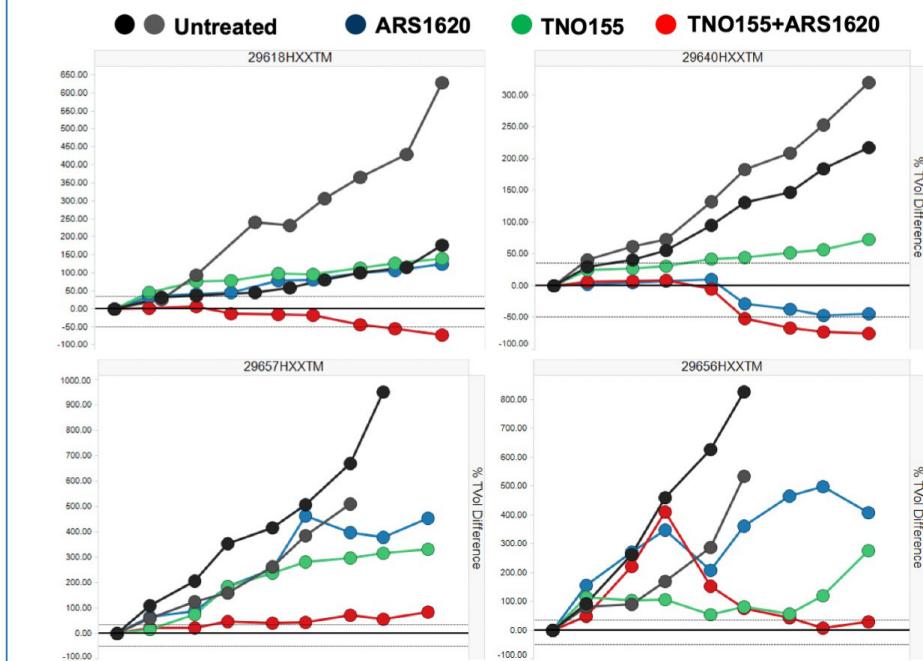


1. Leonetti Br J Cancer 2019. 2. Dagogo-Jack, Clin Canc Res, 2020. 3. Dardaei Nat Med 2018.

# Strong pre-clinical synergy between SHP2i and KRAS<sup>G12C</sup>i informs TKI combination approach



## TNO155 + KRAS<sup>G12C</sup>i shrink tumors in KRAS<sup>G12C</sup> NSCLC PDX pre-clinical models



# Early clinical activity with MRTX849 + TNO155 in KRAS<sup>G12C</sup> mutant cancers

Patient is a 53 year-old male current smoker who was diagnosed with metastatic NSCLC in April of 2017

Patient had received several prior treatments:

- Chemotherapy
- Immunotherapy
- Chemotherapy + immunotherapy
- **AMG510** x 3 mos
- **RMC4630**+cobimetinib x 1 cycle
- Experimental CDK4/6i

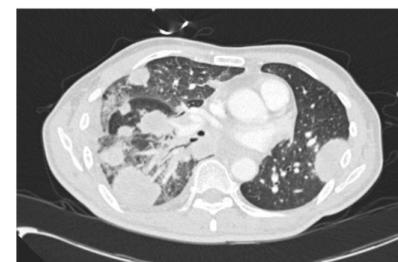
Patient enrolled in combination trial **MRTX849+TNO155**

Patient showed rapid resolution of cancer symptoms, PR on first scans (shown on right panel)

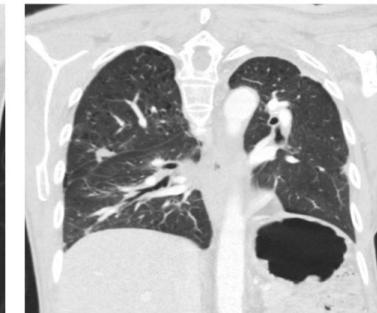
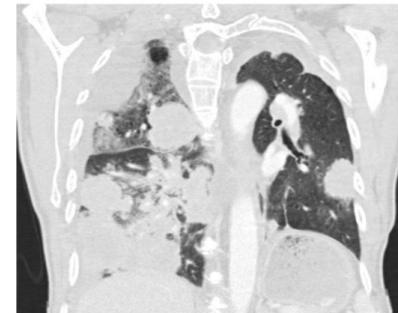
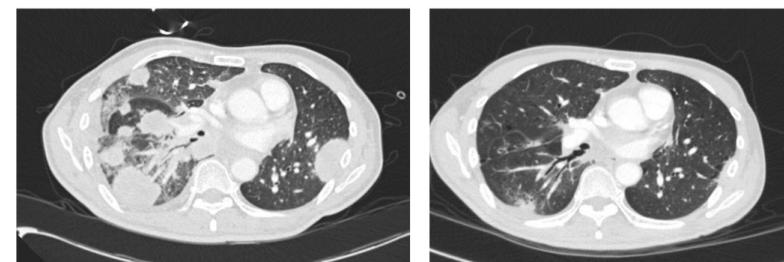
Mild grade 1 toxicities

CT scan of NSCLC patient before treatment and one month after treatment with MRTX849 and TNO155

Pretreatment



1mo after treatment



Courtesy of Dr. Zhu (UCI)

## Multiple TNO155 combinations are being explored clinically

		Est. frequency	FPFV
	TNO155 + EGF816	EGFR mutant NSCLC, post osimertinib	<b>10-40% of NSCLC</b> September 2020
	TNO155 + lorlatinib	ALK+ NSCLC, post lorlatinib	<b>3-5% of NSCLC</b> Q1 2021
	TNO155 + PDR001	KRAS <sup>G12C</sup> NSCLC, ≥1% PD-L1 post-chemo and aPD-(L)1	<b>~13% of NSCLC</b> August 2019
	TNO155 + ribociclib	KRAS-mut CRC post-SOC, per local standard	<b>30-40% of CRC</b> August 2019
	TNO155 + MRTX849	KRAS <sup>G12C</sup> NSCLC and CRC	<b>~13% of NSCLC</b> <b>~4% of CRC</b> April 2020

# LXH254

Low molecular weight  
B/C-RAF inhibitor

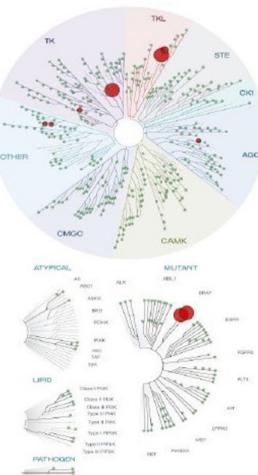
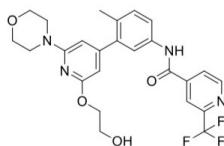
Phase 1

## Key highlights

- 40% of cutaneous melanomas harbor BRAF mutations, 20% harbor NRAS mutations
  - Current standard of care in BRAF<sup>V600E</sup> melanoma includes BRAFi + MEKi, but resistance to pathway activation occurs in most patients
  - No effective treatments in NRAS mutant melanoma following first line IO therapies
- LXH254 is a potent and selective B/C RAF inhibitor which can block both dimeric and monomeric B/C RAF kinases
- Pre-clinical studies have shown robust LXH254 activity in NRAS mutant models when combined with MEK, ERK, and CDK4/6 inhibitors
- Combination studies ongoing in BRAF-mutant and NRAS-mutant melanomas with **FPFV achieved in the Ph2 trial in October 2020**
- Combinations also being tested in NSCLC harboring KRAS mutations or atypical (non-V600) BRAF mutations

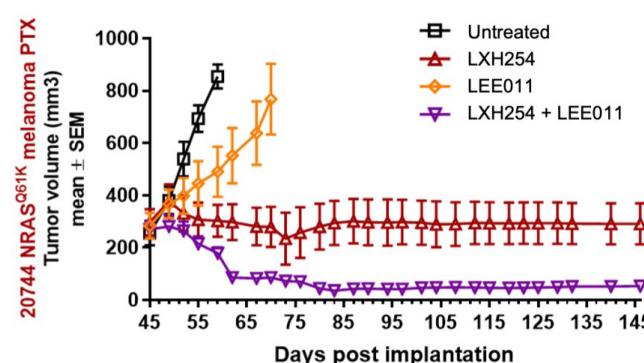
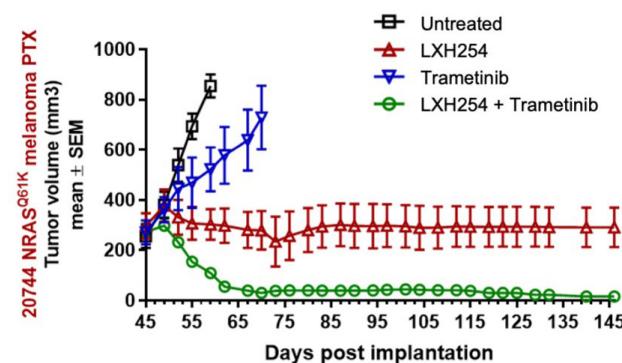
# LXH254: Potentially best-in-class B/C-RAF inhibitor in RAS/RAF mutant melanomas and lung cancers

## Highly potent and selective



- LXH254 inhibits both dimeric and monomeric B- and C-RAF kinases
- B/C-RAF inhibition targets RAS-mutant tumors and BRAF mutants both V600E and non-V600E

