

Meet AZN management: BioPharmaceuticals

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D

Ruud Dobber, Executive Vice President, BioPharmaceuticals Business Unit



25 March 2021

Interactive event for investors and analysts. This webinar is being recorded. <u>https://astrazeneca.zoom.us/webinar/register/WN_bGgqh6nRS120V4JAbnFLvQ</u>

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BioPharmaceuticals Business Unit

BioPharmaceuticals R&D

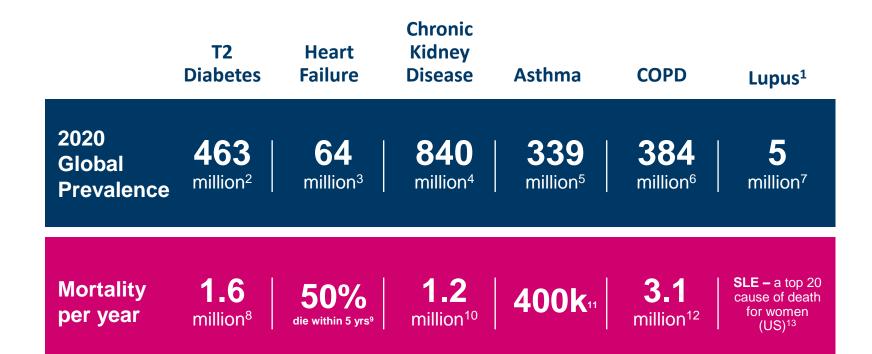
COVID-19

Q&A





Chronic diseases are a staggering, growing burden to patients and society



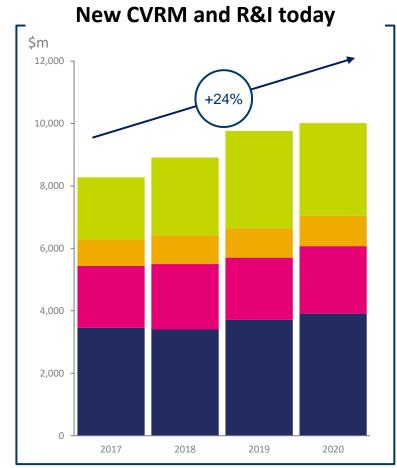
The ambition is to transform treatment for billions of people living with chronic diseases

Systemic lupus erythematosus, Cutaneous lupus, lupus nephritis
 Ogurtsova K, et al. Diabetes Res Clin Pract. 2017;128:40–50
 Global Burden of Disease Study 2016. Lancet. 2017;390:1211-1259
 Jager, et al. Nephrology Dialysis Transplantation 2019;34:1803-1805
 GINA, The Global Asthma Report 2018
 Adeloye D, et al. J Glob Health. 2015;5(2):020415
 Lupus Foundation of America. Lupus facts and statistics [Online]. 709–33
 WHO. Diabetes [online]
 Mozaffarian D, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. Circulation.
 2016;133(4):e38-360
 Carney EF. Nature. 2020:16;251
 Global Asthma Report. 2014 [online]
 The Guardian. 2012 [online]
 Yen EY, Singh RR. Arthritis Rheumatol. 2018; 70(8):1251-55.



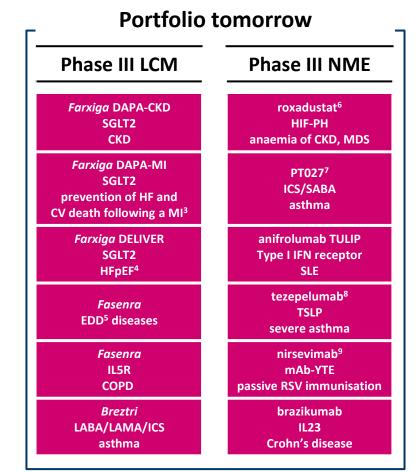
Leading with an unmatched portfolio and growing pipeline





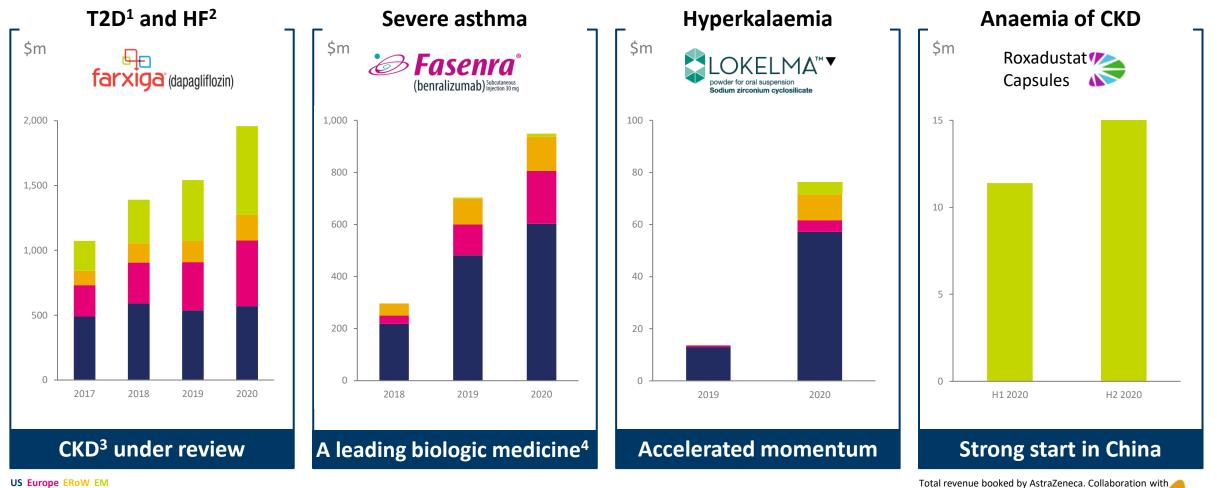
US Europe Established Rest of World (ERoW) Emerging markets (EM)

Product Sales at actual exchange rates. Growth rate at CER.



