



Novartis AG  
Investor Relations

# Meet Novartis Management Overview

Investor Presentation  
May 23, 2019

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This presentation contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995, that can generally be identified by words such as “potential,” “expected,” “will,” “planned,” “pipeline,” “outlook,” or similar expressions, or by express or implied discussions regarding potential new products, potential new indications for existing products, or regarding potential future revenues from any such products; or regarding the potential outcome, or financial or other impact on Novartis, of the spinoff of our Alcon Division, or of the proposed divestiture of certain portions of our Sandoz Division business in the US; or regarding the potential impact of the share buyback plan; or regarding potential future sales or earnings of the Group or any of its divisions or potential shareholder returns; or by discussions of strategy, plans, expectations or intentions. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. You should not place undue reliance on these statements. In particular, our expectations could be affected by, among other things: global trends toward healthcare cost containment, including ongoing government, payer and general public pricing and reimbursement pressures and requirements for increased pricing transparency; regulatory actions or delays or government regulation generally, including potential regulatory actions or delays with respect to the proposed transactions or the development of the products described in this presentation; the potential that the strategic benefits, synergies or opportunities expected from the Alcon and Sandoz transactions may not be realized or may be more difficult or take longer to realize than expected; the inherent uncertainties involved in predicting shareholder returns; the uncertainties inherent in the research and development of new healthcare products, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products that commenced in prior years and will continue this year; safety, quality or manufacturing issues; uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential litigation with respect to the proposed transactions, product liability litigation, litigation and investigations regarding sales and marketing practices, intellectual property disputes and government investigations generally; uncertainties involved in the development or adoption of potentially transformational technologies and business models; our performance on environmental, social and governance measures; general political, economic and trade conditions, including uncertainties regarding the effects of ongoing instability in various parts of the world; uncertainties regarding future global exchange rates; uncertainties regarding future demand for our products; uncertainties regarding potential significant breaches of data security or data privacy, or disruptions of our information technology systems; and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this presentation as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.

# Our external environment is reshaping what it takes to lead in the long-term



- Explosion in data science
- New understanding of human biology
- New therapeutic platforms



- Rising standard of care
- Pricing pressure
- Convergence of tech and health



→ Companies that focus their capital on leading science, cutting-edge platforms, and medicines with substantial absolute efficacy, will win

# We aim to become a leading medicines company

Powered by advanced therapy platforms and data science

We are a diversified  
medicines company



Driving growth  
through cutting-  
edge platforms



Passionate about  
productivity and  
margins



Building a new  
culture and lasting  
impact



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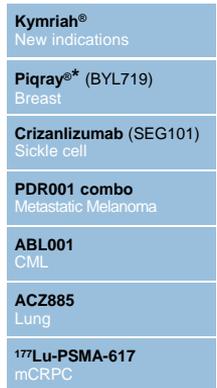
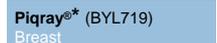
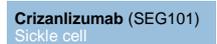
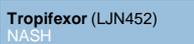
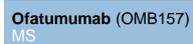
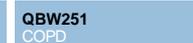
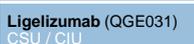
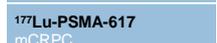


# Focused on medicines, diversified across therapeutic areas and platforms

Company	Revenue split, % medicines <sup>1</sup>	Presence in advanced therapy platforms <sup>4</sup>								
		Rx	Gx	Other	TAs <sup>2</sup>	Blockbusters <sup>3</sup>	Cell	Gene	RLT	RNAi
<b>Novartis</b>	100%				10	15	X	X	X	X
Company 1	100%				3	8				
Company 2	98%				6	3				
Company 3	97%				2	8	X			
Company 4	96%				4	6	X			
Company 5	94%				6	7				X
Company 6	93%				6	8				
Company 7	82%				9	8		X		
Company 8	81%				2	4				
Company 9	80%				6	6				X
Company 10	71%				8	11				
Company 11	70%				9	5				
Company 12	63%				10	4		X		
Company 13	48%				9	11				X
Company 14	44%				11	4				
Company 15	41%				4	4	X			

EvaluatePharma data for FY 2018 See appendix for references

# Building depth across our core therapeutic areas

		PHARMACEUTICALS					BIOPHARMA
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory	
Select commercial assets							
							
Select pipeline assets and opportunities							
							
							
							
							
							
							

\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country. See appendix for references.

# Expanding the game-board with advanced therapy platforms

(illustrative)	Small molecules	Large molecules	Cell therapy	Gene therapy	Radioligand therapy	RNAi therapy	
 Oncology	Targeted protein degradation	Novel biomaterials <sup>1</sup>	Bispecific antibodies <sup>2</sup>	CAR-T	NET	PSMA	Early targets
 Cardio-Metabolic				CRISPR <sup>3</sup>	Novel manufacturing		
 IHD							
 Neuroscience	Transcription factors				AAV9		
 Ophthalmology		Novel biomaterials			Experimental serotypes	AAV2 <sup>4</sup>	
 Respiratory		Inhaled biologics					

1. Partnership with the Wyss Institute for Biologically Inspired Engineering at Harvard University and the Dana-Farber Cancer Institute 2. Collaboration with Xencor 3. Collaborations with Intellia Therapeutics and Caribou Biosciences  
4. Collaboration with Spark on Luxturna® 5. Collaboration with Akcea

# Advancing a highly productive and valuable pipeline

## Scale

**200+** Projects in clinical development

**500+** Ongoing clinical trials<sup>2</sup>

**60+** Major submissions planned 2019-2021<sup>3</sup>

## Value

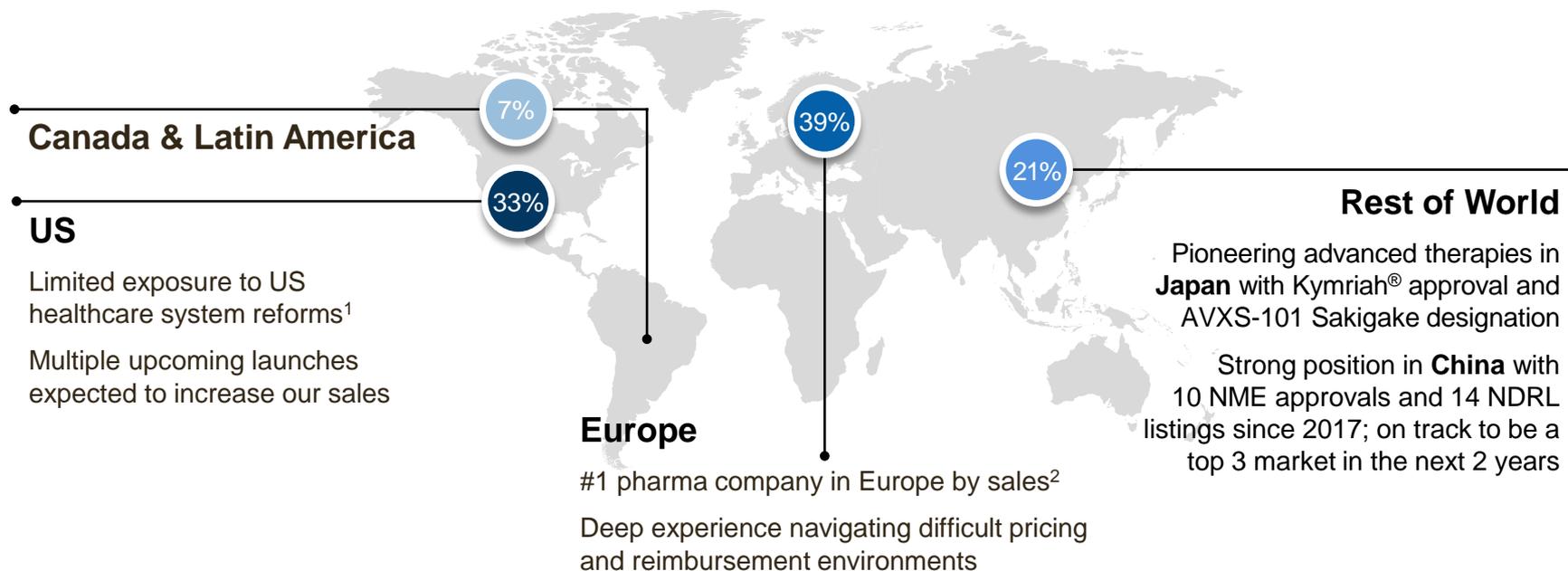
**25+** Potential blockbusters<sup>1</sup> in development

**18** Advanced platform therapies in clinical development

**#1** Most valuable pipeline according to external ranking<sup>4</sup>

1. Blockbuster defined as peak sales >USD 1bn for either a new molecular entity across all indications or for a single new indication of a previously launched product 2. Across NIBR and GDD 3. Submissions in US/EU/JP 2019-21  
4. Source: Evaluate Pharma 2018, outlook to 2024. Ranked #1 in terms of: (1) value creation from advanced therapies, (2) highest pipeline value by sales 2018-24, and (3) value creation 2018-24 from recently launched and pipeline products.

# Global scale and leadership in strategic markets



% of 2018 FY sales excluding Alcon and Sandoz proposed US portfolio sale to Aurobindo 1. Due to highly innovative and differentiated portfolio, limited exposure to Medicare Part B, 340B 2. Source: EvaluatePharma 2018 FY sales

# Building data science and digital capabilities

## Sense Bridge

Transforming clinical trial operations



- Tracks, analyzes and predicts the status of 500+ active trials in 70+ countries involving 80k+ patients in real time
- Other modules enable selection of best trial sites, enrollment tracking, predicting trial risks, drug supply calculations, etc.

## ACTalya

Making sales reps more efficient



- Combines predictive analytics with digital campaign management tools to guide our sales reps towards the “next best action” with each customer they serve
- Piloted in 2018 with 500 reps across 6 countries; scaling up to 7k reps in 2019

## AI-driven Finance

Improving finance operations



- Leveraging AI to improve all planning, forecasting and resource allocation activities
- Initial focus is on sales, P&L and cash forecasting & optimization; results show AI is at least as good as internal plans

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

## Novartis priorities

1. Investments in organic business

Renewed focus on core medicines business with successful spin-off of Alcon

2. Growing annual dividend in CHF

Committed to maintain strong and growing dividend with no adjustment for Alcon spin-off

3. Value-creating bolt-ons

Announced acquisition of Xiidra<sup>®1</sup>; aim to spend up to ~5% of market cap per year on M&A and BD&L

4. Share buybacks

Repurchased 12.6m shares on the 2<sup>nd</sup> trading line 2019 YTD<sup>2</sup>; plan to complete share buyback<sup>3</sup> of up to USD 5bn by end of 2019

1. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions 2. As of May 17, 2019 3. Share buyback of up to USD 5bn announced on June 29, 2018

# Xiidra<sup>®</sup> acquisition: Strong strategic fit and attractive economics<sup>1</sup>

Strong strategic fit	with Novartis leading ophthalmic portfolio and pipeline
Clear blockbuster potential	given high unmet medical need with strong product profile
Significant synergies	with Novartis front-of-the-eye commercial infrastructure
Good financial return profile	strict financial discipline applied; expected to be profitable 2020 and margin accretive 2021; deal structure adds tax benefit

  
Xiidra<sup>®</sup>  
(lifitegrast)  
ophthalmic solution 5%  
  
**Xiidra<sup>®</sup>  
complements  
the Novartis  
ophthalmology  
portfolio**

  
**LUCENTIS**<sup>2</sup>  
RANIBIZUMAB INJECTION

  
**DUREZOL**<sup>®</sup>  
(difluprednate ophthalmic emulsion) 0.05%

  
**ILEVRO**<sup>™</sup>

  
**Pazeo**<sup>®</sup>  
(olopatadine hydrochloride ophthalmic solution) 0.7%

  
**Azopt**<sup>®</sup>

  
**TRAVATAN Z**<sup>®</sup>

  
**SIMBRINZA**<sup>®</sup>  
(brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%

  
**LUXTURNA**<sup>™2</sup>  
voretigene neparvovec-rzyl  
for subretinal injection

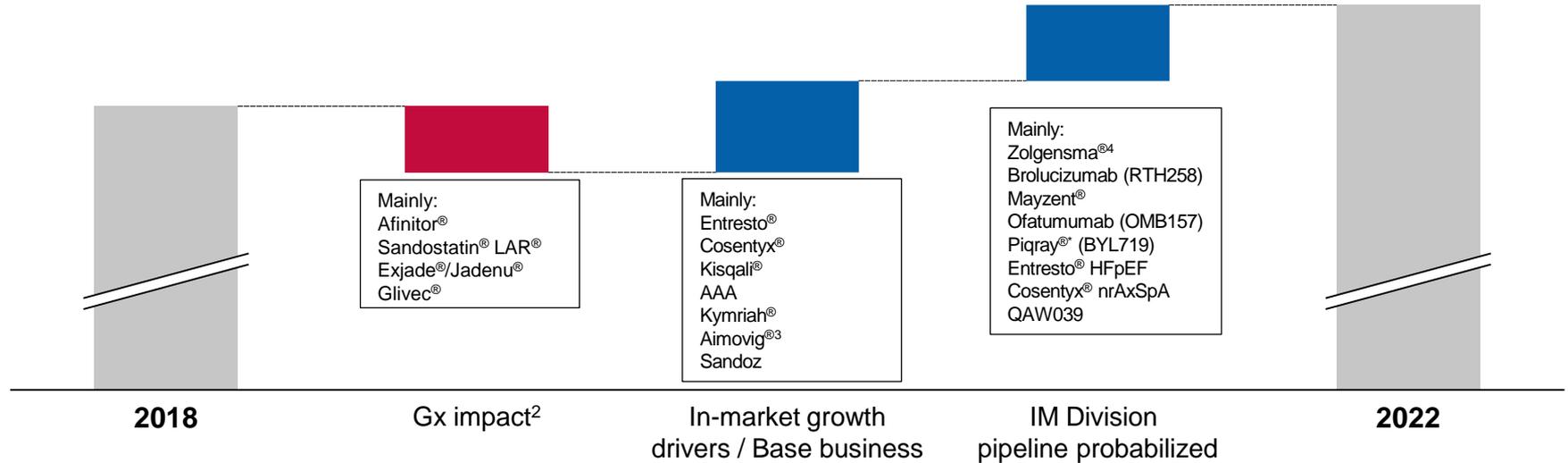
1. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions 2. Ex-US only

# Our growth prospects are strong

Expecting strong sales growth regardless of Gilenya<sup>®</sup> Gx

## Illustrative sales<sup>1</sup> FY 2018–2022

in cc

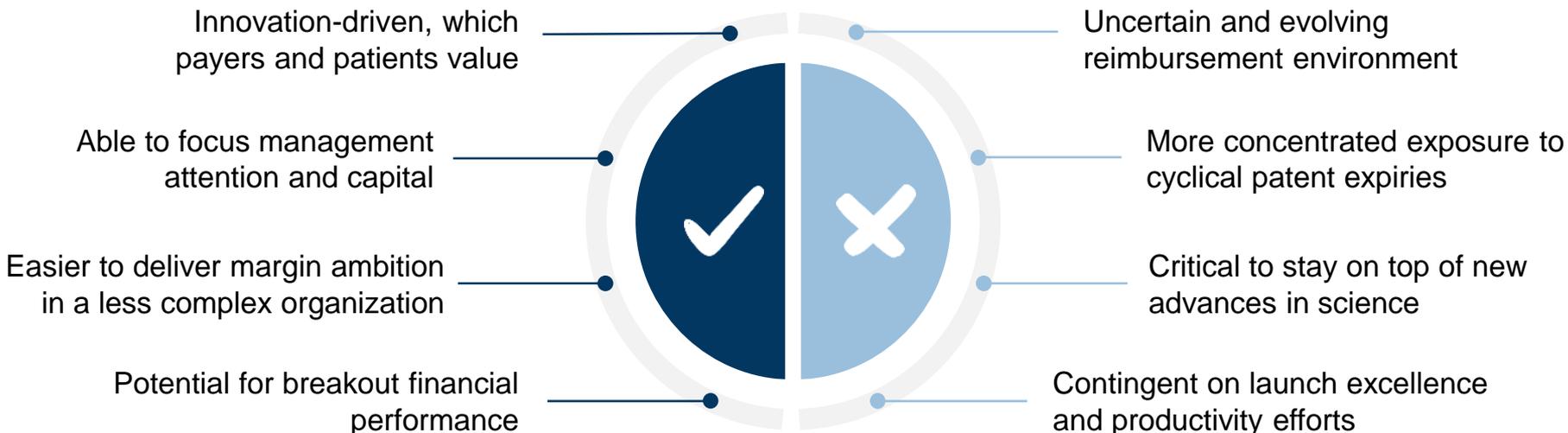


\*The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Benefits and risks to the new focused Novartis

## Benefits

## Risks



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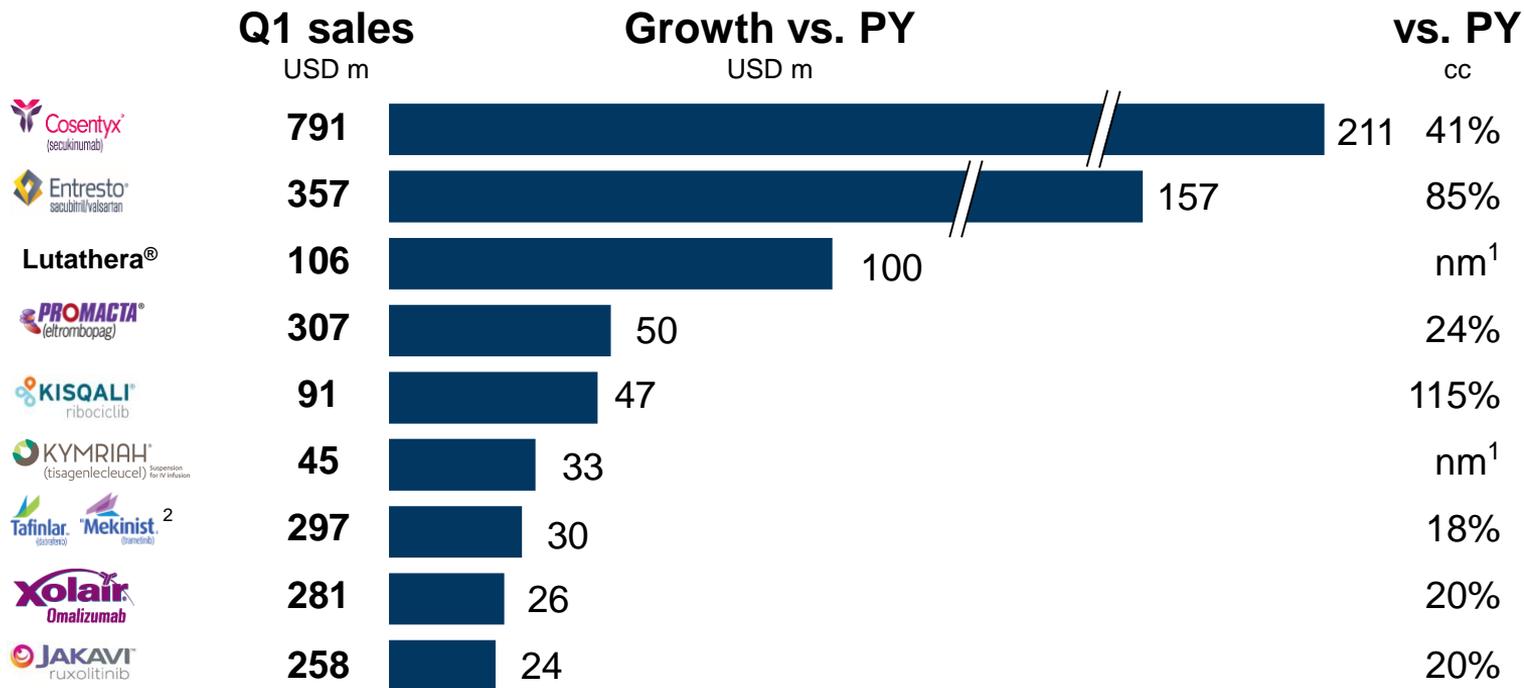
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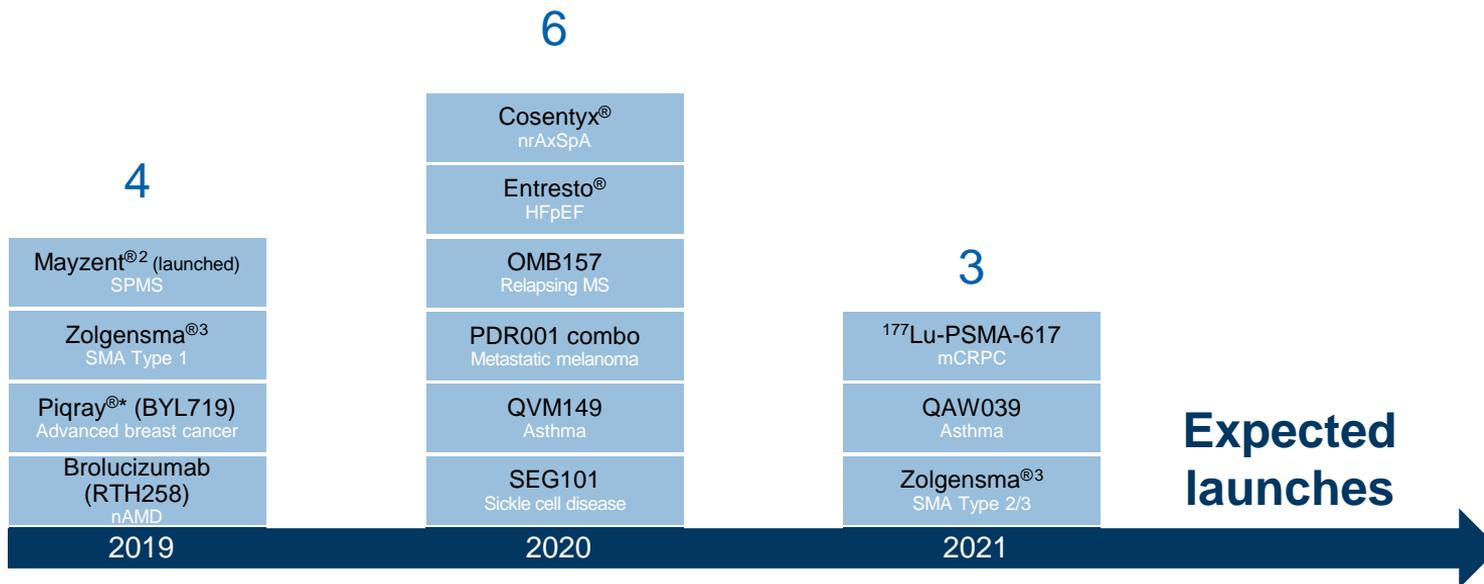


# In-line brands provide strong foundation for growth



1. Not meaningful 2. Combined sales of Tafinlar<sup>®</sup> and Mekinist<sup>®</sup>

# 10+ potential blockbuster launches<sup>1</sup> planned up to 2021



<sup>1</sup>The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country. See appendix for references.

# Zolgensma® (AVXS-101): Robust data show clinically transformative impact across broad spectrum of SMA



Pre-symptomatic

**SPRINT**

Ph3, open-label, single-arm, multi-center trial to evaluate safety and efficacy of IV Zolgensma® in **pre-symptomatic SMA patients with 2 or 3 copies of SMN2 <6 weeks**



Type 1

**STRIVE**

Ph3, open-label, single-arm, single-dose, multi-center trial to evaluate efficacy and safety of IV Zolgensma® in **SMA Type 1 patients <6 months**



Type 1

**START** Long-term follow-up

Voluntary, ongoing, observational, long-term follow-up study in patients from the Ph1 open-label, single-site trial to evaluate safety and efficacy of IV Zolgensma® in **SMA Type 1 patients <6 months**



Type 2

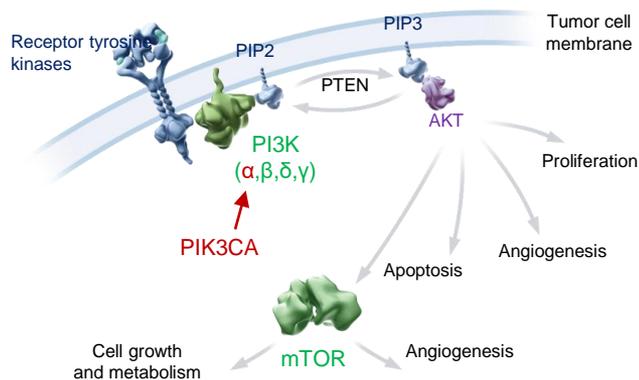
**STRONG**

Ph1, open-label, dose-comparison, multi-center trial to evaluate safety and tolerability of intrathecal (IT) Zolgensma® in **SMA Type 2 patients 6 months – 5 years**

1. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

# Piqray®\* (BYL719): Potential to be the first and only therapy for the most common mutation in HR+ aBC

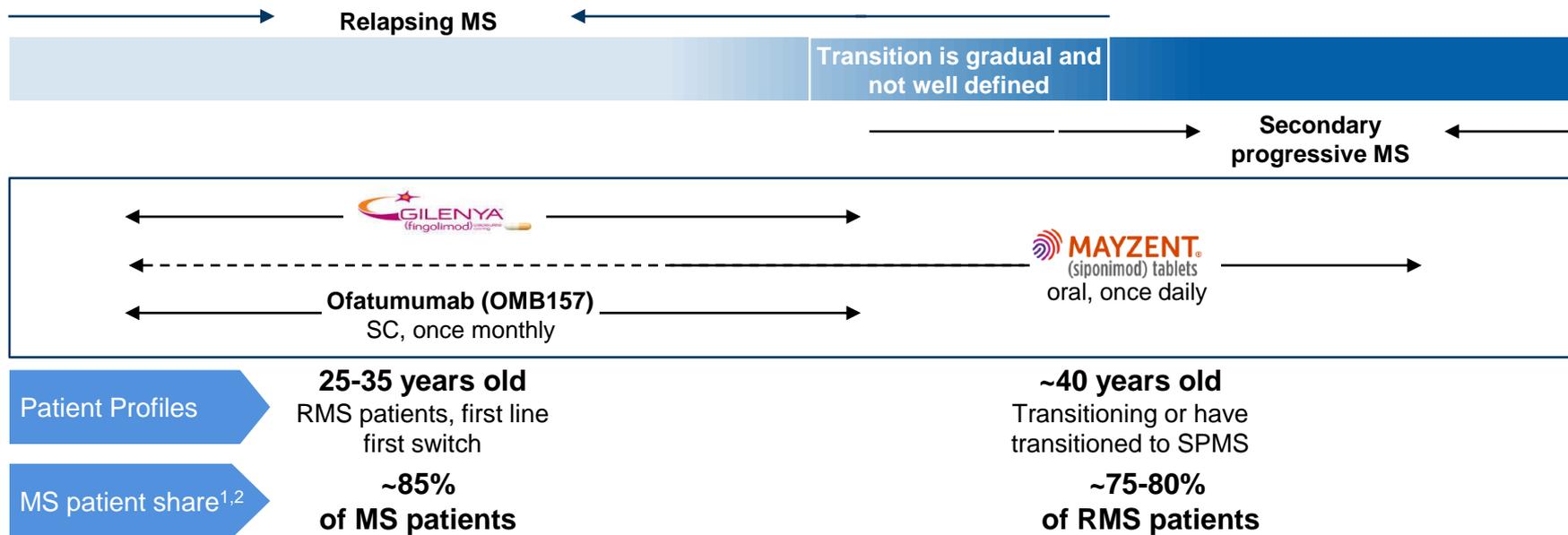
## PI3K: Central oncogenic pathway deregulated in cancer



- Poised to be the first and only therapy for advanced breast cancer (aBC) patients with a PIK3CA mutation
- ~40% of HR+/HER2- breast cancer patients have a PIK3CA mutation, associated with poor prognosis<sup>1,2</sup>
- Nearly doubled median PFS in SOLAR-1 study<sup>3</sup>
- Ready to launch with FDA-approved companion diagnostic
- Initiating pivotal clinical trials in HER2+ aBC and TNBC; planning additional studies across PIK3CA-mutation driven cancers

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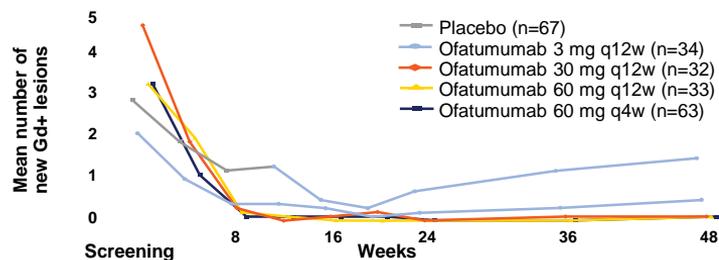
# With new and planned launches, Novartis continues to lead across the MS disease spectrum



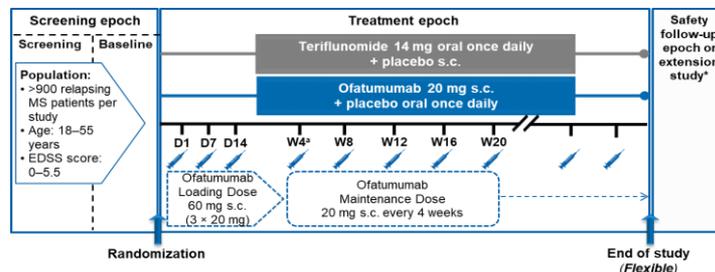
MS – multiple sclerosis; PPMS – primary progressive MS; RRMS – relapsing–remitting MS; SPMS – secondary progressive MS; EDSS – Expanded Disability Status Scale 1. National MS society 2. AntelJ et al. Acta Neuropathol2012;123:627–38.

