AstraZeneca Mölndal

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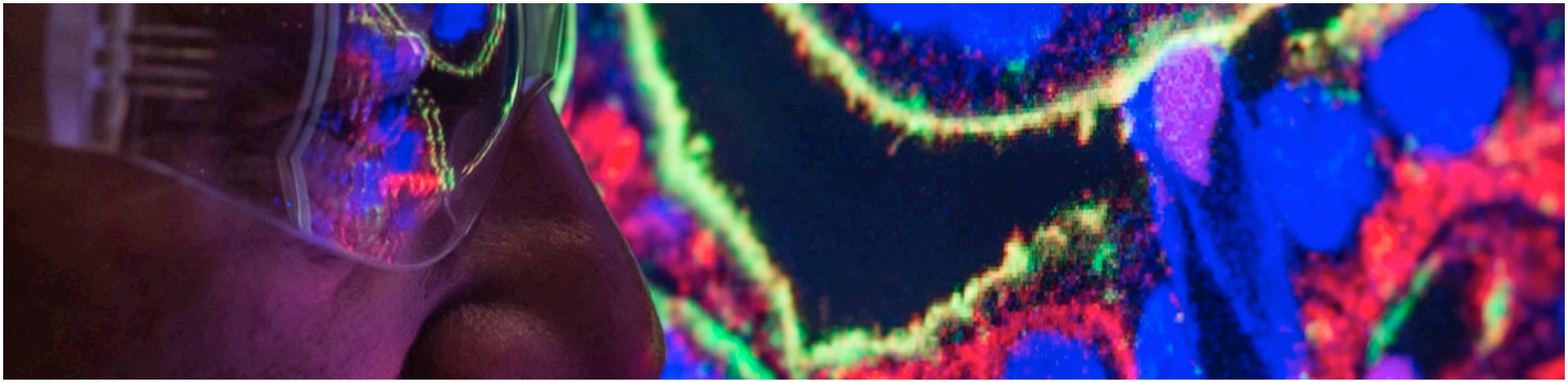
May 2015



AstraZeneca
What science can do

Welcome & introduction

Thomas Kudsk Larsen
Head of Investor Relations

Programme

10.00-10.30	Registration and coffee
10.30-10.45	**Introduction to AZ Sweden:** Jan-Olof Jacke (President, AZ Sweden)
10.45-11.15	**Innovative Medicines Biotech Unit:** Mene Pangalos (EVP, Innovative Medicines)
11.15-11.45	**Respiratory inhaled medicines early-stage pipeline:** Maarten Kraan (Head of RIA, Innovative Medicines)
11.45-12.15	Q&A
12.15-13.15	Lunch
13.15-14.45	Lab tours (RIA and CVMD alternating) 
14.45-15.15	**Cardiovascular & Metabolic Diseases late-stage pipeline:** Elisabeth Björk (VP, Head of Cardiovascular & Metabolic Disease GMD)
15.15-15.45	**'What Science Can Do':** Marcus Schindler (VP, Head of Cardiovascular & Metabolic Disease iMed)
15.45-16.15	Q&A

The AstraZeneca IR Team

Main contacts for Sweden:

Christer Gruvris & Craig Marks

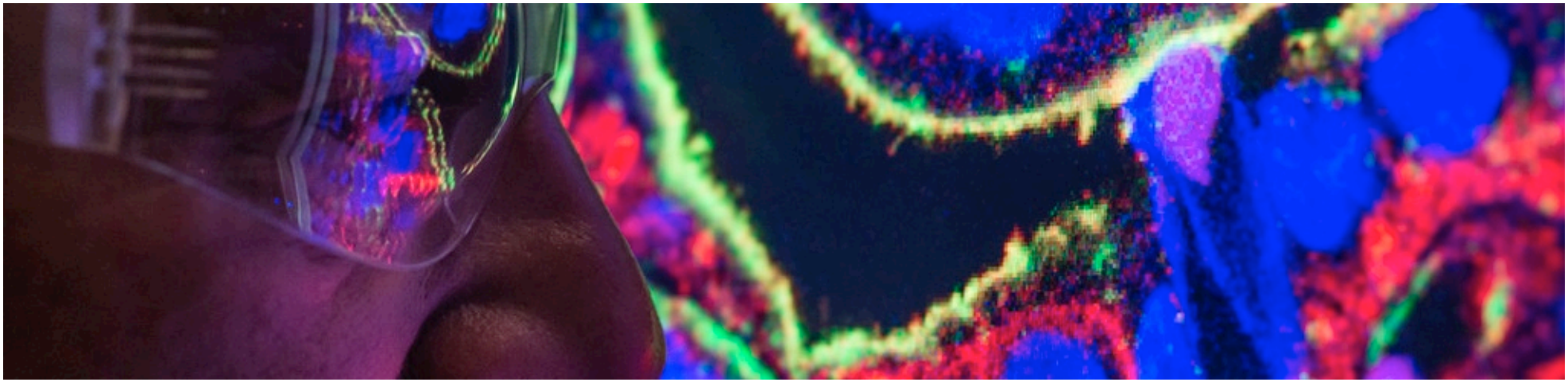
+ two new colleagues in the US

Feedback always welcome!

AstraZeneca
What science can do

Introduction to AstraZeneca Sweden

Jan-Olof Jacke
President, AstraZeneca Sweden



An important player

Key numbers

39 mdr kr — Export from Sweden

25% — Proportion of AZ's total investment in research & development

2 mdr kr — Sales in Sweden (including parallel imports)

110,000 — Number of registered Swedish shareholders

10% — Percentage of Swedish ownership (of total shares)

AstraZeneca has extensive research and manufacturing presence in Sweden

Mölndal
2,400

+

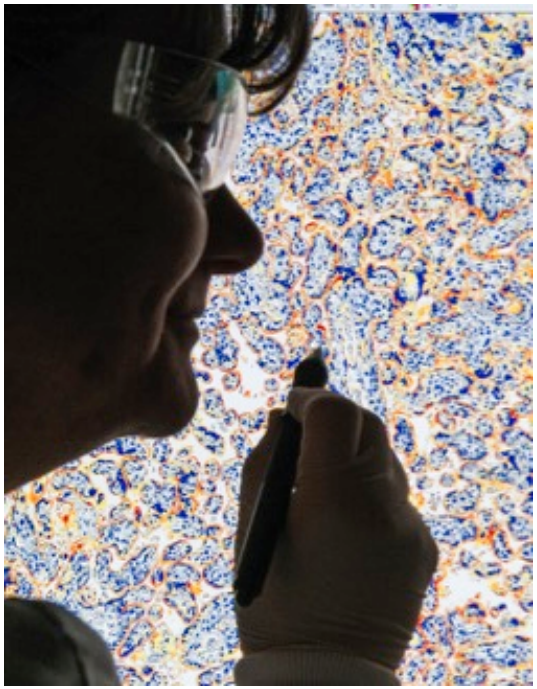
Södertälje
3,800

= 6,200

Mölndal

Mölndal

One of three strategic R&D centres



- Research in Mölndal is focused on:
  - Cardiovascular and Metabolic disease
  - Respiratory, Inflammation and Autoimmunity
- The site has around 2,400 employees, including more than 300 scientists from 30 different countries
- Our scientists work in close collaboration with all of the leading Swedish academic centres, as well as through global networks
- Mölndal represents around 25% of global research and development resources
- In 2014 we invested around 100m SEK per day in R&D

Södertälje

Södertälje

Our largest high-tech manufacturing and supply site

- Sweden Operations manufacture the active pharmaceutical substance and formulate & package the final products
- Launch site for new medicines in form of tablets and capsules entering the global market
- More than 35% of Product Sales value
- Approximately 10bn tablets every year
- Produce substances and 30 different medicines for more than 100 markets
- Three out of 10 largest medicines by Product Sales

What are we doing to strengthen the life-science ecosystem in the Nordics?