3. Acute myocardial infarction 4. Heart failure with preserved ejection fraction 5. Eosinophilic driven diseases including: eosinophilic granulomatosis with polyangiitis, eosinophilic esophagitis, hypereosinophilic syndrome, nasal polyps, bullous pemphigoid 6. Collaboration with FibroGen Inc. 7. Collaboration with Avillion LLP. 8. Collaboration with Amgen Inc. 9. Collaboration with Sanofi S.A.

Strong commercial execution



FibroGen Inc. which booked in-market sales (\$72.5m) in

China in 2020.

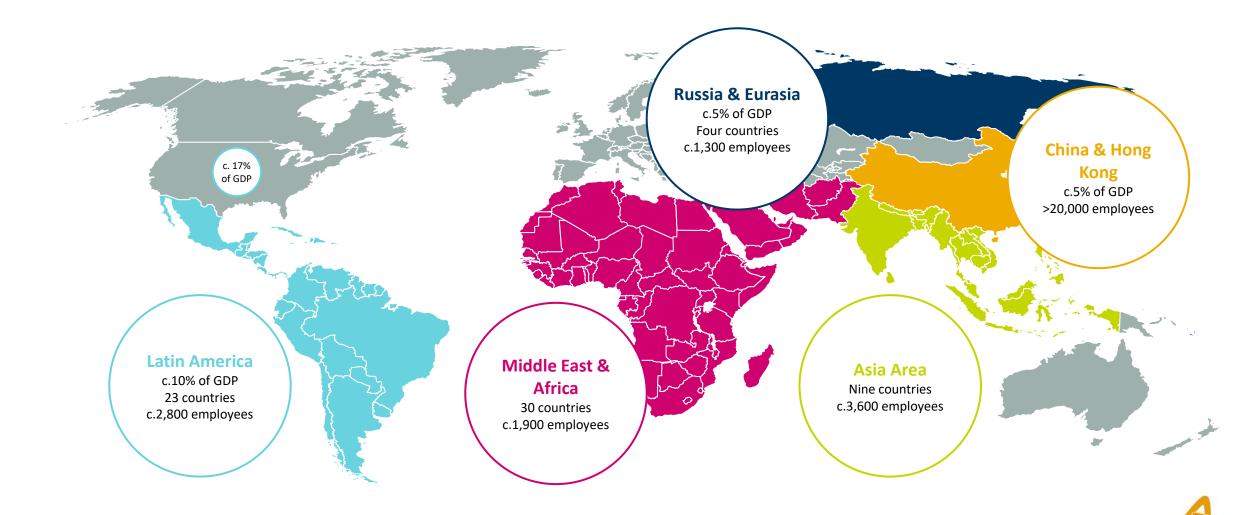
US Europe ERoW EM

Product Sales at actual exchange rates. 1. Type-2 diabetes 2. Heart failure 3. Chronic kidney disease 4. Leading novel biologic medicine in severe asthma in many markets based on new to brand prescriptions. Market shares are total patient share in severe, uncontrolled asthma; specialty pharmacies and 'buy and bill' market, IQVIA market research.