# Ofatumumab (OMB157) subcutaneous anti-CD20 for relapsing MS on track for submission Q4 2019

OFA suppresses new MS lesions >90% (MIRROR Ph 2b)<sup>1</sup>



Phase 3 program for Ofatumumab<sup>2</sup>



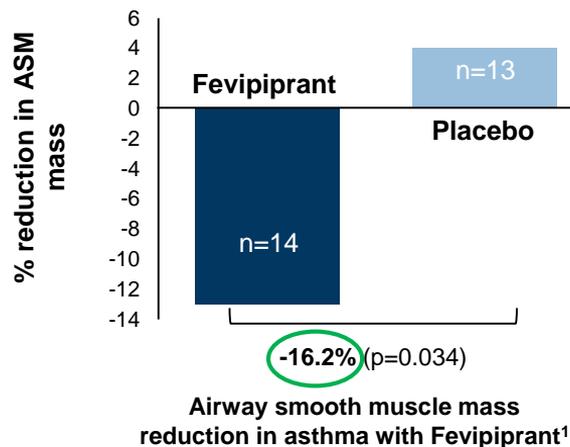
## Potential key benefits for patients:

- Similar efficacy to other anti-CD20s, but in a low dose (20mg) monthly subcutaneous administration, due to higher affinity to CD20<sup>3</sup>
- Faster B cell repletion upon discontinuation<sup>4</sup>
- Targeted to the lymph nodes with potential to partially preserve the immune system<sup>5</sup>
- No need for pre-medications; convenience of at-home injections

See appendix for references

# Fevipiprant (QAW039): Disease-modifying potential in asthma, Ph3 readouts on track for end 2019

## Potential for disease modification

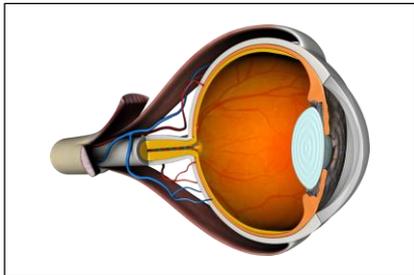


## Robust clinical program to realize full potential

All five Ph3 enrolled	<b>LUSTER 1 &amp; 2</b> (GINA 4/5)	exacerbation trial
	<b>SPIRIT</b> (GINA 3/4/5)	safety
	<b>ZEAL 1 &amp; 2</b> (GINA 3/4)	lung function FEV1
Ph2 data	Reduced sputum eosinophils by 72% <sup>2,3</sup>	
Pre-clinical data	Highly selective DP2 <ul style="list-style-type: none"> <li>▪ Superior potency</li> <li>▪ High selectivity</li> <li>▪ Clean safety profile</li> </ul>	

1. Saunders et al. Sci Trans Med 2019; 11, eaao6451 1\*EP: primary endpoint; FEV<sub>1</sub>: forced expiratory volume in one second; ASM: airway smooth muscle mass. 2. Gonen et al. Lancet Respir Med 2016;4:699–707. 3. Green et al. Lancet 2002;360(9347):1715–1721

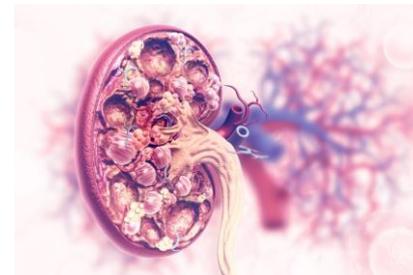
# Phase 2 pipeline with multiple potentially transformational programs



**Presbyopia**



**CNI-free transplantation**



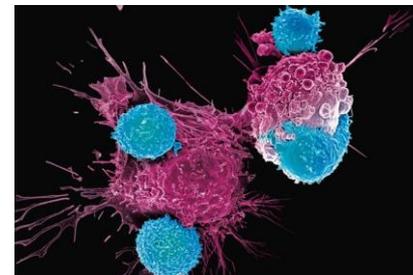
**Chronic renal diseases**



**Cartilage regeneration**



**Stroke recovery**



**Novel CAR-T manufacturing**

# Progressing gene, cell and radioligand platforms with 18<sup>1</sup> projects in development

## Gene therapy



Product	Indication	Preclinical PoC	IND Enabling	First-in-Human	Confirmatory	Launched
Zalgensma <sup>®</sup>	SMA (IV)					
AVXS-101 (IT)	SMA (IT)					
CGF166	Hearing loss					
CPK850	Retinitis pigmentosa					
AVXS-201	Ret Syndrome					
AVXS-301	Amyotrophic Lateral Sclerosis (ALS)					
AVXS-401	Undisclosed					
AVXS-501	Undisclosed					
AVXS-601	Undisclosed					

## Cell therapy



CAR-T type	Indication	Phase 1	Ph 2/Pivotal	Phase 3	Submitted	Approved
CD19 CAR-T	Pediatric & young adult r/r ALL					US, EU
CD19 CAR-T	r/r DLBCL					US, EU
CD19 CAR-T	DLBCL in 1 <sup>st</sup> relapse			Starting 2018		
CD19 CAR-T	r/r FL			Started 2018		
CD19 CAR-T	r/r DLBCL in combination with pembrolizumab	Started 2018				
CD19 CAR-T	Adult r/r ALL			Starting 2018		
CD19 CAR-T	r/r CLL combination with ibrutinib			Starting 2018		
CD19 CAR-T	Pediatric NHL			Starting 2018		
CD19 CAR-T	1st L high risk pediatric and young adult ALL			Starting 2018		
CD19 CAR-T	r/r DLBCL combo with ibrutinib			Starting 2018		
Other targets (UPenn partner)	BCMA&CD19, CD22&CD19, CD123, EGFRv3	Started 2018				

## Radioligand therapy



Product	Disease (target)	Preclinical	Phase I	Phase II	Phase III	Filing	Market	Status
177Lu PSMA-617 (PSMA)	Prostate cancer (PSMA)		Therapeutic					Ph III VISION study initiated 2Q 2018
177 Lu PSMA-R2			Therapeutic					Ph III study initiated 2Q 2018
68Ga PSMA-R2			PET Diag					Ph III study initiated 2Q 2018
18F CTT1067			PET Diagnostic					Ph I study completed
177Lu NeoB	Breast cancer GIST Neuroblastoma		Therapeutic					Phase I study to open 1H 2019
68Ga NeoB	Ovarian Head & Neck Oesophageal (GPRPR)		PET Diagnostic					Phase II study initiated 2Q 2018
177Lu FF-10158	Glioblastoma (integrin Alpha/beta 3/5)		Therapeutic					Preclinical
68Ga FF-10158			PET Diag					Preclinical

1. Gene therapy: 3 (AVXS-101, CGF166, CPK850); cell therapy: 12 (DLBCL in 1st relapse, r/r follicular lymphoma, r/r DLBCL in combo with pembro, adult r/r ALL, r/r CLL in combo with ibrutinib, pediatric NHL, 1st line high risk pediatric and young adult ALL, r/r DLBCL in combo with ibrutinib, BCMA&CD19, CD22&CD19, CD123, EGFRv3); radioligand: 3 (177Lu-PSMA-617, 177Lu-PSMA-R2, 177Lu-NeoB) 2. Luxturna<sup>®</sup> marketed ex-US

# 2019 expected catalysts to continue the momentum

Catalysts		Selected examples		
Key approvals	15	<b>Zolgensma<sup>®1</sup></b> SMA Type 1 (US/EU/JP)  <b>Mayzent<sup>®</sup></b> SPMS (US/EU/JP)	<b>Brolucizumab (RTH258)</b> Neovascular AMD (US)  <b>Piqray<sup>®2</sup> (BYL719)</b> Breast cancer (US)	
Major submissions	20	<b>Ofatumumab (OMB157)</b> Relapsing MS (US/EU)  <b>Crizanlizumab (SEG101)</b> Sickle cell disease (US/EU)	<b>Brolucizumab (RTH258)</b> Neovascular AMD (US/EU/JP)  <b>INC280</b> NSCLC (US/JP)	<b>PDR001 combo</b> Metastatic melanoma (US/EU)
Major late-stage readouts	6	<b>Zolgensma<sup>®1</sup></b> SMA Type 2  <b>Fevipirant (QAW039)</b> Asthma	<b>Entresto<sup>®</sup></b> HFpEF  <b>Cosentyx<sup>®</sup></b> nrAxSpA	<b>Ofatumumab (OMB157)</b> Relapsing MS  <b>PDR001 combo</b> Metastatic melanoma

1. The brand name Zolgensma<sup>®</sup> has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities 2. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country

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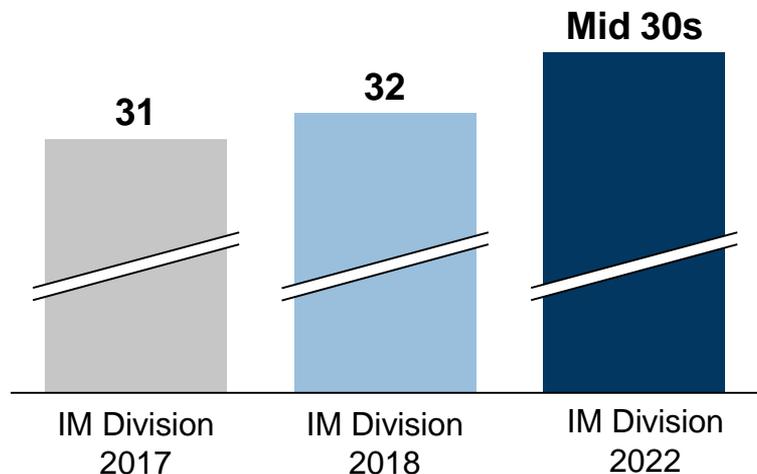
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# Committed to driving consistent margin expansion

## Innovative Medicines

Core margin (%)



1. Gilenya® US compound patent expiration August 2019; dosing regimen patent expiration December 2027

## Key drivers:



- + Acceleration of key growth drivers
- + Resource allocation and productivity programs in commercial units
- + Cross-divisional synergies: Novartis Technical Operations, Novartis Business Services, Procurement



- Generics (mainly Afinitor®, Sandostatin® LAR®, Exjade®/Jadenu®, and tail end of Glivec®)<sup>1</sup>
- Launch investments for potential future blockbusters

# Strong focus on commercial excellence

To create successful, sustained and persistent global brands

## Launch excellence

- Earlier, integrated planning for priority launches
- Deep insights into patient and physician journey
- Leveraging our scale and sharing learnings

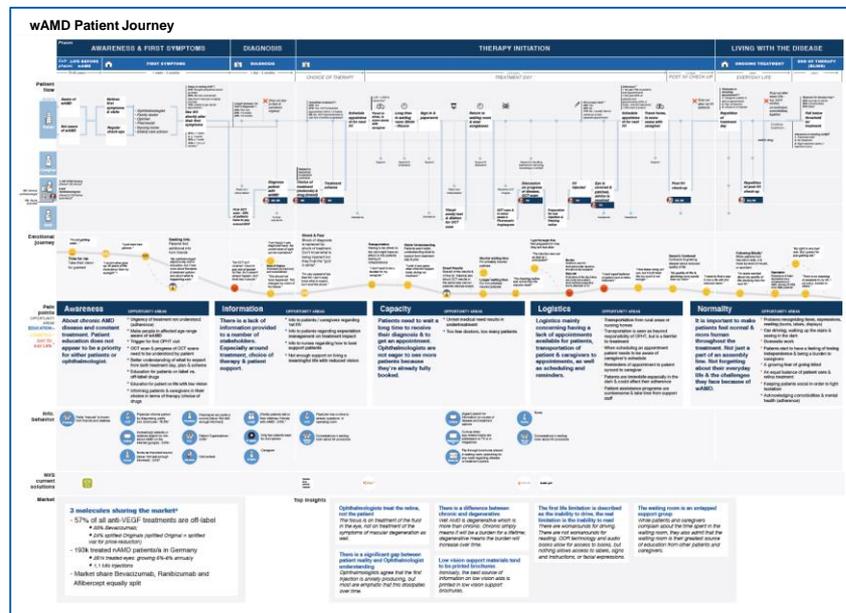
## Post-launch excellence

- Functional upskilling, new capabilities
- Data and analytics to optimize marketing mix
- High-tech, high-touch customer engagement

## Enabled by:

- Externally-focused culture, capabilities and competitive mindset
- Deep discipline in execution

## Select example: In-depth patient journey map



# NTO transformation well underway

Proof-points since end 2016 (post NTO integration, pre-transformation)

## Network transformation

Announced 13 site exits

## Headcount reduction

Reduced 1800+ FTEs

## Warehouse consolidation

Eliminated 95 out of 210 commercial warehouses



## Supplier consolidation

Reduced suppliers for indirect materials by ~30%

Reduced suppliers for FP and API<sup>1</sup> by ~20%

## Data & digital improvement levers

Investing in automation and advanced analytics to drive better performance

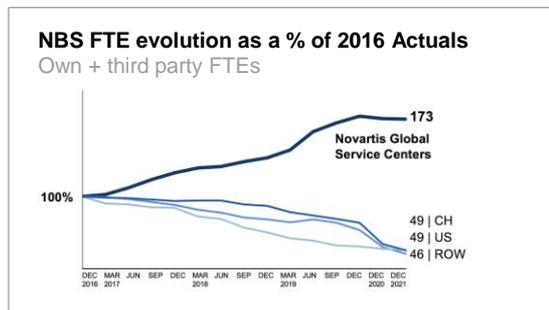
Contributing to goal of ~USD 2bn savings overall<sup>2</sup> by 2020

1. FP = finished product, API = active pharmaceutical ingredient 2. Across NTO, NBS and Procurement

# NBS driving an ambitious efficiency agenda

## Footprint

### Accelerating footprint shift to low-cost locations



## Procurement

### Tightening our approach to Procurement

- ~USD 16bn of 3<sup>rd</sup> party spend across the company
- Revisiting terms with top 50 suppliers
- Consolidating broader supplier base
- Brought in procurement executive from Adidas to lead effort



## Technology

### Investing in automation and next-generation technology to improve efficiency across business services

- M&S content management
- Order-to-cash
- HCP experience platform
- Sales & operations planning



Contributing to goal of ~USD 2bn savings overall<sup>1</sup> by 2020

1. Across NTO, NBS and Procurement

# Sandoz focused on a five-point transformation plan



**Portfolio & Innovation Strategy**



Shift portfolio to more differentiated areas



**Portfolio Delivery**



Ensure timely delivery to key markets



**Cost-competitive & Flexible Supply**



Drive COGS and generic mindset to increase margins



**Resource Allocation**



Agile M&S allocation in fast-changing markets



**Operating Model & Governance**



Simplify how we work

# We aim to become a leading medicines company

Powered by advanced therapy platforms and data science

We are a diversified  
medicines company



Driving growth  
through cutting-  
edge platforms



Passionate about  
productivity and  
margins



Building a new  
culture and lasting  
impact



# Culture transformation is key to our success

Strong focus on developing leaders and empowering associates in 2019

Developing  
leaders

Immersion course for top 300 leaders

Upward feedback for all leaders

Candid Conversations series

Empowering  
associates

Crowdsourcing initiatives

Continuous learning platform

Bold parental leave policy



# Focused effort to build lasting trust with society

Sub-committee of the Executive Committee tracking progress



## Ethical Standards

- Embedding principles-based decision-making
- Strengthened approach to risk management
- Established Ethics, Risk & Compliance function



## Pricing and Access

- Ranked #2 in Access to Medicines Index
- Brought LIC & LMIC prices in line with EU5 average
- Reduced delay from first launch to LMIC to <1 year



## Global Health Challenges

- Renewed commitment to malaria and leprosy
- Launched sickle cell disease partnership in Ghana
- Joined Global Chagas Disease Coalition



## Corporate Citizenship

- Joined the UN Equal Pay International Coalition
- Became the first major pharma company to support the UN LGBTI standards
- New climate targets endorsed by the Science Based Targets initiative



## Stakeholder Engagement

- Published Novartis in Society report with increased level of transparency
- Increased reporting on Financial, Environmental and Social (FES) impact on society

# Concluding thoughts

## Group key messages

- 1 Transformation of Novartis into diversified medicines company is progressing well
- 2 Strong foundation for growth with 15 in-market blockbusters, catalyst-rich pipeline and leadership in advanced therapy platforms
- 3 Clear path to expand margins through acceleration of key growth drivers, together with productivity efforts in NTO and NBS
- 4 Continuing a multi-year journey to build a new culture and lasting impact on society



# Meet Novartis Management 2019 Development: advanced therapy platforms and pipeline summary

**May 23, 2019**

# Catalyst-rich pipeline and strong focus operational execution

- 1 Catalyst-rich pipeline with over 25 submissions with blockbuster potential
- 2 Multiple 2019 pipeline milestones with potential to accelerate 5-10 year growth trajectory
- 3 Building out advanced therapy platform capabilities to complement small molecule / biologics
- 4 Strengthening operational execution with extensive use of data and digital technologies

# Novartis development pipeline leads the industry in its scale and value

## Scale

**200+** Projects in clinical development

**500+** Ongoing clinical trials<sup>2</sup>

**60+** Major submissions planned 2019-2021<sup>3</sup>

## Value

**25+** Potential blockbusters<sup>1</sup> in confirmatory development

**18** Advanced platform therapies in clinical development

**#1** Most valuable pipeline according to external ranking<sup>4</sup>

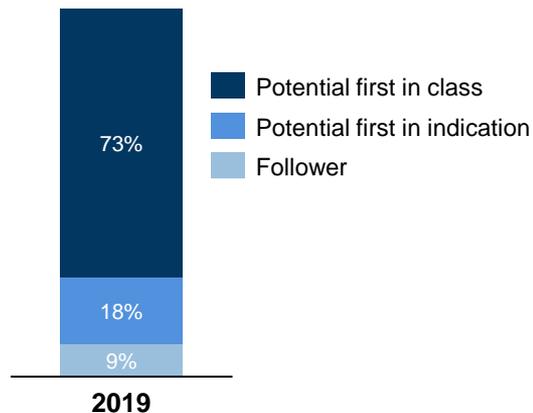
1. Blockbuster defined as peak sales >\$1bn for either a new molecular entity across all indications or for a single new indication of a previously launched product. 2. Across NIBR and GDD. 3. Submissions in US/EU/JP 2019-21. 4. Source: Evaluate Pharma 2018, Outlook to 2024. Ranked #1 in terms of: (1) value creation from advanced therapies, (2) highest pipeline value by sales 2018-24, and (3) value creation 2018-24 from recently launched and pipeline products.

# Novartis size offers unique benefits

## A pipeline to transform Standard of Care

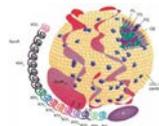
### % of pipeline

No. of programs<sup>1</sup>



## Size and scale to make big bets targeting areas of high unmet need

**TQJ230:**  
antisense oligonucleotide  
against Lipoprotein(a)  
for CVRR<sup>2</sup>



**UNR844:**  
R-Lipoic acid (R-LA)  
choline ester (LACE)  
for presbyopia



## Establishing advanced therapy platforms

**Gene  
therapy**



**Cell  
therapy**



**Radioligand  
therapy**



Internal Data: GDD pipeline as of April 2019. 1. Novartis internal assessment. 2. CVRR = cardiovascular risk reduction. 3. Market ex-US.

# We are delivering on all near-term catalysts ...

Catalysts		Selected examples		
Key approvals	15	<b>Zolgensma™<sup>1</sup></b> SMA Type 1 (US/EU/JP)  <b>Mayzent™<sup>2</sup></b> SPMS (US/EU/JP)	<b>Brolucizumab (RTH258)</b> Neovascular AMD (US)  <b>Piqray®<sup>3</sup> (BYL719)</b> Breast Cancer (US)	
Major submissions	20	<b>Ofatumumab (OMB157)</b> Relapsing MS (US/EU)  <b>Crizanlizumab (SEG101)</b> Sickle Cell Disease (US/EU)	<b>Brolucizumab (RTH258)</b> Neovascular AMD (US/EU/JP)  <b>INC280</b> NSCLC (US/JP)	<b>PDR001 combo</b> Metastatic Melanoma (US/EU)
Major late-stage readouts	6	<b>Zolgensma™<sup>1</sup></b> SMA Type 2  <b>Fevipirant (QAW039)</b> Asthma	<b>Entresto®</b> HFpEF  <b>Cosentyx®</b> nrAxSpA	<b>Ofatumumab (OMB157)</b> Relapsing MS  <b>PDR001 combo</b> Metastatic Melanoma

1. The brand name Zolgensma™ has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparovect-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities 2. Approved by the FDA in Q1 3. The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country

# ... and building a pipeline with 25+ potential blockbusters

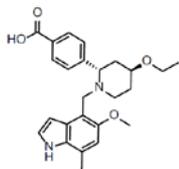
## Potential blockbusters<sup>1</sup> by planned submission year<sup>2</sup>

Cosentyx® nrAxSpA								
Entresto® HFpEF								
OMB157 Relapsing MS								QBW251 COPD
PDR001 combo Metastatic Melanoma								
QVM149 Asthma	<sup>177</sup> Lu-PSMA-617 mCRPC	ABL001 CML	ECF843 Dry Eye		CFZ533 Transplant	LJN452 <sup>4</sup> NASH		SAF312 COSP
RTH258 nAMD	QAW039 Asthma	ACZ885 Lung cancer	UNR844 Presbyopia		CNP520 Alzheimer's Disease	LNP023 Nephropathy		TQJ230 CVRR
SEG101 Sickle Cell Disease	Zolgensma™ <sup>3</sup> SMA Type 2/3	QGE031 CSU / CIU	ZPL389 Atopic Dermatitis		CSJ117 Severe Asthma	LOU064 CSU		VAY736 Sjogren's syndrome
2019	2020	2021	2022		≥ 2023			

1. Blockbuster defined as peak sales >\$1bn for either a new molecular entity across all indications or for a single new indication of a previously launched product. 2. For NMEs submission year represents year of lead indication. 3. The brand name Zolgensma™ has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities. 4. Including NASH portfolio of combination products.

# Early innovative assets target areas of high unmet need

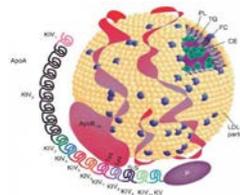
## LNP023



### Oral complement Factor B inhibitor

Potential first disease modifying treatment option for several rare renal diseases

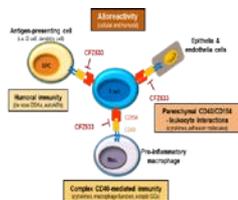
## TQJ230



### Antisense oligonucleotide

Potential to be first medicine approved to treat high Lp(a)

## Iscalimab (CFZ533)

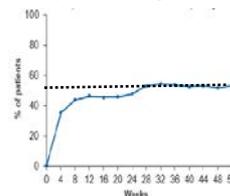


### Fully human IgG1 mAb against CD40

Potential for one organ transplant to last the patient's lifetime

## Ligelizumab (QGE031)

% of patients achieving UAS7=0



### Humanized anti-IgE Antibody

Potential for disease modification in chronic spontaneous urticaria

# Progressing gene, cell and radioligand platforms with 18<sup>1</sup> projects in development

## Gene therapy



Product	Indication	Preclinical PoC	IND Enabling	First-in-Human	Confirmatory	Launched
Zalgensma®	SMA (IV)					
AVXS-101 (IT)	SMA (IT)					
CGF166	Hearing loss					
CPK850	Retinitis pigmentosa					
AVXS-201	Rest Syndrome					
AVXS-301	Amyotrophic Lateral Sclerosis (ALS)					
AVXS-401	Undisclosed					
AVXS-501	Undisclosed					
AVXS-601	Undisclosed					

## Cell therapy



CAR-T type	Indication	Phase 1	Ph 2/Pivot	Phase 3	Submitted	Approved
CD19 CAR-T	Pediatric & young adult r/r ALL					US, EU
CD19 CAR-T	r/r DLBCL					US, EU
CD19 CAR-T	DLBCL in 1 <sup>st</sup> relapse			Starting 2019		
CD19 CAR-T	r/r FL			Starting 2019		
CD19 CAR-T	r/r DLBCL in combination with pembrolizumab	Started 2019				
CD19 CAR-T	Adult r/r ALL			Starting 2019		
CD19 CAR-T	r/r CLL in combination with ibrutinib			Starting 2019		
CD19 CAR-T	Pediatric NHL			Starting 2019		
CD19 CAR-T	1 <sup>st</sup> L high risk pediatric and young adult ALL			Starting 2019		
CD19 CAR-T	r/r DLBCL in combo with ibrutinib			Starting 2019		
Other targets (UPenn partner)	BCMA&CD19, CD22&CD19, CD123, EGFRv3	Started 2019				

## Radioligand therapy



Product	Disease (target)	Therapeutic	Phase I	Phase II	Phase III	Filed	Market	Status
177Lu PSMA-617 (PSMA)	Prostate cancer (PSMA)	Therapeutic						Ph III VISION study initiated 2Q 2018
177 Lu PSMA-R2		Therapeutic						Ph III study initiated 2Q 2018
68Ga PSMA-R2		PET Diag						Ph III study initiated 2Q 2018
18F CTT1287		PET Diagnostic						Ph I study completed
177Lu NeoB	Breast cancer GIST GBM Neuroblastoma	Therapeutic						Phase I study to open 1H 2019
68Ga NeoB	Ovarian Head & Neck Oesophageal (SFRP)	PET Diagnostic						Phase II study initiated 2Q 2018
177Lu FF-10158	Glioblastoma (integrin Alpha/beta 3/5)	Therapeutic						Preclinical
68Ga FF-10158		PET Diag						Preclinical

1. Gene therapy: 3 (AVXS-101, CGF166, CPK850); cell therapy: 12 (DLBCL in 1st relapse, r/r follicular lymphoma, r/r DLBCL in combo with pembro, adult r/r ALL, r/r CLL in combo with ibrutinib, pediatric NHL, 1st line high risk pediatric and young adult ALL, r/r DLBCL in combo with ibrutinib, BCMA&CD19, CD22&CD19, CD123, EGFRv3); radioligand: 3 (177Lu-PSMA-617, 177Lu-PSMA-R2, 177Lu-NeoB) 2. Luxturna® marketed ex-US

# Reimagining Novartis as a medicines company powered by data and digital technologies

## Data for insights



## Patient engagement

FOCAL<sup>VIEW</sup>

TrialSpark



## Process effectiveness



TriNetX

BIOME

Digital Innovation Lab by Novartis

All trademarks are the property of their respective owners

# Focus on operational excellence through Data & Digital



## Time

Indicator	2017	2018	Trend
Study start-up <sup>1</sup>	7.3	4.1	↓
Enrollment <sup>2</sup>	41.9	39.6	↓
Data-analysis & reporting <sup>3</sup>	27.5	22.5	↓



## Cost

Indicator	2017 vs 2018	Trend
Patient recruitment cost <sup>4</sup>	-24%	↓
Site visit cost <sup>5</sup>	-11%	↓
Data analysis cost <sup>6</sup>	-53%	↓



## Productivity

Indicator	2017 vs 2018	Trend
Monitoring efficiency <sup>7</sup>	+12%	↑
Dataset production <sup>8</sup>	+37%	↑
Tables, listings and figures production <sup>9</sup>	+34%	↑

1. Time from final protocol to final protocol package 2. Time from first patient first visit to 25% enrollment (weeks) 3. Time from database lock to clinical study report 4. Grant cost paid to investigators per patient 5. Resources cost per monitoring visit 6. Resources cost per page 7. Monitoring visits per clinical research associate per week 8. Datasets per FTE 9. Tables, listings, figures per FTE

# Conclusion - Development



Robust mid- and late-stage pipeline in place, including advanced platform technologies



Focus on operational excellence, on track to deliver all near-term pipeline goals



Early pipeline focus addressing significant unmet need



Embracing data & digital technologies to accelerate innovation in drug development