BIO VENTURE HUB

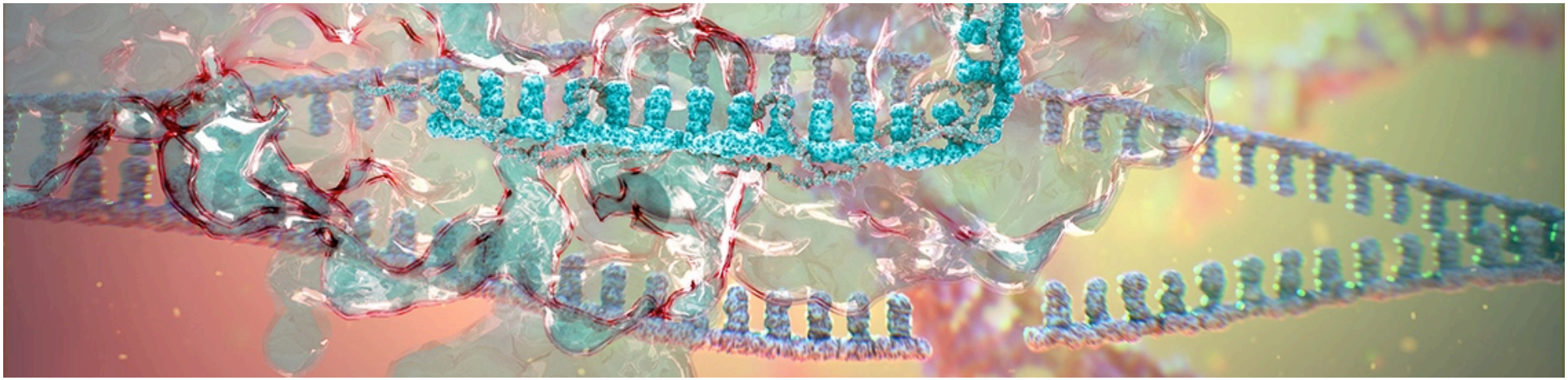
- 300 lab & office seats
- Seven biotech companies and more to come

Collaboration to nurture Nordic innovative ideas in life science

AstraZeneca
What science can do

Creating an environment where science thrives

Mene Pangalos
EVP Innovative Medicines



Strategic priorities

1
Achieve scientific leadership

2
Return to growth

3
Be a great place to work

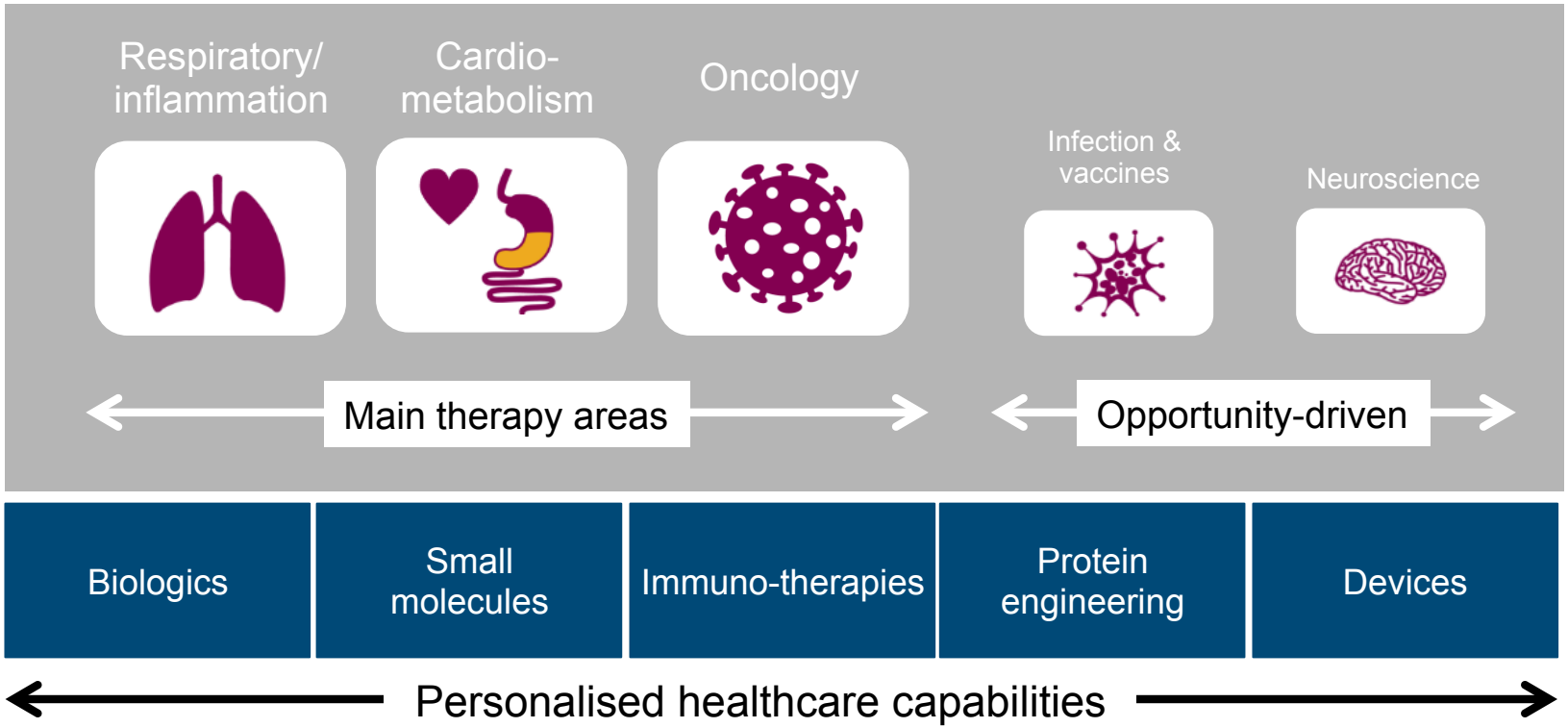
Completing the first phase of the journey

2012-2014
Building strong foundations

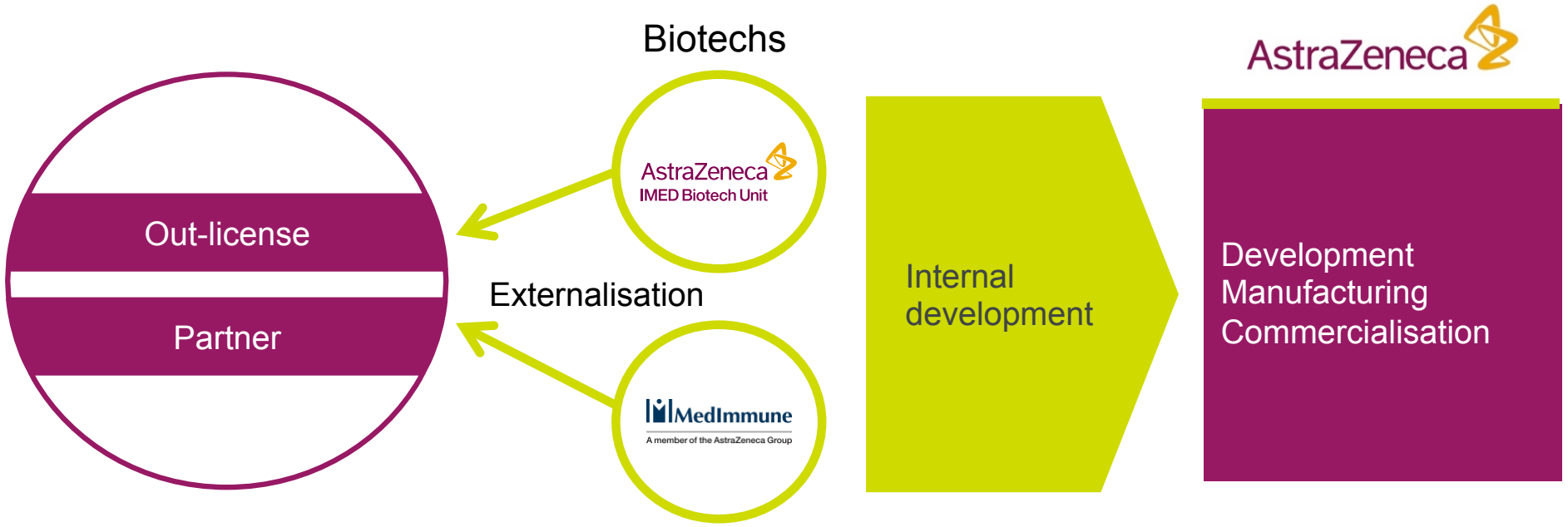
2015-2017
Delivering on return to growth

2018+
Sustainable delivery and growth

As we move forward, we will remain focused in our R&D approach…



…and continue to evolve our business model to create maximum value from strong R&D productivity



Value creation through internal development and externalisation

We have a strong, well balanced pipeline

RIA | CVMD | Oncology | Infection | Neuroscience

Phase 1
30 New Molecular Entities

Small molecule	Large molecule
AZD1419# TLR9 asthma	MEDI4920 CD40L-Tn3 Primary Sjögrens
AZD7594 Inhaled SGRM asthma, COPD	MEDI5872# B7RP1 SLE
AZD7986 DPP1 COPD	MEDI7863 IL-13 asthma
AZD8999 MABA asthma, COPD	MEDI0382 GLP-1/glucagon diabetes, obesity
AZD3759 EGFR NSCLC	MEDI6012 LCAT ACS
AZD5312# androgen receptor prostate	MEDI8111 Rh-Factor II trauma, bleeding
AZD6738 ATR CLL, H&N	MEDI0562# hOX40 solid tumours
AZD8186 PI3Kβ solid tumours	MEDI0639# DLL-4 solid tumours
AZD8835 PI3Kα solid tumours	MEDI0680 PD-1 solid tumours
AZD9150# STAT3 haems & solids	MEDI3617# ANG-2 solid tumours
AZD9496 SERD ER+ breast	MEDI-565# CEA BITE GI tumours
AZD8108 NMDA suicidal ideation	MEDI6383# Ox40 FP solid tumours
	MEDI6469# mOx40 solid tumours
	MEDI3902 PsI/PcrV pseudomonas
	MEDI-550 pandemic influenza virus vaccine
	MEDI7510 sF+GLA-SE RSV prevention
	MEDI8852 influenza A treatment
	MEDI1814 amyloidβ Alzheimer's