6

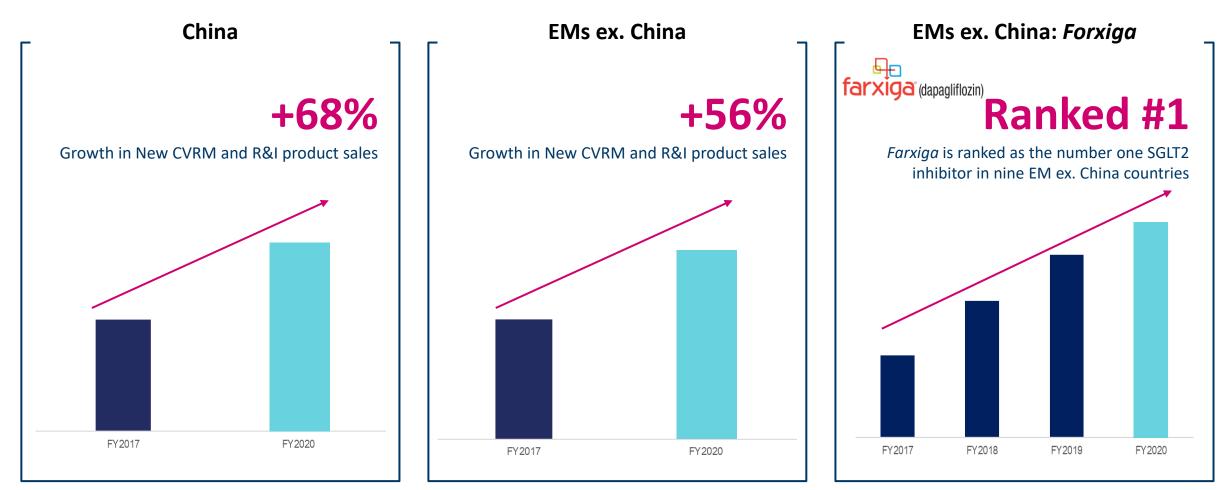
Emerging markets

Footprint across four continents and over 70 countries



Emerging markets

Strong growth both in China and other EMs





Unique opportunity to transform kidney care by 2025

Underdiagnosed and undertreated



>2 billion People at risk of developing CKD¹

c.840 million

Estimated people with CKD²

+12%

Actual people diagnosed with CKD³

Expanding early diagnosis and care



and care



Transforming CKD

management

Partnerships

Will increase treatment at Stage 3 by 2025

1. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, Zhao MH, Lv J, Garg AX, Knight J, Rodgers A, Gallagher M, Kotwal S, Cass A, Perkovic V. Worldwide access to treatment for end-stage kidney disease: a systematic review. The Lancet. 2015 May 16;385(9981):1975-82. doi: 10.1016/S0140-6736(14)61601-9. Epub 2015 Mar 13. PMID: 25777665 2. Kitty J Jager, Csaba Kovesdy, Robyn Langham, Mark Rosenberg, Viekanand Jha, Carmine Zoccali, A single number for advocacy and communication - worldwide more than 850 million individuals have kidney diseases, Nephrology Dialysis Transplantation, Volume 34, Issue 11, November 2019, Pages 1803–1805, https://doi.org/10.1093/ndt/gfr174 3. Vaidya SR, Aeddula NR. Chronic Renal Failure 2019. Available at: https://knowledge.statpearls.com/chapter/0/28357 (Accessed Oct 2020)

Transforming care for 1m patients with severe asthma by 2030 Aiming for biologics uptake similar to other inflammatory diseases

Headroom for growth



34 million

Patients with severe asthma^{1,2}

45% treated in primary care³

15% eligible patients receive a biologic^{3,4}

Accelerating uptake and access



Digital Activation and referral tools driving specialist treatment review Enabling @home monitoring treatment



39 thousand

Patients enrolled

42% Patients self-administer *Fasenra*



1. GINA, The Global Asthma Report 2018 2. Wenzel S, et al. Am J Respir Crit Care Med. 2005;172:149-160 3. AstraZeneca 4. Versus 45% in rheumatoid arthritis (US).

Building the BioPharmaceuticals team of the future



Reimagining healthcare delivery



Data analytics Omnichannel Go-to-market models

Strong & diverse talent pipeline



Building next generation capabilities in new specialty areas





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BioPharmaceuticals R&D

COVID-19

Q&A





AstraZeneca's 5R framework has increased productivity



Identifying the **right target**



Making sure the molecule gets to the right tissue where it is needed



Ensuring the right safety with minimal side effects



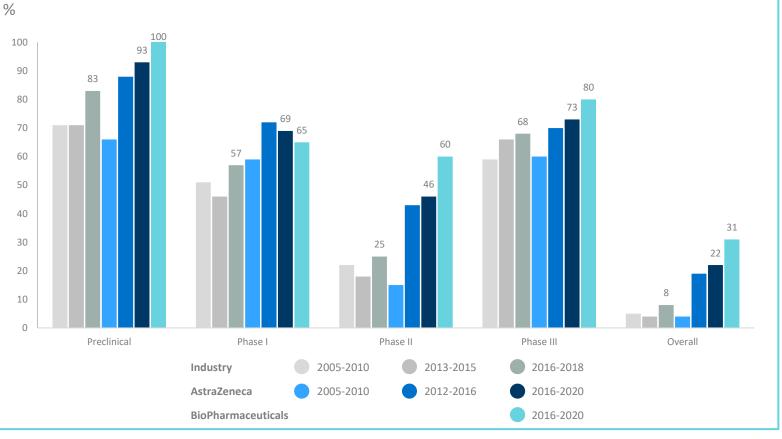
Selecting the **right patients** that will benefit



Defining the right commercial value and future viability

Embedding the right digital solutions to improve efficiency and deliver quality gains

Industry success rates vs. AstraZeneca and BioPharmaceuticals





R&D productivity in 2020 Progress made across all R&D

high-impact journal¹ manuscripts published in 2020 (vs. four in 2012)

123

890

journal publications overall in 2020 (vs. 367 in 2012)

projects with regulatory designations in 2020

2. TR five year IF. 3. High-quality peer-reviewed journals with IF ≥5 <15 using TR five year IF score. Contains exception list considered by AstraZeneca as high quality but has IF <5. Source: Scopus retrieval (algorithm includes journal publications up to Phase III), AstraZeneca analysis.

1. High-impact peer-reviewed journals are those with an impact factor (IF) exceeding 15 using Thomson Reuters (TR) five year IF score.

200

projects with validated mechanism of action in 2016-2020

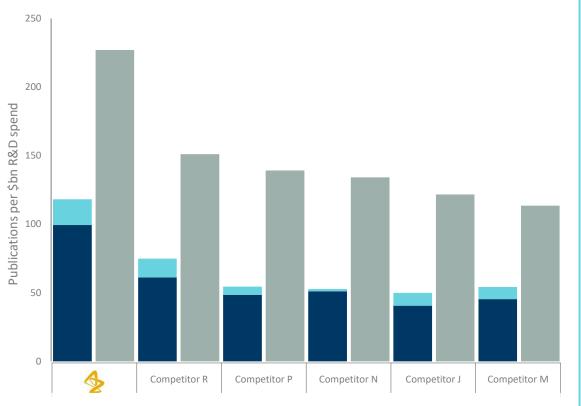
regulatory approvals in 2020

39% 250

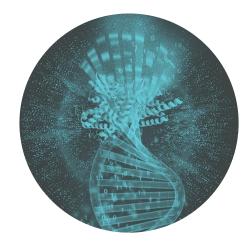
increase in the number of Phase II projects from 2016-2020