# Planned filings 2019 to ≥ 2023

2019	2020	2021	2022	≥ 2023		
<b>Cosentyx®</b> nr-axSpA <sup>12</sup>	177Lu-PSMA-617 mCRPC <sup>26</sup>	ABL001 CML 3rd line	ACZ885 Adjuvant NSCLC <sup>5</sup>	ABL001 CML 1st line	KAF156 Malaria	MOR106 Atopic Dermatitis
<b>Entresto®</b> Heart failure (PEF) <sup>13</sup>	<b>Cosentyx®</b> PsA H2H <sup>17</sup>	ACZ885 1 <sup>st</sup> Line NSCLC <sup>5</sup>	AVXS-201 Rett Syndrome	BYL719 HER2+ adv. breast cancer	<b>Kisqali®</b> HR+, HER2 (-) BC <sup>2</sup> (adjuvant)	QBW251 COPD <sup>2</sup>
<b>INC280</b> NSCLC <sup>5</sup>	<b>Entresto®</b> Post-acute myocardial infarction	ACZ885 2 <sup>nd</sup> Line NSCLC <sup>5</sup>	<b>Cosentyx®</b> AS H2H <sup>19</sup>	BYL719 TNBC <sup>2</sup>	<b>Kymriah</b> + pembrolizumab - r/r DLBCL	PDR001 combo Metastatic Melanoma
<b>OMB157</b> Relapsing multiple sclerosis	<b>Jakavi®</b> Chronic GVHD <sup>14</sup>	<b>Kymriah®</b> r/r Follicular Lymphoma	<b>Cosentyx®</b> Hidradenitis suppurativa	CAD106 Alzheimer's disease	LJC242 NASH <sup>18</sup>	RTH258 Retinal vein occlusion
<b>PDR001+Tafinlar®+Mekinist®</b> Metastatic BRAF V600+ melanoma	<b>Jakavi®</b> Acute GVHD <sup>14</sup>	<b>Kymriah®</b> r/r DLBCL <sup>19</sup> in 1st relapse	ECF843 Dry eye	CFZ533 Solid Organ Transplant	LJN452 NASH <sup>18</sup>	SAF312 Chronic ocular surface pain
<b>QMF149</b> Asthma	<b>QAW039</b> Asthma	LAM320 MDR <sup>9</sup> tuberculosis	<b>Kymriah®</b> CLL <sup>4</sup>	CFZ533 Sjogren's Syndrome	LNP023 IgA nephropathy	TQJ230 CVRR <sup>1</sup>
<b>QVM149</b> Asthma	<b>Zolgensma®</b> SMA Type 2/3 <sup>25</sup>	QGE031 CSU/CIU <sup>16</sup>	<b>Rydapt®</b> AML <sup>20</sup> (FLT3 wild type)	CNP520 Alzheimer's disease	LNP023 Membranous nephropathy	VAY736 Autoimmune Hepatitis
<b>SEG101</b> Sickle cell disease		RTH258 Diabetic macular edema	UNR844 Presbyopia	CSJ117 Severe Asthma	LNP023 C3 glomerulopathy	VAY736 Primary Sjogren's syndrome
<b>Xolair®</b> Nasal Polyps			ZPL389 Atopic dermatitis	HDM201 Acute myeloid leukemia	LMI070 Spinal muscular atrophy	VAY785 NASH <sup>18</sup>
				KAE609 Malaria	LOU064 Chronic spontaneous urticaria	VPM087 CRC 1L/RCC 1L <sup>24</sup>

- Secondary prevention of cardiovascular events in patients with elevated levels of lipoprotein (a)
- Triple negative breast cancer
- Paroxysmal nocturnal hemoglobinuria
- Chronic myeloid leukemia
- Long-acting release
- Non-small cell lung cancer
- Neovascular age-related macular degeneration
- Chronic lymphocytic leukaemia
- Breast cancer
- Diffuse large B-cell lymphoma
- Indolent Non-Hodgkin's lymphoma
- Non-radiographic axial spondyloarthritis
- Preserved ejection fraction
- Graft-versus-host disease
- Neuroendocrine tumors
- Chronic spontaneous urticaria / chronic idiopathic urticaria

- Psoriatic arthritis head-to-head study versus adalimumab
- Non-alcoholic steatohepatitis
- Ankylosing spondylitis head-to-head study versus adalimumab
- Acute myeloid leukemia
- Chronic Obstructive Pulmonary Disease
- Secondary Progressive Multiple Sclerosis
- IV formulation Spinal Muscular Atrophy Type 1
- 1<sup>st</sup> line colorectal cancer / 1<sup>st</sup> line renal cell carcinoma
- IT formulation Spinal Muscular Atrophy Type 2/3
- Metastatic castration-resistant prostate cancer

#### Combination abbreviations:

fulv fulvestrant  
tmx tamoxifen  
gsn goserelin  
NSAI Non-steroidal aromatase inhibitor  
Taf Tafinlar® (dabrafenib)  
Mek Mekinist® (trametinib)



Novartis AG  
Investor Relations

# Meet Novartis Management 2019 Pharmaceuticals pipeline and in-market brands

May 23, 2019

# Index – select pipeline and in-market brands

## Select pipeline

	SLIDE
Brolucizumab (RTH258)	37
Fevipirant (QAW039)	39 – 41
Mayzent <sup>®</sup>	21 – 23
Ofatumumab (OMB157)	24 – 25
Zolgensma <sup>®</sup>	27 – 31

## In-market brands

	SLIDE
Aimovig <sup>®</sup>	26
Cosentyx <sup>®</sup>	11 – 14
Entresto <sup>®</sup>	6 – 8
Gilenya <sup>®</sup> / MS disease	19 – 20
Xiidra <sup>®</sup>	34 – 36

# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets	     			  	  	
	Kymriah® New indications Piquay® (BYL719) Breast Crizanlizumab (SEG101) Sickle Cell PDR001 combo Metastatic Melanoma ABL001 CML ACZ885 Lung <sup>177</sup> Lu-PSMA-617 mCRPC	<b>Entresto®</b> HFpEF, post-MI <b>LNP023</b> Renal diseases <b>TQJ230</b> CVRR	<b>Cosentyx®</b> nrAxSpA <b>CFZ533</b> Transplant / Sjögren's <b>Tropifexor (LJN452)</b> NASH <b>VAY785</b> NASH <b>LOU064</b> CSU <b>Ligelizumab (QGE031)</b> CSU / CIU <b>ZPL389</b> AD <b>MOR106</b> AD	<b>Zolgensma®<sup>2</sup></b> SMA <b>LMI070</b> SMA <b>Ofatumumab (OMB157)</b> MS <b>CNP520</b> Alzheimer's	<b>Brolucizumab (RTH258)</b> nAMD, DME, RVO <b>UNR844</b> Presbyopia <b>ECF843</b> Dry eye <b>SAF312</b> Chronic Ocular Pain	<b>Fevipirant (QAW039)</b> Asthma <b>QVM149</b> Asthma <b>CSJ117</b> Asthma <b>QBW251</b> COPD

\*The brand name Piquay® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country. See appendix for references.

# Cosentyx<sup>®</sup>, Entresto<sup>®</sup> and multiple near-term potential blockbuster launches expected to drive strong growth

1 Continued strong momentum for key growth drivers Cosentyx<sup>®</sup> and Entresto<sup>®</sup>, based on growing evidence base

2 Ready to launch 5 blockbuster candidates – Mayzent<sup>®</sup>, Zolgensma<sup>®1</sup>, Brolucizumab (RTH258), Ofatumumab (OMB157), Fevipiprant (QAW039)

3 With recently launched products and rich pipeline, Novartis expects double-digit growth in China, capitalizing on faster and broader access

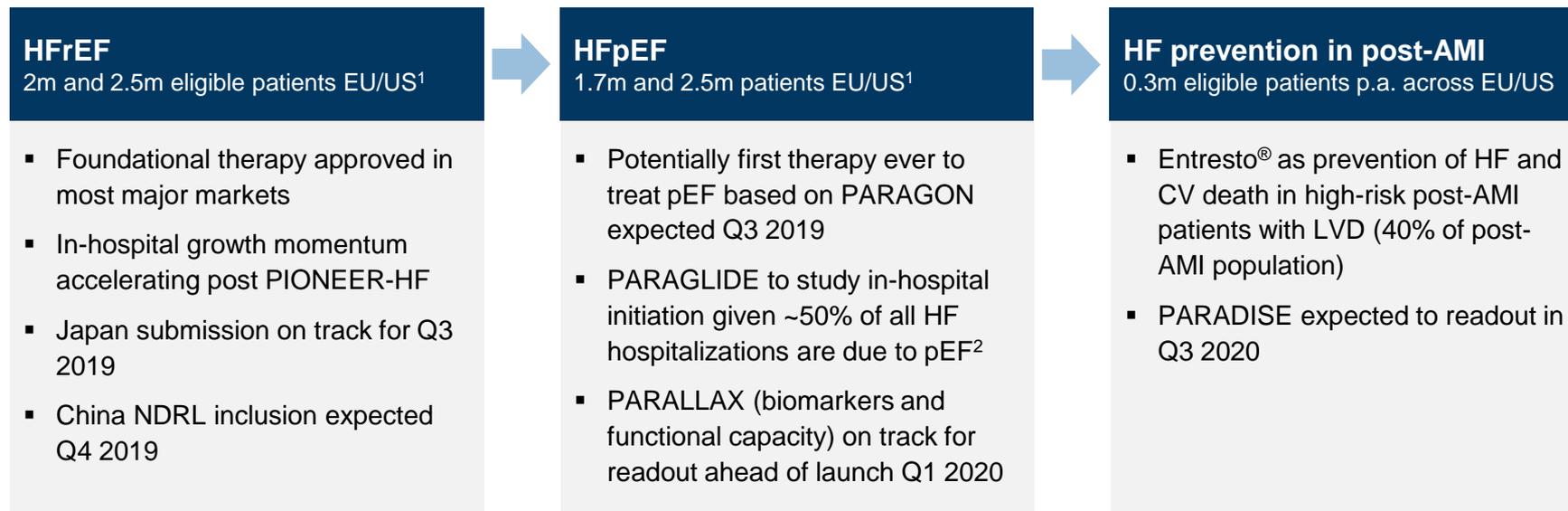
1. The brand name Zolgensma<sup>®</sup> has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets	   			  	  	
	Kymriah® New indications Piqray® (BYL719) Breast Crizanlizumab (SEG101) Sickle Cell PDR001 combo Metastatic Melanoma ABL001 CML ACZ885 Lung <sup>177</sup> Lu-PSMA-617 mCRPC	<b>Entresto®</b> HFrEF, post-MI <b>LNP023</b> Renal diseases <b>TQJ230</b> CVRR	<b>Cosentyx®</b> nrAxSpA <b>CFZ533</b> Transplant / Sjögren's <b>Tropifexor (LJN452)</b> NASH <b>VAY785</b> NASH <b>LOU064</b> CSU <b>Ligelizumab (QGE031)</b> CSU / CIU <b>ZPL389</b> AD <b>MOR106</b> AD	<b>Zolgensma®<sup>2</sup></b> SMA <b>LMI070</b> SMA <b>Ofatumumab (OMB157)</b> MS <b>CNP520</b> Alzheimer's	<b>Brolucizumab (RTH258)</b> nAMD, DME, RVO <b>UNR844</b> Presbyopia <b>ECF843</b> Dry eye <b>SAF312</b> Chronic Ocular Pain	<b>Fevipiprant (QAW039)</b> Asthma <b>QVM149</b> Asthma <b>CSJ117</b> Asthma <b>QBW251</b> COPD

\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Entresto® expected to expand into new indications to become the foundational treatment in all HF



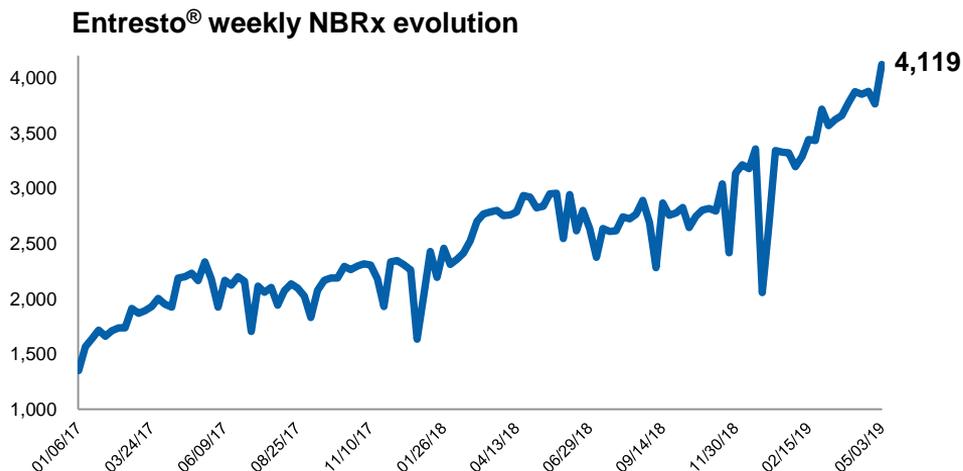
CV = Cardiovascular; HF = Heart Failure; HFrEF = Heart Failure with reduced Ejection Fraction; HFpEF = Heart Failure with Preserved Ejection Fraction; AMI = Acute Myocardial Infarction; LVD = Left Ventricular Dysfunction; NDRL = National Drug Reimbursement List; Post-AMI: post-acute myocardial infarction; eGFR = glomerular filtration rate. 1. Based on NYHA II-IV and eGFR criteria 2. Goyal 2016; DOI:10.1016/j.amjmed.2016.02.007

# Entresto® NBrx acceleration driven by operational excellence and PIONEER data

New data on beneficial and safe in-hospital initiation in significant part of patient population...

- HF Prevalence 7.4m in US and 6.2m in EU5 of which 50% are HFREF patients<sup>3</sup>
- 0.5m hospitalizations in US and 0.7m in EU5 due to HFREF p.a.<sup>2</sup>
- Hospitalizations are an important trigger point to initiate and change treatment
- PIONEER-HF and TRANSITION provided the evidence for safe and beneficial in-hospital initiation of Entresto®<sup>4</sup>

... showing positive impact on overall U.S. prescriptions<sup>1</sup>



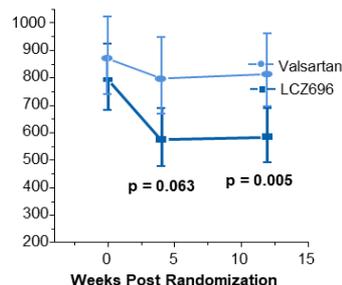
NBRx = New-to-Brand prescriptions; HF = Heart Failure; HFREF = Heart Failure with reduced Ejection Fraction. See appendix for references

# Entresto® dataset in HFpEF to exceed 8000 patients

## PARAMOUNT<sup>1</sup> – successful Ph2

### Hemodynamic

Cardiac stress – prognostic of outcome<sup>2</sup>



$p = 0.063$        $p = 0.005$

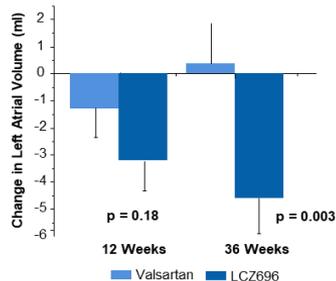
Weeks Post Randomization

Prim. Endpoint: NT-proBNP

23% reduction by week 12

### Structural

Left ventricular pressures – prognostic of outcome<sup>2</sup>



$p = 0.18$        $p = 0.003$

12 Weeks      36 Weeks

■ Valsartan      ■ LCZ696

Sec. Endpoint: Atrial size

7.6% reduction by week 36

LVEF  $\geq 45\%$ , N=301 vs. valsartan

## PARAGON – pivotal Ph3

## PARALLAX, PARAGLIDE – supportive data

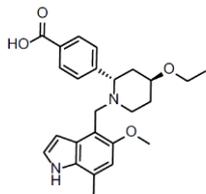
Trial	Indication / population	Endpoints	Next expected milestones
	LVEF $\geq 45\%$ N=4822 vs. valsartan	Novel primary composite endpoint: CV death and total (first & recurrent) HF hospitalization	FIR Q3 2019 Basis for planned filing in Q4 2019
	LVEF $> 40\%$ N=2500 vs. valsartan, enalapril, placebo	NT-proBNP, functional measures, symptoms	Fully enrolled, FIR Q1 2020 Supportive data at launch

HFpEF- heart failure with preserved ejection fraction    LVEF - left ventricular ejection fraction    ADHF – acute decompensated heart failure    FIR – first interpretable results    FPFV – first patient, first visit

1. Solomon et al. LANCET 2012    2. Komajda 2011; Anand 2003; Massie 2008;    3. Zile 2011; Brenyo 2011; Meris 2009; Geris 2007.

# The next wave of cardiometabolic programs are now advancing into late stage development

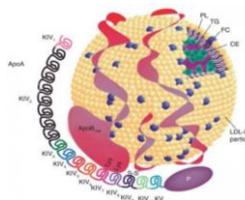
## LNP023



### Oral complement Factor B inhibitor

- Potential first disease modifying treatment option for several rare renal diseases
- Under development for IgA and Membranous Nephropathies, and C3 Glomerulopathy
- Single Ph2a/b studies in all 3 indications potentially enabling direct initiation of single Ph3 studies in coming years

## TQJ230



### Antisense oligonucleotide against Lipoprotein(a)

- Lp(a) is an independent inherited CV risk factor and 20-30% of patients with established CV disease have elevated Lp(a)
- Estimated pt potential 4m in US and 5m in EU<sup>1,2</sup>
- Currently, no medicines are approved to treat high Lp(a)
- TQJ230 demonstrated 80% Lp(a) reduction in patients with CV disease in Ph2b
- Ph3 trial to assess TQJ230 effect on CV outcomes to be initiated in Q1 2020

Lp(a) = Lipoprotein a; CV = cardiovascular; 1. Potential patients are defined by the indication to be studied in the planned phase III trial for patients with elevated Lp(a) and MI, stroke or PAD. Potential eligible population dependent on trial results and label. 2. US AHA (Heart Disease & Stroke Stats 2018 update), EU5 & JP Kantar Health EPI database, DRG Database, REACH Registry, Odyssey Outcome Trial. Estimates vary based on regional/ethnic variability.

# Building depth across our core therapeutic areas

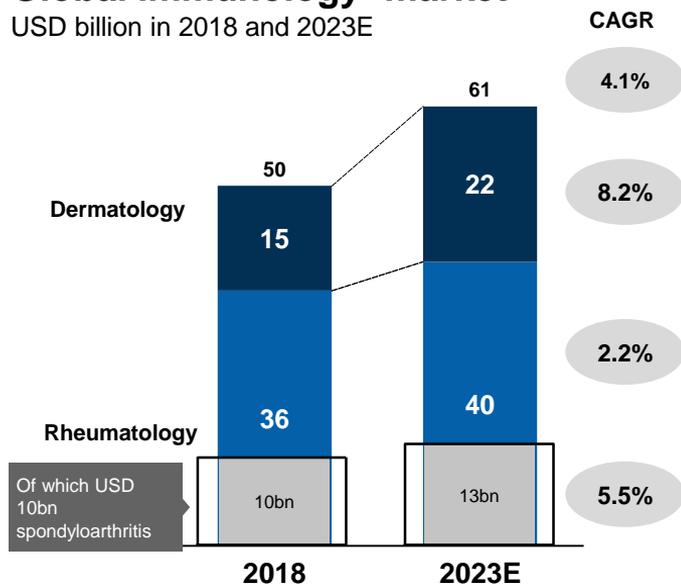
		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets	   					
	Kymriah® New indications Piqray® (BYL719) Breast Crizanlizumab (SEG101) Sickle Cell PDR001 combo Metastatic Melanoma ABL001 CML ACZ885 Lung <sup>177</sup> Lu-PSMA-617 mCRPC	Entresto® HFpEF, post-MI LNP023 Renal diseases TQJ230 CVRR	<b>Cosentyx®</b> nrAxSpA <b>CFZ533</b> Transplant / Sjögren's <b>Tropifexor (LJN452)</b> NASH <b>VAY785</b> NASH <b>LOU064</b> CSU <b>Ligelizumab (QGE031)</b> CSU / CIU <b>ZPL389</b> AD <b>MOR106</b> AD	Zolgensma® <sup>2</sup> SMA LMI070 SMA Ofatumumab (OMB157) MS CNP520 Alzheimer's	Brolicizumab (RTH258) nAMD, DME, RVO UNR844 Presbyopia ECF843 Dry eye SAF312 Chronic Ocular Pain	Fevipiprant (QAW039) Asthma QVM149 Asthma CSJ117 Asthma QBW251 COPD

\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Cosentyx<sup>®</sup> well-positioned to continue to grow in attractive segments of the immunology market

## Global immunology<sup>1</sup> market

USD billion in 2018 and 2023E



PsA = Psoriatic Arthritis. See appendix for references

## Psoriasis

- USD 15bn market expected to grow >8% p.a. through 2023 mainly driven by expansion of biologics usage<sup>16</sup>
- Cosentyx<sup>®</sup> uniquely positioned to win based on strong evidence
  - Cosentyx<sup>®</sup> superiority to Enbrel<sup>®</sup> and Stelara<sup>®</sup><sup>2,3</sup>
  - 5-year data on sustained control of signs and symptoms<sup>4</sup>
  - Strong data in joints in PsA patients and hard-to-treat persistent manifestations<sup>5-9</sup>
  - ARROW study comparing IL-17 vs. IL-23 on track for read-out end 2019

## Spondyloarthritis

- IL17s expected to grow faster than the market
- Mainly driven by increasing diagnosis rate and biologics usage
- Cosentyx<sup>®</sup> uniquely positioned compared to anti-TNFs and IL23s
  - Sustained control of signs and symptoms up to 5 years<sup>10-13</sup>
  - High level of enthesitis resolution<sup>10</sup>
  - Promising structural data across PsA and AS<sup>14, 15</sup>

# Nr-axSpA indication would complete Cosentyx<sup>®</sup> label across the SpA spectrum

## US and EU patient population by indication<sup>1</sup>

Thousands

	Spondyloarthritis								RA	
	PsA		AS		nr-axSpA		Total SpA			
	US	EU	US	EU	US	EU	US	EU	US	EU
Prevalence	1,642	1,541	894	789	904	807	<b>3,440</b>	<b>3,137</b>	2,588	2,308
Diagnosed patients <sup>2</sup>	832	738	532	509	360	396	<b>1,724</b>	<b>1,643</b>	2,254	1,956
% diagnosed	51%	48%	60%	65%	40%	49%	<b>50%</b>	<b>52%</b>	87%	85%
Patients treated <sup>3</sup>	437	397	452	432	252	278	<b>1,141</b>	<b>1,107</b>	1,623	1,392
% treated	53%	54%	85%	85%	70%	70%	<b>66%</b>	<b>67%</b>	72%	71%
Patients on biologics	136	107	92	90	10	22	<b>238</b>	<b>219</b>	885	552
% treated <sup>4</sup>	31%	27%	20%	21%	4%	8%	<b>21%</b>	<b>20%</b>	55%	40%

- SpA patient population is at least as big as RA population
- 1.7m patients in EU and US suffer from nr-axSpA
- 10–40% of patients progress from nr-axSpA to AS over a period of 2–10 years<sup>5</sup>
- Diagnosis of nr-axSpA based on MRI imaging and HLA-B27 biomarker<sup>6,7</sup> gradually increasing, but rates remain low
- Biologics penetration in nr-axSpA only 4-8%

SpA = Spondyloarthritis; nr-axSpA = non-radiographic axial Spondyloarthritis; PsA = Psoriatic Arthritis; AS = Ankylosing Spondylitis; RA = rheumatoid arthritis; HLA = Human Leukocyte Antigen. See appendix for references

# Cosentyx<sup>®</sup> Ph3 PREVENT readout in non-radiographic axial spondyloarthritis expected in Q4 2019

A **Ph3**, randomized, double-blind, placebo-controlled, multicenter study to evaluate the **efficacy and safety of secukinumab** in patients with **non-radiographic axial spondyloarthritis**

Enrolled

555 patients

Population

NSAID-IR, open  
for biologic-IR  
and DMARD-IR

Study start date

April 2016

LPFV (enrollment)  
completion date

May 2018



Primary efficacy  
endpoint at  
Weeks 16 and 52

ASAS40 response  
rate with secukinumab  
vs. placebo

ASAS40, Assessment of SpondyloArthritis International Society criteria (ASAS) 40% criteria; biologic-IR, biologic inadequate responders; DMARD-IR, disease-modifying anti-rheumatic drug inadequate responders; NSAID-IR, non-steroidal anti-inflammatory drug inadequate responders; Biologic-IR patients are patients who have had an inadequate response to not more than 1 anti-TNF agent; ClinicalTrials.gov (NCT02696031)

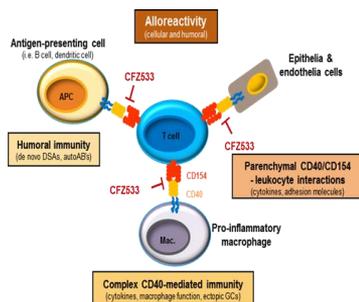
# Generating further evidence on sustained benefit of Cosentyx<sup>®</sup> across SpA indications

Trial	Objectives	Readout expected
<b>PREVENT</b> (nr-axSpA)	Efficacy and safety of Cosentyx <sup>®</sup> in nr-axSpA, compared to placebo and progression of structural changes (at 2 years)	Q4 2019
<b>EXCEED</b> (PsA)	Double-blinded H2H superiority vs. Humira <sup>®</sup> in active PsA patients who are intolerant or have inadequate response to DMARDs (e.g. methotrexate)	2019/ 2020
<b>SURPASS</b> (AS)	H2H vs. proposed adalimumab biosimilar on impact on radiographic progression (mSASSS) in active AS	2022

SpA = Spondyloarthritis; nr-axSpA = non-radiographic axial Spondyloarthritis; PsA = Psoriatic Arthritis; AS = Ankylosing Spondylitis; H2H = Head to Head; DMARDs = disease modifying anti-rheumatic drugs; mSASSS = modified Stoke Ankylosing Spondylitis Spinal Score 1. Humira<sup>®</sup> is a registered trademark of AbbVie Biotechnology Ltd.

# Next wave of immunology programs well advanced in late stage development

## Iscalimab (CFZ533)

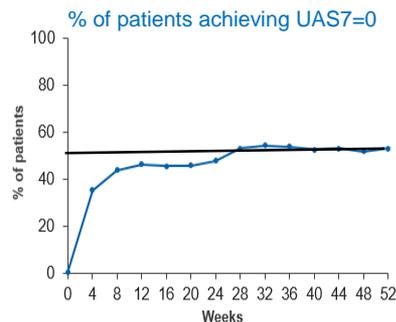


Fully human, Fc-silenced non-depleting, IgG1 mAb blocking the CD40 receptor

- Under development for renal / liver transplant and for Primary Sjögrens Syndrome
- Ph2b CIRRUS I Study (Renal Transplant) ongoing
- Ph2b TWINSS Study (Sjögren's) initiation expected in Q3
- Potential for first organ transplant to last the patient's lifetime

CSU – chronic spontaneous urticarial CIU – chronic idiopathic urticaria

## Ligelizumab (QGE031)



Humanized anti-IgE antibody, in Ph3 head-to-head superiority studies against Xolair® in CSU patients

- Under development for CSU/ CIU
- Ph2 data show complete responses (UAS7=0) sustained in over 50% of patients through 1 year of treatment
- LT (1 year) treatment well tolerated, no unexpected safety signals
- Potential for disease modification based on Ph2 data

# Tropifexor (LJN452) – an FXR agonist for the treatment of NASH

A novel and highly potent non-bile acid FXR agonist that has shown efficacy in preclinical models of NASH<sup>1,2</sup>

Safe and well-tolerated in healthy volunteers at single doses up to 3000 µg

Dose-dependent pharmacodynamic elevation of fibroblast growth factor 19 (FGF19) was demonstrated as a marker of target engagement in the gut<sup>3</sup>

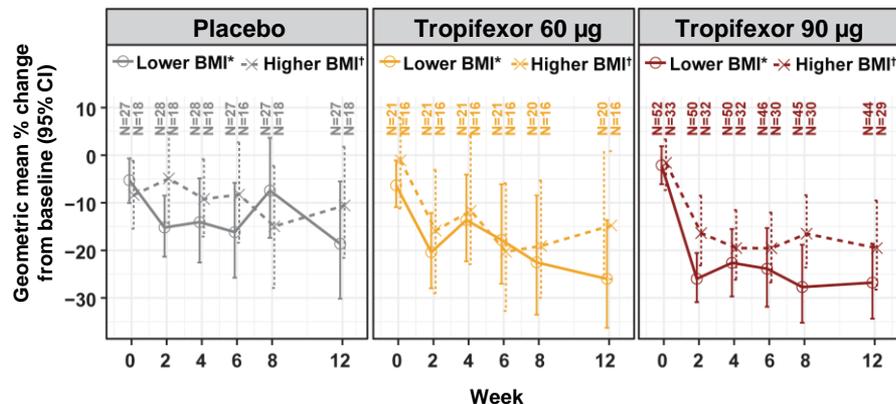
Currently being evaluated in FLIGHT-FXR, a Phase 2 clinical trial in patients with NASH



## Effect of tropifexor on marker of hepatic inflammation: ALT

A rapid and sustained decline in ALT levels from baseline was observed with tropifexor 90 µg doses in patients from both BMI subgroups, more marked in the group with lower BMI

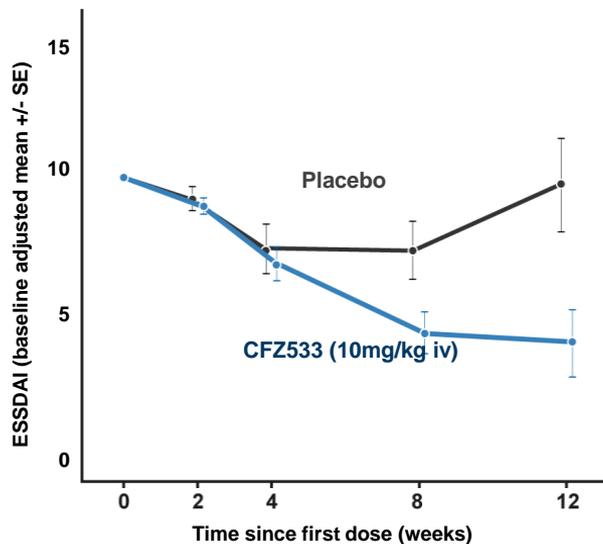
Geometric mean percentage change from baseline of ALT (U/L) at week 12 by BMI subgroups<sup>4</sup>



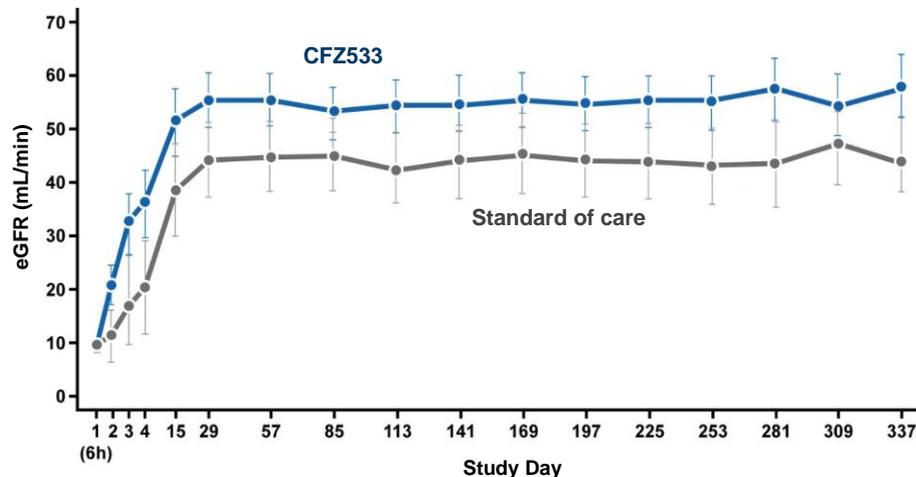
1. Tully DC, et al. *J Med Chem.* 2017;60:9960-73 2. Laffitte B, et al. *J Hepatol.* 2018;68:S341 3. Badman MK, et al. *Hepatology.* 2016;64:16A 4. Sanyal A, et al. *J Hepatol* 2019 70(S1) e796-797 Data is investigational. Efficacy & safety not yet established

# Iscalimab (CFZ533) – first-in-class anti-CD40 medicine for transplantation and autoimmune disease

Reduces disease activity in Sjögren's syndrome

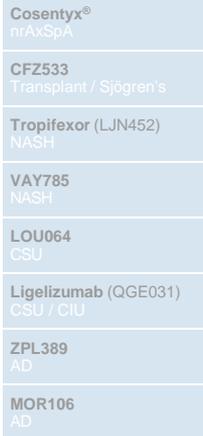
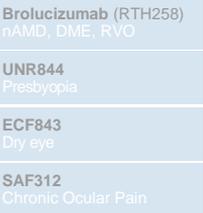
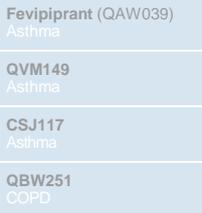


Prevents rejection and improves kidney function after kidney transplantation



Data is investigational. Efficacy & safety not yet established.

# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets						
						

\*The brand name Piquay® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Disease area leadership in multiple sclerosis supported by cutting edge innovation



Progression is recognized to start earlier than previously thought<sup>1</sup>



Patient relevant outcomes measured through digital is the expectation<sup>2</sup>



Real-world data and advanced analytics used to gain insights and inform decisions

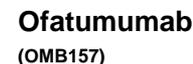


Potential biomarkers, beyond MRI are becoming more accessible



Portfolio aligns to the full spectrum of Disease

Category Leadership

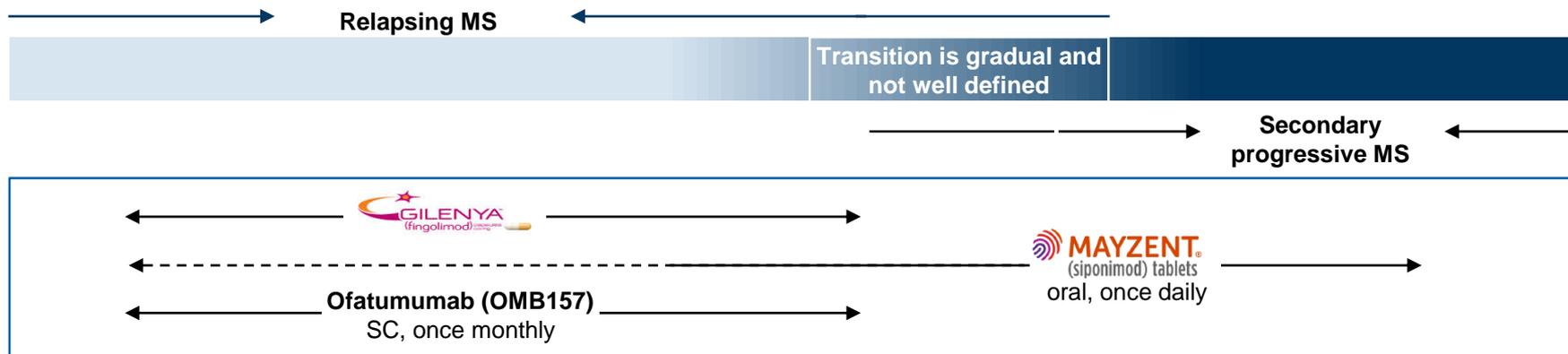


- 1<sup>st</sup> oral
- 1<sup>st</sup> in NfLs
- 1<sup>st</sup> in pediatric MS
- 1<sup>st</sup> s.c. B-cell therapy
- 1<sup>st</sup> successful study in typical SPMS

1. Kremenchutzky M, et al. The natural history of multiple sclerosis: a geographically based study 9: observations on the progressive phase of the disease. Brain. 2006 Mar;129(Pt 3):584-94 NFL: Neurofilaments light chain, s.c. subcutaneous

2. <https://www.novartis.com/news/media-releases/novartis-presents-first-its-kind-algorithm-based-tool-help-ms-patients-and-physicians-evaluate-and-discuss-early-signs-progression-secondary-progressive-ms>

# With new and planned launches, Novartis continues to lead across the MS disease spectrum



<p><b>Patient Profiles</b></p>	<p><b>25-35 years old</b> RMS patients, first line first switch</p>	<p><b>~40 years old</b> Transitioning or have transitioned to SPMS</p>
<p><b>MS patient share<sup>1,2</sup></b></p>	<p><b>~85% of MS patients</b></p>	<p><b>~75-80% of RMS patients</b></p>

MS = multiple sclerosis; PPMS = primary progressive MS; RRMS = relapsing–remitting MS; SPMS = secondary progressive MS EDSS -Expanded Disability Status Scale.  
 1. National MS society. 2. Antel J et al. Acta Neuropathol 2012;123:627–38.



# Mayzent® EXPAND study resulted in first and only oral drug proven to impact progression in typical SPMS patient

## EXPAND study<sup>2</sup>: typical SPMS population with unmet need

Age (mean): 48 years

Moderate to severe disability: EDSS 5.4 / 6.0 (mean/ median)

Years since onset of MS (mean): 17 years

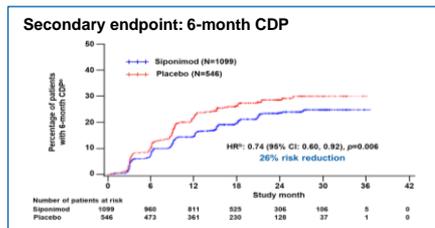
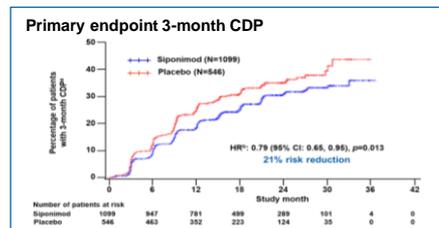
Relapse-free for prior 2 years (%): 64%

### Disability progression<sup>3</sup>

#### Reduction in risk of CDP vs. placebo

21% 3-month p<0.013  
26% 6-month p<0.006

Primary end-point



### Confirmed relapses

55% reduction ARR<sup>3</sup> vs. placebo (p < 0.0001)

### Cognitive processing<sup>4</sup>

SDMT<sup>2</sup>: 2.48 points improvement from baseline, vs. placebo<sup>3</sup> (p<0.0004)

### Brain volume loss

23.4% reduction in brain volume loss vs. placebo<sup>3</sup> (p = 0.0002)

ARR – annualized relapse rate. CDP – confirmed disability progression. EDSS – Expanded Disability Status Scale. DMT – Disease modifying treatment See appendix for references

# Mayzent® showed significant effects on cognitive processing speed in SPMS patients<sup>1</sup>

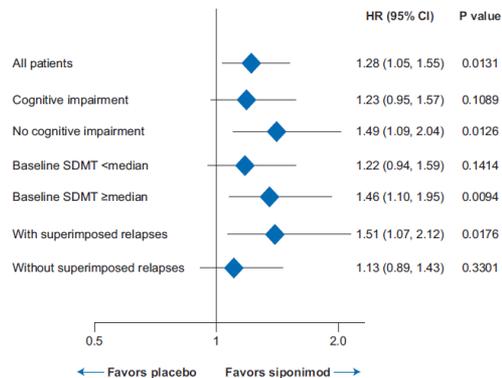
Decreased Cognitive Processing Speed (CPS) is a core underlying deficit in SPMS, affecting up to 70%<sup>3</sup> of the patients

EXPAND study (>1600 patients):

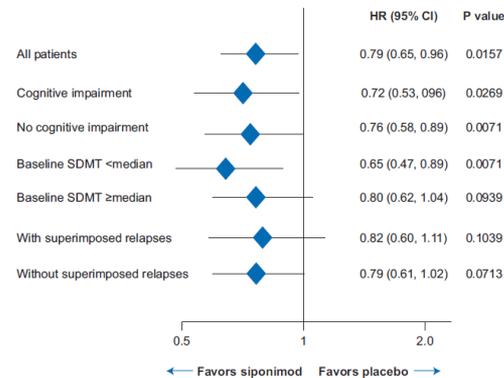
- Mayzent® (siponimod) is a brain penetrant S1P<sub>1,5</sub> receptor modulator that reduces brain volume loss, reducing disability progression in patients with SPMS
- CPS assessed with the Symbol Digit Modality Test (SDMT)

Subgroup analyses:

Higher proportions of sustained CPS improvement<sup>2</sup> with Mayzent® vs. placebo



Lower proportions of sustained CPS deterioration<sup>2</sup> with Mayzent® vs. placebo



HR = hazard ratios See appendix for references

# Mayzent® the first and only oral treatment successfully studied and approved for active SPMS<sup>1</sup>

## Unique label and clinical data

- ✓ Full range of RMS indication
- ✓ Active SPMS<sup>2</sup> (EDSS range: 3.0 to 6.0)
- ✓ Efficacy
- ✓ Safety and tolerability
- ✓ No FDO (~70%)<sup>3</sup>



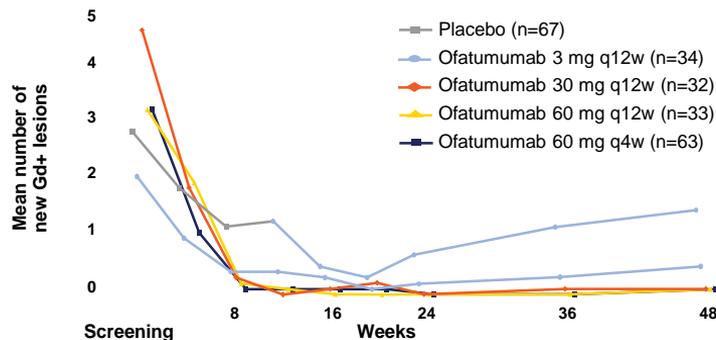
## For a large population with unmet need

- ✓ ~250K target active SPMS patients in US
- ✓ Awareness of Mayzent® >50% of physicians in most major markets
- ✓ Initial focus on disease education
- ✓ MSProDiscuss™ launched to help target patient identification

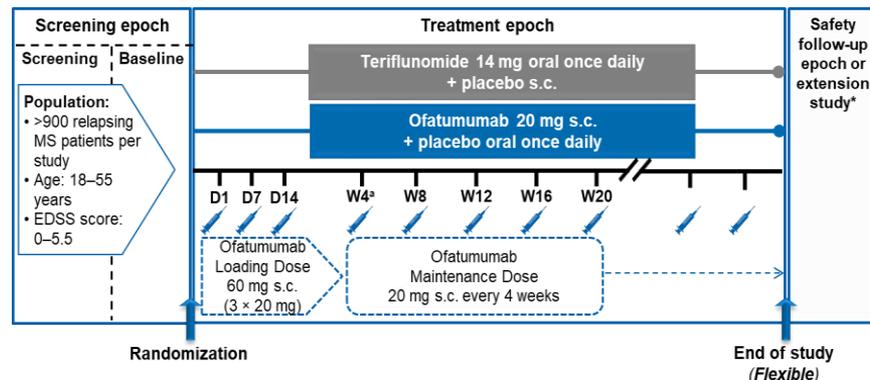
RRMS – Relapsing Remitting Multiple Sclerosis; SPMS – Secondary Progressive Multiple Sclerosis; CPS – Cognitive Processing Speed; FDO – first dose observation See appendix for references

# Ofatumumab (OMB157) subcutaneous anti-CD20 for relapsing MS on track for submission Q4 2019

Ofatumumab suppresses new MS lesions >90% (MIRROR Ph2b)<sup>1</sup>



Ph3 program for Ofatumumab<sup>2</sup> (ASCLEPIOS 1 & 2)



Ph3 ASCLEPIOS 1 & 2 readout expected Q3 2019

1. Bar-Or et al., April 2018, Neurology, 2018; 90:e1805-e1814. 2. Kappos L, et al. Presented at EAN 2017. EP2154. 3. Savelieva M, et al. Presented at AAN 2017. 4. Savelieva M, et al. Presented at ECTRIMS 2016. P730; P5.348. 5. Theil D, et al. Presented at ECTRIMS 2017. P657; Gd+ = gadolinium-enhancing

# Ofatumumab (OMB157): potentially first and only highly potent precision B-Cell therapy tailored for MS patients

## Maximizing unique B-cell biology ...

- More potent B-cell lysis as Ofatumumab binds to unique CD20 epitopes, with higher affinity<sup>1,2,3</sup>
- SC administration favorable vs. IV route due to improved lymph node targeting, sparing B-cells in the spleen, higher uptake in the spinal cord and improved CNS uptake<sup>5,6,7</sup>
- Low dose Q4W dosing: preservation of immunity through faster B-cell repletion<sup>4</sup> upon discontinuation

## ... with potential for best-in-class efficacy, safety and convenience

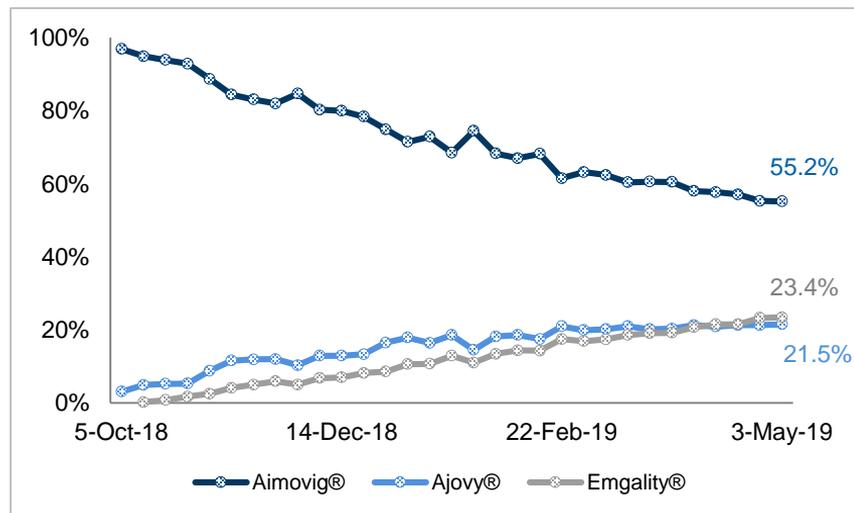
- Expected to have high efficacy on all key measures of disease activity enabling low dose
- Fewer side effects due to specific B-cell subset targeting and faster repletion<sup>4</sup>
- Potential for at-home once-a-month injection, requiring no pre-treatment, offering high degree of convenience

See appendix for references

# Aimovig® the leading CGRP in US with further growth expected from ongoing ex-US launches

## US CGRP Market TRx Share

Source IQVIA



- In US Aimovig® leads with 55% TRx share
- Further US opportunity in diagnosis rates (currently 13%) and penetration of preventive treatments (currently 12%)
- >200k patients treated to date worldwide
- Aimovig® now approved in 38 countries, available in 27 countries

All trademarks are the property of their respective owners. Aimovig is co-commercialized with Amgen in the US, where Amgen records sales, and Novartis has exclusive commercialization rights for all territories excluding US and Japan.

# Speed, efficacy and durability demonstrated by robust Zolgensma<sup>®1</sup> data at AAN

Please see posters/ AAN Novartis investor presentation (click [link](#))

## **SPRINT**

Pre-symptomatic data show benefit of early treatment

Pre-symptomatic: 2 or 3 copies of SMN2, <6 weeks of age at dosing

Rapid, age-appropriate improvement in motor function and milestone achievement:

- 8.9-point increase from baseline in CHOP-INTEND one-month post-dosing
- 4 patients could sit without support for ≥30 secs; 1 patient could stand with assistance for ≥2 secs

All patients alive, with no new safety signals relative to other Zolgensma<sup>®</sup> studies

Supports use of Zolgensma<sup>®</sup> as a key therapy in SMA identified through newborn screening

**Open label, data as of March 8, 2019**

2 copies: median 5.4 months of follow-up  
3 copies: median 2.2 months of follow-up

## **STRIVE**

Rapid measurable gains in motor function, confirming START data

Type 1: <6 months of age at dosing

New interim data continued to show Zolgensma<sup>®</sup> has the potential to provide prolonged event-free survival, increases in motor function and significant milestone achievement:

- 11 infants (50%) sitting at a mean of 8 months post-treatment, mean age of 11.9 months
- 21/22 patients have achieved a CHOP-INTEND score ≥40

One death independently deemed unrelated

STRIVE continues to reinforce foundational role of Zolgensma<sup>®</sup> for SMA Type 1

**Open label, data as of March 8, 2019**

Median 10.1 months of follow-up

## **START** Long-term follow-up

Long-term durability with no waning effect, reconfirms long-term value

Type 1: <6 months of age at dosing

No loss of milestones or waning of effect nearly four years post-dosing adds to evidence of long-term durability of Zolgensma<sup>®</sup>

All enrolled Cohort 2 patients (n=10) maintained motor function and milestone achievements

No patient experienced a worsening of nutritional or ventilatory requirements:

- 2 of 4 patients who used BiPAP at the start of the LTFU period no longer require it regularly

No new treatment-related adverse events have emerged during the follow-up period

Mean (range) age at last follow-up:  
3.9 (3.4–4.8) years

Mean (range) time since treatment:  
3.7 (3.3–4.3) years

## **STRONG**

Rapid gains through IT administration, shows promise for Type 2

Type 2: 6 months - 5 years of age at dosing

Intrathecal data reported for 1<sup>st</sup> time show rapid motor function gains and promising milestone achievements in SMA Type 2:

- 22 milestones in 10 patients achieved after a median 6.5 months of follow-up
- In the lower age cohort at dosing, 2 patients could stand independently, 1 went on to walk; in the older age cohort at dosing, 1 patient could walk with assistance

Plan to initiate discussions with regulators to define the path to registration for intrathecal administration of Zolgensma<sup>®</sup>

**Open label, data as of March 8, 2019**

Median 6.5 months of follow-up

Source: Novartis investor presentation on Zolgensma<sup>®</sup> at American Academy of Neurology Annual meeting 2019 <sup>1</sup> The brand name Zolgensma<sup>®</sup> has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

# Data show potential impact of Zolgensma<sup>®</sup> in broad spectrum of SMA

- ✓ START, STRIVE, SPRINT data indicate Zolgensma<sup>®</sup> provides **rapid** improvement in motor function and durable milestone achievement
- ✓ SPRINT data shows early treatment could lead to **near-normal development** for pre-symptomatic patients
- ✓ START long term follow-up shows the **long-term durability** of Zolgensma<sup>®</sup> with no waning effect
- ✓ Expansive program with >150 patients treated & <5% of patients excluded due to elevated anti-AAV9 antibodies<sup>2</sup>

Zolgensma<sup>®</sup> potentially transformational therapy for SMA

See appendix for references

# Zolgensma<sup>®</sup>: on approval, ready to meet immediate launch demand independent of label scenario

Institutional	<ul style="list-style-type: none"><li>▪ &gt;150 patients treated at 26 US sites</li><li>▪ Delivery infrastructure validated for HUB, AAV9 testing and rapid product delivery</li><li>▪ Expect &gt;60 top centers ready at launch, covering 80% of infants with SMA</li></ul>
Manufacturing	<ul style="list-style-type: none"><li>▪ Continuing to build supply</li><li>▪ Footprint growing with ~1 million square-feet of manufacturing space (See supplement)</li></ul>
Access	<ul style="list-style-type: none"><li>▪ Engaged with &gt;70 payers covering &gt;80% of the SMA infant population</li><li>▪ High interest in innovative contracts, expect 30% of commercial lives contracted within 30 days</li></ul>

The brand name Zolgensma<sup>®</sup> has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

# Broad clinical program for potentially transformative spinal muscular atrophy therapy

Delivery	SMA Type	2014-2017	Q1 2018	Q2 2018	Q3 2018	Q4 2018	2019	Completion
Intravenous (IV)	Pre-symptomatic Type 1,2,3			<b>SPRINT</b> Phase 3 22 / 27 patients enrolled – data at AAN 2019				2021
	Type 1	<b>START</b> 15 patients	<b>START</b> Long-term follow-up START dose-escalation study to identify therapeutic dose 13 / 15 patients enrolled – data at AAN 2019					2033
			<b>STRIVE</b> Phase 3 22 / 22 patients, fully enrolled – data at MDA 2019 and AAN 2019					2020
			<b>STRIVE-EU</b> Phase 3 26 / 30 patients enrolled					2021
							<b>STRIVE-AP</b> Planned start Will enroll 6 patients	TBC
Intrathecal (IT)	Type 2		<b>STRONG</b> Phase 1 31 / 51 patients; fully-enrolled in low-, mid-dose cohorts – data at AAN 2019					2020
	Type 1,2,3						<b>REACH</b> Pending	TBC

Final design of REACH to be informed by STRONG; cutoff as of April 2019. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities.

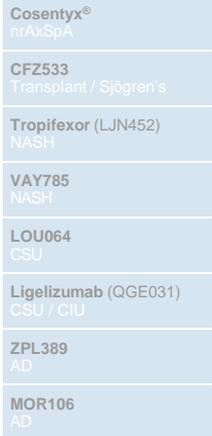
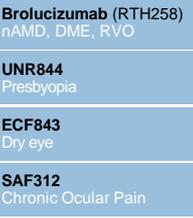
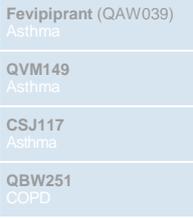
# Ongoing development program to address incident and prevalent populations across SMA types and regions

Region	Incident population			Prevalent population <sup>4</sup>		
	Type 1	Type 2	Type 3	Type 1	Type 2	Type 3
<b>US</b>	270-300 <sup>1</sup>	135-150 <sup>1</sup>	45-50 <sup>1</sup>	1,260-1,400	4,590-5,100	3,150-3,500
<b>Europe</b>	330-360 <sup>2</sup>	165-180 <sup>2</sup>	55-60 <sup>2</sup>	1,540-1,680	5,610-6,120	3,850-4,200
<b>Japan</b>	24-30 <sup>3</sup>	12-15 <sup>3</sup>	4-5 <sup>3</sup>	112-140	408-510	280-350

- SPR1NT studies pre-symptomatic population, in patients with 2 or 3 copies of SMN2
- START and STRIVE studies Type 1
- STRONG studies Type 2

1. Symphony claims data 2. [J Neurol](#), 2017 Jul;264(7):1465-1473 3. Data on file 4. Spinal Muscular Atrophy: Introduction to SMA families: SMA Foundation

# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets						
						
Select pipeline assets and opportunities						

\*The brand name Piquay® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country. See appendix for references

# Ophthalmology – building a portfolio to address high unmet need ocular surface diseases



## Unmet needs

### Ocular Surface Diseases

An incipient, poorly understood epidemic with high unmet patient needs

Heterogeneous population with lack of consistent diagnosis and segmentation

Limited Rx therapies available, and diverse scientific hypotheses

Superior response rates, tolerability and onset of action are needed for better treatment outcomes

Widespread use of OTC therapies

Medical Experts expect an Ocular Surface Disease epidemic

## Ocular surface diseases strategy

Segmented approach targeting transformative best- or first-in-class disease-modifying treatments; Novartis has capabilities and assets in each key segment

Inflammation induced Dry Eye Disease	Treat signs and symptoms by inhibiting the inflammatory cascade	<b>Xiidra</b> <sup>®1</sup> LFA-1 antagonist
Dry Eye Disease & Primary Sjogren's Syndrome	Next generation multi-modal biologic restoring ocular homeostasis	<b>ECF843</b> <i>rh</i> Lubricin
Ocular Surface Pain	Ocular pain	<b>SAF312</b> TRPV1 antagonist
Meibomian Gland Dysfunction	Targeting underlying disease pathophysiology	<b>Preclinical Asset</b>

1. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions

# Xiidra® acquisition: Strong strategic fit and attractive economics<sup>1</sup>

Strong strategic fit	with Novartis leading ophthalmic portfolio and pipeline
Clear blockbuster potential	given high unmet medical need with strong product profile
Significant synergies	with Novartis front-of-the-eye commercial infrastructure
Good financial return profile	Strict financial discipline applied, expected to be profitable 2020 and margin accretive 2021; deal structure adds tax benefit

  
Xiidra®  
complements  
the Novartis  
ophthalmology  
portfolio

  
LUCENTIS<sup>2</sup>  
RANIBIZUMAB INJECTION

  
DUREZOL<sup>®</sup>  
(difluprednate ophthalmic emulsion) 0.05%

  
ILEVRO™

  
Pazeo<sup>®</sup>  
(olopatadine hydrochloride ophthalmic solution) 0.7%

  
Azopt<sup>®</sup>

  
TRAVATAN Z<sup>®</sup>

  
SIMBRINZA<sup>®</sup>  
(brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%

  
LUXTURNA™<sup>2</sup>  
voretigene neparvovec-rzyl  
for subretinal injection

1. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions 2. Ex-US only

# Novartis industry leadership and commercial infrastructure setup to continue Xiidra® success and maximize its potential

## US Infrastructure

- 375 FF in-line products
- Market access expertise
- Field medical
- Retina team for anticipated RTH258 launch in Q4 2019<sup>1</sup>

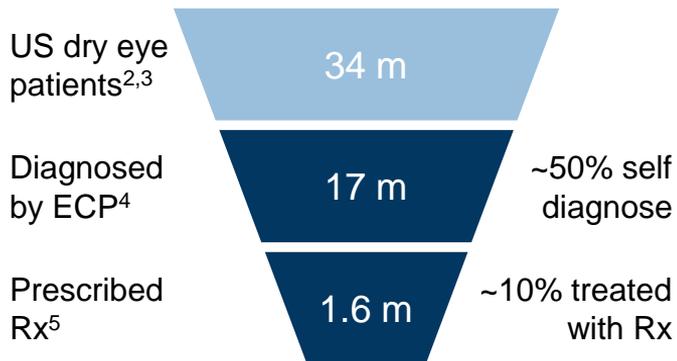
## Novartis global ophthalmic 2018 sales<sup>2</sup>

- #1 in Anti-inflammatory
- #1 in Anti-allergy
- #1 in Anti-infective
- #2 in Glaucoma
- #2 in Retina (outside US)

1. Pending regulatory approval. 2. Rankings based on 2018 sales from IQVIA

# Xiidra® uniquely positioned to treat both signs and symptom of dry eye disease

Dry eye disease underdiagnosed, undertreated<sup>1</sup>, increasing in incidence



First and only treatment approved for both signs and symptom of dry eye that targets inflammation

- Fast onset of action, 2 weeks to 3 months
- Tolerable safety profile

Well positioned as 2nd line therapy – vast majority of ophthalmologists want additional treatment options<sup>1</sup>

US prescriptions expected to increase with increasing incidence and use of more effective therapies