Phase 2
29 New Molecular Entities

Small molecule	Large molecule
abediterol (AZD0548) LABA asthma, COPD	anifrolumab# IFNαR SLE
AZD7624 Inhaled p38 inhibitor COPD	AZD9412# Inhaled βIFN asthma, COPD
PT010 LABA/LAMA/ICS COPD	mavrilimumab# GM-CSFR rheumatoid arthritis
RDEA3170 SURI hyperuricemia, gout	MEDI2070# IL-23 Crohns
AZD4901 PCOS	MEDI-551# CD19 neuromyelitis optica∂
tenapanor# NHE3 ESRD-Pi/CKD	MEDI7183# α4β7 Crohns, ulcerative colitis
AZD1775# Wee-1 ovarian	MEDI9929# TSLP asthma
AZD2014 mTOR 1/2 solid tumours	sifalimumab# INFα SLE
AZD4547 FGFR solid tumours	MEDI-551# CD19 CLL, DLBCL
AZD5363# AKT breast cancer	MEDI-573# IGF metastatic breast cancer
AZD6094# MET pRCC	MEDI4893 staph alpha toxin SSI
ATM AVI# BL/BLI SBI	MEDI8897# RSV passive prophylaxis
AZD5847 oxazolidinone TB	
CXL# BLI/cephalosporin MRSA	
AZD3241 MPO Multiple System Atrophy	
AZD3293# β-secretase Alzheimer's	
AZD5213 H3R Tourettes, neuropathic pain	

Phase 3
12 New Molecular Entities

Small molecule	Large molecule
PT003 LABA/LAMA COPD	benralizumab# IL-5R severe asthma
roxadustat# HIFPH anaemia CKD/ESRD	brodalumab# IL-17R psoriasis
AZD9291 EGFRm T790M NSCLC >2L	tralokinumab IL-13 severe asthma
cediranib VEGF PSR ovarian	MEDI4736# ATLANTIC¶ PD-L1 NSCLC 3L
selumetinib# SUMIT MEK uveal melanoma	moxetumomab# CD22 HCL
CAZ AVI# RECLAIM BLI/cephalosporin SBI	tremelimumab¶ CTLA-4 mesothelioma

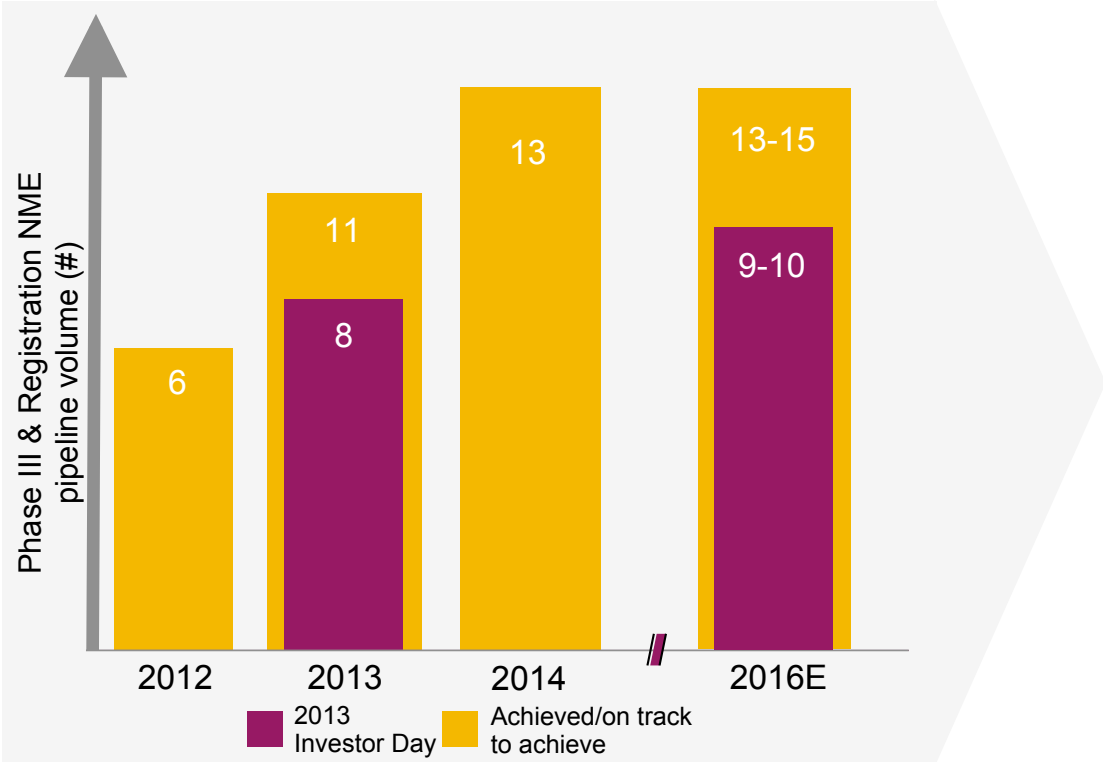
Applications Under Review
1 New Molecular Entities

Small molecule	Large molecule
lesinurad SURI gout	

Terminations in Q1 2015
AZD2115 (COPD) in P2, brodalumab (asthma) in P2, MEDI-559 (RSV prophylaxis) in P1
Divestitures in Q1 2015
AZD0914 (infection) in P2

† Includes significant fixed dose combination projects, and parallel indications that are in a separate therapeutic area *(See LCM chart for other parallel indications and oncology combination projects)*
# Partnered
¶ Registrational P2/3 study
∂ Neuromyelitis optica now lead indication (Multiple sclerosis P1 study continuing)

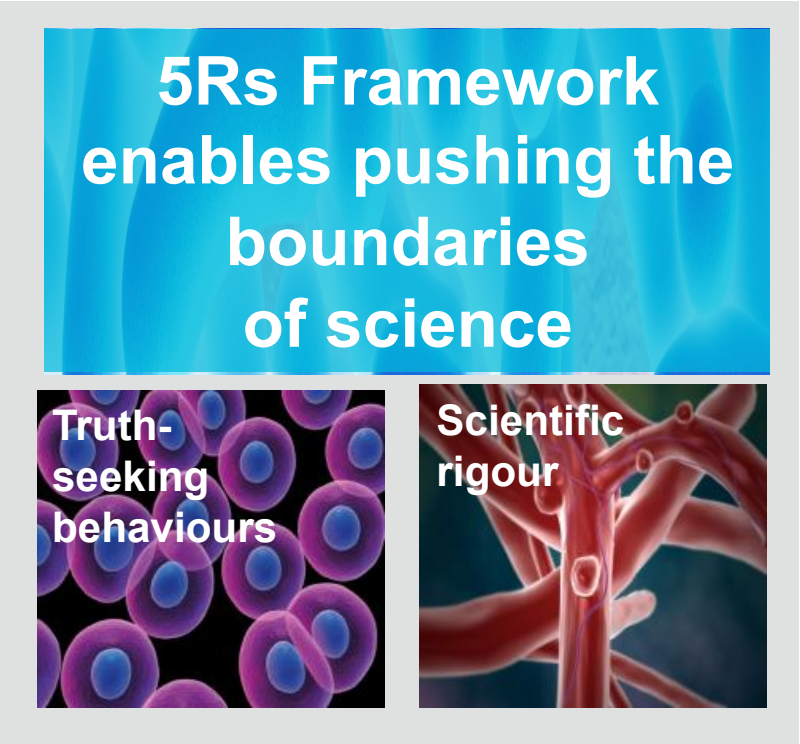
…and are delivering late-stage pipeline well ahead of plan

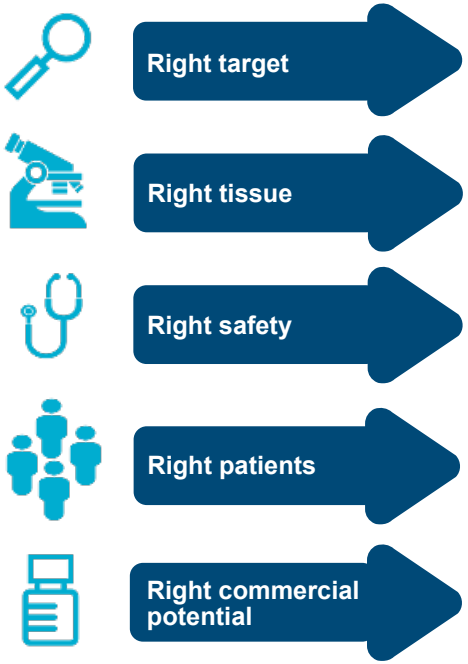


Pipeline events since 2014 Investor Day

- *Lynparza* approvals (US, EU)
- *Moventig* approval (EU)
- *Duaklir* approval (EU)
- BACE (AZD3293) Phase II/III trial start
- Saxa/dapa submission (US)
- Lesinurad submissions (US, EU)
- *Brilinta* PEGASUS positive data; submissions (US, EU)
- PT003 positive Phase III read-out
- Orphan-Drug Designation: selumetinib, tremelimumab
- Fast-Track Designation: MEDI8897, MEDI4736
- Licensing agreement with Omnis