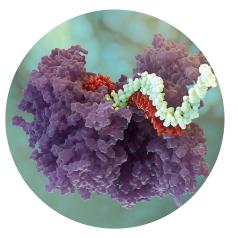
Benchmark: publications per \$bn R&D spend²

High impact publications High quality publications² Total publications



Focus areas to further improve productivity









Enhancing disease understanding

Broadening therapeutic platforms

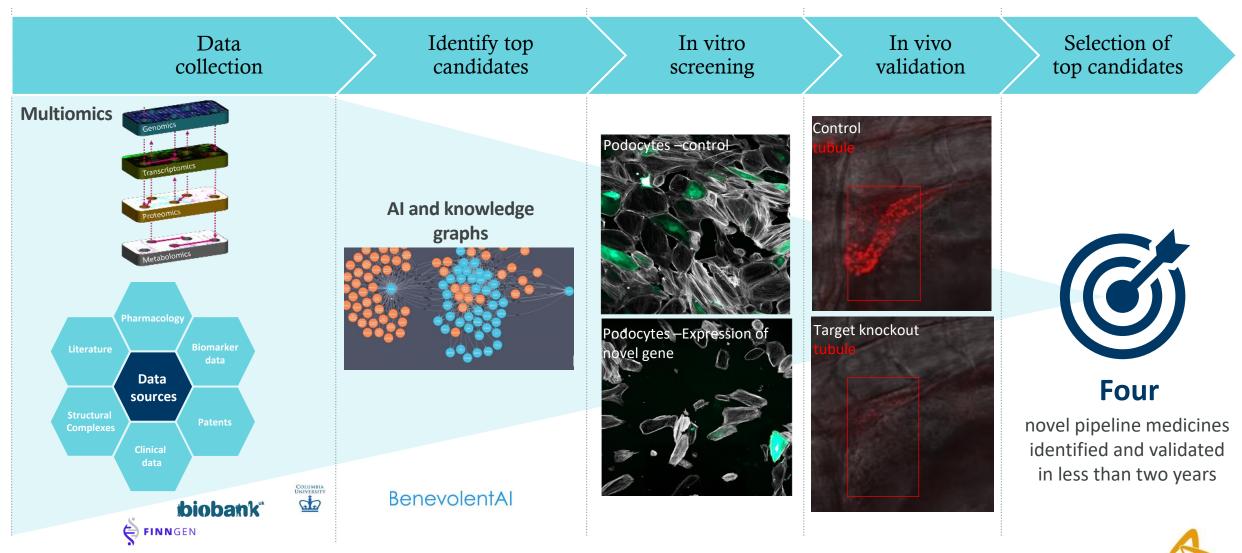
Predicting clinical outcomes

Pioneering new approaches in the clinic

Data science and artificial intelligence (AI)

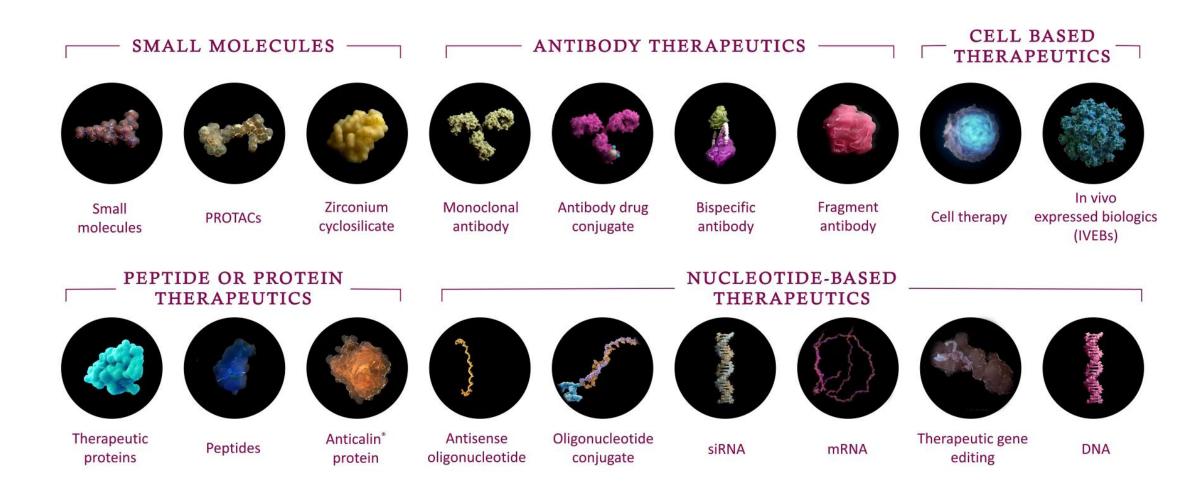


Identifying new targets through AI-enabled big data



Source: Groopman et al. NEJM (2019); Povysil et al. JAMA (2020); Kumar et. al. American Society of Nephrology Congress October (2020).