See appendix for references

# Brolucizumab (RTH258) achieved robust visual gains<sup>‡</sup> and superior fluid resolution\* – on track for 4Q19 US launch<sup>1</sup>

## HAWK & HARRIER outcomes on primary and key secondary end points<sup>2</sup>

Visual acuity	<ul style="list-style-type: none"><li>▪ Non-inferior to aflibercept in BCVA change from baseline to Week 48<sup>‡</sup></li></ul>
Anatomical outcomes	<ul style="list-style-type: none"><li>▪ Significantly fewer patients with IRF and/or SRF at Weeks 16 and 48*; difference maintained at Week 96<sup>†</sup></li><li>▪ Superior reductions in CST at Weeks 16 and 48*; difference maintained at Week 96<sup>†</sup></li><li>▪ Fewer patients with sub-RPE fluid at Weeks 16<sup>#</sup>, 48<sup>#</sup>, and 96<sup>†</sup></li><li>▪ Significantly fewer patients with disease activity at Week 16*</li></ul>
q12w dosing	<ul style="list-style-type: none"><li>▪ &gt;50% of patients maintained on q12w interval after loading through Week 48</li><li>▪ Over 75% of those who completed Week 48 on a q12w interval were maintained on q12w interval until Week 96</li></ul>

- Global anti-VEGF market ~10bn USD in 2018, 70% of market nAMD<sup>3</sup>
- On track for launch Q4 2019 US<sup>1</sup>, Q1 2020 Australia/ Canada<sup>1</sup>, Q2 2020 Europe/Japan<sup>1</sup>
- DME submission expected Q2 2021
- Brandname Beovu™ has provisionally been approved by FDA for Brolucizumab<sup>4</sup>

See appendix for references

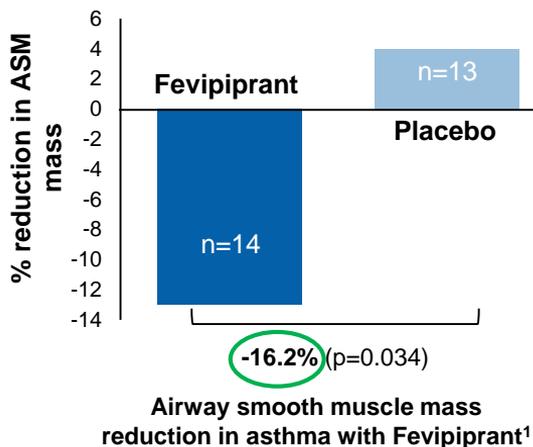
# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets	     			  	  	
	Kymriah® New indications Piqray® (BYL719) Breast Crizanlizumab (SEG101) Sickle Cell PDR001 combo Metastatic Melanoma ABL001 CML ACZ885 Lung <sup>177</sup> Lu-PSMA-617 mCRPC	Entresto® HFpEF, post-MI LNP023 Renal diseases TQJ230 CVRR	Cosentyx® nrAxSpA CFZ533 Transplant / Sjögren's Tropifexor (LJN452) NASH VAY785 NASH LOU064 CSU Ligelizumab (QGE031) CSU / CIU ZPL389 AD MOR106 AD	Zolgensma® <sup>2</sup> SMA LMI070 SMA Ofatumumab (OMB157) MS CNP520 Alzheimer's	Brolicizumab (RTH258) nAMD, DME, RVO UNR844 Presbyopia ECF843 Dry eye SAF312 Chronic Ocular Pain	Fevipiprant (QAW039) Asthma QVM149 Asthma CSJ117 Asthma QBW251 COPD

\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Feviprant (QAW039) showing asthma disease-modifying potential with Ph3 readouts on track end 2019

## Potential for disease modification

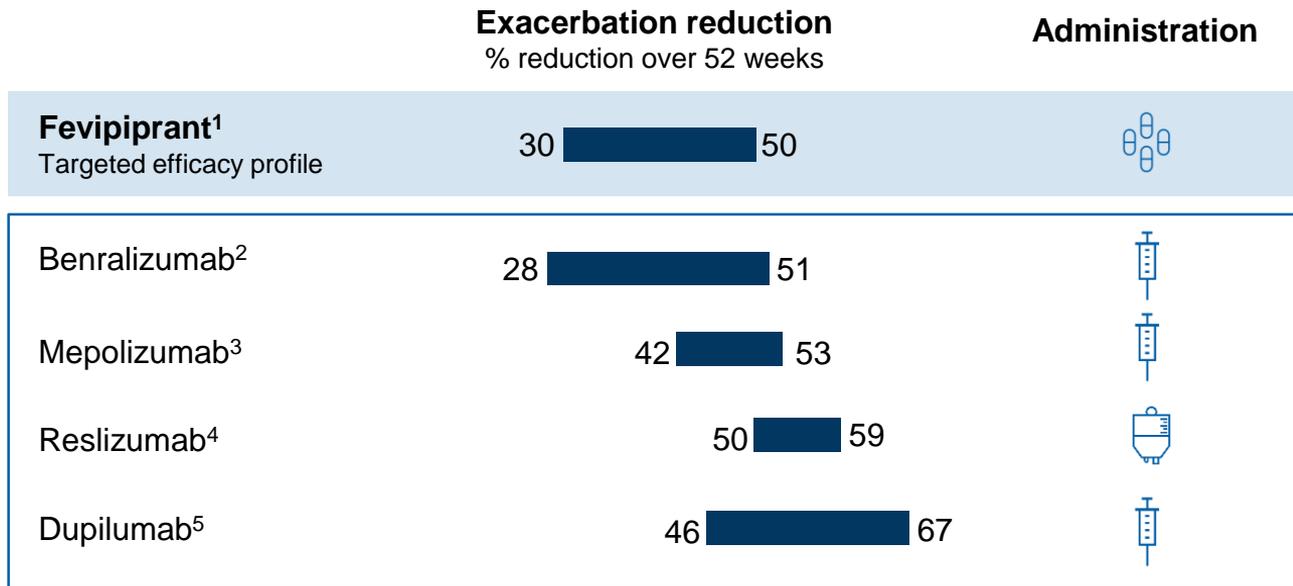


## Robust clinical program to realize full potential

All five Ph3 enrolled	<b>LUSTER 1 &amp; 2</b> (GINA 4/5)	exacerbation trial
	<b>SPIRIT</b> (GINA 3/4/5)	safety
	<b>ZEAL 1 &amp; 2</b> (GINA 3/4)	lung function FEV1
Ph2 data	Reduced sputum eosinophils by 72% <sup>2,3</sup>	
Pre-clinical data	Highly selective DP2 <ul style="list-style-type: none"> <li>▪ Superior potency</li> <li>▪ High selectivity</li> <li>▪ Clean safety profile</li> </ul>	

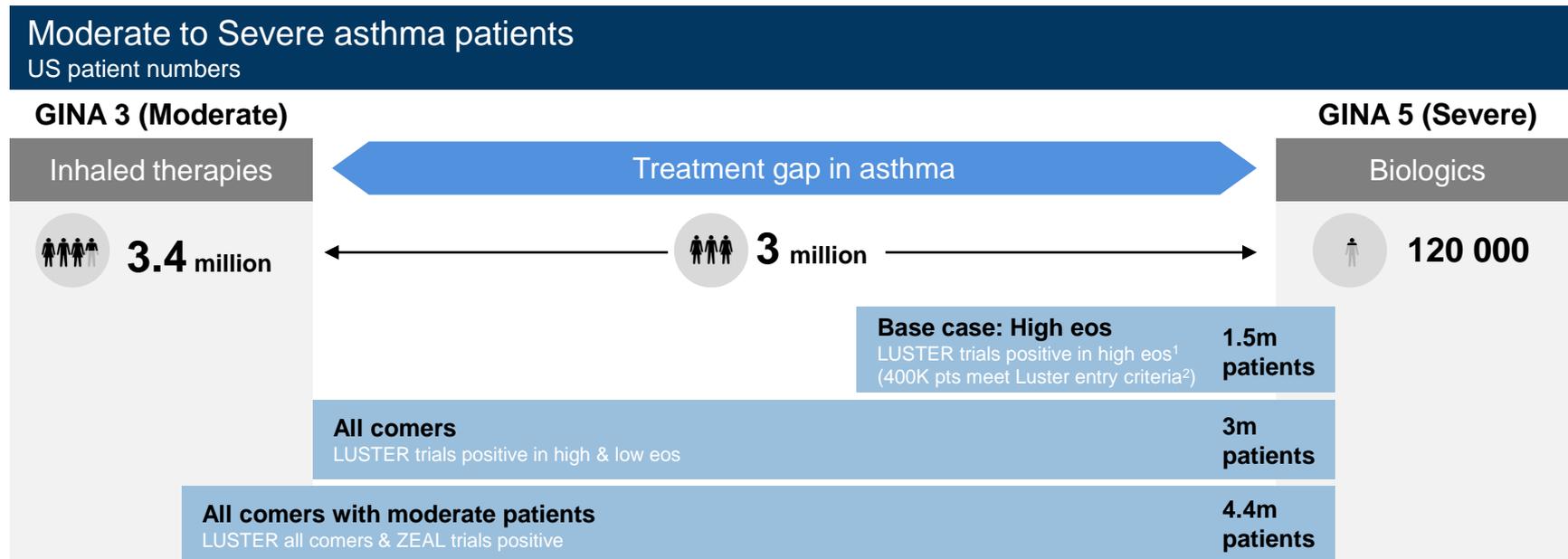
1. Saunders et al. Sci Trans Med 2019;11, eaao6451 1<sup>st</sup> EP; primary endpoint; FEV<sub>1</sub>: forced expiratory volume in one second; ASM: airway smooth muscle mass 2. Gonet et al. Lancet Respir Med 2016;4:699–707 3. Green et al. Lancet 2002;360(9347):1715–1721

# Fevipiprant (QAW039) development: targeting biologic efficacy with oral simplicity



See appendix for references

# Fevipiprant (QAW039) has the potential to address significant treatment gap in patients with unresolved asthma



1. High eosinophils defined as  $\geq 250$  cells/ $\mu$ L 2. Moderate to Severe refers to patients on GINA step 4/5 therapies (i.e ICS/LABA  $\pm$  LAMA). Sources: CDC; US claims data.

# Ready for first- and best-in-class launches

## 2019 Pharma launch priorities in US

Brolucizumab (RTH258)	<ul style="list-style-type: none"><li>▪ U.S. FDA filing accepted in April with use of Priority Review Voucher</li><li>▪ Pending FDA approval, US launch anticipated in Q4 2019</li><li>▪ Deep US Medical and Commercial team in place with extensive retina expertise</li></ul>
Zolgensma® <sup>1</sup>	<ul style="list-style-type: none"><li>▪ &gt;150 patients treated at 26 US sites</li><li>▪ Delivery infrastructure validated for HUB, AAV9 testing and rapid product delivery</li><li>▪ Expect &gt;60 top centers ready at launch, covering 80% of infants with SMA</li><li>▪ Manufacturing footprint growing with ~1 million square-feet of manufacturing space (See supplement)</li><li>▪ Engaged with &gt;70 payers covering &gt;80% of the SMA infant population</li><li>▪ High interest in innovative contracts, expect 30% of commercial lives contracted within 30 days</li></ul>
Xiidra®	<ul style="list-style-type: none"><li>▪ Strong US commercial presence of 375 field force associates promoting 7 in-line products</li><li>▪ Decades of experience within Optometry and Ophthalmology, deep customer relationships and insights</li><li>▪ Extensive commercial and market access expertise with payers</li><li>▪ Proven ability to successfully manage brands in a genericized marketplace</li></ul>

1. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities.

# With recently launched products and rich pipeline, Novartis expects double-digit growth in China, capitalizing on faster and broader access

Novartis position in China is strong ...

... expected to expand significantly based on a rich pipeline

## Approvals

Novartis is one of the leading MNCs in NDA approvals

## Reimbursement

All in-line brands launched before 2017 are reimbursed

## Execution

Entresto® best ever primary care launch in China, even pre-reimbursement

Year	Actual / pursued approvals	NDRL actual / pursued listings
2017	+6; incl. Entresto® HFpEF, Xolair® Asthma, Ultibro® COPD, Exelon® Patch AD, Galvus®5, Diovan® FCT	+8: Lucentis® wAMD; Galvus®, Exforge®, Co-Diovan®, Onbrez®, Lescol XL®, Simulect®, Patanol®
2018	+6; Lucentis® DME/RVO/PM, Vigamox®, Seebri® COPD	(Oncology only)
2019e	+3; Cosentyx® PsO <sup>3</sup> , Gilenya® MS	+6: Entresto®, Lucentis® RVO/DME/CNV, Vigamox®, Exelon® Patch, Ultibro®, Xolair®
2020e	+5; Cosentyx® AS, Mayzent® SPMS	+3
2021e	+5; Entresto® HFpEF, Xolair® CIU/CSU, Fevipirant <sup>4</sup> Asthma;	+5
2022e	+1; Entresto® Post-AMI	+5
2023e	+3; Brolucizumab (RTH258) wAMD/DME; Aimovig® CM/EM	+1

NDRL expected to be updated dynamically

NDA – New Drug Applications NDRL – National Drug Reimbursement List COPD – Chronic Obstructive Pulmonary Disease AD – Alzheimer’s Disease DME – Diabetic Macular Edema RVO – Retinal Vein Occlusion CNV – choroidal neovascularization PM – pathologic myopia CM – Chronic Migraine EM – Episodic Migraine See appendix for references

# Enhancing productivity, patient care and engagement through digital solutions – examples

**DRIVING PRODUCTIVITY** 

**ACTalya Personal Assistant**



Unleashing the power of data and technology to give our reps real-time, streamlined, personalized data to make their **100 000 daily interactions with HCPs more personalized, efficient and impactful**

**PLAN OF SCALE & IMPACT:**  
Equip all Novartis sales reps with ACTalya worldwide

**TRANSFORMING ENGAGEMENT** 

**Patient Engagement Platform**



Improving the patient experience from pre-diagnosis to post-Rx through transformative patient-centric solutions helping **address specific pain points along the patient journey**

**PLAN OF SCALE & IMPACT:**  
Form large-scale partnerships across all major markets

**IMPROVING PATIENT CARE** 

**Automated inhaler tracking**



Improving Respiratory Care by **combining a sensor and app together with the Breezhler device**, uniquely enabling confirmation of the inhalation and providing precise medication reminders & objective reports

**PLAN OF SCALE & IMPACT:**  
Partnership with Propeller Health to launch in major markets across the EU starting this year

\*All Trademarks are property of their respective owners

★ Solution live in at least 1 market

# Conclusion - Pharmaceuticals



Continued strong momentum for Cosentyx<sup>®</sup> and Entresto<sup>®</sup>



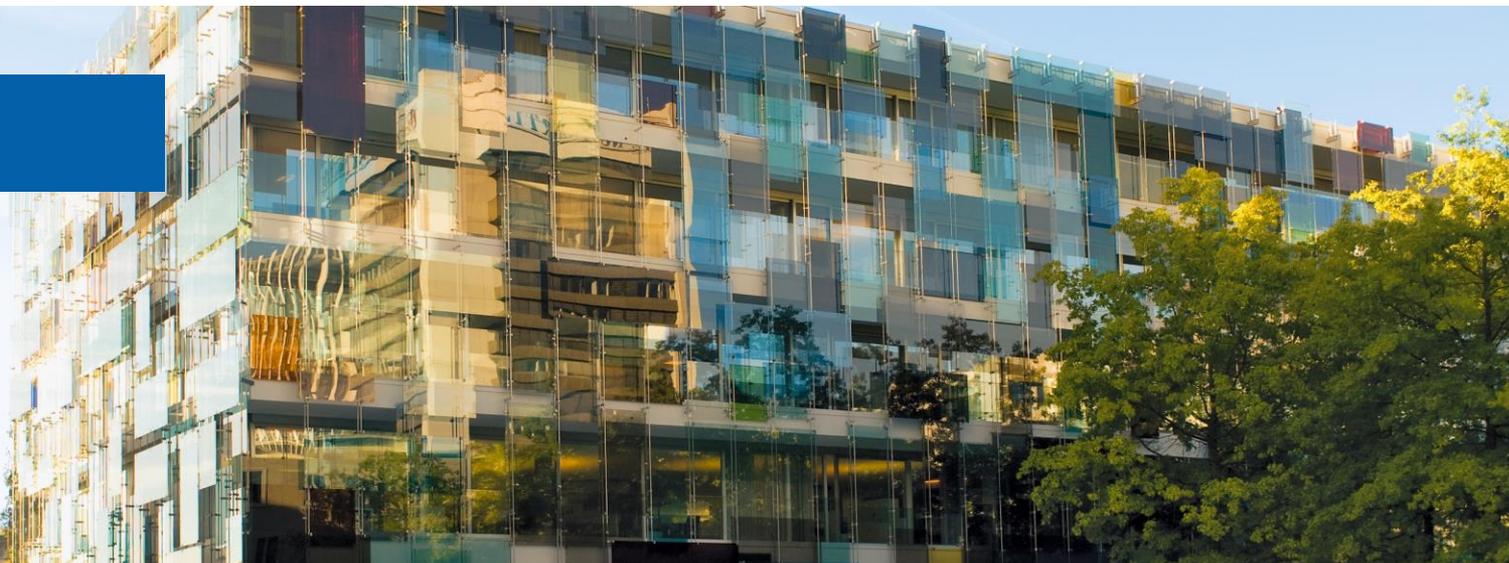
Ready to launch 5 blockbuster near-term candidates



With recently launched products and rich pipeline, Novartis expects double-digit growth in China



Novartis AG  
Investor Relations



# **Meet Novartis Management 2019 Oncology pipeline and in-market brands**

**May 23, 2019**

# Index – select commercial and pipeline assets

## Anchor commercial assets

	SLIDE
Key in-market blockbusters	8
Kisqali <sup>®</sup>	9 – 10
Kymriah <sup>®</sup>	20
Lutathera <sup>®</sup>	15

## Select pipeline assets

	SLIDE
<sup>177</sup> Lu-PSMA-617	18
ABL001	12
Canakinumab (ACZ885)	25 – 26
Crizanlizumab (SEG101)	11
Piqray <sup>®1</sup> (BYL719)	10

1. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country

# Building depth across our core therapeutic areas

		PHARMACEUTICALS				
		Cardio-Metabolic	IHD	Neuroscience	Ophthalmology	Respiratory
Select commercial assets	ONCOLOGY					
						
Select pipeline assets and opportunities	Kymriah® New indications	Entresto® HFpEF, post-MI	Cosentyx® nrAxSpA	Zolgensma® <sup>2</sup> SMA	Brolicizumab (RTH258) nAMD, DME, RVO	Fevipiprant (QAW039) Asthma
	Piqray®* (BYL719) Breast	LNP023 Renal diseases	CFZ533 Transplant / Sjögren's	LMI070 SMA	UNR844 Presbyopia	QVM149 Asthma
	Crizanlizumab (SEG101) Sickle Cell	TQJ230 CVRR	Tropifexor (LJN452) NASH	Ofatumumab (OMB157) MS	ECF843 Dry eye	CSJ117 Asthma
	PDR001 combo Metastatic Melanoma		VAY785 NASH	CNP520 Alzheimer's	SAF312 Chronic Ocular Pain	QBW251 COPD
	ABL001 CML		LOU064 CSU			
	ACZ885 Lung		Ligelizumab (QGE031) CSU / CIU			
	<sup>177</sup> Lu-PSMA-617 mCRPC		ZPL389 AD			
		MOR106 AD				

\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country See appendix for references

# Leading oncology business, driving growth in four distinct platforms

**1** Novartis is one of the leading Oncology companies with growth opportunities in Targeted Therapy, Cell Therapy, Radioligand Therapy and Immunotherapy

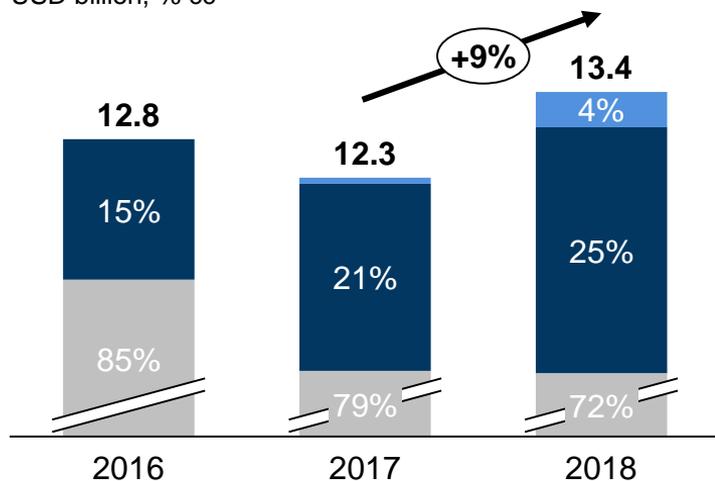
**2** Rich portfolio with 7 in-market blockbusters and 3 recent launches with blockbuster potential and a strong, unique pipeline across our 4 platforms

**3** Promising pipeline, integrating the best from internal and external innovation, positions Novartis to continue to lead in Oncology with 4 potential blockbuster launches planned by 2021

# 2018 Oncology sales up +9% cc driven by recent launches<sup>1</sup> and growth drivers<sup>2</sup>

## Net Sales Oncology BU

USD billion, % cc



■ Recent Launches<sup>1</sup>
■ Growth Drivers<sup>2</sup>
■ Base Business<sup>3</sup>

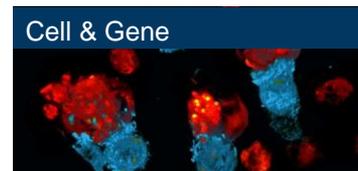
1. Recent launches include Kisqali<sup>®</sup>, Kymriah<sup>®</sup>, Lutathera<sup>®</sup>. 2. Growth drivers include Promacta<sup>®</sup>/Revolade<sup>®</sup>, Jakavi<sup>®</sup> (marketed by Novartis ex-USA), Tafinlar<sup>®</sup>+ Mekinist<sup>®</sup>. 3. Base business – other brands.



## Potential Future Growth

- + Strong uptake of recent launches
- + Growth drivers deliver double-digit performance
- + Resource allocation/productivity to fuel strategic investment (i.e. launches, China)
- Generic impact (Afinitor<sup>®</sup>, Exjade<sup>®</sup>, Glivec<sup>®</sup> and Sandostatin LAR<sup>®</sup>)
- Healthcare cost containment / pricing

# Deep pipeline across four distinct platforms is expected to continue driving differentiation and growth



**Anchor commercial assets**



**Select pipeline assets<sup>1</sup> and opportunities**

**ABL001** in CML (3rd line & 1st line add-on)  
**Piqray<sup>®</sup>**, in PIK3CA mutated HR+/HER2- advanced breast cancer, HER2+ advanced breast cancer, TNBC  
**INC280** in NSCLC, single agent  
**SEG101** in sickle cell disease

**177Lu PSMA-617** in prostate cancer  
**177Lu PSMA-R2** in prostate cancer  
**177Lu NeoB** in breast cancer, GIST, GBM, neuroblastoma, ovarian, head & neck, esophageal

**Kymriah<sup>®</sup>** in

- r/r DLBCL in 1st relapse
- r/r follicular lymphoma
- combinations (pembro; ibrutinib) in r/r DLBCL
- 1st line high risk pediatric and young adult ALL
- Adult ALL
- CLL

**Other targets:** BCMA&CD19, CD22&CD19, CD123, EGFRv3

**ACZ885** in

- adjuvant NSCLC
- 1st line NSCLC
- 2nd line NSCLC

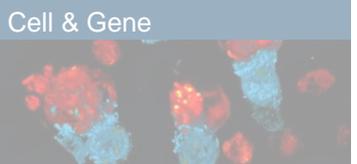
**PDR001+Tafinlar<sup>®</sup>+Mekinist<sup>®</sup>** in metastatic melanoma

**PDR001+LAG525+carboplatin** in TNBC

**PDR001+INC280** in 2nd line NSCLC

Projects included are those with planned filings in US and/or EU 1. All select pipeline assets are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation 2. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country

# Deep pipeline across four distinct platforms is expected to continue driving differentiation and growth

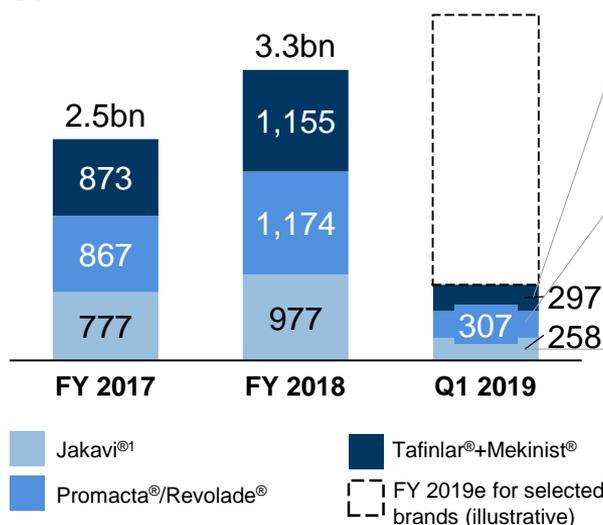
	Targeted therapies (TT)	Radioligand therapies (RLT)	Cell & Gene	Immunotherapies (IO)
<b>Anchor commercial assets</b>	 <p><b>PROMACTA®</b> (eltrombopag) 25mg, 50mg, 75mg tablets</p> <p><b>JAKAVI®</b> ruxolitinib</p> <p><b>KISQALI®</b> ribociclib</p> <p><b>Tafinlar®</b> (dabrafenib)</p> <p><b>Mekinist®</b> (trametinib)</p>	 <p><b>LUTATHERA®</b> Advanced radioligand antagonist (lutetium Lu 177) (radioactive) injection, for intravenous use</p>	 <p><b>KYMRIAH®</b> (tisagenlecleucel) Suspension for IV infusion</p>	
<b>Select pipeline assets<sup>1</sup> and opportunities</b>	<p><b>ABL001</b> in CML (3rd line &amp; 1st line add-on)</p> <p><b>Piqray®</b>, in PIK3CA mutated HR+/HER2- advanced breast cancer, HER2+ advanced breast cancer, TNBC</p> <p><b>INC280</b> in NSCLC, single agent</p> <p><b>SEG101</b> in sickle cell disease</p>	<p><b>177Lu PSMA-617</b> in prostate cancer</p> <p><b>177Lu PSMA-R2</b> in prostate cancer</p> <p><b>177Lu NeoB</b> in breast cancer, GIST, GBM, neuroblastoma, ovarian, head &amp; neck, esophageal</p>	<p><b>Kymriah®</b> in</p> <ul style="list-style-type: none"> <li>- r/r DLBCL in 1st relapse</li> <li>- r/r follicular lymphoma</li> <li>- combinations (pembro; ibrutinib) in r/r DLBCL</li> <li>- 1st line high risk pediatric and young adult ALL</li> <li>- Adult ALL</li> <li>- CLL</li> </ul> <p><b>Other targets:</b> BCMA&amp;CD19, CD22&amp;CD19, CD123, EGFRv3</p>	<p><b>ACZ885</b> in</p> <ul style="list-style-type: none"> <li>- adjuvant NSCLC</li> <li>- 1st line NSCLC</li> <li>- 2nd line NSCLC</li> </ul> <p><b>PDR001+Tafinlar®+Mekinist®</b> in metastatic melanoma</p> <p><b>PDR001+LAG525+carboplatin</b> in TNBC</p> <p><b>PDR001+INC280</b> in 2nd line NSCLC</p>

Projects included are those with planned filings in US and/or EU become commercially available for the use(s) under investigation sale in any country

1. All select pipeline assets are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will  
2. The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for

# Key in-market Oncology blockbusters delivering high double-digit growth since 2017

## Net Sales USD million



### Tafinlar<sup>®</sup> + Mekinist<sup>®</sup> (grew +18% cc in Q1 2019 vs. PY)

- 28k BRAF+ melanoma and NSCLC patients p.a. in G7
- Standard of care in BRAF+ targeted therapy
- Launch of lung and adjuvant melanoma progressing well
- Ph3 triplet with PDR001 study in 1L BRAF+ metastatic melanoma read out expected H2 2019

### Promacta<sup>®</sup>/Revolade<sup>®</sup> (grew +24% cc in Q1 2019 vs. PY)

- 86k eligible ITP patients p.a. in G7
- Market leader in TPO-RA class and gaining share outside of the class in ITP
- Launched 1L SAA in US
- Implemented unique analytical tool, DROID<sup>2</sup>, to optimize marketing mix

### Jakavi<sup>®1</sup> (grew +20% cc in Q1 2019 vs. PY)

- 37k MF and PV patients treated with Jakavi ex-US
- Standard of care in 1L MF and in 2L PV in most countries, where launched
- Ph3 studies in acute and chronic GVHD results expected in H2 2019 12,5k new GVHD cases per year in G6<sup>3</sup>)

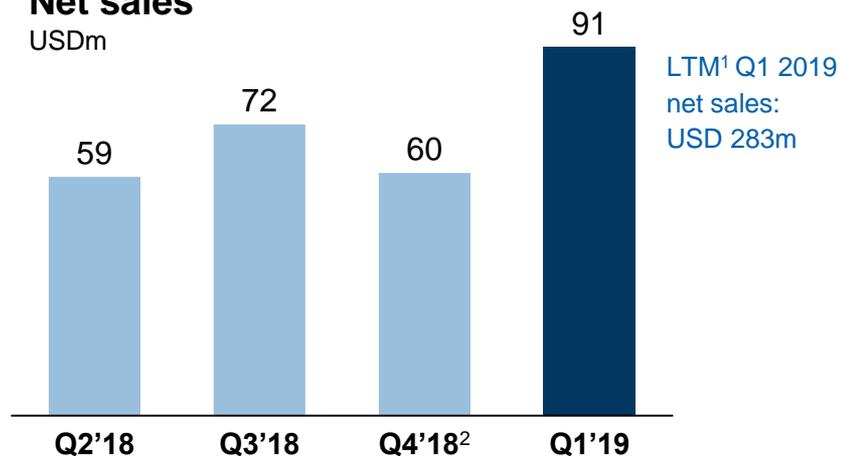
1. Jakavi is a registered trademark of Novartis AG in countries outside the United States. Jakafi is a registered trademark of Incyte Corporation. 2. DROID is an acronym that stands for data repository for optimization, insights and decision-making  
3. UK, France, Germany, Italy, Spain and Japan.