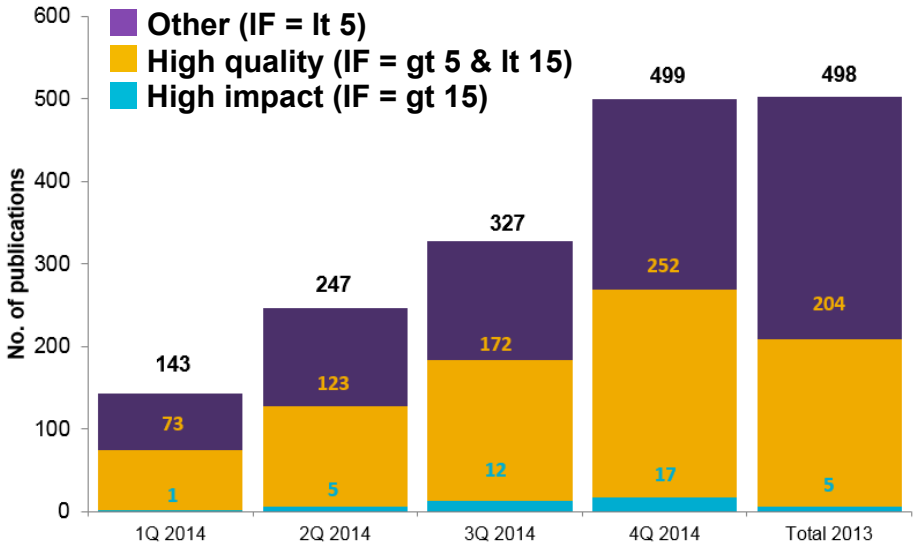
Our 5R framework has created an environment where science thrives





We are strengthening our scientific reputation through a focus on high impact and high quality publications

IMED peer-reviewed publications



Which is enabling us to attract the best scientists

A few examples of recent hires into the IMED Biotech Unit

Jérémie Boucher,
Principal Scientist, Diabetes
Previously Harvard
38 publications including Cell, Nature and Nature Medicine

Tim Eisen
Early Clinical Development & Professor at University of Cambridge
163 publications including NEJM, Lancet, Nature

Ralph Knoll
Chief Scientist, Cardiac Regeneration
Previously Imperial College
54 publications including Cell, J Mol Med

Tony Johnson
Early Clinical Development
Previously Cambridge University / BMS
79 publications including Diabetes Care, Circulation

Donald Stanski
Early Clinical Development
Previously Stanford / Novartis / FDA
110 publications including Journal of Clinical Pharmacology and Therapeutics and Anesthesiology

Robert Unwin
Chief Scientist, Chronic Kidney Disease
Previously UCL
153 publications including Lancet, Science, Nature Medicine, Nature Genetics

Outi Vaarala
Translational Science
Previously Helsinki University
206 publications including NEJM, Lancet, Diabetes

James Matcham
Biometrics
Previously Amgen

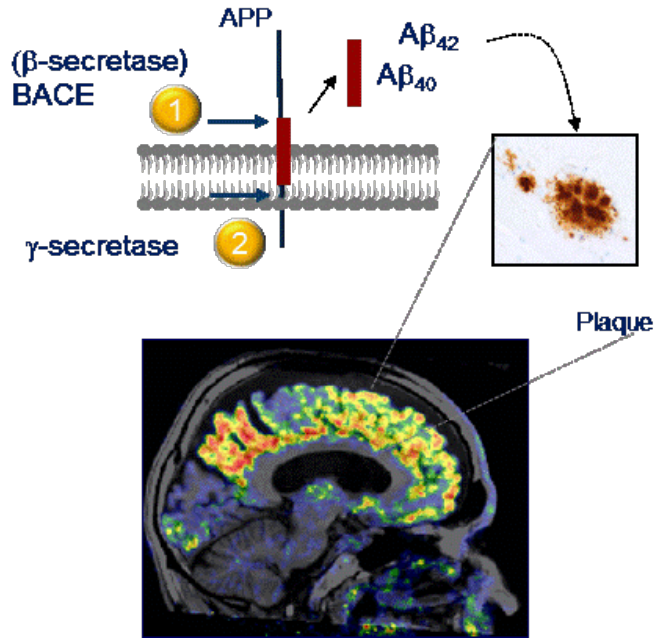
Scientific partnerships and alliances….

…remain a driver of sustainable scientific innovation

Alliance with Lilly to accelerate development of our BACE inhibitor (AZD3293)

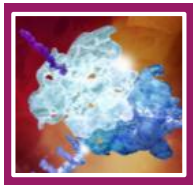
- Familial AD linked to mutations in APP
- Mutations in APP result in increased BACE activity and Aβ production
- Inhibition of BACE1 should reduce production of Aβ and might reduce disease progression
- Agreement to combine AZ science with Lilly experience in late-stage AD development
- Aim to progress rapidly into a Phase II/III clinical trial in patients with early Alzheimer's disease

Highly promising approach to address unmet medical need in Alzheimer's

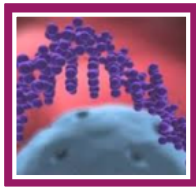


CRISPR/Cas9 won the 2015 Breakthrough Prize in Life Sciences*

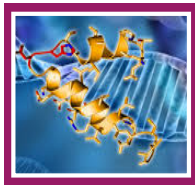
AstraZeneca working collaboratively to embrace the gene-editing revolution



Our IMED Genome Editing Team is unlocking the potential of CRISPR/Cas9



We are collaborating with pioneers and world experts in gene-editing



Exciting technology with the potential to transform our approach to drug discovery

Innovative Genomics Initiative

wellcome trust sanger institute

ThermoFisher SCIENTIFIC

Massachusetts Institute of Technology

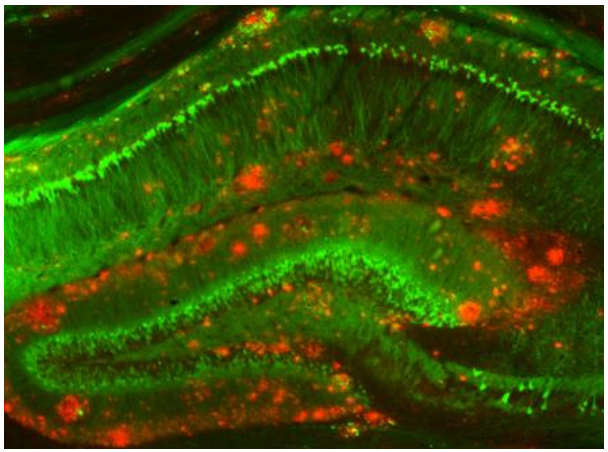
*The Breakthrough Prize in Life Sciences honors transformative advances toward understanding living systems and extending human life. The prize was founded in 2013 by Sergey Brin **(Google)** and Anne Wojcicki **(23andMe)**, Mark Zuckerberg **(Facebook)** and others.

Our commitment to open innovation has uncovered potential new treatments for patients

AZD0530 in trials for Alzheimer's Disease

- AZD0530 - Fyn kinase inhibitor - developed to target cancer
- Yale scientists explored potential treatment for AD by blocking Fyn activity
- Compound successfully reversed adverse brain conditions in mouse models
- Phase I safety study in humans showed compound reaches the brains at levels similar to those beneficial in mice

Mouse model of Alzheimer's disease - amyloid beta plaques (red) build up among neurons (green) in memory-related area of the brain.