## Tumor growth inhibition as single agent or in combination

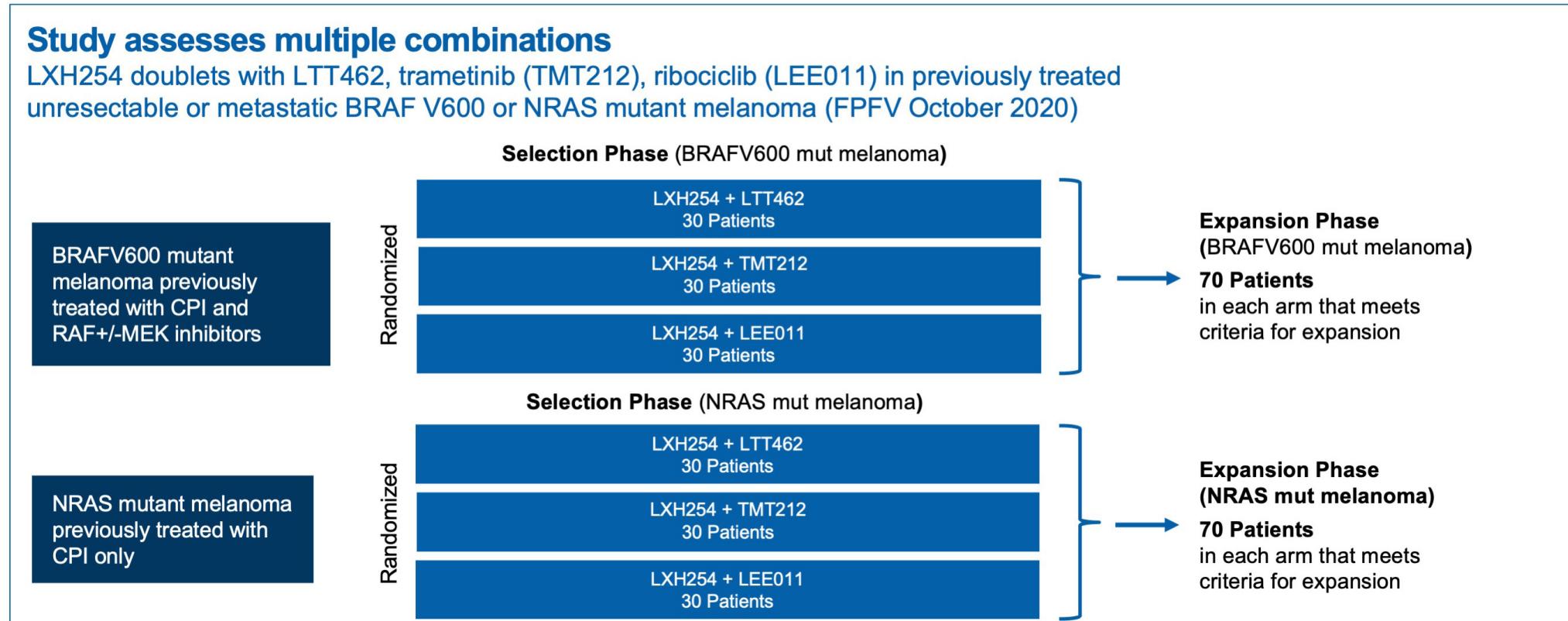


- Antitumor activity of LXH254 single agent was observed in patients with KRAS-mut and BRAF-mut cancers
- Preclinical data show robust activity in vertical combinations with MEK, ERK, and CDK4/6 inhibitors
- Favorable tolerability profile of LXH254 enables combinations
- Clinical studies evaluating LXH254 in combination with LTT462 (ERKi), trametinib (MEKi), ribociclib (CDK4/6) and spartalizumab (anti-PD-1) in RAS/RAF mutant NSCLC and melanoma ongoing

# Design of ongoing LXH254 combination study in melanoma

## Study assesses multiple combinations

LXH254 doublets with LTT462, trametinib (TMT212), ribociclib (LEE011) in previously treated unresectable or metastatic BRAF V600 or NRAS mutant melanoma (FPFV October 2020)



# Oncology: Hematology

**Asciminib**

**Sabatolimab**



Click to view  
**MNM Agenda**

# Asciminib (ABL001)

First-in-class 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 TKI therapy may be associated with increased resistance and intolerance
- Asciminib, a first-in-class STAMP inhibitor, has the potential to address these unmet needs
- The Ph3 ASCEMBL study met its primary endpoint of major molecular response (MMR) rate at 24 weeks; the study evaluated asciminib (ABL001) vs. bosutinib in patients with Philadelphia chromosome positive (Ph+) CML in Chronic Phase (CP) previously treated with two or more TKIs
- X2101/FIH study demonstrated clinical activity and favorable tolerability of asciminib in CML patients harboring T315I mutation (Oral at ASH, December 2020)
- **Global regulatory submissions planned in H1 2021**

# Asciminib in Chronic Myeloid Leukemia (CML)

Transform CML treatment standards to enable more patients to live disease-free

## High unmet need in 3L+ CML-CP

Many patients with CML are at risk of disease progression, and sequential TKI therapy can be associated with increased resistance and-treatment intolerance

## Significant unmet need in CML patients harboring T315I mutation

Many patients develop mutations that cause resistance to TKI therapy; the T315I mutation confers resistance to all approved TKIs except for ponatinib

## Prevalence

Although the incidence of CML is low (1-2/100,000 people), the prevalence is increasing (currently 55,500 US patients), because TKI treatment significantly reduces mortality

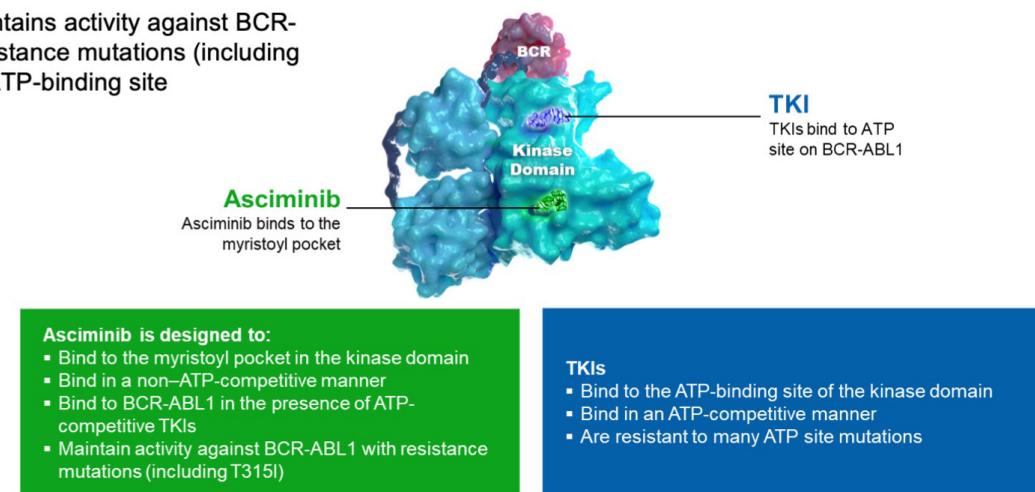
## Addressable market potential

Currently 10% - 15% of patients progress to 3L, but a significant number remain in 2L due to lack of appropriate options; failure rate in 3L is as high as 75% on current therapies

## Asciminib is a fist-in-class STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor and is different from ATP-competitive TKIs

The specificity of asciminib for BCR-ABL1 minimizes off-target activity, which may reduce toxicity

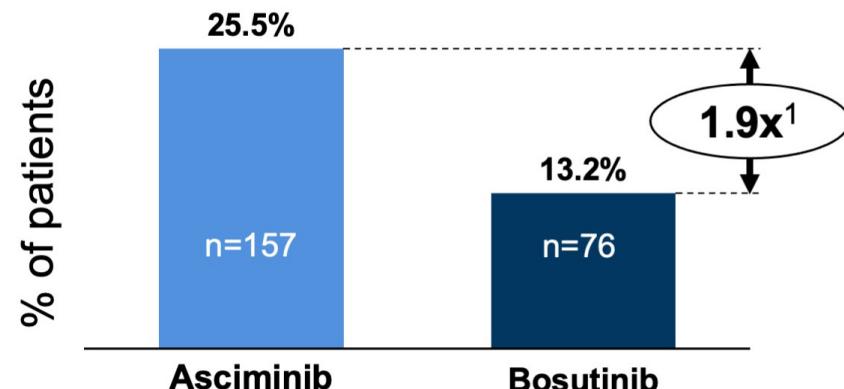
Asciminib maintains activity against BCR-ABL1 with resistance mutations (including T315I) in the ATP-binding site



## Asciminib Ph3 study (ASCEMBL) in 3L+ CML-CP

Primary endpoint met; ~two-fold improvement in MMR rate at 24 weeks

### Major Molecular Response (MMR) rate at 24 weeks



Asciminib demonstrated statistically significant superiority in efficacy compared to bosutinib and a favorable safety profile

- The MMR rate at 24 weeks was 25.5% with asciminib and 13.2% with bosutinib, meeting the study's primary endpoint

Pre-planned analysis showed that the MMR rate at 24 weeks was superior in the asciminib arm vs. the bosutinib arm across most major demographic and prognostic subgroups

Most frequent grade  $\geq 3$  AEs with asciminib vs. bosutinib were thrombocytopenia (17.3%, 6.6%), neutropenia (14.7%, 11.8%), diarrhea (0%, 10.5%), and increased alanine aminotransferase (0.6%, 14.5%)

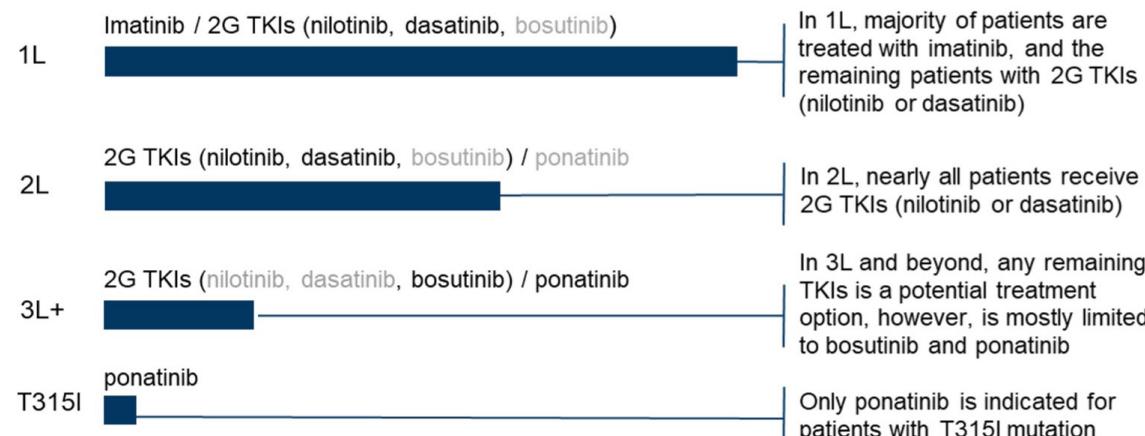
Assessment of asciminib line extension plans is ongoing

1. Difference: 12.2% (95% CI, 2.19-22.3; two-sided p = 0.029) per the Cochran-Mantel-Haenszel test which is stratified by baseline major cytogenetic response status

# Asciminib first launch in 3L+ CML with expansion to earlier lines

## Asciminib has the potential to transform standard of care in CML

### Patient Journey in CML, treatment options and preferences<sup>1</sup>



#### Asset maximization

##### Asciminib Label extension



Asciminib  
1<sup>st</sup> launch  
(3L+) 2022

### Market potential

Indication	Market size
1L CML-CP	●●●
3L+ CML-CP	●●○
T315I CML-CP	●○○
	●○○ <USD 500m
	●●○ USD 500m – 1bn
	●●● >USD 1bn

2G TKIs = 2<sup>nd</sup> Generation Tyrosine Kinase Inhibitors, CML-CP = Chronic Myeloid Leukemia in Chronic Phase. Ipsos, February 2020, EU5 countries. 1. Applicable globally where therapies are approved.