A broad set of therapeutic platforms to target any biology





Novel PROTAC chemistry advances project portfolio

16 **PROTAC** projects

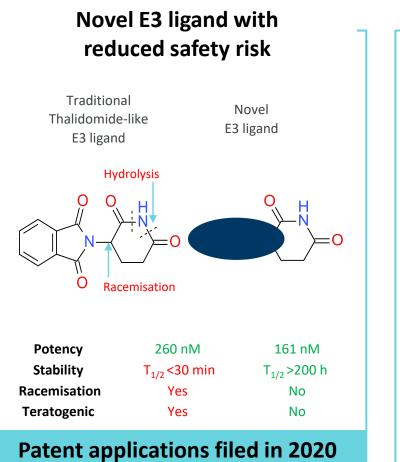
Five Projects with in vivo efficacy

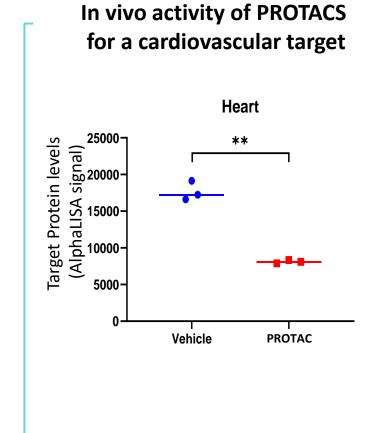
Five E3 ligases enabled for project application

Current status

Three Projects in lead optimisation

Source: Pike et al. Drug Discov. Today (2020); Edmondson et al. BioOrg. Med. Chem. Lett. (2019)

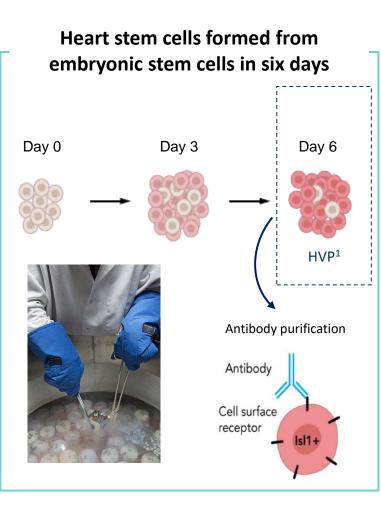




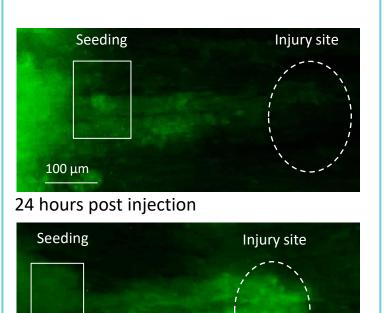
**significance in Welch test (p 0.005).



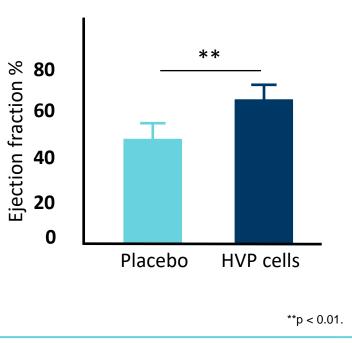
Cell therapy approaches focused on regeneration ongoing across all therapy areas



HVP cells migrate to injury site after injection in damaged NHP² heart



Increased ejection fraction in infarcted mice at two months





Non-human primate.
 Source: Karl-Ludwig Laugwitz / Kenneth R.Chien.

48 hours post injection

HVP cells – attracted to injury site

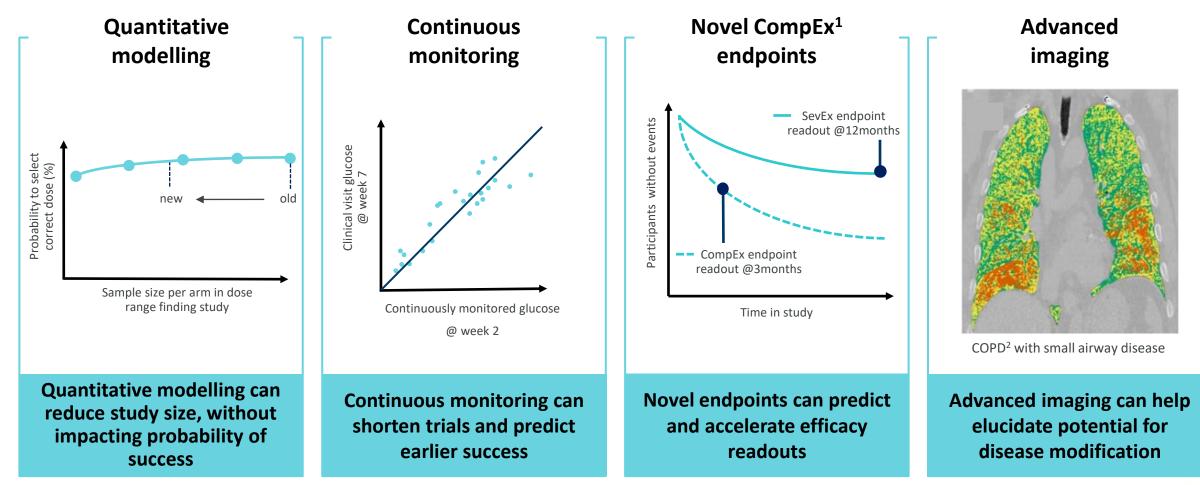
AI-led small molecule discovery is driving 70% efficacy 50% of small molecule projects are applying AI approaches



Source: Kotsias et al. *Nature Machine Intelligence* (2020); Blaschke et al. *J.Chem.Inf.Model.* (2020); Segler et al. *ACS Cent Sci* (2018); Olivecrona et al. J. *Cheminformatics* (2017).