# Kisqali® gaining share in front line



## Net sales

USDm

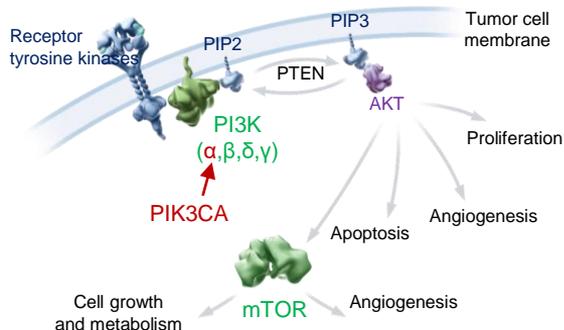


- **CDK 4/6 with largest body of first line evidence** regardless of combination partner or menopausal status while maintaining patients' quality of life
- **Overall survival results from MONALEESA-7 with Kisqali® (ribociclib)\* plus endocrine therapy in premenopausal women with HR+/HER2- advanced breast cancer, to be presented at ASCO**

1. Last twelve months 2. Reimbursement agreements in Europe had a temporary impact on Q4 growth in the region Kisqali® was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals

# Next pioneering medicine, Piqray®\* (BYL719), expected to be the first and only therapy for aBC patients with PIK3CA mutation

PI3K: Central oncogenic pathway deregulated in cancer

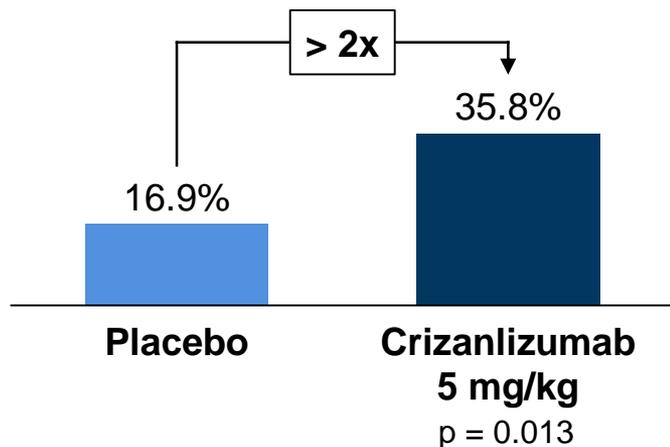


- ~40% of HR+/HER2- breast cancer patients have a PIK3CA mutation, associated with poor prognosis<sup>1,2</sup>
- Nearly doubled median PFS in SOLAR-1 study<sup>3</sup>
- Ready to launch with FDA-approved companion diagnostic
- Initiating pivotal clinical trials in HER2+ aBC and TNBC; planning additional studies across PIK3CA-mutation driven cancers

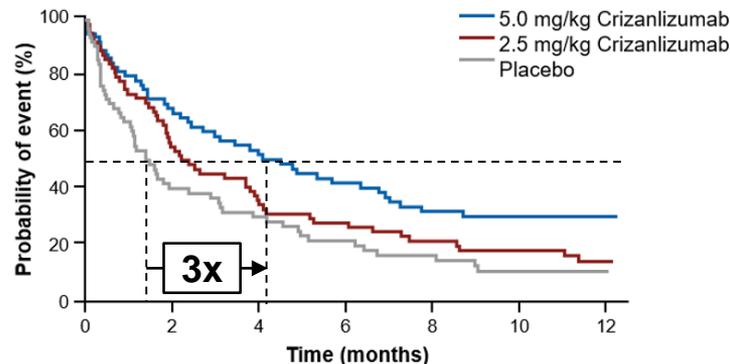
\*The brand name Piqray® has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country 1. Sabine V, Crozier C, Brookes C, et al. Mutational analysis of PI3K/AKT signaling pathway in tamoxifen exemestane adjuvant multinational pathology study. Journal of Clinical Oncology. 2014;32:2951-2958. 2. Juric D, Ciruelos EM, Rubovszky G et al. Alpelisib (ALP) + fulvestrant (FUL) for advanced breast cancer (ABC): Phase 3 SOLAR-1 trial results. Presented at the San Antonio Breast Cancer Symposium (SABCS) (Abstract #GS3-08) on December 6, 2018.

# SEG101 (crizanlizumab) increased proportion of patients free from VOC and delayed these crises

Proportion of patients free from VOC for the study period<sup>1</sup>



Time to first VOC<sup>1</sup>



**Median for crizanlizumab 5 mg/kg vs. placebo**  
4.07 vs 1.38 months

VOCs are associated with increased morbidity / mortality, can result in stroke, as well as organ damage or failure<sup>2</sup>

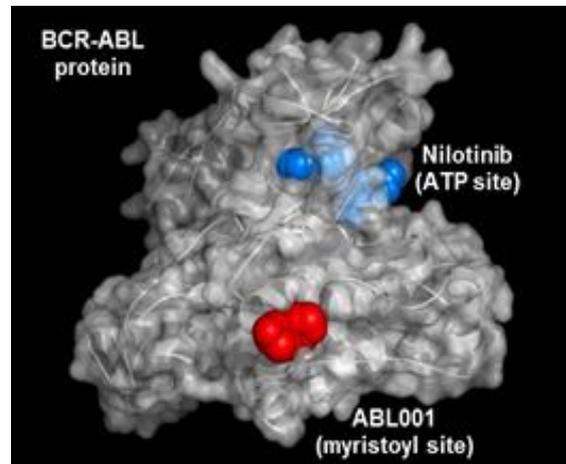
1. VOC that led to healthcare visit; p = 0.001 (log rank p-value); HR (95%CI) = 0.50 (0.33, 0.74); Kutlar et al, Am J Hematol. 2018 Oct 8. doi: 10.1002/ajh.25308. 2. Piel F, Steinberg M, Rees D. Sickle cell disease. N Engl J Med. 2017; 376(16):1561-1573.

# ABL001: Potential game changer to address unmet needs in CML with a unique mechanism of action

Asciminib (ABL001)

Chronic myeloid leukemia

- 50-70% of patients do not achieve MR<sup>4.5</sup> by 5 years with existing treatments<sup>1,2</sup>
- ABL001 is a first-in-class, potent and selective allosteric BCR-ABL inhibitor, which has a complementary mode of action with TKIs
- A potential game changer in CML which may bring more patients into deeper response faster, enabling the opportunity for TFR
- Expect to file in 3L by 2021 and in 1st line add-on in 2024



1. Hochhaus A, et al. Leukemia.2016;30:1044-1054

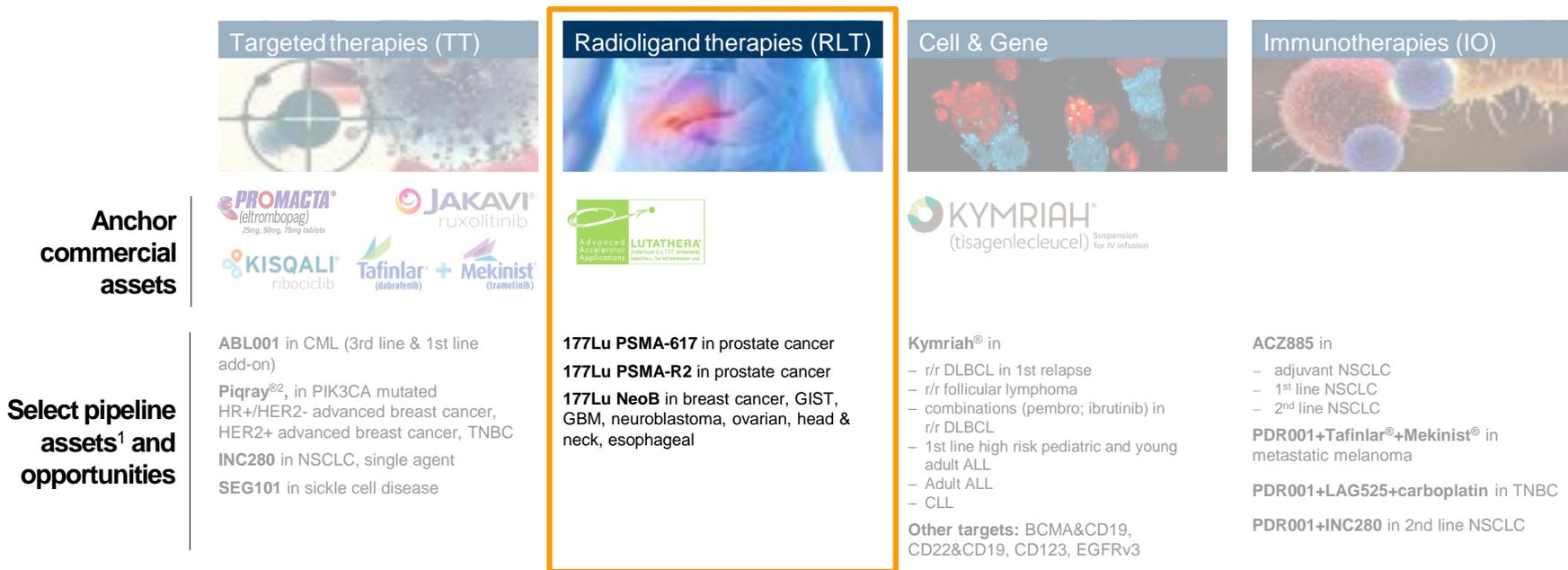
2. Cortes JE, et al. J Clin Oncol. 2016;34:2333-2340;

# Preparing for potential first- and best-in-class launches; select launch examples in US

<b>Piqray<sup>®</sup> (BYL719)</b>	<ul style="list-style-type: none"><li>▪ Anticipated to be launched with FDA approved companion diagnostic for PIK3CA testing (Qiagen)</li><li>▪ Entered into agreement with Foundation Medicine to develop plasma and tissue test</li><li>▪ Engaged with payers covering over 80% of the target population in the US</li></ul>
<b>SEG101 (crizanlizumab)</b>	<ul style="list-style-type: none"><li>▪ Breakthrough therapy designation granted by FDA in December 2018 for the prevention of vaso-occlusive crisis in sickle cell disease</li><li>▪ Filing on track to be completed by 1H 2019</li><li>▪ Engagements with payers and legislators ongoing</li><li>▪ Expected to launch in H1 2020</li></ul>
<b>INC280 (capmatinib)<sup>2</sup></b>	<ul style="list-style-type: none"><li>▪ Achieved Breakthrough Therapy Designation from FDA</li><li>▪ Developing NGS-based CDx for submission using tumor tissue, with plasma-based “liquid biopsy” version to follow</li><li>▪ Expected to launch in H2 2020</li></ul>

RTR = Real-Time Review 1. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country  
2. Capmatinib (INC280) licensed to Novartis by Incyte Corporation

# Deep pipeline across four distinct platforms is expected to continue driving differentiation and growth



Projects included are those with planned filings in US and/or EU. become commercially available for the use(s) under investigation sale in any country

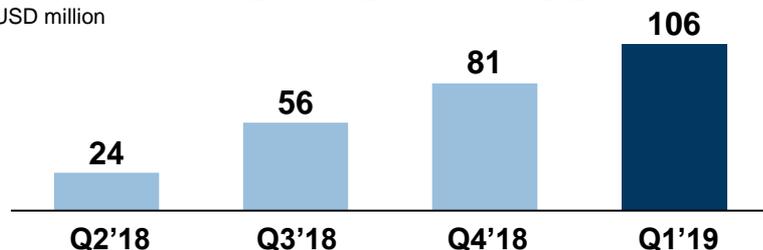
1. All select pipeline assets are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will  
 2. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for

# Successful launch of Lutathera<sup>®</sup> demonstrates high potential of targeted radioligand therapies (RLT)

## Lutathera<sup>®</sup> strong uptake continues

**Net sales**  
USD million

LTM<sup>1</sup> Q1 2019 sales: USD 267m

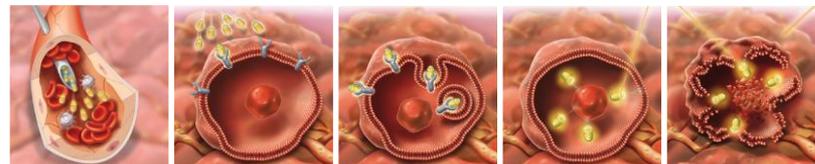


- Over 2,000 NET patients treated in the US since Jan 2018 launch
- Broad US payer coverage with over 85% of lives covered
- Positive momentum in EU launch w/ several favorable reimbursement decisions expected this year
- Expected to reach blockbuster status

1. Last twelve months

## Lutathera<sup>®</sup> is an innovative RLT

- RLT involves the systemic administration of a radiopharmaceutical to deliver cytotoxic radiation to a tumor
- The peptide is designed to target somatostatin receptors with high binding affinity



Intravenous infusion

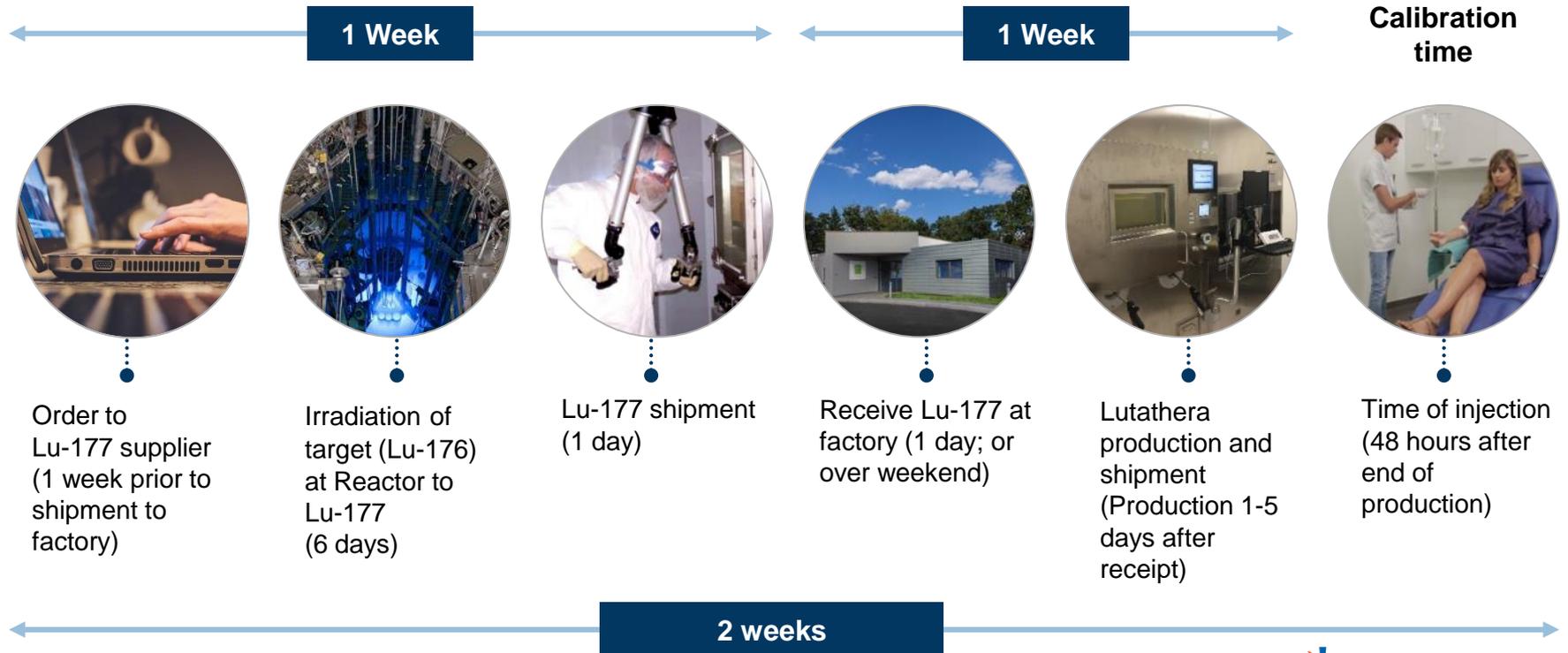
Lutathera<sup>®</sup> binds to somatostatin receptor type 2 (SSTR2) overexpressed by GEP-NETs of the foregut, midgut, and hindgut for adults

Lutathera<sup>®</sup> is internalized into the NET cell

Lutathera<sup>®</sup> delivers radiation within the GEP-NETs cells

Radiation induces DNA strand breaks causing tumor cell death

# Novartis building leadership in RLT with highly-complex, scaled, on-demand manufacturing capability



# RLT platform with growing pipeline in solid tumors

RLT being explored across wide range of solid tumors

Product	Disease (target)	Preclinical	Phase I	Phase II	Phase III	Filing	Marketed	Status
177Lu PSMA-617	Prostate cancer (PSMA)	Therapeutic						Ph III VISION study initiated 2Q 2018
177 Lu PSMA-R2		Therapeutic						Ph I/II study initiated 2Q 2018
68Ga PSMA-R2		PET Diag.						Ph I/II study initiated 2Q 2018
18F CTT1057		PET Diagnostic						Ph I study completed
177Lu NeoB	Breast cancer GIST GBM Neuroblastoma Ovarian	Therapeutic						Phase I study to open 1H 2019
68Ga NeoB		PET Diagnostic						Phase II study initiated 2Q 2018
177Lu FF-10158	Glioblastoma (Integrin Alphabeta 3/5)	Therapeutic						Preclinical
68Ga FF-10158		PET Diag.						Preclinical

Endocyte further establishes leadership position

## Expands Novartis RLT platform

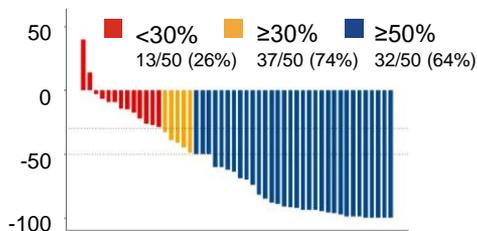
- 177Lu-PSMA-617 potentially first-in-class PSMA radioligand therapy in mCRPC
- Opportunity to further develop 177Lu-PSMA-617 to enter earlier lines of therapy

## Ph3 VISION trial enrollment ongoing for 177Lu-PSMA-617 in mCRPC

- Expected read-out and filing in 2020

# <sup>177</sup>Lu-PSMA-617 has strong Ph2 data in mCRPC<sup>1,2</sup>

## PSA response % (N=50)



## Treatment emergent adverse events attributable to <sup>177</sup>Lu-PSMA-617

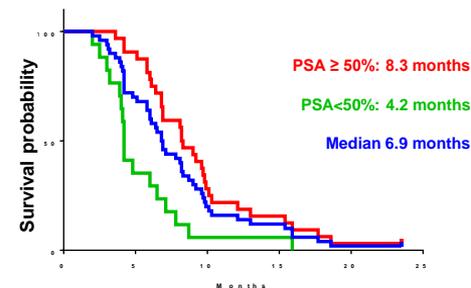
	Grade 1	Grade 2	Grade 3	Grade 4
Dry mouth	29 (58%)	4 (8%)	0 (0%)	0 (0%)
Lymphocytopenia	7 (14%)	13 (26%)	16 (32%)	0 (0%)
Thrombocytopenia	11 (22%)	3 (6%)	4 (8%)	1 (2%)
Fatigue	15 (30%)	3 (6%)	1 (2%)	0 (0%)
Nausea	20 (40%)	4 (8%)	0 (0%)	0 (0%)
Anaemia	3 (6%)	6 (12%)	5 (10%)	0 (0%)
Neutropenia	6 (12%)	6 (12%)	3 (6%)	0 (0%)
Bone Pain	5 (10%)	4 (8%)	0 (0%)	0 (0%)
Vomiting	11 (22%)	2 (4%)	0 (0%)	0 (0%)
Anorexia	8 (16%)	0 (0%)	0 (0%)	0 (0%)
Dry eyes	4 (8%)	1 (2%)	0 (0%)	0 (0%)
Renal injury	4 (8%)	1 (2%)	0 (0%)	0 (0%)
Weight loss	3 (6%)	1 (2%)	0 (0%)	0 (0%)

1. Hofman, Michael et al (2019). Results of a 50-patient single-centre phase II prospective trial of Lutetium-177 PSMA-617 theranostics in metastatic castrate-resistant prostate cancer. J Clin Oncol. 2019;37(suppl 7S): 228. 2. <sup>177</sup>Lu-PSMA-617 is an investigational drug not approved for use - study protocol is not designed to confirm efficacy or safety.

## PSA PFS

50 patients

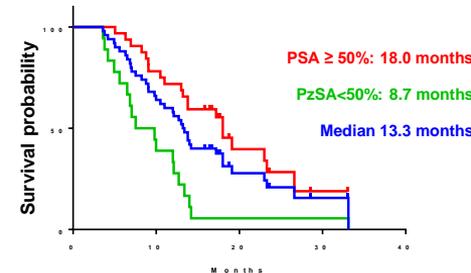
PSA ≥50% vs <50%:  
median PFS 8.3 vs  
4.2 months (p<0.001)



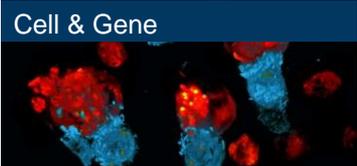
## Overall Survival

50 patients

PSA ≥50% vs <50%:  
median OS 18.0 vs  
8.7 months (p=0.001)



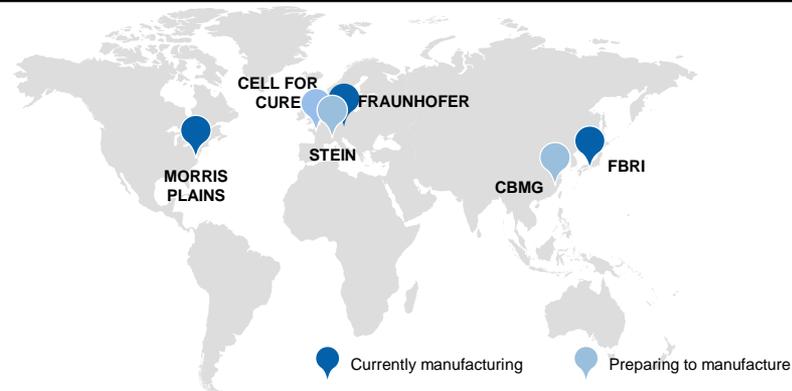
# Deep pipeline across four distinct platforms is expected to continue driving differentiation and growth

	Targeted therapies (TT)	Radioligand therapies (RLT)	Cell & Gene	Immunotherapies (IO)
<b>Anchor commercial assets</b>	     	 	 	
<b>Select pipeline assets<sup>1</sup> and opportunities</b>	<p><b>ABL001</b> in CML (3rd line &amp; 1st line add-on)</p> <p><b>Piqray<sup>®2</sup></b>, in PIK3CA mutated HR+/HER2- advanced breast cancer, HER2+ advanced breast cancer, TNBC</p> <p><b>INC280</b> in NSCLC, single agent</p> <p><b>SEG101</b> in sickle cell disease</p>	<p><b>177Lu PSMA-617</b> in prostate cancer</p> <p><b>177Lu PSMA-R2</b> in prostate cancer</p> <p><b>177Lu NeoB</b> in breast cancer, GIST, GBM, neuroblastoma, ovarian, head &amp; neck, esophageal</p>	<p><b>Kymriah<sup>®</sup></b> in</p> <ul style="list-style-type: none"> <li>- r/r DLBCL in 1st relapse</li> <li>- r/r follicular lymphoma</li> <li>- combinations (pembro; ibrutinib) in r/r DLBCL</li> <li>- 1st line high risk pediatric and young adult ALL</li> <li>- Adult ALL</li> <li>- CLL</li> </ul> <p><b>Other targets:</b> BCMA&amp;CD19, CD22&amp;CD19, CD123, EGFRv3</p>	<p><b>ACZ885</b> in</p> <ul style="list-style-type: none"> <li>- adjuvant NSCLC</li> <li>- 1st line NSCLC</li> <li>- 2nd line NSCLC</li> </ul> <p><b>PDR001+Tafinlar<sup>®</sup>+Mekinist<sup>®</sup></b> in metastatic melanoma</p> <p><b>PDR001+LAG525+carboplatin</b> in TNBC</p> <p><b>PDR001+INC280</b> in 2nd line NSCLC</p>

Projects included are those with planned filings in US and/or EU 1. All select pipeline assets are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation 2. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for sale in any country

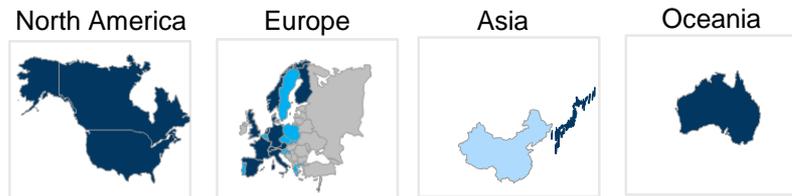
# Progressing with capacity expansion and reimbursement to deliver Kymriah® to every patient in need

## Global capacity expansion



- Completed CellforCure acquisition
- Wider commercial specifications are approved in EU, Switzerland, Australia, Japan, Canada
- Cleared by the FDA to further increase Morris Plains capacity

## Global reimbursement expansion



- LTM<sup>1</sup> Q1 2019 net sales: USD 109 m
- Treated over 900 patients worldwide<sup>2</sup>
- Reimbursed at least with 1 indication in 16 countries

1. Last twelve months. 2. Includes patients treated with Kymriah® in both clinical trial and commercial settings.

# Select pipeline examples for cell therapy platform

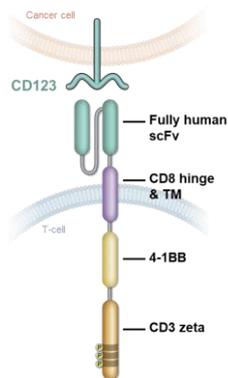


## Pipeline of 10 clinical programs and 4 FIH, with large pre-clinical effort

CAR-T type	Indication	Phase 1	Ph 2/Pivotal	Phase 3	Submitted	Approved
CD19 CAR-T	Pediatric & young adult r/r ALL					US, EU
CD19 CAR-T	r/r DLBCL					US, EU
CD19 CAR-T	DLBCL in 1 <sup>st</sup> relapse	Started 2019				
CD19 CAR-T	r/r FL	Started 2018				
CD19 CAR-T	r/r DLBCL in combination with pembrolizumab	Started 2018				
CD19 CAR-T	Adult r/r ALL	Starting 2019				
CD19 CAR-T	r/r CLL combination with ibrutinib	Starting 2019				
CD19 CAR-T	Pediatric NHL	Starting 2019				
CD19 CAR-T	1st line high risk pediatric and young adult ALL	Starting 2019				
CD19 CAR-T	r/r DLBCL combo with ibrutinib	Starting 2019				
Other targets (UPenn partner)	BCMA&CD19, CD22&CD19, CD123, EGFRv3	Started 2018				

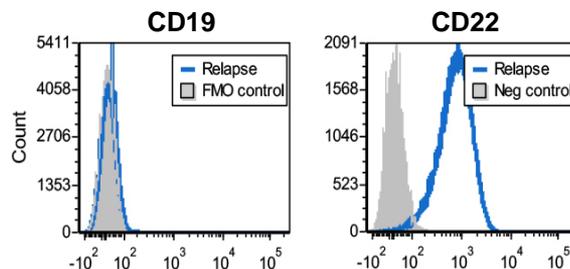
# Advances in novel CAR-Ts as monotherapies and combination strategies in collaboration with UPenn

## aCD123 CAR-T for AML



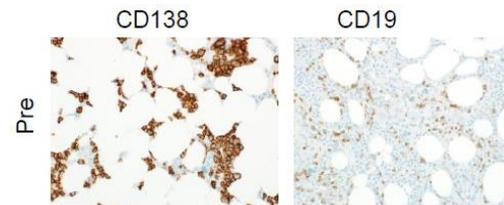
- JEZ567: lentivirally transduced T cells expressing anti-CD123 chimeric antigen receptors in r/r adult AML
- Opened Dec 2018, 2 patients treated and no safety issues

## CAR-T aCD22 + CAR-T aCD19 combo for ALL



- JJO686 + LXG250 in r/r adult and ped ALL to prevent resistance
- Opened Oct 2018, 6 patients treated with aCD22 monotherapy and no safety issues
- Clinical activity to be presented at upcoming meeting

## CAR-T aBCMA + CAR-T aCD19 combo for MM



- MCM998 + LXG250 in MM, opened June 2018
- Phase A – r/r MM responding to last line of therapy – 6 patients treated, no new safety signals
- Phase B – randomized, upfront MM – 2 patients treated

# Deep pipeline across four distinct platforms is expected to continue driving differentiation and growth

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 2. The brand name Piqray<sup>®</sup> has been provisionally approved by the FDA for the investigational product alpelisib (BYL719), but the product itself has not been approved for

# Novartis is taking a rigorous approach to IO assets for development, setting a high bar for advancement

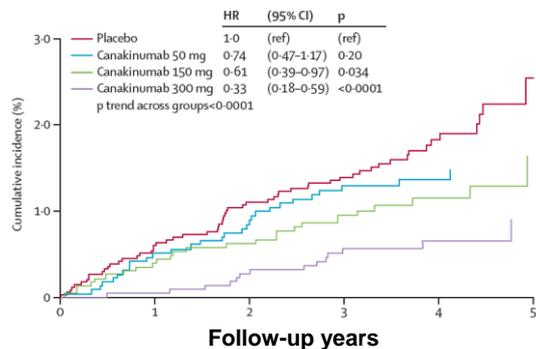
- Taking a rigorous approach to prioritizing assets for development
- Looking for single agent activity, or synergetic combinations with appropriate control arms

Asset	Indication	Phase 1	Phase 2	Phase 3
PDR001+Tafinlar®+Mekinist®	Melanoma			
ACZ885	NSCLC, 1st line			
ACZ885	NSCLC, 2nd line			
ACZ885	NSCLC, adjuvant			
Lutathera® + nivolumab	SCLC	Started in 2017		
PDR001+LAG525+carboplatin	TNBC	Started in 2018		
PDR001+INC280	2nd line NSCLC	Started in 2018		
Kymriah® + pembrolizumab	r/r DLBCL	Started in 2018		

# ACZ885 (canakinumab) reduced lung cancer incidence and mortality based upon exploratory analysis in CANTOS

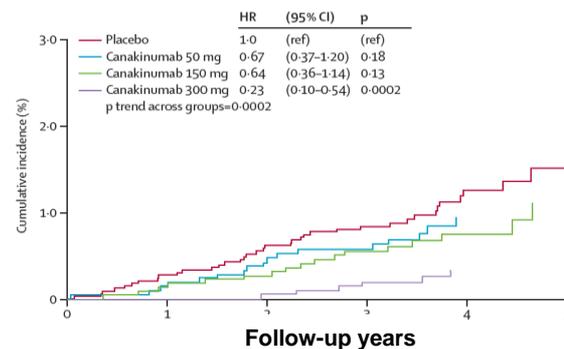
## Lung cancer incidence

Dose-dependent effect, 67% relative risk reduction (canakinumab 300mg)



## Lung cancer mortality

Dose-dependent effect, 77% relative risk reduction (canakinumab 300mg)



>70% baseline samples with detectable ctDNA with lung cancer driver mutations (p53, EGFR, etc.)