# Sabatolimab (MBG453)

First in class anti-TIM-3 monoclonal antibody, a unique opportunity in MDS/AML to target both immune and myeloid cells

Phase 3

## Key highlights

- Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) are related myeloid disorders with very high unmet medical need
  - 5-years survival is 20% in Higher-Risk (HR) MDS and 28% in AML
  - Significant toxicity impacts the benefit of current therapies
- High annual incidence rate (MDS: ~10,000/year; AML: ~ 20,000/year in US) makes it particularly important to develop novel therapies
- Sabatolimab may have both immunomodulatory and direct anti-leukemic effects which synergize with hypomethylating agents to enhance efficacy in MDS/AML
- Pivotal Ph2 study in **HR-MDS** is ongoing with read-out and **first submission expected H2 2021**
- Ph2 study in **Unfit AML** started in 2020 with Ph3 **read-out projected for 2025**

TIM-3, T cell immunoglobulin domain and mucin domain-3.

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

## Overall survival

**5-year survival is poor<sup>1</sup>:**

20% for HR-MDS

28% for AML

## Tolerability

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

## Lack of innovation

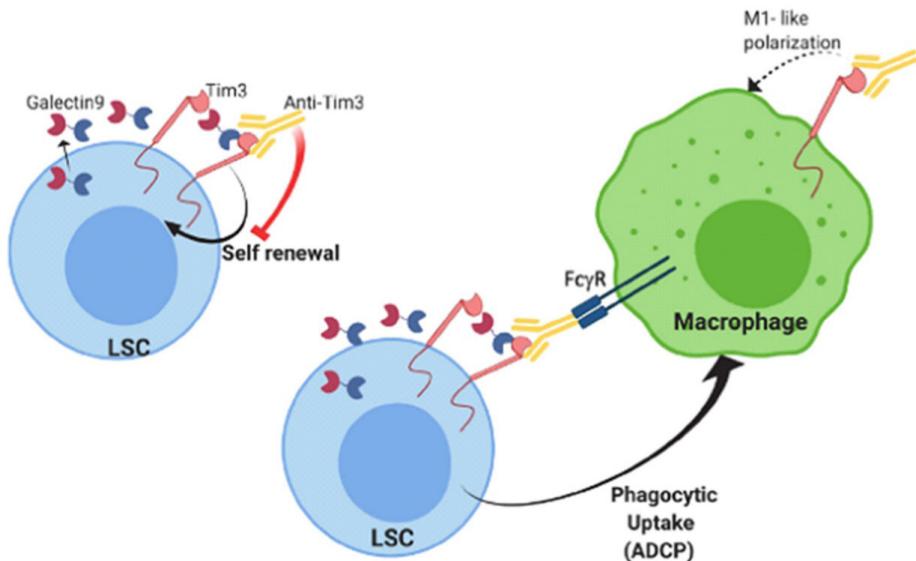
No regulatory approvals in over **10 years<sup>2</sup>** in HR-MDS

- Emerging data pointing to a strong role of immune dysfunction in MDS
- Higher Risk-MDS (HR-MDS) is a more aggressive type of MDS where patients have a worse prognosis and a higher chance of progressing to AML
- Unfit AML patients are often older and have general health status that precludes intensive chemotherapy
- Age at diagnosis is ~75 years for MDS and ~68 years for AML
- G7 annual incidence is ~15,300/year for HR-MDS and ~13,300/year for unfit AML<sup>3</sup>

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. AML: SEER data 2009-2015; High-riskMDS: Pfeilsticker et al., 2016.   2. VidazaEMA approval 2008, FDA 2004.   3. MDS Epidemiology: Greenberg et al, 1997/2012.

# Sabatolimab inhibits TIM-3, a dual target on immune cells and leukemic stem cells in AML and MDS

## Sabatolimab MoA



TIM-3 is expressed on myeloid immune cells and leukemic stem cells (LSC) but not on normal hematopoietic stem cells, making it a promising target in MDS/AML<sup>1-5</sup>

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

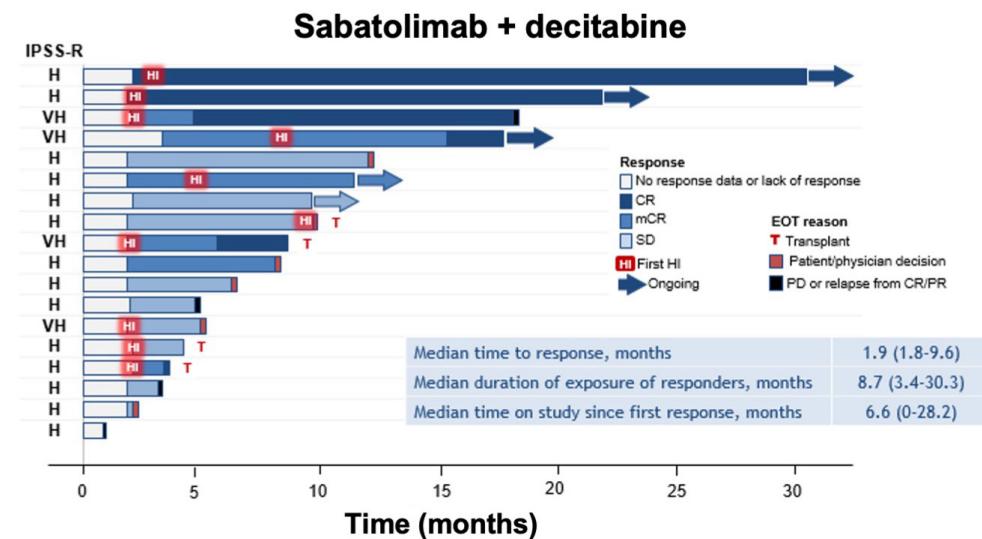
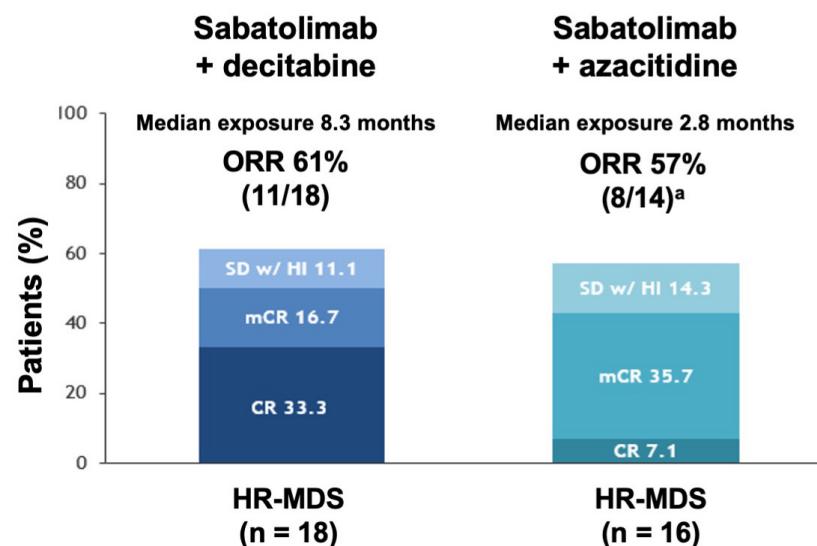
- Restore effector T-cell activity and promote antitumor activity<sup>3,6,7</sup>
- Disrupt the LSC galectin-9/TIM-3 autocrine loop and trigger ACDP<sup>8</sup>

Hypomethylating agents (HMA) upregulate TIM-3 on LSC

1. Wolf Y et al., Nature Immunology, 2019. 2. Asamaya T et al., Oncotarget 2017. 3. Kikushige Y et al., CellStemCells, 2010. 4. Goncalves Silva I et al., EBioMedicine, 2017. 5. Kikushige Y et al., CellStemCells, 2015. 6. DamaP et al., J. ImmunotherapyCancer, 2019. 7. Kong Y et al., Blood Cancer J., 2015. 8. Sabatos-Peyton C et al., SITC 2020.