Predictive science continues to improve our clinical trial performance

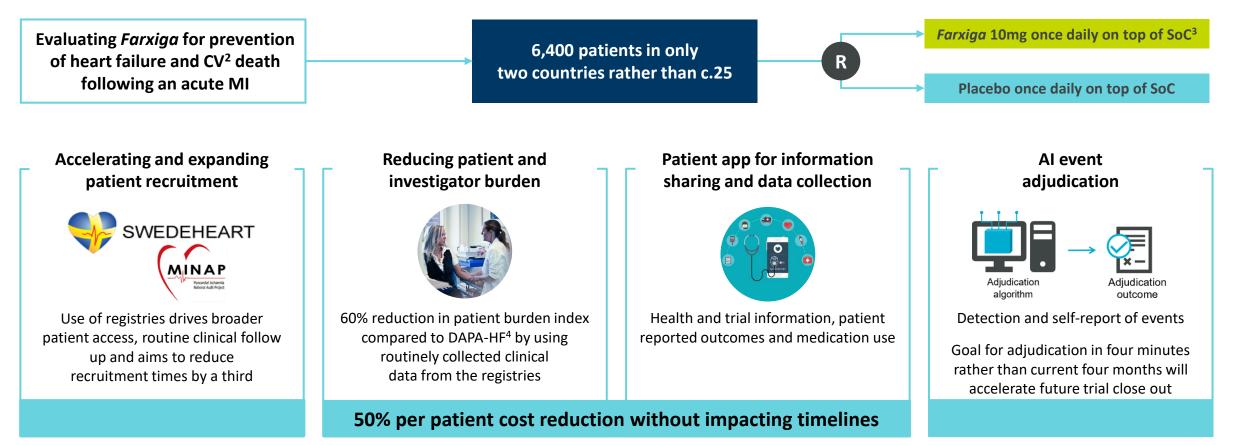




2. Chronic obstructive pulmonary disease.

1. Composite exacerbation.

Accelerating clinical efficiency through digital innovation DAPA-MI¹ is world's first indication-seeking registry-based randomised controlled outcomes trial





1. Myocardial infarction 2. Cardiovascular.

Overall BioPharmaceuticals pipeline

Innovation to fuel sustainable growth

Phase I	Phase II			Phase III		Under Review
AZD0284 RORg ¹ psoriasis	anifrolumab Type I IFN ¹³ receptor LN ¹⁴	cotadutide GLP-1 ³¹ /glucagon T2D ³²	MEDI6012 LCAT ³⁹ CV	AZD7442 LAAB ⁵¹ combination COVID-19	Fasenra NATRON IL5R HES ⁵⁹	anifrolumab TULIP Type I IFN receptor SLE
AZD0449 Inhaled JAK ² inhibitor asthma	anifrolumab Type I IFN receptor SLE ¹⁵ SC ¹⁶	cotadutide GLP-1/glucagon obesity	MEDI6570 LOX-1 ⁴⁰ CV disease	brazikumab¶ IL23 Crohn's disease	Fasenra OSTRO, ORCHID IL5R nasal polyps	Farxiga DAPA-CKD SGLT2 CKD
AZD2373 Podocyte health nephropathy	AZD1402# inhaled IL4Ra ¹⁷ asthma	cotadutide GLP-1/glucagon NASH	MEDI7352 NGF ⁴¹ /TNF ⁴² OA pain	<i>Breztri</i> KALOS LABA ⁵² /LAMA ⁵³ /ICS ⁵⁴ asthma	Fasenra RESOLUTE ILSR COPD	
AZD2693 NASH ³	AZD4831 MPO ¹⁸ HFpEF ¹⁹	cotadutide GLP-1/glucagon DKD ³³	MEDI7352 NGF/TNF PDN ⁴³	Farxiga DAPA-MI SGLT2 prevention of heart failure and CV death following an MI ⁵⁵	nirsevimab# mAb-YTE ⁶⁰ passive RSV ⁶¹ immunisation	
AZD3366 CD39L3 ⁴ CV ⁵ disease	AZD5718 FLAP ²⁰ CKD	Fasenra ARROYO IL5R ³⁴ CSU ³⁵	navafenterol# MABA ⁴⁴ COPD	<i>Farxiga</i> DELIVER SGLT2 HFpEF	PT027# ICS/SABA ⁶² asthma	
AZD3427 Relaxin ThP ⁶ CV disease	AZD5718 FLAP CAD ²¹	Fasenra HILLIER IL5R AD ³⁶	roxadustat# HIF ⁴⁵ -PHI ⁴⁶ CIA ⁴⁷	Fasenra FJORD ILSR BP ⁵⁶	roxadustat# HIF-PHI anaemia MDS ⁶³	
AZD4041# orexin 1 receptor antagonist opioid use disorder	AZD7986# DPP1 ²² COPD ²³	MEDI3506 IL33 ³⁷ DKD	suvratoxumab alpha-Toxin Staphylococcus pneumonia	<i>Fasenra</i> MANDARA ILSR EGPA ⁵⁷	tezepelumab# NAVIGATOR TSLP severe uncontrolled asthma	
AZD8154 Inhaled PI3Kgd ⁷ asthma	AZD8233 PCSK9 ²⁴ hypercholesterolemia	MEDI3506 IL33 AD	tezepelumab# TSLP ⁴⁸ AD	Fasenra MESSINA IL5R EOE ⁵⁸		
MEDI0618# PAR2 ⁸ antagonist mAb ⁹ OA ¹⁰	AZD8601# VEGF-A ²⁵ cardiovascular	MEDI3506 IL33 COPD	tezepelumab# TSLP COPD			
MEDI1341# alpha synuclein Parkinson's disease	AZD9567 SGRM ²⁶ CID ²⁷	MEDI3506 IL33 asthma	verinurad URAT1 ⁴⁹ CKD / HFpEF			
MEDI1814# amyloid beta Alzheimer's disease	AZD9977+ <i>Farxiga</i> MCR ²⁸ +SGLT2 ²⁹ heart failure	MEDI3506 IL33 COVID-19 ³⁸	Zibotentan <i>+Farxiga</i> ETA1 ⁵⁰ +SGLT2 CKD		Highlighte	d in breakout sessions
MED18367 avb8 ¹¹ CKD ¹²	brazikumab IL23 ³⁰ ulcerative colitis	MEDI5884# cholesterol modulation CV			Other pipe	line medicines