- In agreement with FDA in 2010, incident cancers were adjudicated by a blinded independent committee of Oncologists
- Data on incident cancers including cancer deaths were collected as (serious) adverse events and analyzed in a prospective fashion

Source: Ridker PM, et al. Lancet. (2017); DOI: 10.1016/S0140-6736(17)32247-X

# Development programs for three Ph3 trials (CANOPY) of canakinumab in NSCLC on track

Indication	Ph3 trial name and code	Patient population	Trial design	Planned filing
Adjuvant NSCLC	CANOPY-A NCT03447769	High-Risk Stage II-III	Canakinumab vs. placebo (N=1500 with 1:1 randomization) after post-resection chemotherapy	2022
1 <sup>st</sup> line mNSCLC	CANOPY-1 NCT03631199	No prior therapy Stage IIIb or IV, Squamous or Non-Squamous, No EGFR, ALK alterations	Platinum doublet chemotherapy and pembrolizumab with or without canakinumab (N=627 with 1:1 randomization)	2021
2 <sup>nd</sup> line mNSCLC	CANOPY-2 NCT03626545	Stage IIIb or IV, previously treated with platinum-based doublet chemotherapy and PD-(L)1 inhibitor, No EGFR, ALK alterations	Docetaxel with or without canakinumab (N=226 with 1:1 randomization)	2021

# Uniquely positioned to create new standards of care through novel immuno-therapy and combinations

## Novel Immuno-therapy (IO)

Solo or combo	TGFβ (NIS793) +/- PD1 Adenosine R (NIR178) +/- PD1 CD73 (NZV930) +/- PD1 Het IL-15 (NIZ985) +/- PD1 TLR7 ISAC (NJH395) +/- PD1 TLR7 (LHC165) +/- PD1 LAG3 (LAG525) +/- PD1 Degradar (DKY709) +/- PD1 TIM3 (MBG453) +/- PD1 TIM3 (MBG453) + HMA +/- PD1 STING (MIW815) <sup>1</sup> +/- PD1 or CTLA4 CSF-1 (MCS110) +/- PD1 CSF-1R (BLZ945) +/- PD1
Solo	PD1 (PDR001) CD123 x CD3 (SQZ622) <sup>2</sup> GITR (GWN323)

## Novel Combinations<sup>4</sup>

IO/IO	CD73 + Adenosine R (NIR178) +/- PD-1 in multiple solid tumors PDR001 + TGFβ Multiple Solid Tumors
CAR-T/IO	CAR-T EGFRviii + pembrolizumab in Glioblastoma Kymriah <sup>®</sup> + pembrolizumab in DLBCL
TT/IO	Tafinlar <sup>®</sup> + Mekinist <sup>®</sup> + PDR001 in Melanoma MET (INC280) + PDR001 in Lung Cancer SHP2 (TNO155) + PDR001 in Lung Cancer
RLT/IO	Lutathera <sup>®</sup> + PD1 in Neuroendocrine Tumors PSMA-617 + PD1 in mCRPC <sup>3</sup>

1. Collaboration / licensing with Aduro 2. Collaboration / licensing with Xencor 3. Collaboration with Peter MacCallum Cancer Centre. 4. Selected trials



# Conclusion - Oncology



Unique position across 4 platforms with expertise in innovating within and across the platforms



Growing our current and future in-market blockbusters and focused on success of new launches



Robust pipeline across diverse platforms to create innovative medicines, alone and in combination, to treat cancer



Novartis AG  
Investor Relations

# Meet Novartis Management Research overview

May 23, 2019

# Leading center of therapeutics discovery research with proven record of delivering innovative therapies

**1** Deep pipeline of ~90 new molecular entities prioritized and optimized for transformative potential and resourced for competitive advantage

**2** Advanced therapy platforms and technologies, including targeted protein degradation, cell & gene therapy and expansive chemical libraries

**3** Focused research strategy leveraging internal and external innovation, fueled also by strategic out-licensing to capture ROI and enable patient access



**NIBR**

**6,000**  
Scientists

**340**  
Discovery  
programs

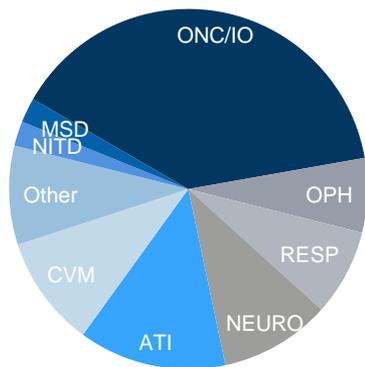
**8**  
Disease  
areas

**~90**  
New molecular  
entities

**USD 2.6bn**  
Research & early  
development

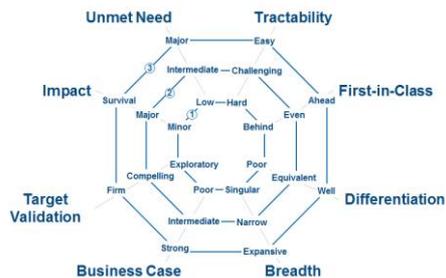
# Portfolio perspective

## Strategic disease area leadership



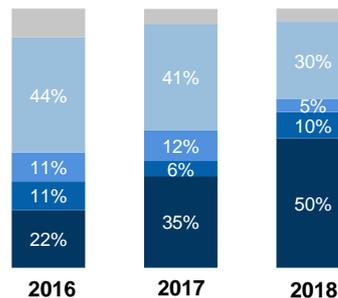
Focused commitment in our disease areas

## Disciplined project selection



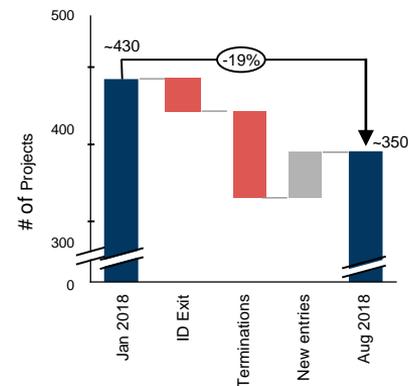
Critically evaluated against expanded set of parameters

## Best at first-in-class



With emphasis on pursuing transformative innovation

## Ruthless prioritization



And commitment to making decisions that enable focused resourcing

ONC/IO - Oncology/Immuno-Oncology; OPH - Ophthalmology; RESP - Respiratory; NEURO - Neuroscience; ATI - Autoimmunity, Transplantation, and Inflammation; CVM - Cardiovascular Metabolic; NITD - Novartis Institutes for Tropical Diseases; MSD - Musculoskeletal Diseases; FIC - First-in-Class; BIC - Best-in-Class; ID - Infectious Diseases

# A productive internal therapeutics engine



1. Kymriah® and Gilenya® were in-licensed into NIBR pre-PoC

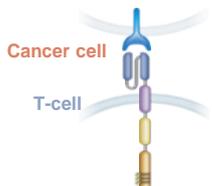
# NIBR vital to delivering a promising pipeline through origination, execution and evaluation of external opportunities

Oncology	Cardio-Metabolic	Neuroscience	IHD	Respiratory	Ophthalmology	Global Health
						
<b>Kymriah®</b> New indications	<b>LNP023</b> Renal disease	<b>Gilenya®</b> MS	<b>Cosentyx®</b> nrAxSpA	<b>Fevipiprant (QAW039)</b> Asthma	<b>Brolucizumab (RTH258)</b> nAMD, DME	<b>KAF156</b> Malaria
<b>Piqray®</b> (BYL719) Breast cancer	<b>Entresto®</b> HFpEF	<b>Mayzent®</b> SPMS	<b>Tropifexor</b> NASH	<b>CSJ117</b> Asthma	<b>Lucentis®</b> AMD	<b>KAE609</b> Malaria
<b>ACZ885, Capmatinib (INC280)</b> Lung	<b>TQJ230</b> High Lp(a)	<b>LMI070</b> SMA	<b>Ligelizumab</b> CSU / CIU	<b>QBW251</b> COPD	<b>Luxturna®</b> RPE65 mutations	<b>Crizanlizumab (SEG101)</b> Sickle cell disease
<b>PDR001 Combo</b> Melanoma		<b>CNP520</b> Alzheimer's	<b>LOU064</b> CSU	<b>Xolair®</b> Asthma	<b>UNR884</b> Presbyopia	
<b><sup>177</sup>Lu-PSMA-617</b> mCRPC		<b>Aimovig®</b> Migraine	<b>CFZ533</b> Transplant / Sjögren's	<b>QVM149</b> Asthma	<b>ECF843</b> Dry eye	
<b>VPM087</b> CRC / RCC		<b>Zolgensma®</b> <sup>1</sup> SMA	<b>VAY736</b> Multiple diseases		<b>SAF312</b> COSP	
<b>Lutathera®</b> NET		<b>Ofatumumab (OMB157)</b> Relapsing MS	<b>VAY785</b> NASH			
			<b>ZPL389</b> Atopic dermatitis			
			<b>MOR106</b> Atopic dermatitis			

1. Aimovig® is developed in collaboration with Amgen. 2. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities. 3. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions. 4. Luxturna® marketed ex-US. 5. Per license agreement, EirGenix Inc. is responsible for development and manufacturing; Sandoz has rights to commercialize in all markets except China and Taiwan. 6. Per license agreement, Gan&Lee is responsible for development and manufacturing; Sandoz has rights to commercialize in EU, US, Switzerland, Japan, South Korea, Canada, Australia and New Zealand. 7. The brand name Piqray® has been provisionally approved by the FDA for the investigational product apelisib (BYL719), but the product itself has not been approved for sale in any country.

# Technology platforms accelerating drug discovery

**CAR-T**



Cancer cell  
T-cell



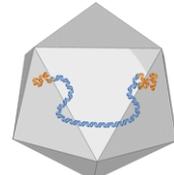
**KYMRIAH**  
(tisagenlecleucel)

**CRISPR**



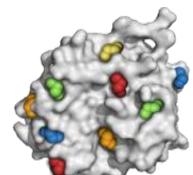
**Intelia** **CARIBOU**  
THERAPEUTICS BIOSCIENCES

**AAV**



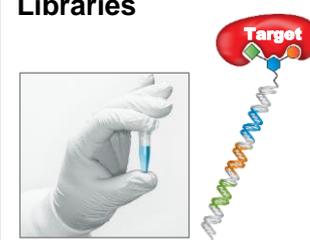
**HOMOLOGY** **avenue**  
Medicines, Inc.

**Covalent Binders**

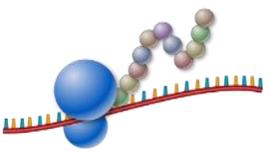


**Berkeley**  
UNIVERSITY OF CALIFORNIA

**DNA Encoded Libraries**



**mRNA**

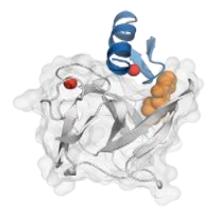


**DARPA**

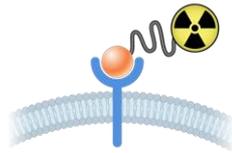
**Novel IO Rx Delivery**



**Targeted Protein Degradation**



**Radiopharmaceuticals**



**Advanced  
Accelerator  
Applications**

**Digital Therapeutics**



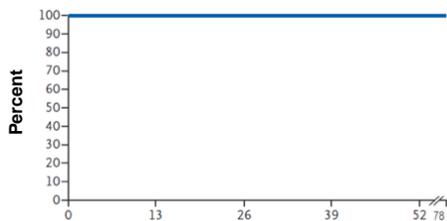
**PEAR**  
THERAPEUTICS

All trademarks are the property of their respective owners.

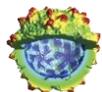
# Novartis cell & gene therapy

## AAV<sup>1</sup>

Zolgensma®  
Spinal muscular atrophy



Probability of event-free survival



Recombinant AAV9  
Capsid Shell



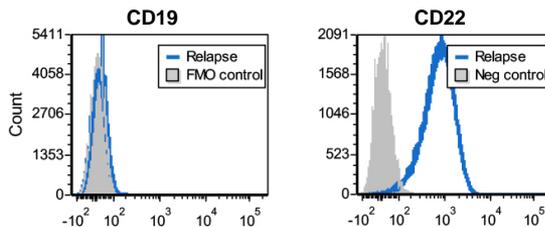
Neuroscience



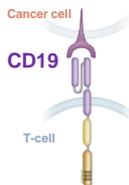
Ophthalmology

## CAR-T<sup>2</sup>

CD22 CAR-T (JJO686) in Ph1 studies in combination with  
CD19 CAR-T (LXG250) to prevent resistance



CD19- relapse patient



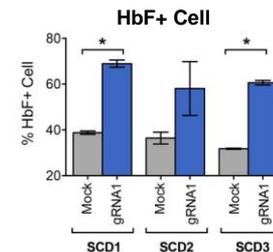
B-Cell malignancies

AML

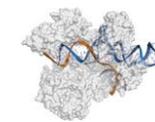
Solid tumors

## CRISPR<sup>3</sup>

Increase in F-cell number and HbF expression upon  
editing of SCD patient PB derived CD34+ cells



N=3/experiment, 4 independent experiments, data show  
mean+SEM



CRISPR Machinery



Hematology



Ophthalmology

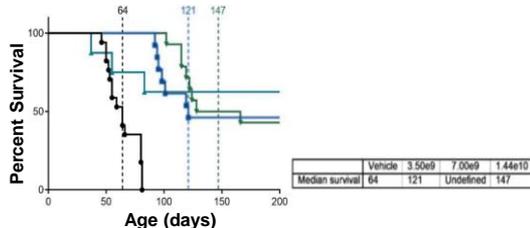
All trademarks are the property of their respective owners. 1. Mendell JR, et al, N Engl J Med 2017; 377:1713-1722 Data is investigational. Efficacy & safety not yet established. 2,3. Data is investigational. Efficacy & safety not yet established.

# Establishing leadership in AAV gene therapy

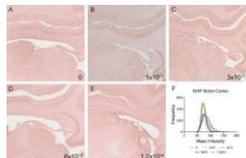
## AVXS-201<sup>1</sup>

Rett Syndrome

Treatment of male rett mice with GMP AVXS-201 increases survival



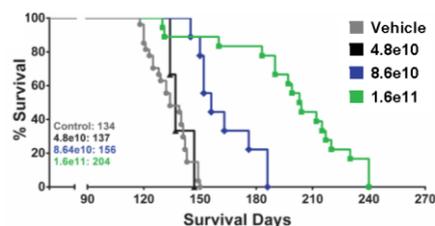
MeCP2 Immunohistochemistry in the Brains of Control and AVXS-201-Treated NHPs



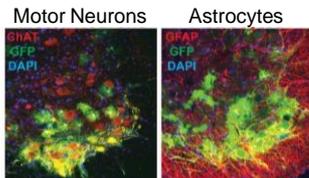
## AVXS-301<sup>2</sup>

SOD-1 Amyotrophic lateral sclerosis (ALS)

AVXS-301 ICV dose response



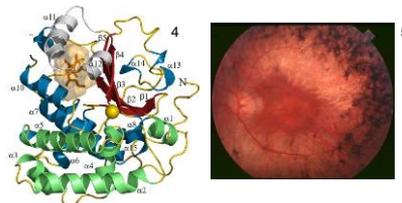
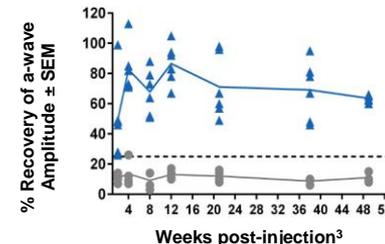
AAV9-GFP Spinal cord transduction



## CPK850

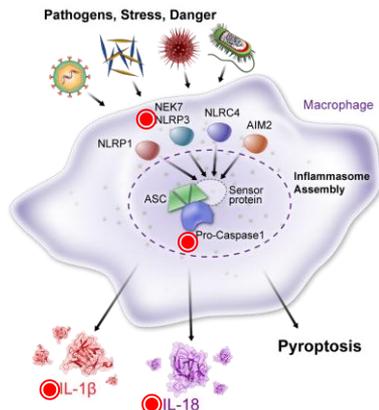
Retinitis pigmentosa (RP)

Gene therapy improved dark adaptation in a mouse model of RP



1. "Efficacy and safety in mice and non-human primates of csf-delivered AVXS-201 for the treatment of Rett syndrome," K. Foust, et al. ASGCT, 2019. Data is investigational. Efficacy & safety not yet established. 2. "Intrathecal administration of AVXS-301 for amyotrophic lateral sclerosis: survival extension and SOD1 reduction in mice and nonhuman primates," G. Thomsen, et al. ASGCT, 2019. Data is investigational. Efficacy & safety not yet established. 3. Choi et al., Mol Ther Methods Clin Dev. 2015 Data is investigational. Efficacy & safety not yet established. 4. He et al., PNAS, 2009. 5. Hamel, Orphanet Journal of Rare Diseases 2006.

# The inflammasome



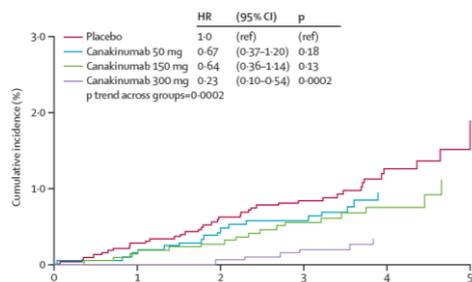
The **NLRP3** (nucleotide-binding domain, leucine-rich repeat-containing receptor pyrin domain containing 3) pathway plays a critical role in the body's innate immune system, serving as a danger sensor. When activated, NLRP3 triggers an inflammatory response via the assembly of a multi-protein complex called the inflammasome

1. Glynn et al., | Lancet | Vol 390 | October 21, 2017 Data is investigational. Efficacy & safety not yet established. 2. Data is investigational. Efficacy & safety not yet established.

## IL-1 $\beta$ Inhibition as cancer therapy

Dose dependent risk reduction with canakinumab in fatal lung cancer incidence of up to 77%

### Cumulative incidence fatal lung cancer<sup>1</sup>

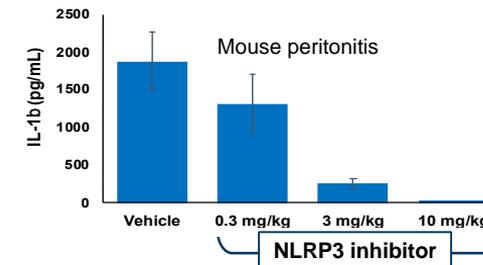


**Hypothesis:** Inhibition of IL-1 $\beta$  blocks the tumor-promoting effects of myeloid cells in the tumor microenvironment, inhibiting cancer cell growth and metastasis, and promoting a protective immune response augmented by PD-1 inhibition

## Novartis Inflammasome pipeline

Description	Status	Indications
<b>Canakinumab;</b> <b>Anti-IL-1<math>\beta</math></b> ACZ885	Ph3	Excl. marketed indications: Lung cancer, Bechet
<b>Gevokizumab;</b> <b>Anti-IL-1<math>\beta</math></b> VPM087	Ph2	Colorectal, gastroesophageal, renal cell cancers
<b>Anti-IL-18</b>	Ph1	TBD
<b>IFM2427</b> NLRP3	Ph1	TBD
<b>NLRP3 LMW</b>	Research	TBD

### Identification of potent inhibitors with excellent overall profile<sup>2</sup>



# Novartis Oncology – balanced mid-stage pipeline

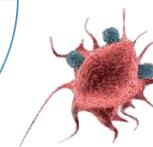
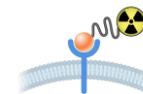
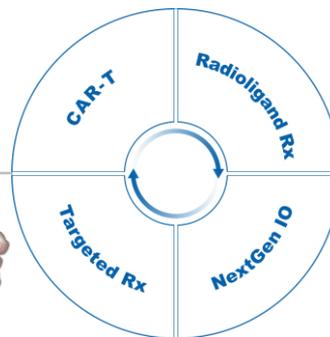
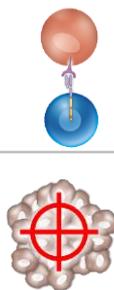
Uniquely positioned to create new standards of care through combinations of treatment approaches

Targeted Therapies	Immunotherapies	CAR-T	Radioligand Therapy
Tafinlar® + Mekinist®	PDR001	Kymriah®	Lutathera® (Somatostatin Receptor)
Capmatinib (INC280) (cMet)	Anti-IL-1β	BCMA	PSMA-617 & PSMA-R2 (Prostate-Specific Membrane Antigen)
LXH254 (B,C Raf)	CSF-1	CD22	NeoB (Gastrin-Releasing Peptide Receptor)
TNO155 (SHP2)	Anti-TGFβ	CD123	FF10158 (Integrin)

Potential next wave combinations -  
Integration of therapeutic approaches

Kymriah® + Pembro  
EGFRviii + PDR001

Tafinlar® + Mekinist® + PDR001  
INC280 + PDR001  
LXH254 + Trametinib  
SHP2 + PDR001



Lutathera® + Nivolumab  
PSMA-617 + Pembro

Jakavi® + TGFβ  
PDR001 + TGFβ

Selected compounds

# External innovation

300+ academic and 50+ industry alliances focused on areas of mutual scientific interest

Alliances bring ideas, capabilities and talent to complement internal innovation

Few companies bring scientific and platform expertise along with resources to pursue external innovation so ambitiously

## Bringing outside innovation inside



## New paths to patients

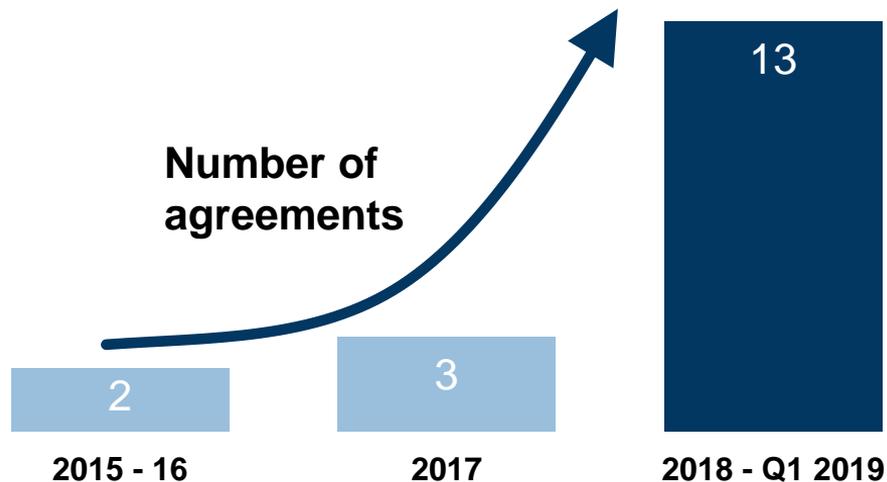


All trademarks are the property of their respective owners.

# Strategic out-licensing to capture return on investment and enable patient access

18 agreements from 2015 to date

- Significant cash upfronts
- Equity stake
- Upside potential from future royalties



# Conclusion - Research



Deliver transformative innovation and curate a first-in-class pipeline



Partner of choice, unbiased acceleration of the most promising internal and early external opportunities



Deploy a suite of advanced technology platforms in an effort to drug targets that were previously considered “undruggable”



Sustain focus on targeted cancer therapies while expanding into new modalities alone and in combination



Novartis AG  
Investor Relations



# Meet Novartis Management 2019 Sandoz

**May 23, 2019**

# Sandoz a global leader in generics and biosimilars, transforming to stay ahead of the competition

**1** Sandoz a global leader in generic and biosimilar medicines, focusing on higher-margin differentiated products. Ex-US >70% of sales, driving gross margin expansion

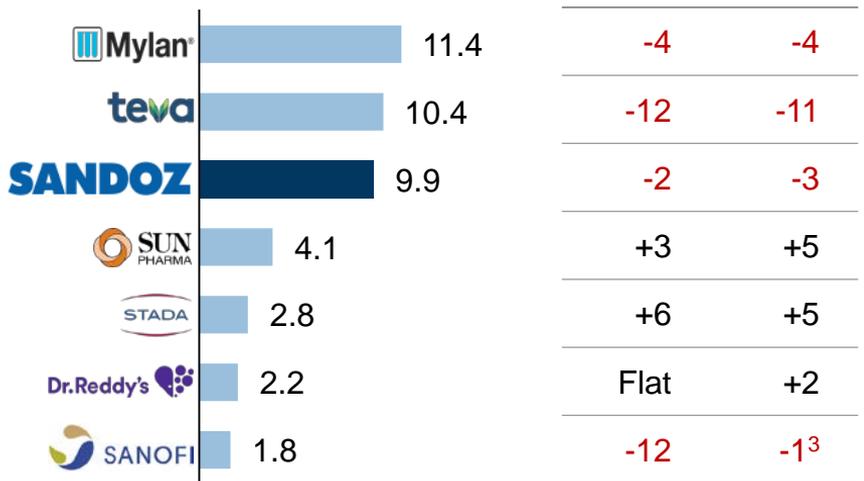
**2** Biosimilars remain key global growth driver  
Leading with 8 biosimilars on the market and 10+ in the pipeline

**3** Sandoz becoming leaner and more agile to drive sustainable sales and margin growth in a rapidly-moving generics environment

# Sandoz outperforming key competitors in a challenging and fragmented environment

## Top global Gx players

by 2018 net sales (USD bn)<sup>1, 2</sup>



## Global generics industry 2018<sup>2</sup>

Global USD 224bn sales (+3% vs. PY)

- US USD 71bn (-4%)
- Ex-US USD 153bn (+6%)

1. Sales based on published figures; absolute net sales for Sun, DRR, Stada and Sanofi were converted to USD using internal Novartis exchange rates; growth rates in cc are **organic** growth estimates, internal analysis. All trademarks are the property of their respective owners. 2. IQVIA figures, including Bio and OTC. 3. Sanofi organic growth rate includes negative impact of Zentiva divestment, while estimated cc growth rate is inorganic only.