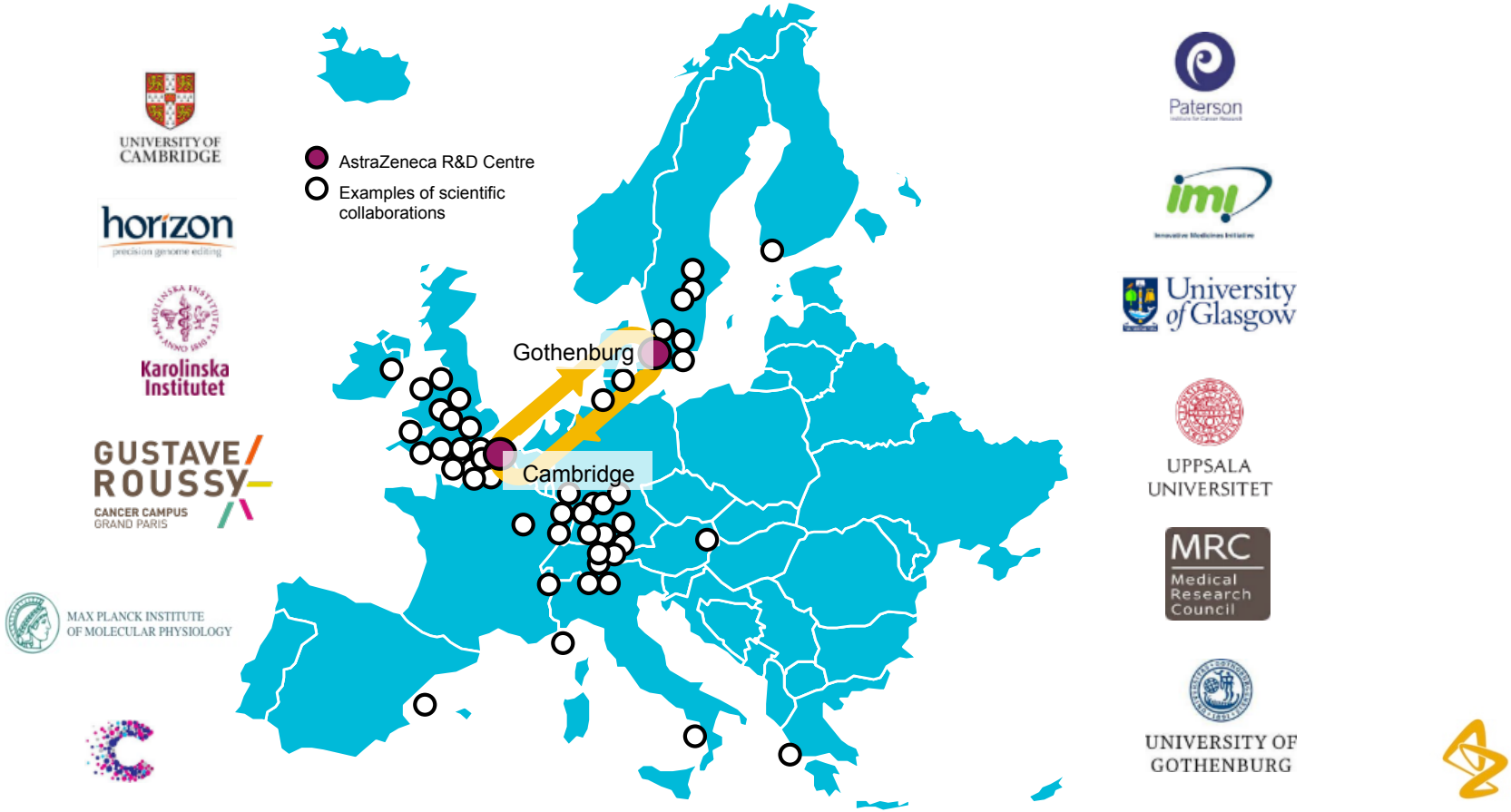
(Yale University Photo/Strittmatter Lab)

NCATS National Center for Advancing Translational Sciences

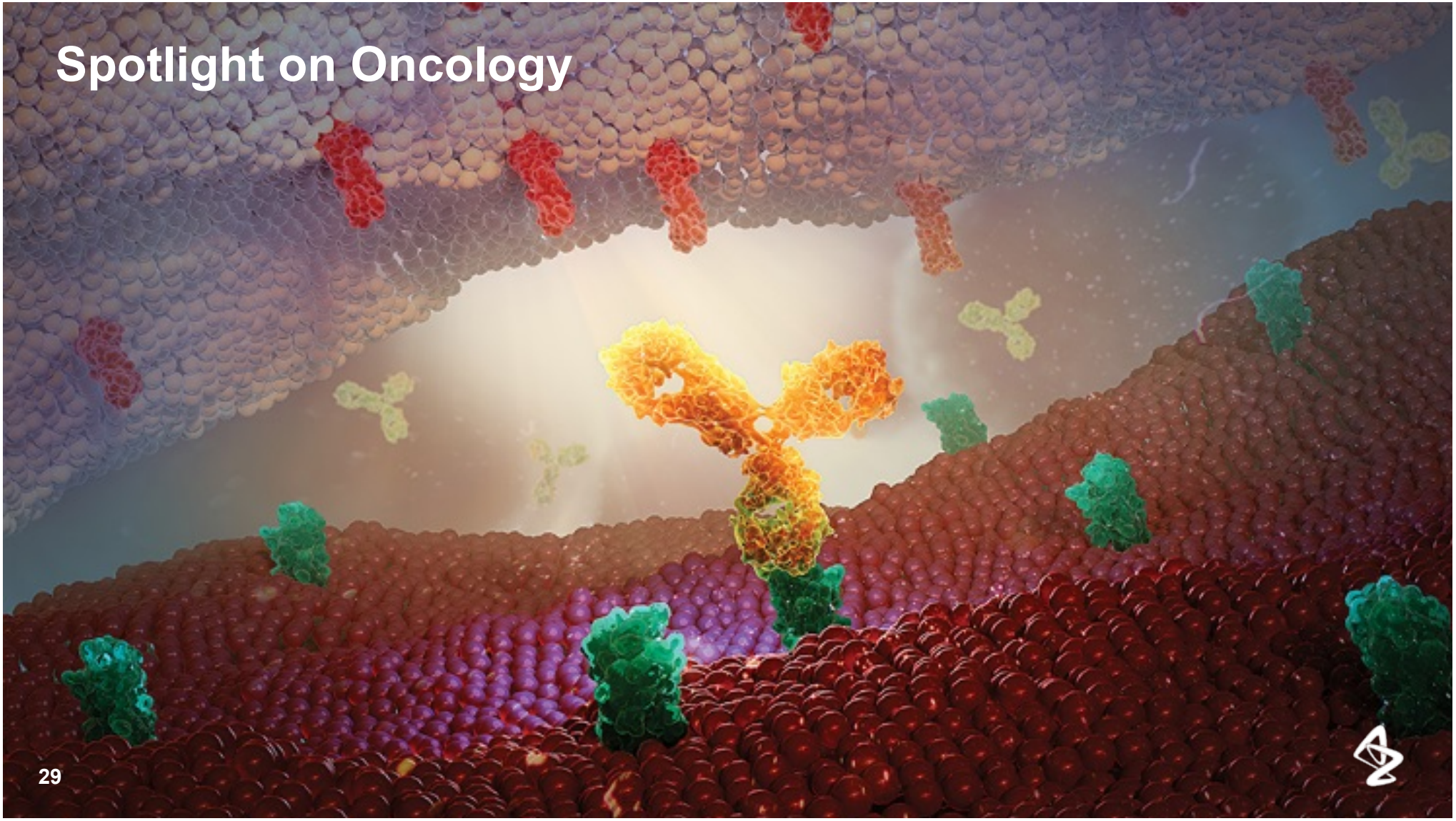
LUX ET VERITAS

Enhanced collaboration is a key driver behind our new UK facility at the Cambridge Biomedical Campus...

…and by connecting Cambridge & Gothenburg we will create a scientific powerhouse in Europe

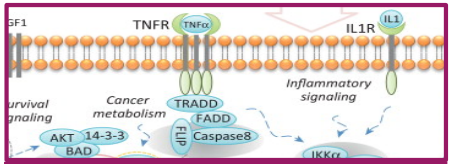


Spotlight on Oncology



AstraZeneca/MedImmune: Oncology pipeline

Four key areas under research development

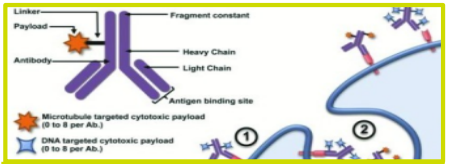


Tumor drivers and Resistance Mechanisms

- AZD9291 (*EGFR*m)
- Selumetinib (MEK)
- AZD2014 (TORC1/2i)
- AZD4547 (FGFR)
- AZD5363 (AKT)
- AZD6094 (cMET)
- AZD8186 (PI3Kβ)
- AZD8835 (PI3Kα)
- MEDI0639 (aDLL4)
- MEDI-573 (aIGF1/2)
- AZD9496 (SERD)
- AZD5312 (AR antisense)

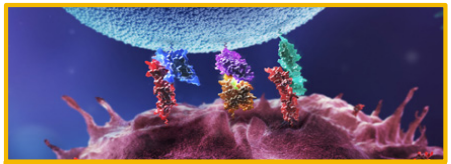
DNA Damage Response

- Olaparib (PARP)
- Cediranib (VEGF)
- AZD1775 (Wee1)
- AZD6738 (ATR)
- AZD0156 (ATM)
- AZD2811 (AKB)



Immuno-Oncology

- MEDI4736 (PD-L1)
- Tremelimumab (CTLA-4)
- MEDI0680 (PD-1)
- MEDI6469 (murine OX40)
- MEDI6383 (OX40 Fusion Protein)
- MEDI0562 (OX40 humanised mAb)
- AZD9150 (STAT3)
- AZD5069 (CXCR2)



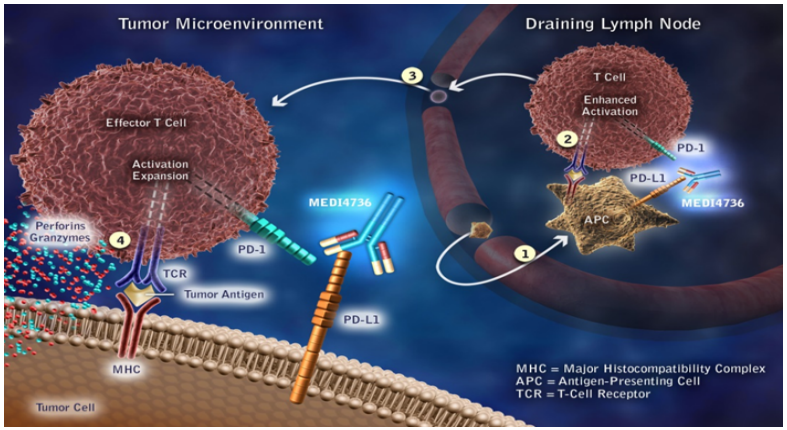
Armed Antibodies/ Antibody Drug Conjugates