# Sabatolimab + HMA lead to promising and durable response rates in an ongoing Ph1 trial

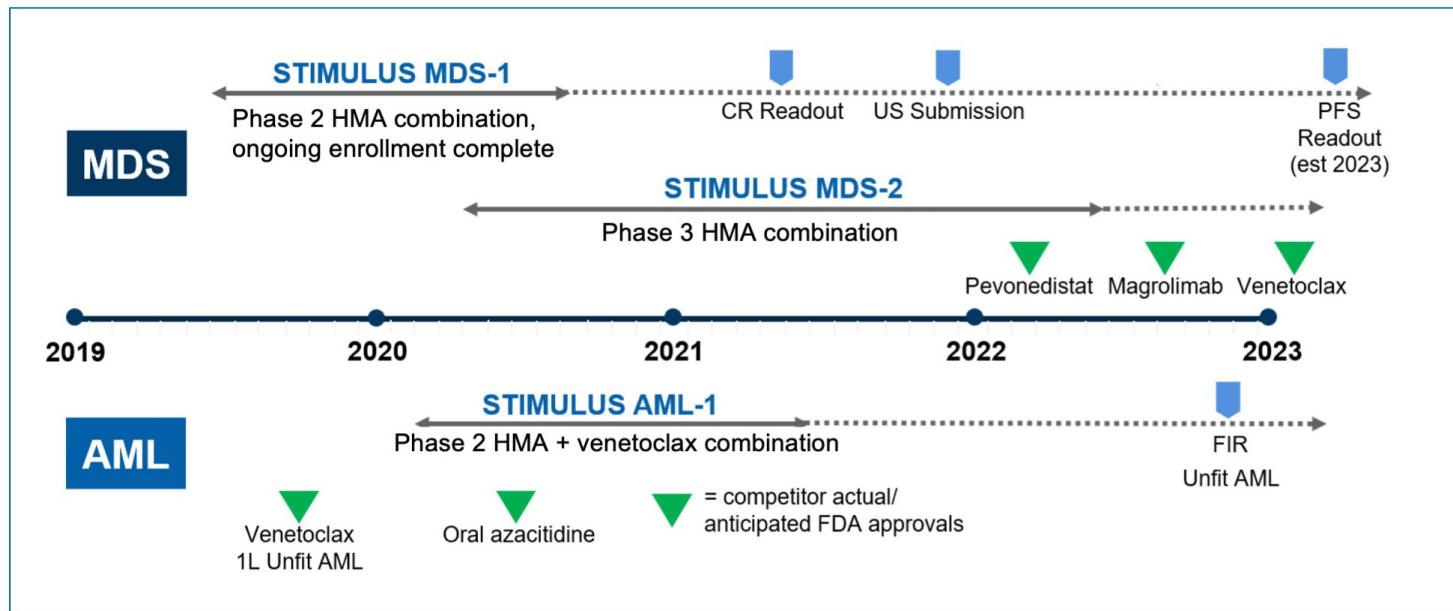
High CR/mCR rate with a favorable safety profile and emerging durability in high- and very-high IPSS-R risk MDS



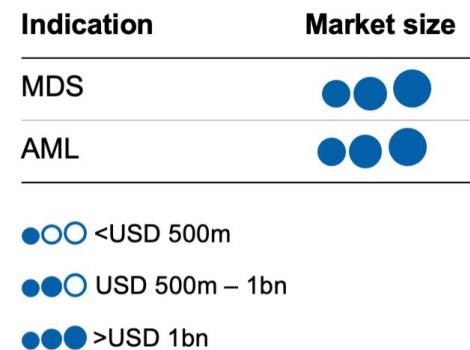
<sup>a</sup> Denominator is 14 (vs n = 16 in category label) due to 2 patients not yet reaching the timepoint for their first scan. CR, complete response; EOT, end of treatment; HI, haematological improvement; HMA, hypomethylating agent; HR-MDS, high-risk MDS; mCR, marrow complete response; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease. Borate U, et al. EHA 2020. Oral presentation. Wei A, et al. ESH Acute Leukaemia 2020. Oral presentation.

# STIMULUS program fully deployed in a competitive landscape

Pivotal studies initiated and first read-out expected in H2 2021



## Market potential



### Novel combinations

#### MDS/AML

Phase 1, HDM201<sup>a</sup> combination

### Myelofibrosis

Phase 1b/2, ruxolitinib combination

Phase 1, combination, post-JAK inhibitor patients

NCT03946670, NCT04266301, NCT04150029, NCT03940352, NCT04283526, NCT04097821. Available from (for example): <https://clinicaltrials.gov/ct2/show/NCT03946670>.

<sup>a</sup> HDM201: MDM2 inhibitor. JAK, Janus kinase.

# Sandoz

Where we are today

Strategy

Biosimilars & Antibiotics

Conclusion

Click to view  
**MNM Agenda**



# Sandoz aspires to drive growth, in order to deliver on pioneering access for patients

## Purpose

Pioneering access  
for patients



## Growth

Our ultimate measure  
of purpose



## Ambition

To be the world's leading  
and most valued  
generics company



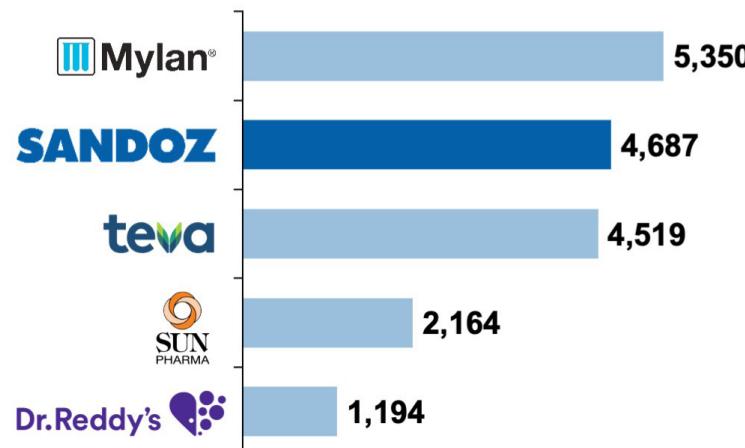
# Sandoz is a top two Gx player, with an unmatched presence across all three major regions...

The only global Gx company ranking top 3 across Europe, US and RoW

## H1 2020 market performance summary

### Gx Net Sales

USD million



Based on IQVIA MIDAS MAT 06 2019-20 data. Gx (Rx+ OTC + Bio) based on Gross IQVIA sales. IQVIA RoW data excludes key markets, incl. India. Source: Company qtrly reports, press releases; Sdzo financials.

## Sandoz rankings

Global	Biosimilars only	Gx Antibiotics	Gx Oncology
	1	1	1

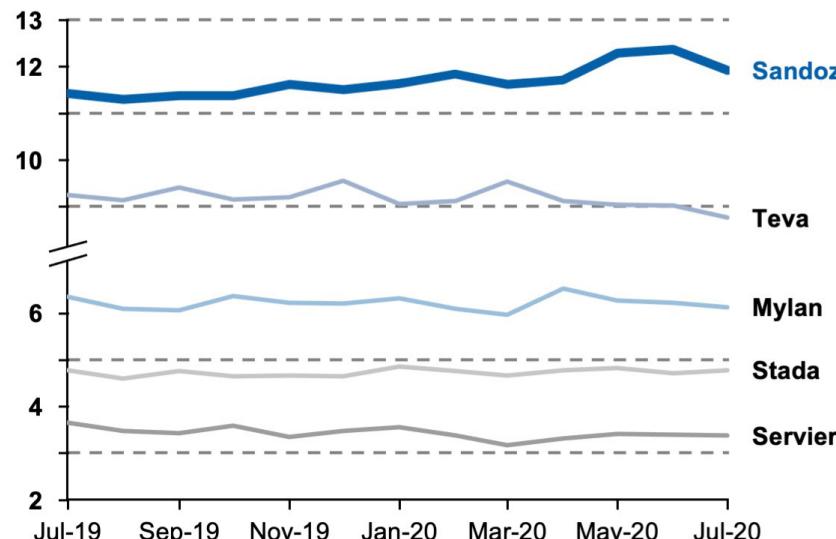
Regional	Gx EU	Gx US	Gx RoW <sup>1</sup>
	1	3	2

Source: IQVIA MIDAS data (MAT 06 2020). Gross sales in USD. QTR database updated till Jun 2020, currency impact included in RoW. 1. #5 across Latam/APAC

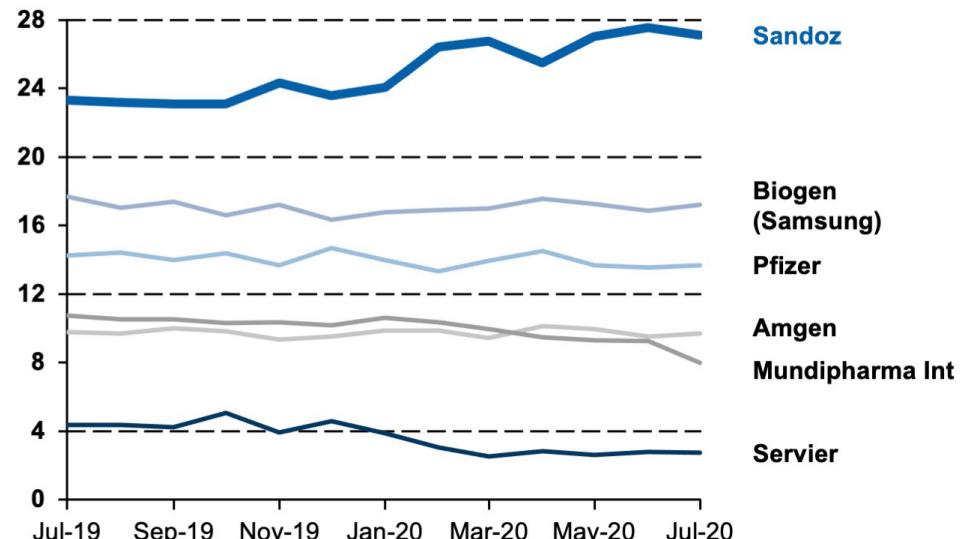
# ...number 1 Generics company in Europe...

## Monthly Gx market share development for Sandoz and key competitors

Market share is calculated in **Total Gx market** (in %)



Market share is calculated in **Total Biosimilar market** (in %)



Source: IQVIA PADDS July 2020 Value: @TGT 2020. Total Gx (OTC, Bio, Rx) excluding Kazakhstan, Baltics & Ireland.