# Sandoz shaping its portfolio to drive sustainable and profitable growth

Sandoz portfolio (sales 2018)

Expected market growth  
(CAGR 2018-23, approximate<sup>4</sup>)

Biopharmaceuticals <sup>1</sup>			15%
	1.4	USD bn Sandoz sales	
	8	Products in market	
	10+	Assets in pipeline	
	80	USD bn originator product sales in scope	
Differentiated Therapeutics			7%
	~30-35%	of Sandoz Retail Gx sales, mostly branded Gx <sup>2</sup>	
	1 <sup>st</sup>	Prescription digital therapeutics in US	
	20+	Value-added medicines <sup>3</sup> in development	
Standard generics			1%
	~65-70%	of Sandoz Retail Gx sales Deep global development & production expertise Strong capabilities in select segments (e.g. injectables)	

1. Biopharmaceuticals comprises biosimilars, contract manufacturing and Glatopa<sup>®</sup>. 2. Branded Gx are products that are promoted / branded, definition is internal and largely dependent on market type rather than molecule. 3. VAMs are known molecules that offer improvements, address unmet needs and add value by a) improving efficacy, safety or tolerability, b) Improving administration, ease of use, c) offering new therapeutic use (indication, population). Include 505(b)(2) in US. 4. Internal estimates.

# Sandoz is outperforming competition in Europe – Region Europe delivers 50% of total Sandoz sales

#1 off-patent medicines company with **11.3%** market share<sup>1</sup>

#1 or #2 generics player in **11** geographies<sup>2</sup>

Growing above market across **14** countries

European leader in **six** therapeutic areas<sup>3</sup>

**Strong brands** across Rx, OTC and biosimilar markets

PORTFOLIO SEGMENTS



- Maximize value of launches
- Continue to drive market share of in-line brands



- Clear portfolio choices
- Expand presence in Western Europe
- Build OTC in markets with strong existing presence



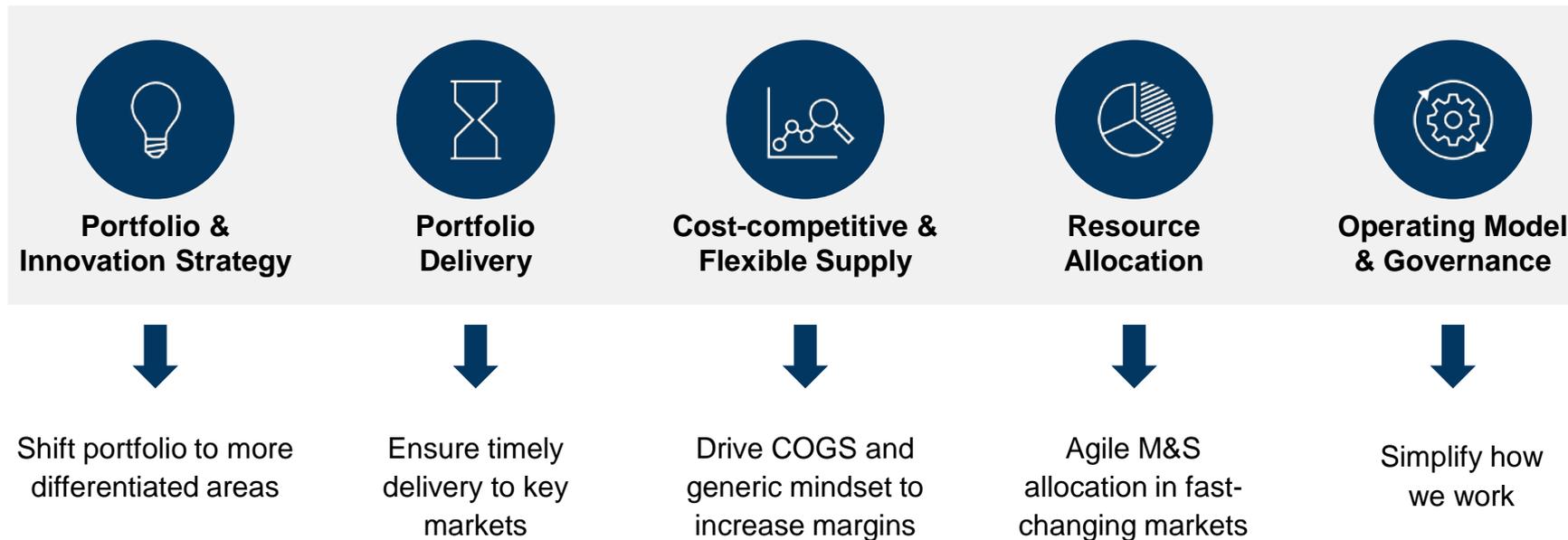
- Broad portfolio, covering >80% of market needs
- Competitiveness in future LoEs



1. EU Gx Market (Rx + OTC + Bio), excl. Mature Brands 2. 11 geographies represent 48% of EU Gx market sales except for growing above market: Full year 18), Internal sales FY 2018.

3. Cardiovascular and Metabolism, Pain, Oncology, Hormones, Derma, Transplant. Source: IQVIA Midas data (Feb. 19

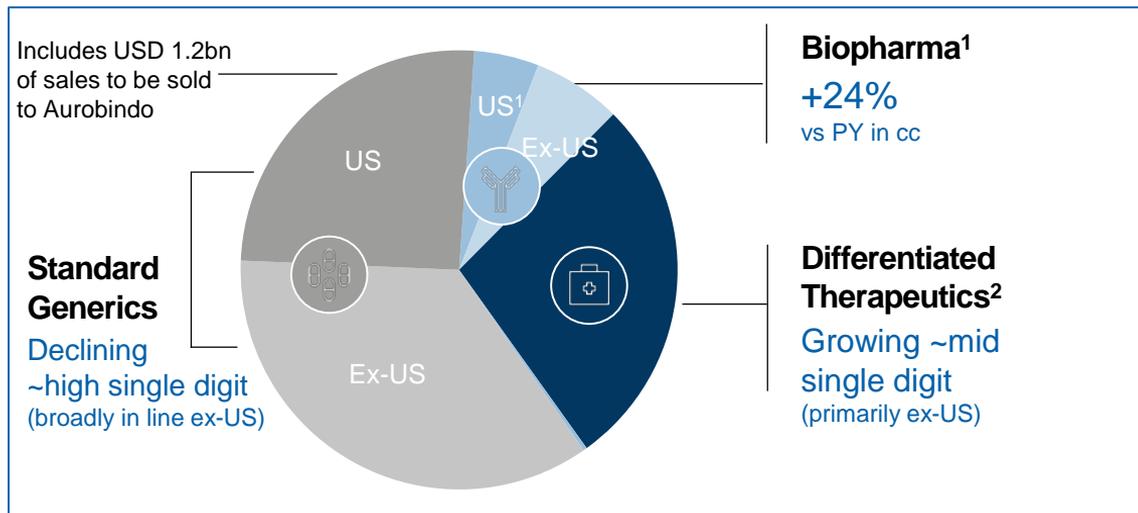
# Sandoz focused on a five-point transformation plan



# Sandoz continues to drive growth in Biopharmaceuticals and Differentiated Therapeutics

**FY 2018 net sales USD 9.9bn**

Illustrative sales split



**Global leader in biosimilars,**  
eight molecules on market

**Global #1**  
in Gx oncology and antibiotics

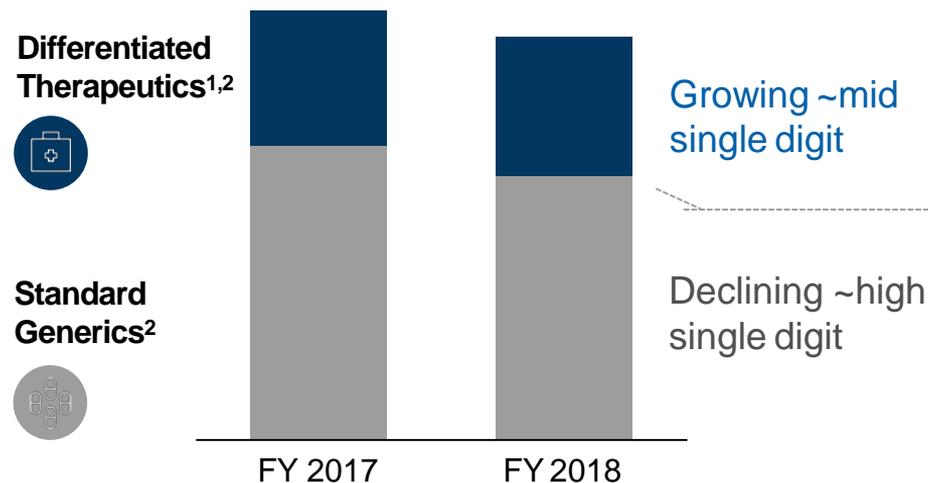
**#1 in Europe**  
and #1-3 in >20 countries

1. Biopharmaceuticals comprises biosimilars, contract manufacturing and Glatopa®. 2. Differentiated Therapeutics comprise branded Gx, OTC, Value Added Medicines (VAMs), Digital Therapeutics (DTx).

# Sandoz driving growth in differentiated therapeutics and emerging markets, offset by US price erosion

## Retail net sales

Illustrative sales split and growth



- Growth driven by Europe and emerging markets
- Maintaining strong position across established markets
- Broadly in line ex-US
- Focusing US on complex generics and biosimilars, plus opportunities in digital therapeutics and VAMs; plan to divest standard Gx segments to Aurobindo

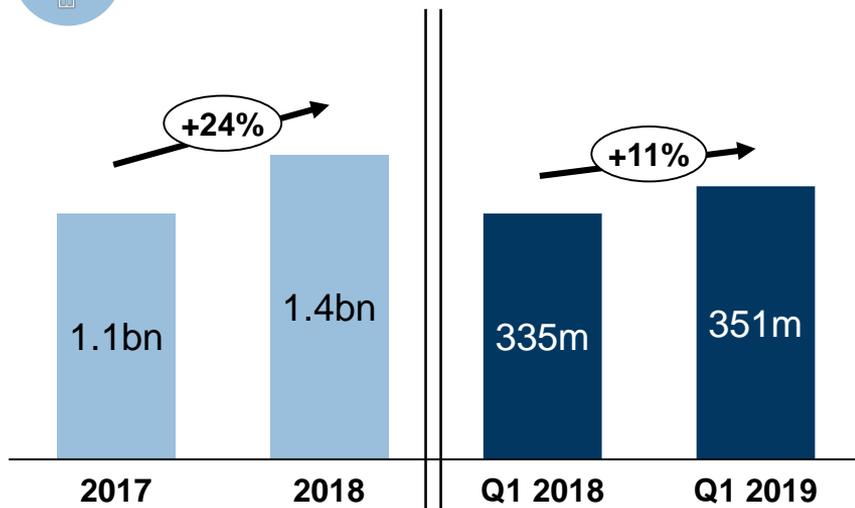
1. Differentiated Therapeutics comprise branded Gx, OTC, Value Added Medicines (VAMs), Digital Therapeutics (DTx). Standard Gx comprises other products (excluding Biopharma). 2. Sales by segment are approximate, non-audited figures.

# Biopharmaceuticals<sup>1</sup> continue to grow double-digit



## Biopharma y-o-y sales growth

USD, % cc



- Europe growing high double-digit; Q1 slower due to US price competition
- Ongoing progress in all three key areas: oncology, immunology, endocrinology
- Omnitrope<sup>®</sup>, Binocrit<sup>®</sup> and Zarzio<sup>®</sup>/Zarxio<sup>®</sup> all #1 biosimilar globally
- Zarxio<sup>®</sup> the first US biosimilar, tracking ahead of originator since April 2018<sup>2</sup>
- Pipeline continues to advance, including strategic deals

1. Biopharmaceuticals comprises biosimilars, contract manufacturing, Glatopa<sup>®</sup>. 2. IQVIA

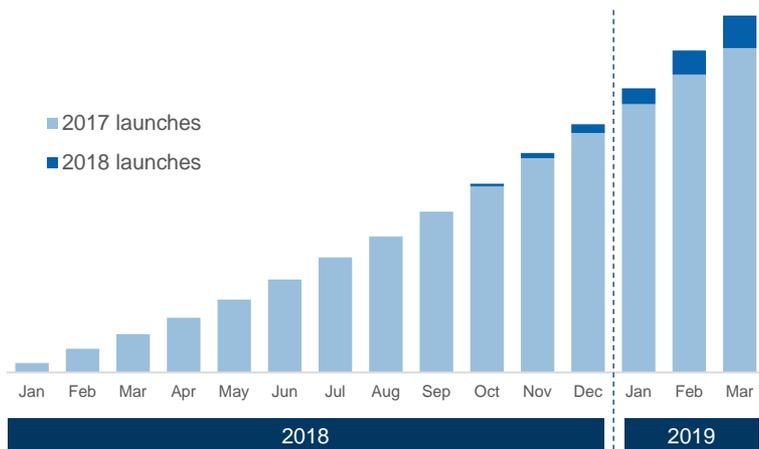
# Sandoz a leader in biosimilars; eight marketed products and a broad pipeline

EU / ROW	  	 	  	<p>ROW rollout</p>    
US	 			<p>Pending approval</p>  <p>Pending litigation</p> 
	2006-2016	2017	2018	2019
Launch				

# Biosimilar launches continue to drive Sandoz growth

## Cumulative net sales from launches

USD million (illustrative only)



## Leading pipeline

- Strong pipeline of 10-plus molecules, targeting ~USD 80bn in originator net annualized value
- Focus on **oncology, immunology and endocrinology**
- Further expanding portfolio through **partnerships<sup>1</sup>**:
  - Three insulins with Gan&Lee<sup>2</sup>
  - Several new molecules via collaboration with Biocon
  - Collaboration with EirGenix on biosimilar trastuzumab

**Erelzi**  
etanercept

**RIXATHON**

**Hyrimoz**  
adalimumab

**Zessly**  
infliximab

**Ziextenzo**<sup>TM</sup>

1. Rights for each deal are for defined geographies 2. Glargine: Lantus<sup>®</sup>; Lispro: Humalog<sup>®</sup>; Aspart: NovoLog<sup>®</sup> (US), NovoRapid<sup>®</sup> (EU).

# Sandoz continues to be optimistic on the global biosimilar market outlook

## Critical for healthcare systems

- Accessibility
- Affordability
- Sustainability

## Opportunities

- Continued LoE opportunities (approx. USD 80bn in originator sales, 2019-2028)<sup>1</sup>
- Improving EU uptake, EGM potential
- Legislative reform potential in US (e.g. Medicare reimbursement)
- Positive early performance in Japan

## Challenges

- Tender market dynamics
- US legislative and regulatory barriers
- Need to continue educating patients and physicians about biosimilars, particularly in the US, which has seen less biosimilar launches than Europe

1. Internal analysis: USD 10bn through 2018, USD 8bn 2019-21, USD 70 bn 2022-28. Represents value of molecules in our pipeline, not total market.

# Sales growth ex-US and product mix drive 10 straight quarters of core gross margin expansion<sup>1</sup>

## Core gross margin

in ppts vs. PY



- Ex-US sales growth (+4%, 72% of 2018 sales) fueled by higher-margin biosimilars
- Underlying Retail sales growth ex-US (+2%<sup>2</sup>):
  - Driven by all regions
  - Steadily moving to more differentiated portfolio
- Acting decisively to drive profitable growth in new US environment

Total +5 ppts core gross margin improvement since Q4 2016

1. Including segments planned to be divested to Aurobindo. 2. Underlying growth, excl. one-timers (i.e. items that are included in reported gross margin, but not in core gross margin). Incl. one-timers: +0%.

# Sandoz leading in data and digital, aiming to drive further productivity and sales

## Pioneering in digital therapeutics



- First FDA-cleared prescription digital therapeutic (reSET®<sup>1</sup>)
- reSET-O®<sup>2</sup> launched in US in January 2019
- Working with Pear™ to expand access to these new cognitive therapies

1. For treatment of Substance Use Disorder. 2. For treatment of opioid use disorder

## Pioneering use of AI in tender markets



- Optimizing bidding strategies in tender markets by use of advanced algorithms
- Pilot in Germany already driving sales and margin
- Potential to create significant AI-based competitive advantage

# Sandoz becoming leaner and simpler, in order to invest in innovation and growth tomorrow

## Laying strong foundations

- Simplifying how we operate, with workforce **reduction of ~900 FTEs** (~7% of total workforce)<sup>1</sup>
- Aiming to realize **productivity gains** across total functional costs by end 2020
- **Streamlining development network**, with planned closure of Holzkirchen Development Center<sup>1</sup>

## Building the future

- **Driving greater efficiency in manufacturing<sup>2</sup>**, to achieve significant longer-term savings
- **Driving digital enablement** across every aspect of our business
- **Reinvesting into growth areas** and **securing core business** competitiveness – expected to drive core ROS towards mid-20s
- Creating a **sustainable growth mindset**

1. These are proposed plans for cost reduction, pending agreement by local works councils. 2. Part of USD 2bn manufacturing savings target for Novartis Group.

# Conclusion – Sandoz



Transforming to succeed long-term in a rapidly-evolving global generics market



Expects to continue to drive growth in biosimilars and Differentiated Therapeutics



Continues to grow sales ex-US and margin globally

# References: Overview

## Slide

## Footnotes

Focused on medicines, diversified across therapeutic areas and platforms

1. Revenue split based on EvaluatePharma data for FY 2018. Revenue from medicines includes sales reported as Rx or Gx. Novartis revenue excludes Alcon and Sandoz proposed US portfolio sale to Aurobindo. 2. TA count if >\$500m only 3. Blockbusters defined as sales >\$1bn in Rx only 4. Presence = company expected to market a product in cell therapy, gene therapy and radioligand therapy (RLT) by 2024, according to EvaluatePharma; for RNA interference therapy (RNAi), presence based on review of available public information (EvaluatePharma, annual reports, press releases).

Building depth across our core therapeutic areas

1. Aimovig® is developed in collaboration with Amgen. 2. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparovvec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities. 3. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions. 4. Luxturna® marketed ex-US. 5. Per license agreement, EirGenix Inc is responsible for development and manufacturing; Sandoz has rights to commercialize in all markets except China and Taiwan. 6. Per license agreement, Gan&Lee is responsible for development and manufacturing; Sandoz has rights to commercialize in EU, US, Switzerland, Japan, South Korea, Canada, Australia and New Zealand

Growth prospects

1. Chart reflects new focused medicines company, which excludes Alcon and Sandoz proposed US portfolio sale to Aurobindo from all periods, and does not include impacts from Xiidra announced acquisition. 2. Illustrative sales assume no Gilenya® US generic entry in the forecasted period. Gilenya® US compound patent expiration August 2019; dosing regimen patent expiration December 2027. 3. In collaboration with Amgen; companies co-commercialize in the US (Amgen to book Sales to third party), Novartis has exclusive rights in rest of world excluding Japan. 4. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparovvec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

10+ potential blockbuster launches

1. Launch of a new molecular entity or new indication with expected peak sales >USD 1bn. 2. Approved by the FDA in Q1 3. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparovvec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities

Piqray®

1. Sabine V, Crozier C, Brookes C, et al. Mutational analysis of PI3K/AKT signaling pathway in tamoxifen exemestane adjuvant multinational pathology study. Journal of Clinical Oncology. 2014;32:2951-2958. 2. Lee JJX, Loh K, Yap Y-S. PI3K/Akt/mTOR inhibitors in breast cancer. Cancer Biol Med. 2015 ;12(4):342-354. 3. Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3\_PR) on October 20, 2018

Ofatumumab (OMB157)

1. Bar-Or et al., April 2018, Neurology, 2018; 90:e1805-e1814. 2. Kappos L, et al. Presented at EAN 2017. EP2154. 3. Savelieva M, et al. Presented at AAN 2017. 4. Savelieva M. et al. Presented at ECTRIMS 2016. P730; P5.348. 5. Theil D, et al. Presented at ECTRIMS 2017. P657; Gd+ = gadolinium-enhancing

# References: Pharmaceuticals (1/2)

## Slide

## Footnotes

Building depth across our core therapeutic areas

1. Aimovig® is developed in collaboration with Amgen. 2. The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvovec-xioi), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities. 3. Announced acquisition of global rights; closing expected in 2H19, subject to customary closing conditions. 4. Luxturna® marketed ex-US. 5. Per license agreement, EirGenix Inc is responsible for development and manufacturing; Sandoz has rights to commercialize in all markets except China and Taiwan. 6. Per license agreement, Gan&Lee is responsible for development and manufacturing; Sandoz has rights to commercialize in EU, US, Switzerland, Japan, South Korea, Canada, Australia and New Zealand

Cosentyx® is well-positioned to continue to grow in attractive segments of the immunology market

1. DRG disease landscape forecast for G7: Dec'18, PsA: Nov'18, RA: Jan'19, PSO: Nov'18. 2. Langley R, et al. NEJM 2014;371:326. 3. Blauvelt A., et al. JAAD 2017 Jan;76(1):60-69.e9  
Enbrel® is a registered trademark of Wyeth LLC in Europe and Immunex Corporation in the US. Stelara® is a registered trademark of Janssen Biotech, Inc. 4. Bissonnette R., et al. JEADV 2018 Sep;32(9):1507-1514. 5. Bagel J et al. JAAD 2017;77:667-674. 6. Gottlieb A et al. JAAD 2017;76:70-80. 7. Reich K., et al. BJD 2018 doi: 10.1111/bjd.17351. [Epub ahead of print]. 8. Mease PJ, et al. RMD Open. 2018 Aug 13;4(2):e000723. 9. McInnes IB, et al. Lancet 2015;386:1137-46. 10. Mc Innes IB et al. Rheumatology (Oxford) 2017 Nov; 56(11): 1993-2003. 11. Mease PJ, et al. Ann. Rheum. Dis. 2017; 76 (suppl 2): 952. 12. Marzo-Ortega H, et al. Arthritis Care Res (Hoboken). 2017;69:1020-9. 13. Braun J, et al. Ann Rheum Dis. 2017;76:1070-1077. 14. Mease P et al. Ann Rheum Dis. 2018 Jun;77(6):890-897. 15. Braun J. et al. Rheumatology. 2018 Dec 19. doi:10.1093/rheumatology/key375. 16. DRG disease landscape forecast for G7

Nr-axSpA indication would complete Cosentyx® label across the SpA spectrum

1. DRG Epidemiology database - axSpA: release Dec'18; PsA: Nov'18; RA: Jan'19. Patients on biologics: PsA and AS - Calculated Patient equivalent based on IQVIA Midas volume Dec'18, Indication split IQVIA medical data Dec'18; nr-axSpA - DRG disease landscape forecast release Dec'18, RA: Corrona Study 2017. 2. Moderate-severe psoriasis diagnosis. 3. Systemic treated patients. 4. Out of patients treated. 5. Protopopov M and Poddubnyy D, Expert Rev Clin Immunol. 2018;14:525-533. 6. Sieper J, van der Heijde D, Arthritis Rheum. 2013;65:543-51. 7. Poddubnyy D, Rudwaleit M. Rheum Dis Clin North Am. 2012;38:387-403.

Entresto®: PIONEER landmark study demonstrated superiority to enalapril, unlocked new patient segment

1. Velazquez et al. N Engl J Med. 2019 Feb 7;380(6):539-548; Epub 2018 Nov 11. 2. Morrow et al. Circulation. 2019;139:00-00. ADHF: acute decompensated heart failure; SoC: standard of care; HFREF: heart failure with reduced ejection fraction; HF: heart failure; CV: cardiovascular; NT-proBNP: N-terminal pro-brain natriuretic peptide.

Entresto® NBRx acceleration

1. IMS New to Brand w/e 03 May 2019. 2. The Global Health and Economic Burden of Hospitalizations for Heart Failure A. P. Ambrosy, G.C. Fonarow, et al. JACC Apr 2014, 63 (12) 1123-1133 and internal calculations 3. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Card Fail Rev. 2017;3(1):7-11. doi:10.15420/cfr.2016.25:2 4. Velazquez et al. N Engl J Med. 2019 Feb 7;380(6):539-548; Epub 2018 Nov 11 and TRANSITION: Wachter R. et al., Initiation of sacubitril/valsartan in hospitalized patients with heart failure with reduced ejection fraction after hemodynamic stabilization: Primary results of the TRANSITION study. Data presented at: ESC 2018, Aug 25-29; Munich, Germany.

Mayzent® the first and only oral treatment successfully studied in SPMS

1. Largest trial performed in SPMS: Kappos L et al. Siponimod versus placebo in secondary progressive multiple sclerosis: a double-blinded randomized, phase 3 study. The Lancet. 2018; DOI 10.1016/S0140-6736(18)30475-6. 2. FDO is only recommended for patients with certain pre-existing cardiac conditions -sinus bradycardia, first or second-degree[Mobitz type I] AV block, or a history of myocardial infarction or heart failure.

EXPAND study results

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Mayzent® showed significant effects on cognitive processing speed in SPMS

1. Benedict et al. Effect of Siponimod on cognition in patients with secondary progressive multiple sclerosis (SPMS): Phase 3 EXPAND study subgroup analyses. American Academy of Neurology, Philadelphia 2019. P2-051. 2. Sustained CPS improvement – SDMT ≥4-point increase from baseline; sustained CPS deterioration – SDMT ≥4-point decrease from baseline 3. Planche et al. 2015: Cognitive impairment in a population-based study of patients with multiple sclerosis: differences between late relapsing/remitting, secondary progressive and primary progressive multiple sclerosis

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Slide	Footnotes
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Data show potential impact of Zolgensma® in broad spectrum of SMA	The brand name Zolgensma® has been provisionally approved by the FDA for the investigational product AVXS-101 (onasemnogene abeparvec-xxxx), but the product itself has not received marketing authorization or BLA approval from any regulatory authorities. 1. STRONG, STRIVE, SPR1NT, START long term follow up data presented at AAN 2019. 2. Day J. et al. "Adeno-Associated Virus Serotype 9 Antibodies in Patients With Spinal Muscular Atrophy Screened for Treatment With Onasemnogene Abeparvec." Muscular Dystrophy Association (MDA) 2019.
Fevipirant (QAW039) targeting biologic efficacy with oral simplicity	1. Fevipirant: Study defines high eosinophil levels ≥250 cells/μL. Targeted efficacy profile studied with GINA step 4/5 patients. 2. Benralizumab: Fitzgerald et al, CALIMA study - Lancet 2016;388: 2128-2141 & Bleecker et al. SIROCCO study - Lancet 2016, 388: 2115-2127. 3. Mepolizumab: Ortega et al. MENSA study - N Engl J Med 2014;371:1198-1207 & Chupp et al. MUSCA study - Lancet Resp Med 2017, 5:390–400. 4. Reslizumab: Castro et al. Lancet Respir Med. 2015;3:355-366. 5. Dupilumab: Castro et al. QUEST study - N Engl J Med. 2018; 378:2486-2496.
Xiidra® fits strategically within Novartis' leading ophthalmic portfolio, pipeline and existing infrastructure	1. 2018 calendar year sales. 2. Ex-US only. 3. Paulsen AJ et al. Am J Ophthalmic. 2014;157(4):799-806. 4. US Census Bureau. Annual estimates of the resident population for selected age groups by sex for the United States, States, Counties, and Puerto Rico Commonwealth and Municipios: April 1, 2010 to July 1, 2014. 5. Schaumberg et al, 2013, Prevalence of diagnosed dry eye in the US, Marketscope 2018 report – Diagnosed Dry Eye patients in the US. 6. Novartis Dry Eye market forecasts in the US, Mar 2019, validated with IQVIA TRx and NBRx claims data
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Brolucizumab achieved robust visual gains <sup>‡</sup> and superior fluid resolution*—on track for 4Q19 US launch <sup>1</sup>	1. Pending regulatory approvals. 2. Data on file, HAWK & HARRIER Ph3 3. Source: Evaluate pharma (Accessed Mar 29 2019); Regeneron, Bayer, Novartis and Roche Annual Reports. Accounted anti-VEGF sales in nAMD, DME and RVO indications. 4. Brolucizumab (RTH258) has not received marketing authorization or BLA approval from any regulatory authorities. *Prespecified secondary endpoints in both HAWK and HARRIER, with confirmatory superiority analysis in HAWK only. †Primary endpoint. ‡Descriptive P-values at Week 96 related to prespecified secondary endpoints assessed at Weeks 16 and 48. # Prespecified secondary endpoint in both HAWK and HARRIER. BCVA - Best Corrected Visual Acuity; CST - Central Subfield Thickness; IRF - Intraretinal Fluid; RPE - Retinal Pigment Epithelium; SRF - Subretinal Fluid; MAA - Marketing Authorization Application; BLA - Biologic Licensing Application; DME - Diabetic Macular Edema.
China	1. IQVIA data. 2. CFDA website. 3. Approval received Q1 2019. 4. Best of best case. 5. Add-on insulin and add-on SU; scenario: China's limited data from global studies could be accepted for NDA approval

# References: Oncology

## Slide

Building depth across our core therapeutic areas

## Footnotes

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