- Moxetumomab (CD22)
- ADC-Spirogen
- ADC-Bispecific

Two of our most exciting and talked-about programmes…

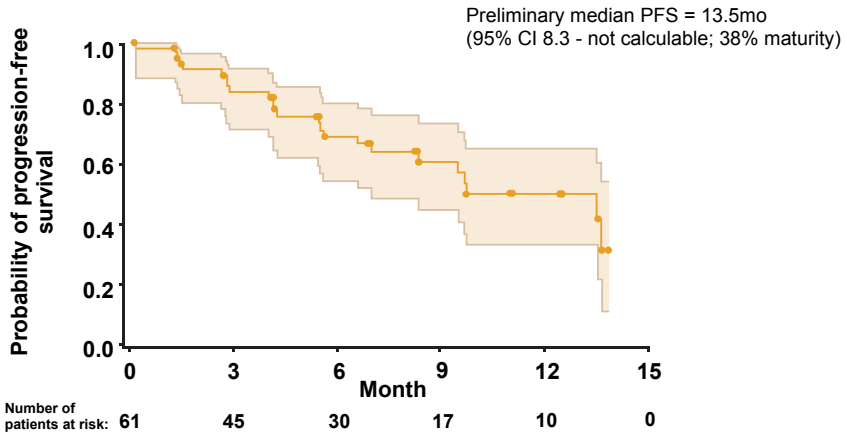
MEDI4736: An engineered PD-L1 antibody

- PD-L1 inhibits cancer immunity
- Expressed on multiple tumours
- MEDI4736 binds to PD-L1 and allows T cells to recognise and kill tumour cells



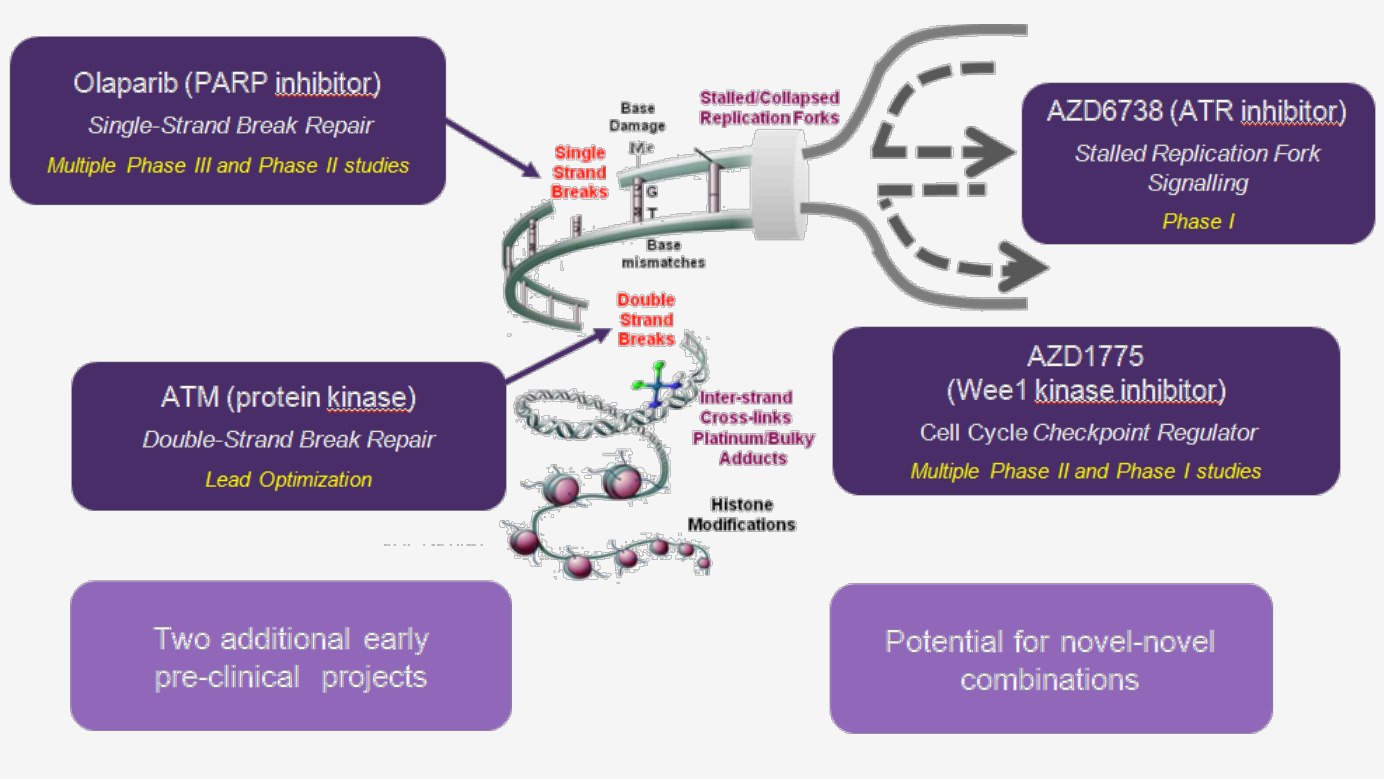
AZD9291

- Updated PFS for AZD9291 (NSCLC; AURA study) of 13.5 months in T790M, 80mg cohort, independent review



Source: European Lung Cancer Conference 2015

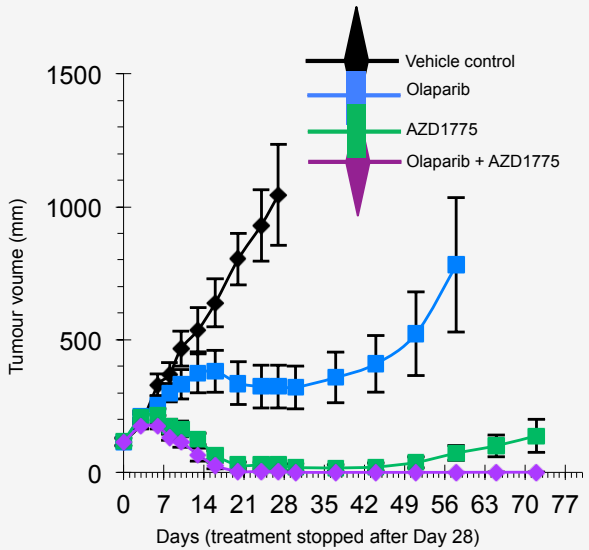
Leading ‘first-in-class’ DDR portfolio



Breadth of portfolio allows combinations with strong scientific rationale

	*Lynparza* & AZD1775 in TNBC
	*Lynparza* & AZD6738 in ATM-deficient GC
	*Lynparza* & AZD1775 in NSCLC and SCLC
	*Lynparza* & AZD1775 in platinum-resistant ovarian cancer

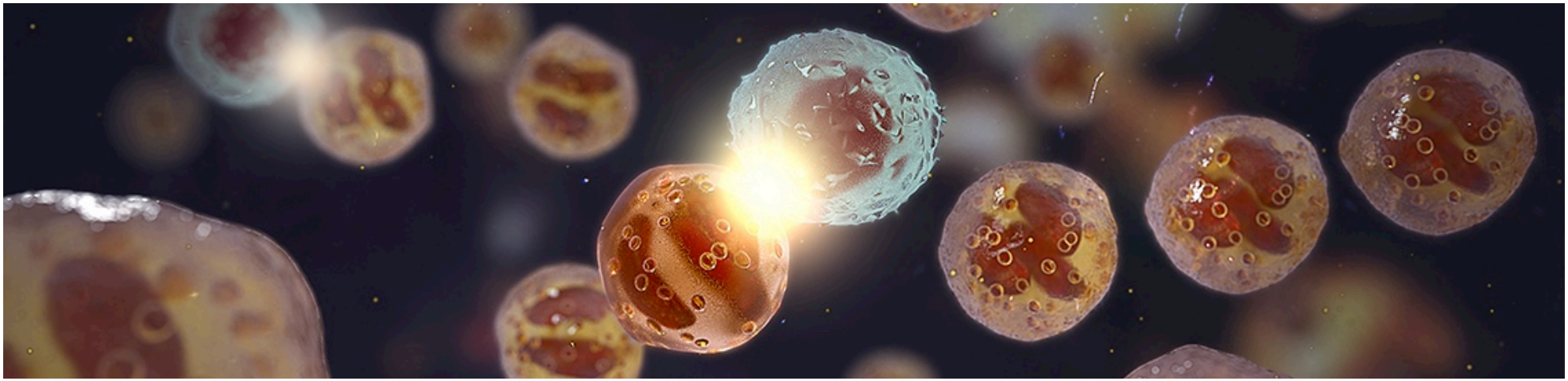
AZD1775 combination with *Lynparza* in a TNBC PDX model