## ...number 3 in US but committed to succeed with a goal to return to share growth

Sandoz is on track to submit ~40 first-to-files in US by 2024



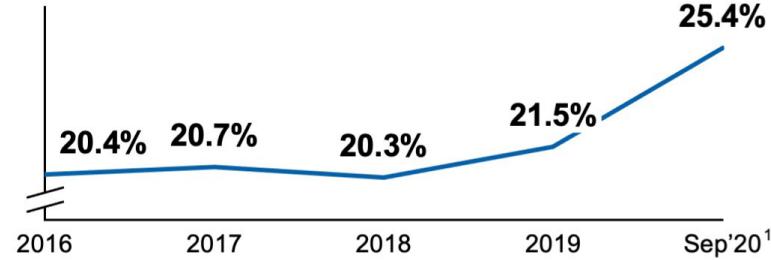
Segments	Oral Solids & Derm	Biosimilars	Specialty
Status	<p>Aurobindo termination maintains volume / scale</p> <p><b>Market size<sup>1</sup></b> USD ~53bn</p> <p>Termination of Aurobindo deal makes us #3 in US</p>	<p>Biosimilars continue to drive growth with 3 biosimilars in-market</p> <p><b>Market size<sup>1</sup></b> USD ~3bn</p> <p><b>Market growth</b> 2020-23 CAGR, % ~55%+</p>	<p>Injectables, respiratory and ophthalmology in focus</p> <p><b>Market size<sup>1</sup></b> USD ~42bn</p> <ul style="list-style-type: none"> <li>High-margin segments</li> <li>Growing market</li> <li>#1 in Ophthalmology</li> </ul>
Strategy	<p>Stabilize business to enable growth</p>	<p>Double down on biosimilars</p>	<p>Drive growth in specialty through innovation (e.g. KitCheck)</p>

1. MAT June 2020, USD

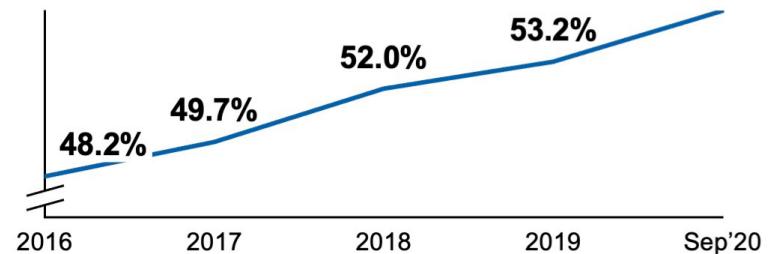
# Sandoz is driving value and delivering on its strategic goals...

## Financial progress

### Core ROS



### Gross Margin



## Strategic successes in key markets



Biosimilars in Europe are outgrowing the competition in a rapidly growing market



Two key strategic deals (KitCheck, Civica), with first products already launched



Successful Aspen Japan acquisition and integration

1. COVID favorability included

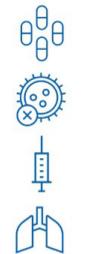
# ...and aiming to grow top line low-to-mid single digit, core margin to mid-to-high 20s with its portfolio and strategy

## Portfolio

### Biosimilars



### Small Molecules



- Oral solids
- Anti-infectives
- Steriles
- Respiratory

## First in, last out

- First-to-market launches
- Cost competitiveness
- Reliable & flexible supply
- Bolt-on M&A

## Enablers



### People & Culture



### Pragmatic autonomy



### Gx setup & mindset



### Complexity reduction



### Data & Digital

## Growth

### Biosimilars

Main growth driver from strong pipeline of 15+ assets leading to sales of up to USD 3.5bn by 2025, maintaining strong position in growing market

### Small molecules

High LoE coverage (EU: >80%, US: >50%) with ~40 first-to-files in US until 2024

## Competitiveness

### Gross margin

Gx TechOps network optimization  
Positive mix from higher biosimilar share

### TFC

Digital to transform commercial model and development

### ROS

Top quartile in industry (mid-to-high 20s in mid-to-long term)

# Pipeline focus on promising segments

## Sandoz priority market segments

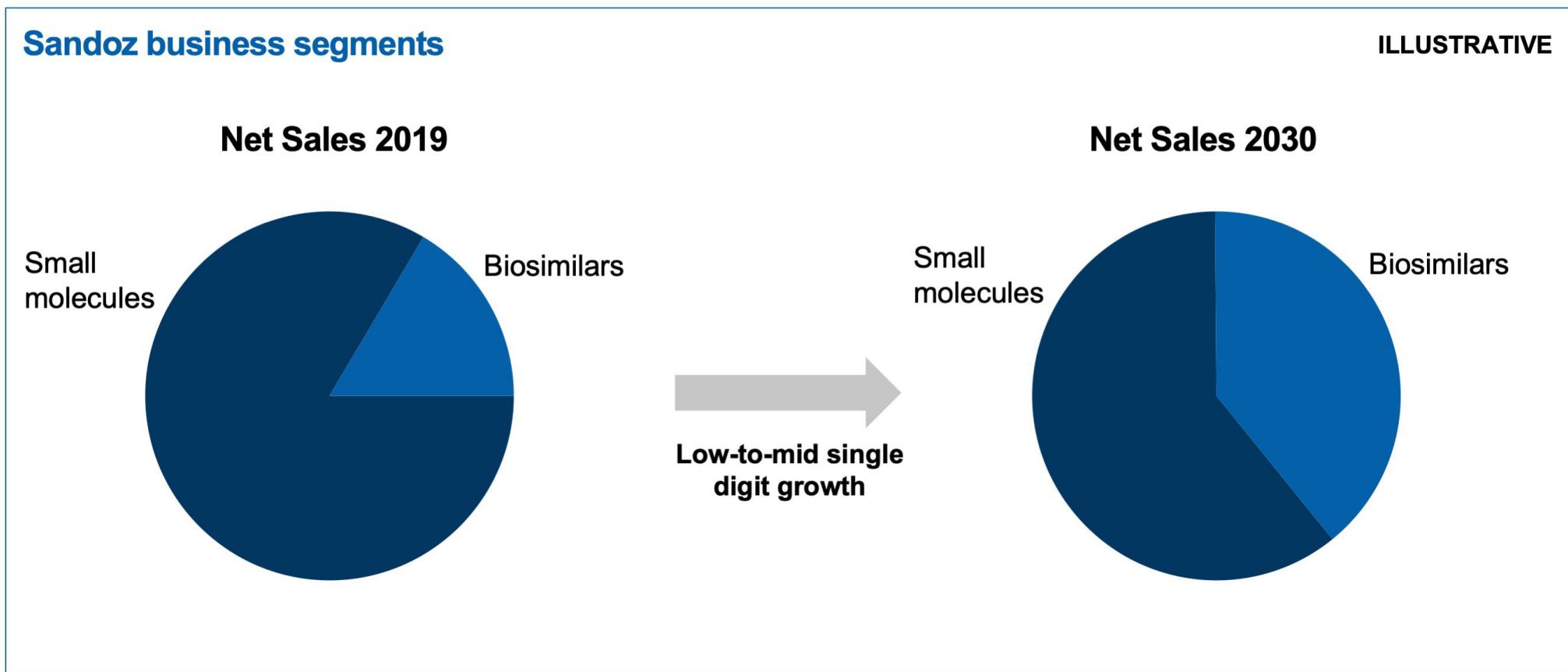
	2030 Gx Market <sup>1</sup> USDbn	2019-30 CAGR <sup>2</sup> %	# of relevant Gx players
 Standard Orals <sup>3</sup>	100	+1	100+
 Injectables <sup>4</sup>	70	+4	20+
 Biosimilars <sup>5</sup>	30	+9	~5
 Respiratory	19	+8	~5
 Antibiotics <sup>6</sup>	9	+1	10+

## De-prioritized market segments

	2030 Gx Market <sup>1</sup> USDbn	2019-30 CAGR <sup>2</sup> %
OTC	20	+2
Gynecology	11	+2
Ophthalmology	7	+4
Dermatology	6	+/-0
HIV/HCV	4	+5

1. Based on IQVIA sales. 2. Based on past sales, IQVIA market prognosis and other industry reports. 3. CVM, CNS, Gastro, Pain etc. 4. Including Oncology and Antibiotics. 5. Incl. Insulins. 6. Non-injectable.

# Growth driven by biosimilar expansion, while strengthening key segments of standard generics



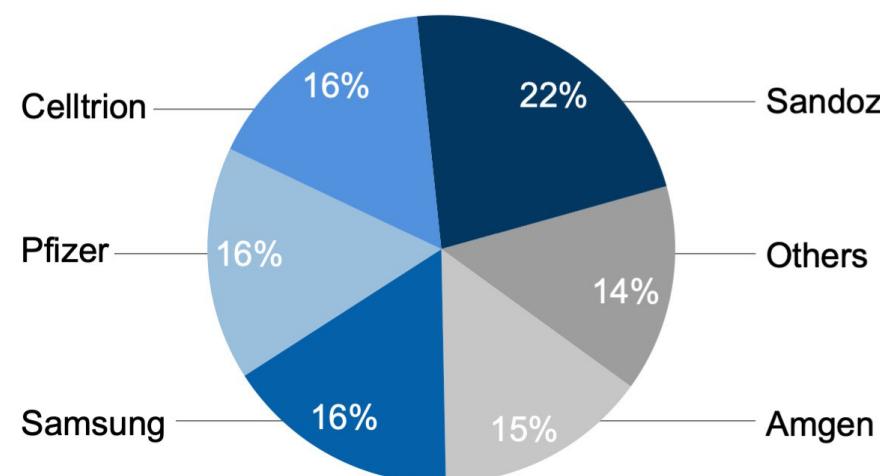
# Strong biosimilars market position, with 8 marketed molecules...