1. RAR-related orphan receptor gamma 2. Janus kinase inhibitor 3. Non-alcoholic steatohepatitis 4. Ectonucleoside triphosphate diphosphohydrolase-3 5. Cardiovascular 6. Human leukaemia monocytic cell line 7. Phosphoinositide 3-kinases gamma delta 8. Protease activated receptor 2 9. Monoclonal antibody 10. Osteoarthritic pain 11. alpha-v-beta-8 integrin 12. Chronic kidney disease 13. Interferon 14. Lupus nephritis 15. Systemic lupus erythmeatosus 16. Subcutaneous 17. Interleukin 4 receptor alpha 18. Myeloperoxidase 19. Heart failure with the preserved ejection fraction 20. 5-lipoxygenase-activating protein 21. Coronary tery disease 22. Dipetidel 32. Toc-2 Chronic inflammatory disease 24. Interleukin 31. Glucagon-ratery disease 23. Dipetide 132. Toc-2 Chronic inflammatory disease 24. Interleukin 33. Coronavirus disease 2019 39. Lecithin – cholesterol avoid receptor 29. Sodium-glucose co-transporter-2 30. Interleukin 33. Coronavirus disease 2019 39. Lecithin – cholesterol avoidised low-density lipoprotein receptor 1 4. Nerve growth factor 42. Tumour necrosis factor 43. Painful diabetic neuropathy 44. Muscarinic beta 2-agonis 45. Hypoxia-inducible factor 46. Prolyt Chronic spontaneous urticaria 36. Atopic dermatitis 37. Interleukin 33. Coronavirus disease 2019 39. Lecithin – cholesterol avoidised low-density lipoprotein receptor 1 41. Nerve growth factor 42. Tumour necrosis factor 43. Painful diabetic neuropathy 44. Muscarinic beta 2-agonis 45. Hypoxia-inducible factor 46. Prolyt hydroxylase inhibitor 47. Cheronotherapy induced anaemia 48. Thymic stromal lymphopoietin 49. Urate transporter 1 50. Endothelin receptor 40. Storg antipody 52. Long-acting antibody 52. Long-acting antibody 52. Long-acting nuscarinic antagonist 54. Inhaled corticosteroid 55. Myocardial infarction 56. Bullous pemphigidi 57. Eosinophilic granulomators with polyangiitis 58. Eosinophilic sophagitis 59. Triple modification, M252Y/S254T/T256E, of the fragment crystallisable region of an IgG antibody which extends its half life - Robbie, G.J., et



BioPharmaceuticals Business Unit

BioPharmaceuticals R&D

COVID-19

Q&A





COVID-19 treatment and prevention approaches Advancing vaccine, antibody, other options

COVID-19 Vaccine AstraZeneca (C19VAZ)



- UK emergency use authorisation;
 EU conditional marketing authorisation
- Real world data from UK rollout showing >80% protection against hospitalisation
- US Phase III met the primary endpoint

Granted conditional approval or emergency use in >70 countries AZD7442 long-acting antibody (LAAB) combo

- Potential to offer immediate protection
- Late-stage trials in both prophylaxis and treatment
- US Government agreements for potential supply of 700,000 doses in 2021

First data

in H1 2021



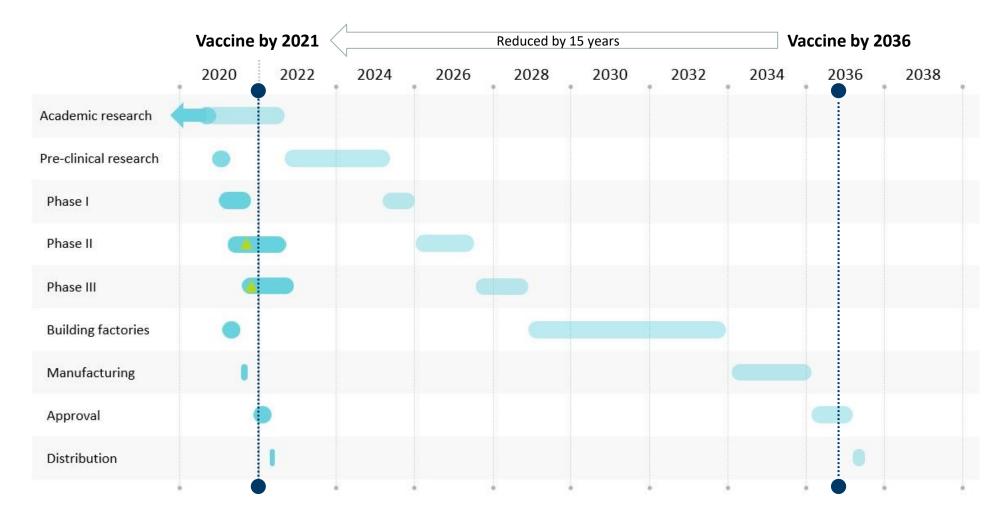
Other COVID efforts continue

- Farxiga
 DARE-19 Phase III trial
- ACCORD Phase II trial
- Symbicort INHASCO Phase IIIa trial
- Pulmicort
 TACTIC-COVID Phase IIIa trial
 STOIC Phase II trial positive