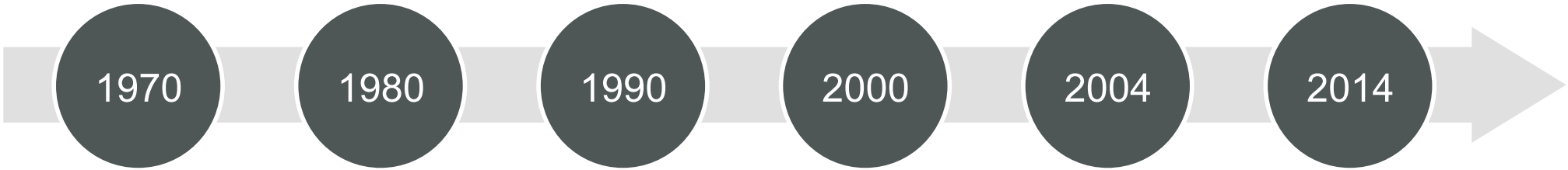
AstraZeneca
What science can do

Advancing inhalation science to change respiratory disease

Maarten Kraan
Head of RIA, Innovative Medicines



Four decades of leading innovation in respiratory disease



Pulmicort

Oxis®

SYMBICORT SMART
Reduced severe exacerbations by 40%
ASTHMA

Eklira Genuair

Duaklir Genuair
aclidinium bromide/formoterol

Terbutaline Sulphate-Astra
Bricanyl
Turbuhaler

Bambec

Twice daily/Oral
ACCOLATE
ZAFIRLUKAST

Symbicort
budesonide/eformoterol

Pearl™
A member of the AstraZeneca Group

Almirall

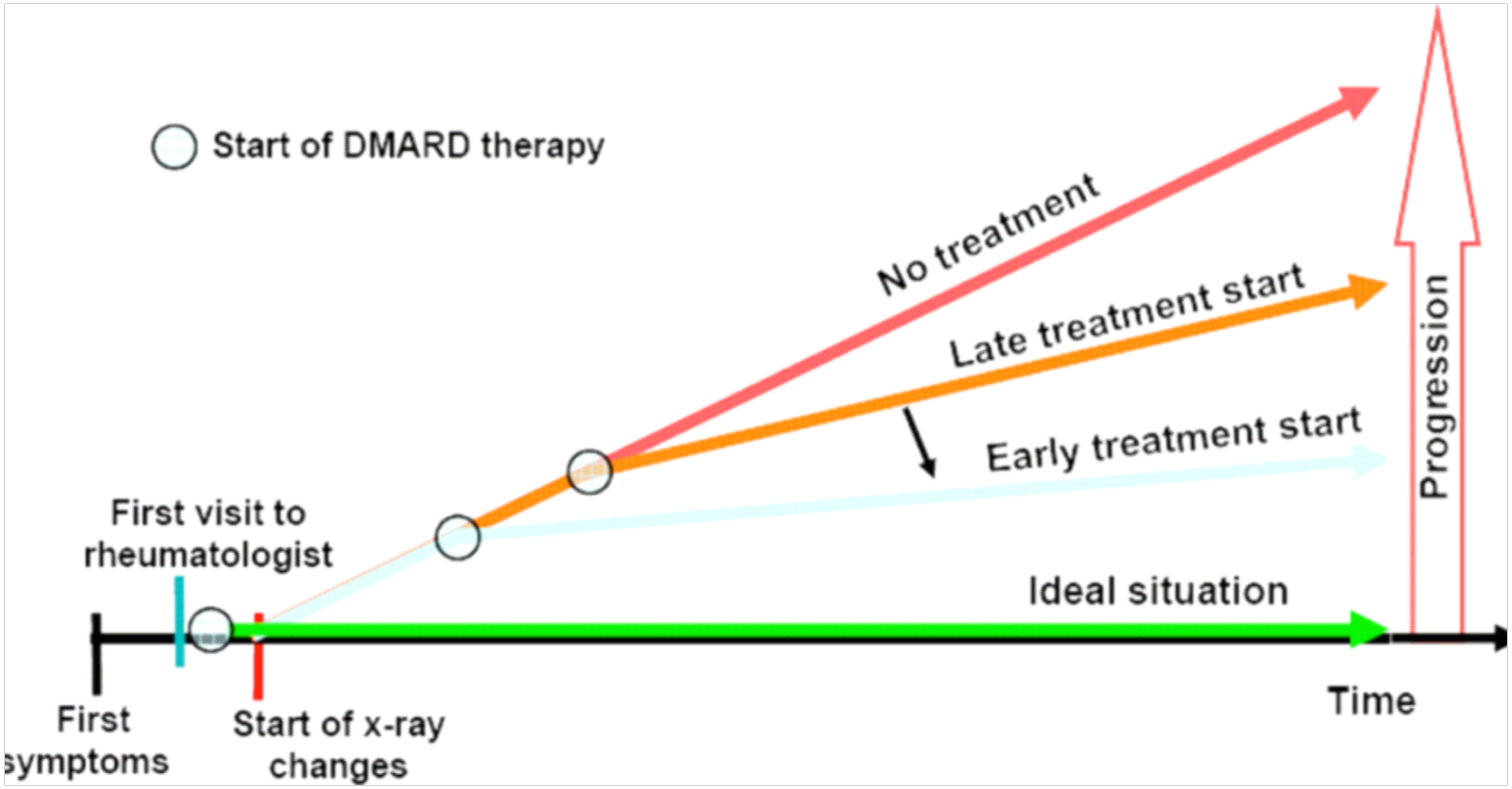
Rhinocort®

ABOUT HALF OF ALL TREATED ASTHMA PATIENTS REMAIN UNCONTROLLED.

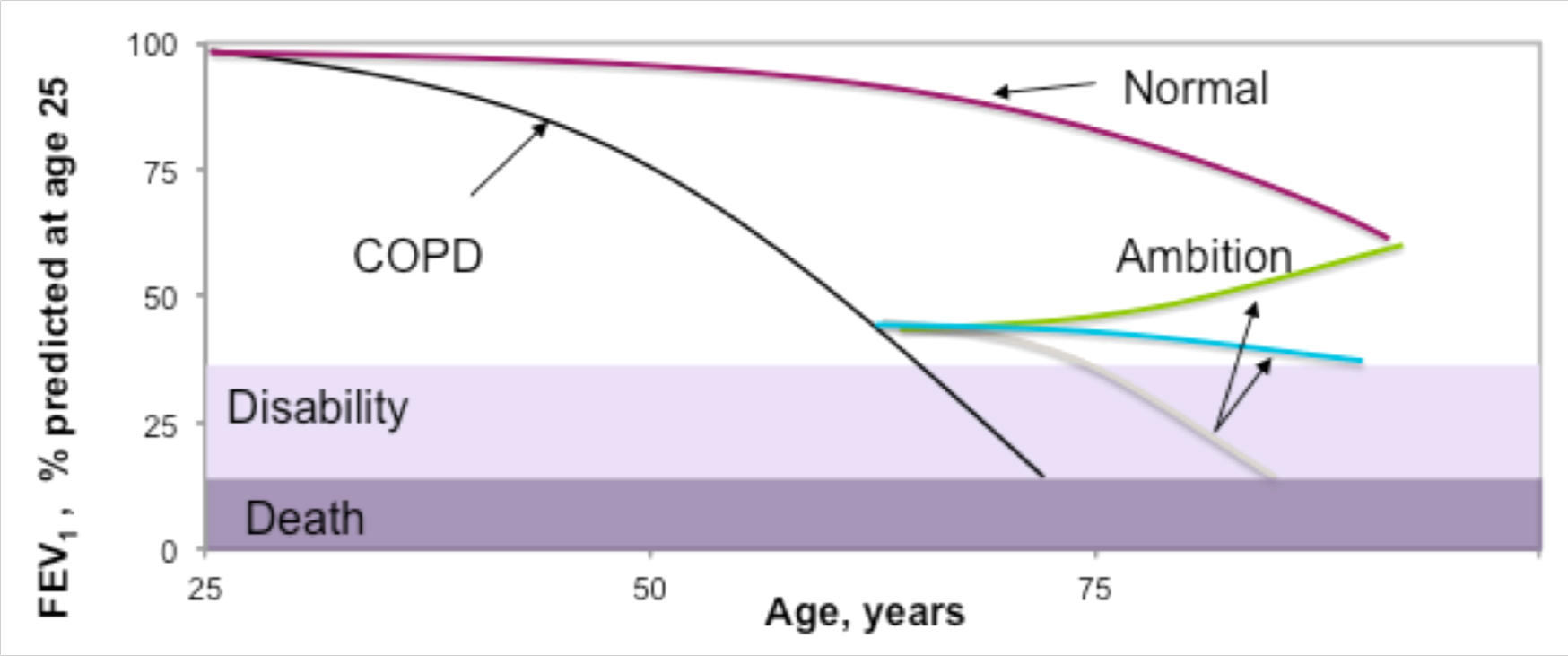
The inhaled portfolio remains the backbone of the respiratory strategy - but new treatments are needed