Biosimilars have grown at CAGR of 23% per year since 2006 to USD 1.6bn in 2019

## The global leader in biosimilars market share<sup>1</sup>

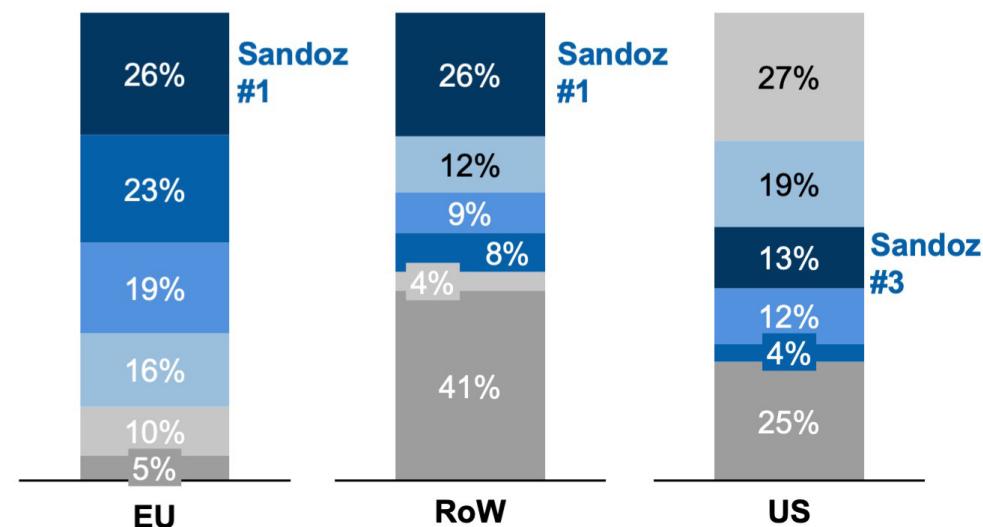
### Global view

Revenues



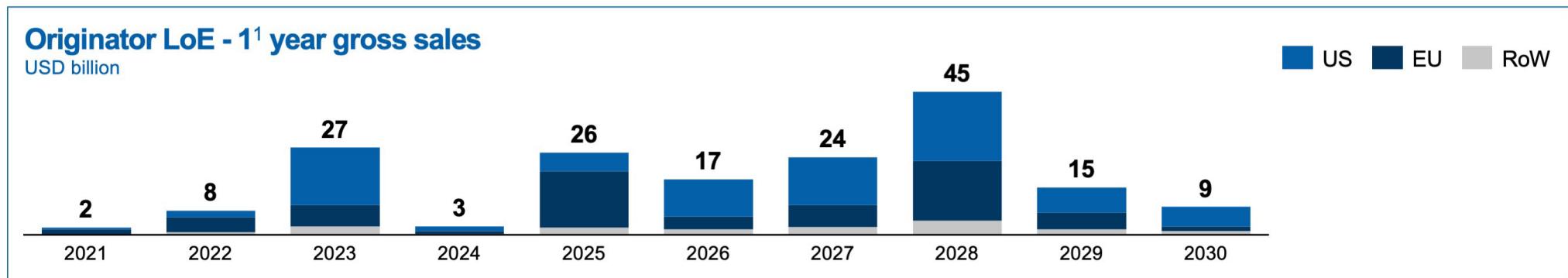
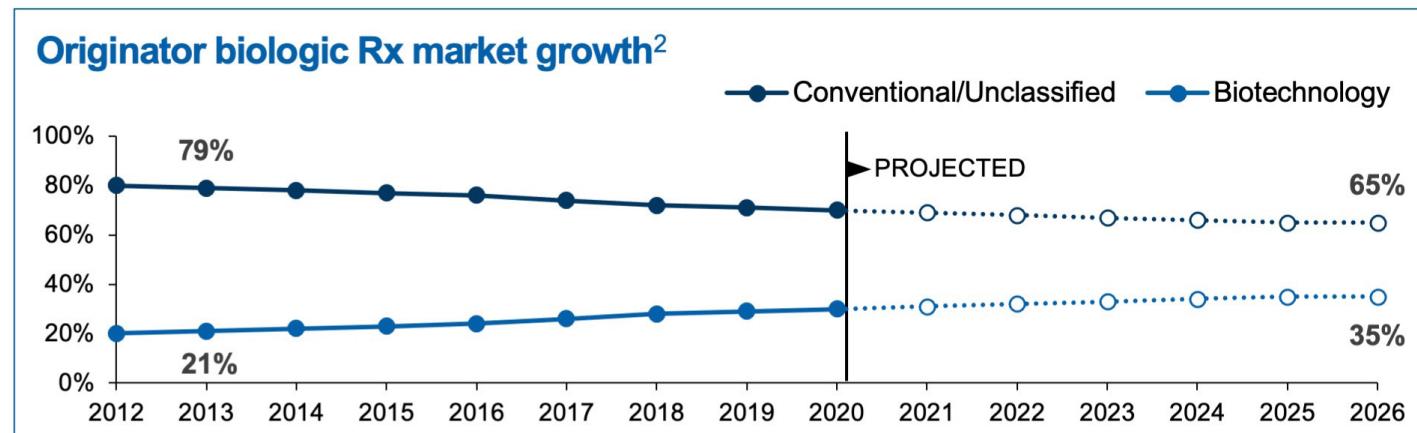
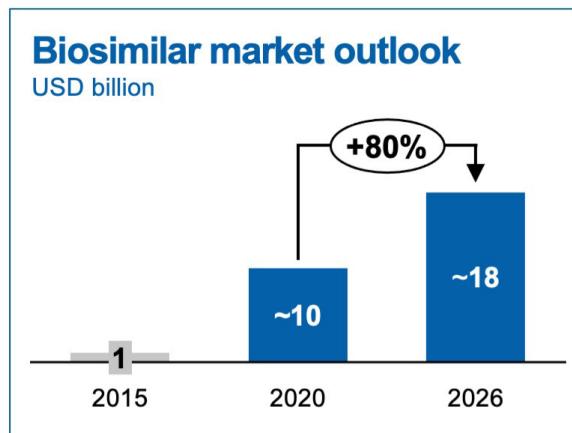
### Regional view

Sandoz  
 Celltrion/Teva  
 Samsung/Biogen  
 Pfizer  
 Amgen  
 Others



1. Without insulins, IQVIA August 2020

## ...the (biosimilar) opportunity continues to be significant and growing...

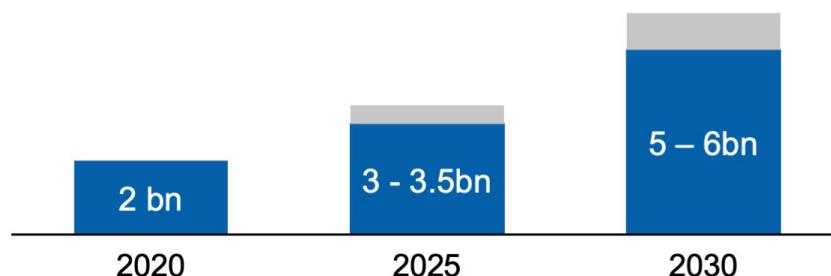


1 Loss of exclusivity. 2 Worldwide prescription drug & OTC pharmaceutical sales.

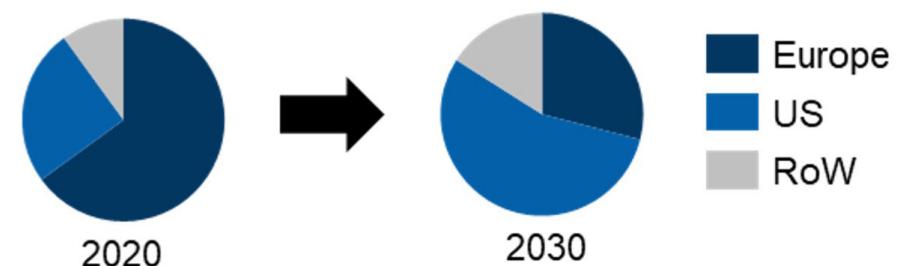
## ...and have a leading (biosimilar) pipeline with 15+ molecules, adding at least 1 new project per year

Potential timeframe (IP dependent)	2021-2023	2024-2026	2027-2029	2030 and beyond
Sandoz planned launches <sup>1</sup> (#)	2+	7+	4+	2+
Est. originator revenue <sup>2</sup> (USD billion)	25	40	50	20
Therapy area (Immuno / Onco/ Other)	Immuno / Other	Onco / Other	Onco	Immuno / Other
<b>Major growth catalysts (USD)</b> Originator LOE annual sales @ Sandoz Entry	~1bn ~18bn ~2bn	Adalimumab Can/Aus US Natalizumab	~6.5bn ~8bn ~6bn	Denosumab Other Onco <sup>3</sup>
				~9bn ~17bn
				Other Immuno <sup>4</sup>

### Revenue ambition



### Source of business



1. Externally partnered biosimilars disclosed in Phase 3: trastuzumab, insulins aspart, lispro, glargine, natalizumab. Other partnered assets not yet in phase 3 and undisclosed by partner. 2. In year of Sandoz biosimilar launch.

3. Refers to 3 of the biosimilars onco major growth catalysts. 4. Refers to 2 of the biosimilars immunology major growth catalysts.

# Sandoz #1 in Gx antibiotics – a USD 1bn business, with a unique integrated European supply chain

## Leading position in antibiotics

### Global #1 in Gx antibiotics

Strong **antibiotic portfolio** with over 150 different product and technology combinations

Flagship product, **AmoxiClav**, has steady market share of >20%, 15 formulations, 60+ strengths

## The only manufacturing network based outside Asia

Main antibiotic **manufacturing site in Kundl, Austria**, is only remaining integrated antibiotics production plant outside Asia, producing >170 million packs every year

**Joint investment** with AT government in Kundl (EUR 150m over 5 years for penicillin API/FDF)

**Dedicated development center in Kundl**, focused on antibiotics

## Strong commitment to access and sustainability

Working jointly on framework to **incentivize robust supply chains** for critical products

Signed 'Davos Declaration' for **collective and dedicated response to AMR**<sup>1</sup>

Driving **balanced approach** (access, responsible use, responsible manufacturing and R&D)

Source: IQVIA MIDAS 1. Antimicrobial Resistance

# Conclusion

## Sandoz remains focused on sustainable growth

1

Sandoz is focused on driving sustainable growth, in order to realize its business ambition and deliver on its Purpose: Pioneering access for patients

2

Sandoz aspires to maintain a strong position in the rapidly-growing biosimilars industry and to outgrow the global generics industry

3

Sandoz is committed to drive overall value by balancing sales growth with continued innovation and an unwavering commitment to social responsibility

# Appendix

**MNM Agenda**

**Portfolio overview**

**Glossary**



# Meet Novartis Management

**November 24, 2020**

All times in CET

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14:00 – 14:45 **Novartis Group** (incl. CEO intro)

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Break / 15 minutes

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15:00 – 15:45 **Pipeline / R&D**

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Break / 60 minutes

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16:45 – 17:30 **Pharmaceuticals**

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Break / 15 minutes

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17:45 – 18:30 **Oncology**

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Break / 15 minutes

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18:45 – 19:30 **Sandoz**

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Click to return to  
Contents page