First data in H1 2021



Vaccine development typically takes a decade or longer *C19VAZ*: an unprecedented acceleration



COVID-19 Vaccine AstraZeneca

Shown to be safe and effective in clinical trials and real-world data



Protection from hospitalisation and severe disease



First dose protection



Increased efficacy with a longer dosing interval US Phase III trial primary analysis

100%

efficacy against severe disease, hospitalisation and death

76%

efficacy from day ≥15 after second dose in all adult age groups

85%

efficacy from day 15 after first dose in adults 65 years and over

Real world effectiveness

<mark>94%</mark>

effective against hospitalisation in enriched elderly population¹

<mark>80%</mark>

effective against hospitalisation in ≥80 years with extensive comorbid disease²

73%

effective from day 35 after first dose in older adults (≥70 years)³

1. Vasileiou E et al. Preprint published online. *The Lancet*. 2021 2. Bernal JL et al. Preprint published online. *The Lancet*. 2021 3. Hyams C et al. Preprint published online. *The Lancet*. 2021.

Clinical priorities



Establishing optimal dosing regimen



Different populations

- Older adults
- Paediatrics started
- Pregnant women



Heterologous boosting

New variants



AZD7442 long-acting antibody (LAAB) combination COVID-19 unmet needs persist even during a successful vaccine rollout

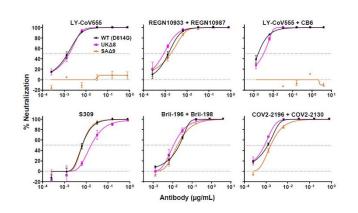
AZD7442

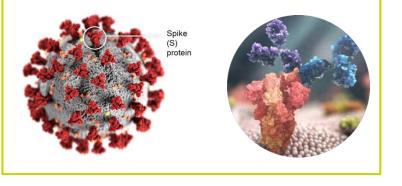
- Extended half-life using YTE¹
- Intra-muscular administration
- Potent and synergistic combination
- >2% of population immune suppressed²

2021 capacity of 1-2m doses

1. Triple modification, M252Y/S254T/T256E, of the fragment crystallisable region of an IgG antibody which extends half life - Robbie, G.J., et al. *Antimicrob Agents Chemother*, 2013. 57(12): p. 6147-53 2. Harpaz, R., et al *JAMA*. 2016;316(23):2547-2548.

Neutralisation profiles of therapeutic mAbs^{3,4}





3. Monoclonal antibody 4. Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization, David D. Ho et al. bioRxiv 2021.01.25.428137.

Phase III trials

- PROVENT and STORMCHASER
 Phase III trial in pre- and postexposure prophylaxis; 300mg IM⁵ dose; potential for 12 months protection
- TACKLE Phase III trial of 600mg IM in outpatient setting and collaborator trials

First data H1 2021





BioPharmaceuticals Business Unit

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COVID-19

Q&A





Questions & Answers

To ask a question

Webinar Click 'Raise Hand' (preferred):

or type your question into the Q&A box (alternative)

Q.

*Phone**6 - Toggle mute/unmute*9 - Raise hand



Meet AZN management: BioPharmaceuticals Four Q&A-focused, virtual breakout sessions

Opening session and Q&A 14:30-15:20 GMT

Mene Pangalos, Ruud Dobber

https://astrazeneca.zoom.us/webinar/register/WN bGgqh6nRS120V4JAbnFLvQ

Webinar ID: 96770774469 | IR moderator: nick.stone@astrazeneca.com

New CVRM: emerging pipeline

Session 1: 15:30 GMT Session 2: 16:15 GMT

Regina Fritsche Danielson, Tomas Andersson, Lori Kreamer

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Webinar ID: 92950815561 IR moderator: christer.gruvris@astrazeneca.com

New CVRM: near-term opportunities

Session 1: 15:30 GMT Session 2: 16:15 GMT

Elisabeth Björk, John Houghton, Joris Silon

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> Webinar ID: 95741428905 IR moderator: nick.stone@astrazeneca.com

Respiratory & Immunology: emerging pipeline

Session 1: 15:30 GMT Session 2: 16:15 GMT

> Maria Belvisi, Ben Fenby, Iain Chessell

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Webinar ID: 95277051413 IR moderator: tom.waldron@astrazeneca.com

Respiratory & Immunology: near-term opportunities

Session 1: 15:30 GMT Session 2: 16:15 GMT

Richard Marshall, Pablo Panella, Gerard O'Malley, Micki Hultquist

https://astrazeneca.zoom.us/webinar/re gister/WN_WkP2l8waRWiCoa9ROqIkUQ

> Webinar ID: 95741428905 IR moderator: josie.afolabi@astrazeneca.com

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