# Pipeline projects at a glance

As presented at Q3 2020 financial results

Projects shown in blue are included in Meet Novartis Management

	Phase 1/2	Phase 3	Registration	Total
<b>ONCOLOGY</b>	52	21	1	74
<b>Solid Tumors</b> Kisqali®, Piqray®, Tabrecta™, Canakinumab, Lu-PSMA-617, TNO155, LXH254	12	4	2	18
<b>Hematology</b> Cosentyx®, Iscalimab, Ligelizumab	27	6	1	34
<b>PHARMACEUTICALS</b>	64	20	6	90
<b>Cardiovascular, Renal, Metabolism (CRM)</b> Entresto®, Leqvio, Pelacarsen, Iptacopan	12	4	2	18
<b>Immunology, Hepatology, Dermatology (IHD)</b> Cosentyx®, Iscalimab, Ligelizumab	27	6	1	34
<b>Neuroscience</b> Kesimpta®, Branaplam	6	3	1	10
<b>Ophthalmology</b> Beovu®	5	3	0	8
<b>Respiratory</b>	8	3	1	12
<b>Global Health</b>	6	1	1	8
<b>BIOSIMILARS</b>	Not disclosed	1	0	1
<b>Total</b>	116	42	7	165

# Novartis pipeline in Phase 1 (1 of 2)

As presented at Q3 2020 financial results

**38 lead indications**

Lead indication

Oncology				
Code	Name	Mechanism	Indication(s)	
177Lu-NeoB	177Lu-NeoB	Radioligand therapy target GRPR	Multiple solid tumors	
177Lu-PSMA-R2	177Lu-PSMA-R2	Radioligand therapy target PSMA	Prostate cancer	
ADPT01	ADPT01	-	TNBC (combos)	Colorectal Cancer (combos)
ADPT03	ADPT03		Sickle cell Anemia	
CSJ137	CSJ137	Growth Factor Inhibitor	Anaemia	
CTL019	Kymriah®	CD19 CART	Lymphoma	r/r DLBCL (+ pembro)
DKY709	DKY709 + spartalizumab	-	Cancers	
EGF816	nazartinib + LXH254, ribociclib, capmatinib, Opdivo, Mekinist	EGFR Inhibitor	NSCLC (combo)	
HDM201	HDM201 + MBG453, venetoclax	MDM2 Inhibitor	Haematological malignancy	
INC424	Jakavi	JAK1 / 2 Inhibitor	Myelofibrosis (combination)	
JBH492	JBH492	-	Haematological Malignancy	
JEZ567	JEZ567	CD123 CART	AML	
KAZ954	KAZ954	-	Solid tumors	
LHC165	LHC165 + spartalizumab	TLR7 Agonist	Solid tumors	
LXF821	LXF821	EGFR CART	Glioblastoma multiforme	
LXH254	LXH254 (combos)	cRAF Inhibitor	Solid tumors	Solid tumors
MAK683	MAK683	EED Inhibitor	Cancers	
MCM998	MCM998, LXG250	BCMA CART, CD19 CART	Multiple myeloma	
MIK665	MIK665	MCL1 Inhibitor	AML (combo)	
NIS793	NIS793, spartalizumab	TGFB1 Inhibitor	Solid tumors	
NIZ985	NIZ985, spartalizumab	IL-15 Agonist	Solid tumors	
NJH395	NJH395	-	Solid tumors	
NZV930	NZV930, spartalizumab, NIR178	CD73 Antagonist	Solid tumors	
PDR001	spartalizumab (combos)	PD1 Inhibitor	AML	Solid tumors (combo)
PHE885	PHE885	BCMA Cell therapy	Multiple Myeloma	
SQZ622	SQZ622	CD123xCD3 Modulator	AML	
TNO155	TNO155	SHP2 Inhibitor	Solid tumors (single agent)	Solid tumors (combo)
VAY736	ianalumab + ibrutinib	BAFF-R Inhibitor	Haematological malignancy	
VOB560	VOB560	-	Cancers	
VPM087	gevokizumab	IL1B Antagonist	CRC 1 <sup>st</sup> line	
WNT974	WNT974 + spartalizumab	Porcupine Inhibitor	Solid tumors	
WVT078	WVT078	-	Multiple myeloma	
YTB323	YTB323 ± ibrutinib	CD19 CART	Haematological malignancy	

# Novartis pipeline in Phase 1 (2 of 2)

As presented at Q3 2020 financial results

**38 lead indications**

Lead indication

## Immunology, Hepatology, Dermatology

Code	Name	Mechanism	Indication(s)			
CEE321	CEE321	Pan JAK Inhibitor	AD			
DFV890	DFV890	-	Anti-inflammatory therapy			
FIA586	FIA586	-	NASH			
MAS825	MAS825	-	Inflammatory diseases			
MHS552	MHS552	-	Autoimmune Indications			
MHV370	MHV370	-	Sjögren's	SLE		

## Global Health

Code	Name	Mechanism	Indication(s)		
KAF156	ganaplaclide	-	Malaria prophylaxis		

## Neuroscience

Code	Name	Mechanism	Indication(s)			
OAV201	AVX-201	MECP2 gene therapy	Rett syndrome			
LMI070	branaplam	mRNA splicing modulator	Huntington			

## Respiratory Disease

Code	Name	Mechanism	Indication(s)		
LTP001	LTP001	-	Respiratory Diseases		

## Cardiovascular, Renal, Metabolism

Code	Name	Mechanism	Indication(s)			
HSY244	HSY244	-	Atrial fibrillation			
MBL949	MBL949	-	Obesity related diseases			

# Novartis pipeline in Phase 2

As presented at Q3 2020 financial results

## Oncology

Code	Name	Mechanism	Indication(s)				
BYL719	alpelisib	PI3K $\alpha$ inhibitor	PROS				
BLZ945	BLZ945	CSF-1 Inhibitor	Solid tumors				
INC280	capmatinib	Met Inhibitor	NSCLC EU <sup>1)</sup>	Solid tumors	NSCLC (Combo)	NSCLC (Combo)	
INC424	Jakavi®	JAK1 Inhibitor	Myelofibrosis (combination)		Pediatrics Acute GVHD	Pediatrics Chronic GVHD	
MBG453	sabatolimab	TIM3 Antagonist	Unfit AML				
NIR178	NIR178, spartalizumab	Ad2AR Inhibitor, PD1 Inhibitor	Cancers				
PDR001	spartalizumab	PD1 Inhibitor	Metastatic melanoma (combo)				
SEG101	crizanlizumab	P-selectin Inhibitor	Ped sickle cell anaemia with crisis				

## Immunology, Hepatology, Dermatology

Code	Name	Mechanism	Indication(s)				
ADTP02	ADTP02	-	NASH (Combos)				
AIN457	Cosentyx®	IL17A Inhibitor	GCA	Lichen Planus			
CFZ533	iscalimab	CD40 Inhibitor	Renal Tx	Sjögren's	HS	Liver Tx	
LJC242	tropifexor&cenicriviroc	FXR agonist, CCR2 Inhibitor	NASH (combos)				
LJN452	tropifexor	FXR agonist	NASH	NASH (combos)			
LNA043	LNA043	ANGPTL3 Agonist	Osteoarthritis				
LOU064	remibrutinib	BTK Inhibitor	CSU / CIU	Sjögren's			
LRX712	LRX712	-	Osteoarthritis				
LYS006	LYS006	Anti-inflammatory	Acne	Colitis ulcerative	HS		
VAY736	ianalumab	BAFF-R Inhibitor	Sjögrens	AIH	SLE		

## Ophthalmology

Code	Name	Mechanism	Indication(s)				
CPK850	CPK850	RLBP1 AAV	RP				
ECF843	ECF843	rh-Lubricin	Dry eye				
LKA651	LKA651	EPO Inhibitor	DME				
SAF312	SAF312	TRPV1 Antagonist	COSP				
UNR844	UNR844	disulfide bonds Modulator	Presbyopia				

1. Approved in US & JP

## Portfolio overview

## 30 lead indications

Lead indication

### Neuroscience

Code	Name	Mechanism	Indication(s)				
BAF312	Mayzent®	S1P1 Modulator	Stroke				
BLZ945	BLZ945	CSF-1 Inhibitor	ALS				
LMI070	branaplam	mRNA splicing modulator	SMA				
MIJ821	MIJ821	NR2B Inhibitor	Depression				

### Respiratory Disease

Code	Name	Mechanism	Indication(s)				
CMK389	CMK389	IL-18 Inhibitor	Pulmonary sarcoidosis				
CSJ117	CSJ117	TSLP Inhibitor	Asthma				
DFV890	DFV890	-	COVID-19 related pneumonia				
LOU064	remibrutinib	BTK Inhibitor	Asthma				
MAS825	MAS825	-	COVID-19 related pneumonia				
QBW251	QBW251	CFTR Potentiator	COPD				
VAY736	ianalumab	BAFF-R Inhibitor	IPF				

### Cardiovascular, Renal, Metabolism

Code	Name	Mechanism	Indication(s)				
CFZ533	iscalimab	CD40 Inhibitor	Lupus Nephritis	T1DM			
LCZ696	Entresto®	Angiotensin II Receptor Neprilysin Inhibitor (ARNI)	nHCM				
LMB763	niduxefor	FXR Agonist	Diabetic Nephropathy				
LNP023	iptacopan	CFB Inhibitor	PNH	IgAN	C3G	iMN	aHUS
LTW980	LTW980	-	Hypertriglyceridemia				

### Global Health

Code	Name	Mechanism	Indication(s)				
AFQ056	AFQ056	mGlu5 Antagonist	Cocaine use disorder				
KAE609	cipargamin	PfATP4 inhibitor	Malaria severe	Malaria uncomplicated			
KAF156	ganaplaciade	-	Malaria uncomplicated				
LXE408	LXE408	Protozoan Inhibitor	Visceral leishmaniasis				

# Novartis pipeline in Phase 3

As presented at Q3 2020 financial results

## 5 lead indications

Lead indication

### Oncology

Code	Name	Mechanism	Indication(s)				
177Lu-PSMA-617	177Lu-PSMA-617	Targeted Radioligand Therapy	mCRPC				
177Lu-oxodotreotide <sup>1)</sup>	Lutathera®	Targeted Radioligand Therapy	GEP-NET 1L G3				
ABL001	asciminib	BCR-ABL Inhibitor	CML 3L				
ACZ885	canakinumab	IL-1b Inhibitor	NSCLC 1L	NSCLC 2L	Adjuvant NSCLC		
BYL719	Piqray®	PI3Kα inhibitor	HER2+ adv BC	TNBC	HNSSC 2/3L	Ovarian cancer	
CTL019	Kymriah®	CD19 CART	r/r Follicular lymphoma	1L high risk ALL, pediatrics and young adults	r/r DLBCL 1st relapse		
ETB115	Promacta®	Thrombopoietin receptor (TPO-R) Agonist	Radiation sickness syndrome		Food effect free formulation		
INC424	Jakavi®	JAK1 Inhibitor	Acute GVHD	Chronic GVHD			
LEO11	Kisqali®	CDK4 Inhibitor	HR+/HER2- BC (adj)				
MBG453	sabatolimab	TIM3 Antagonist	HR-MDS				
SEG101	crizanlizumab	P-selectin Inhibitor	Sickle cell anemia new formulation				

### Immunology, Hepatology, Dermatology

Code	Name	Mechanism	Indication(s)				
AIN457	Cosentyx®	IL17A Inhibitor	Lupus Nephritis	Hidradenitis suppurativa	AS H2H	PsA / axSpA IV/IV	
ACZ885	canakinumab	IL-1b Inhibitor	COVID-19 induced respiratory disease				
QGE031	ligelizumab	IgE Inhibitor	CSU / CIU				

### Ophthalmology

Code	Name	Mechanism	Indication(s)				
RTH258	Beovu®	VEGF Inhibitor	Diabetic retinopathy	RVO	DME		

1. 177Lu-dotatate in US. 2. FDA placed a partial hold on AVXS-101 intrathecal clinical trials for SMA patients based on findings in a small pre-clinical animal study. 3. Not aimed at label change. 4. Approved in US.

### Neuroscience

Code	Name	Mechanism	Indication(s)				
AMG334	Aimovig®	CGRP R antagonist	Ped Migraine				
BAF312	Mayzent®	S1P1 Modulator	Ped MS				
OAV101	AVXS-101	Gene Therapy, Survival motor neuron (SMN1) gene	SMA IT <sup>2)</sup>				

### Respiratory Disease

Code	Name	Mechanism	Indication(s)				
IGE025	Xolair®	IgE Inhibitor	Food allergy	Auto-injector			
INC424	Jakavi®	JAK1 Inhibitor	COVID-19 related pneumonia <sup>3)</sup>				

### Cardiovascular, Renal, Metabolism

Code	Name	Mechanism	Indication(s)				
KJX839	inclisiran	siRNA (regulation of LDL-C)	CVRR-LDLC				
LCZ696	Entresto®	Angiotensin II Receptor Neprilysin Inhibitor (ARNI)	Post-AMI	Pediatric HF <sup>4)</sup>			
TQJ230	pelacarsen	ASO targeting Lp(a)	CVRR-Lp(a)				

### Global Health

Code	Name	Mechanism	Indication(s)			
COA566	Coartem®	-	Malaria uncomplicated, new formulation <5kg patients			

### Biosimilars

Code	Name	Mechanism	Indication(s)				
GP2411	denosumab	anti RANKL mAb	Denosumab BioS				

# Novartis pipeline in registration

As presented at Q3 2020 financial results

**2 lead indications**

Lead indication

## Oncology

Code	Name	Mechanism	Indication(s)
SEG101	Adakveo®	P-selectin Inhibitor	Sickle cell disease <sup>1)</sup>

## Respiratory Disease

Code	Name	Mechanism	Indication(s)
IGE025	Xolair®	IgE Inhibitor	Nasal polyps <sup>2)</sup>

## Immunology, Hepatology, Dermatology

Code	Name	Mechanism	Indication(s)
AIN457	Cosentyx®	IL17A Inhibitor	300 mg AI

## Cardiovascular, Renal, Metabolism

Code	Name	Mechanism	Indication(s)
KJX839	inclisiran	siRNA (regulation of LDL-C)	Hyperlipidemia
LCZ696	Entresto®	Angiotensin II Receptor Neprilysin Inhibitor (ARNI)	HFpEF

## Neuroscience

Code	Name	Mechanism	Indication(s)
OMB157	ofatumumab	CD20 Antagonist	r MS <sup>3)</sup>

## Global Health

Code	Name	Mechanism	Indication(s)
LAM320	Lamprene®	SMPD1 Inhibitor	Tuberculosis <sup>4)</sup>

1. Approved in US, CHMP pos. opinion received. 2. Approved in EU. 3. Approved in US as Kesimpta®. 4. WHO Pre-Qualification.

# Glossary (1/2)

<b>aABC</b>	Advanced breast cancer
<b>ACT</b>	Actual
<b>AD</b>	Atopic Dermatitis
<b>aHUS</b>	atypical Hemolytic Uremic Syndrome
<b>AIH</b>	Autoimmune hepatitis
<b>ALL</b>	Acute lymphoblastic leukemia
<b>ALS</b>	Amyotrophic lateral sclerosis
<b>AMI</b>	Acute myocardial infarction
<b>AML</b>	Acute myeloid leukemia
<b>AS H2H</b>	Ankylosing spondylitis head-to-head study versus adalimumab
<b>ASCVD</b>	Atherosclerotic cardiovascular disease
<b>BC</b>	Breast cancer
<b>C3G</b>	C3 glomerulopathy
<b>CCF</b>	Congestive cardiac failure
<b>CHF</b>	Chronic heart failure
<b>CINDU</b>	Chronic inducible urticaria
<b>CLL</b>	Chronic lymphocytic leukemia
<b>CML</b>	Chronic myeloid leukemia
<b>CONS</b>	Consensus
<b>COPD</b>	Chronic obstructive pulmonary disease
<b>COSP</b>	Chronic ocular surface pain
<b>CRC</b>	Colorectal cancer
<b>CRSwNP</b>	Severe chronic rhinosinusitis with nasal polyps

<b>CSU</b>	Chronic spontaneous urticaria
<b>CVD</b>	Cardiovascular disease
<b>CVRR</b>	Cardiovascular Risk Reduction
<b>CVRR-LDLC</b>	Secondary prevention of cardiovascular events in patients with elevated levels of LDLC
<b>CVRR-Lp(a)</b>	Secondary prevention of cardiovascular events in patients with elevated levels of lipoprotein (a)
<b>D&amp;I</b>	Diversity & Inclusion
<b>DLBCL</b>	Diffuse large B-cell lymphoma
<b>DLBCL</b>	Diffuse large B-cell lymphoma refractory
<b>DME</b>	Diabetic macular edema
<b>DS&amp;AI</b>	Data Science & Artificial Intelligence
<b>E2E</b>	End to end
<b>ESG</b>	Environmental, social and governance
<b>ESMO</b>	European Society for Medical Oncology
<b>FF</b>	Field force
<b>FL</b>	Follicular lymphoma
<b>FPFV</b>	First patient first visit
<b>GCA</b>	Giant cell arteritis
<b>GHCR</b>	Global Health & Corporate Responsibility
<b>GTx</b>	Gene Therapies
<b>GVHD</b>	Graft-versus-host disease
<b>HCC</b>	Hepatocellular carcinoma
<b>HCP</b>	Healthcare provider
<b>HD</b>	Huntington's disease

## Glossary (2/2)

<b>HER2+ aBC</b>	Human epidermal growth factor receptor-2 positive advanced breast cancer
<b>HFpEF</b>	Heart failure with preserved ejection fraction
<b>HFrEF</b>	Heart failure with reduced ejection fraction
<b>HNSCC</b>	Head and neck squamous cell carcinoma
<b>HR-MDS</b>	Myelodysplastic syndrome
<b>HS</b>	Hidradenitis suppurativa
<b>IA</b>	Interim analysis
<b>IgAN</b>	IgA nephropathy
<b>IM</b>	Innovative Medicines
<b>iMN</b>	Membranous nephropathy
<b>IPF</b>	Idiopathic pulmonary fibrosis
<b>jPsA/ ERA</b>	Juvenile psoriatic arthritis / enthesitis-related arthritis
<b>LCM</b>	Lifecycle Management
<b>Lp(a)</b>	Lipoprotein(a)
<b>mCRPC</b>	Metastatic castration-resistant prostate cancer
<b>MDR</b>	Multi-drug resistant
<b>MDS</b>	Myelodysplastic syndrome
<b>MRD</b>	Measurable residual disease
<b>MS</b>	Multiple sclerosis
<b>NASH</b>	Non-alcoholic steatohepatitis
<b>NBS</b>	Novartis Business Services
<b>nHCM</b>	Non-obstructive hypertrophic cardiomyopathy
<b>nrAxSpA</b>	Non-radiographic axial spondyloarthritis

<b>NSCLC</b>	Non-small cell lung cancer
<b>NTO</b>	Novartis Technical Operations
<b>PDR</b>	Proliferative diabetic retinopathy
<b>PedPsO</b>	Pediatric psoriasis
<b>PEF</b>	Preserved ejection fraction
<b>PNH</b>	Paroxysmal nocturnal haemoglobinuria
<b>PROS</b>	PIK3CA related overgrowth spectrum
<b>PsA H2H</b>	Psoriatic arthritis head-to-head study versus adalimumab
<b>RA</b>	Rheumatoid arthritis
<b>RCC</b>	Renal cell carcinoma
<b>rMS</b>	Relapsing multiple sclerosis
<b>ROP</b>	Retinopathy of prematurity
<b>RP</b>	Retinitis pigmentosa
<b>RVO</b>	Retinal vein occlusion
<b>SAA</b>	Severe aplastic anemia
<b>SLE</b>	Systemic lupus erythematosus
<b>SMA Type 1</b>	Spinal muscular atrophy (IV formulation)
<b>SMA Type 2/3</b>	Spinal muscular atrophy (IT formulation)
<b>SpA</b>	Spondyloarthritis
<b>SPMS</b>	Secondary progressive multiple sclerosis
<b>T1DM</b>	Type 1 Diabetes mellitus
<b>TNBC</b>	Triple negative breast cancer
<b>wAMD</b>	Wet (neovascular) age-related macular degeneration