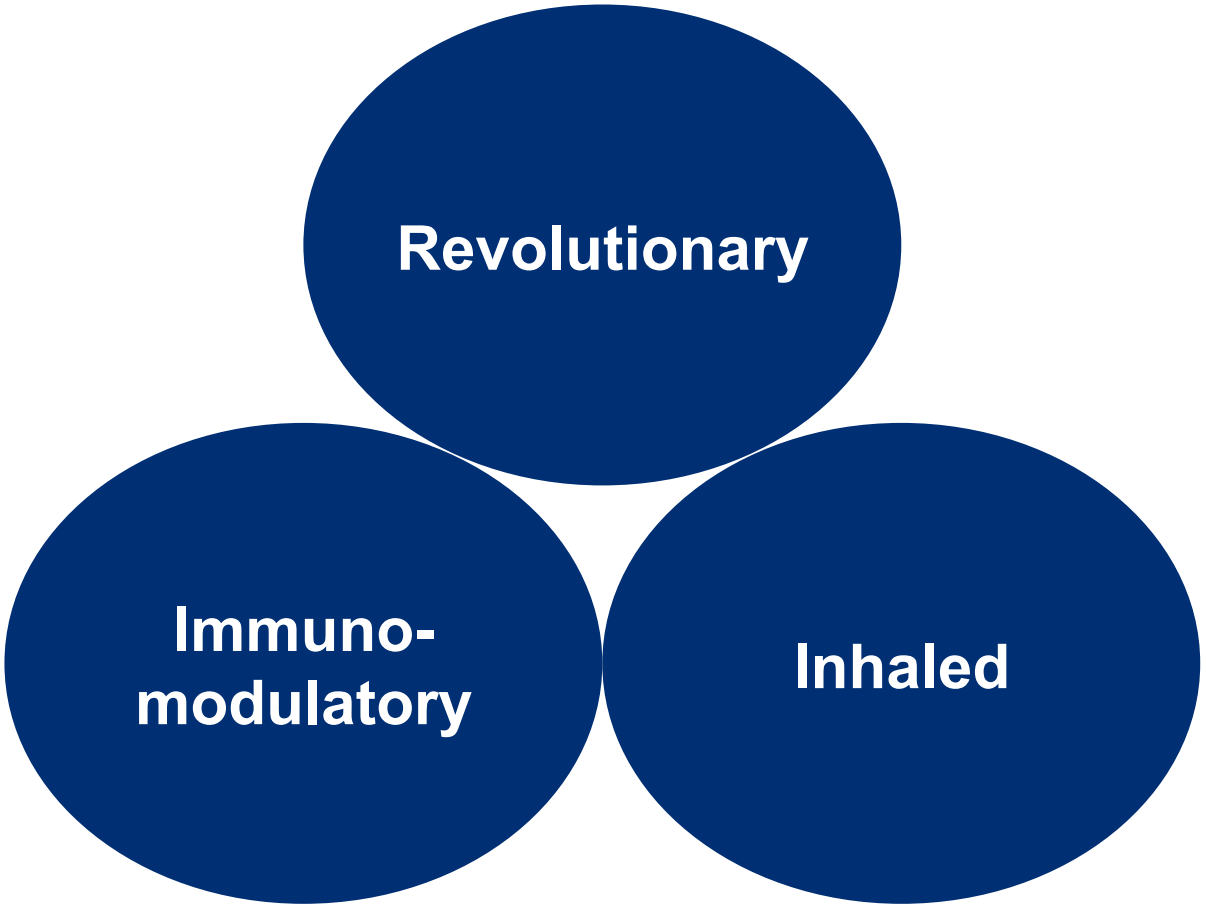
Unique inhaled therapies	1	Continue to differentiate *Symbicort* and *Pulmicort*
	2	Win in triple therapy with the Pearl technology
	3	Leveraging our 'two platform' device strategy
Innovative precision approaches	4	Progress immuno-modulating disease-changing therapies
Transforming disease management	5	Deliver paradigm-shifting evidence with existing combinations

Disease-modifying treatment changed the lives of patients with rheumathoid arthritis

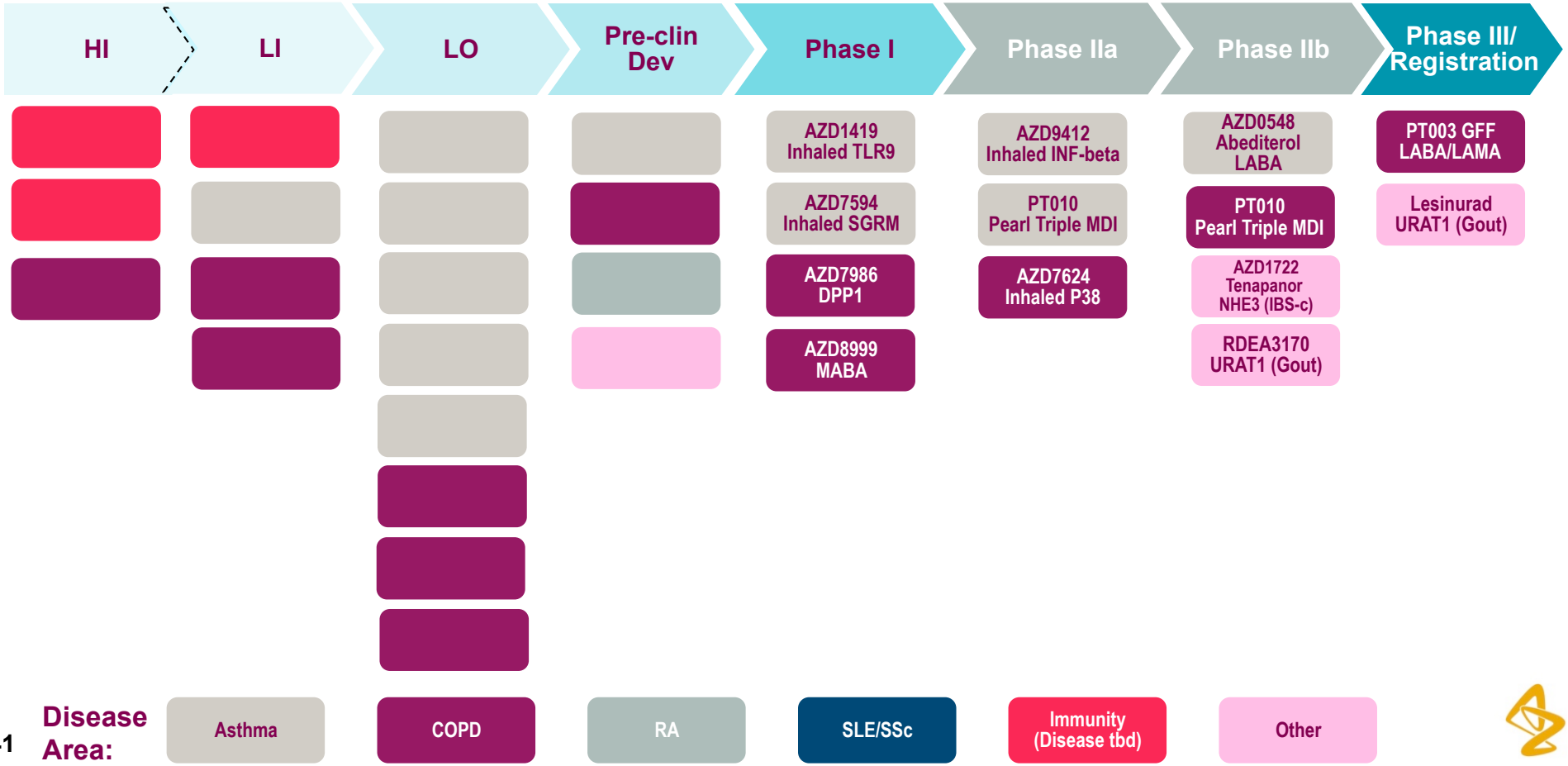


Immuno-modulatory medicine, effective in respiratory disease, is required

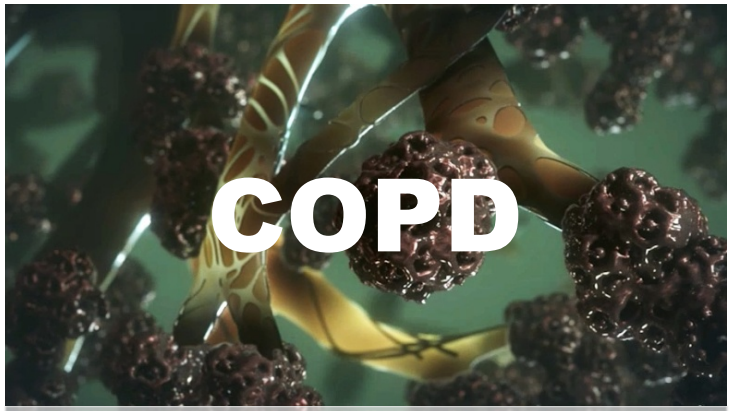



Revolutionary
Immuno-
modulatory
Inhaled

Most promising respiratory pipeline in the industry



Progressing novel, game-changing therapies

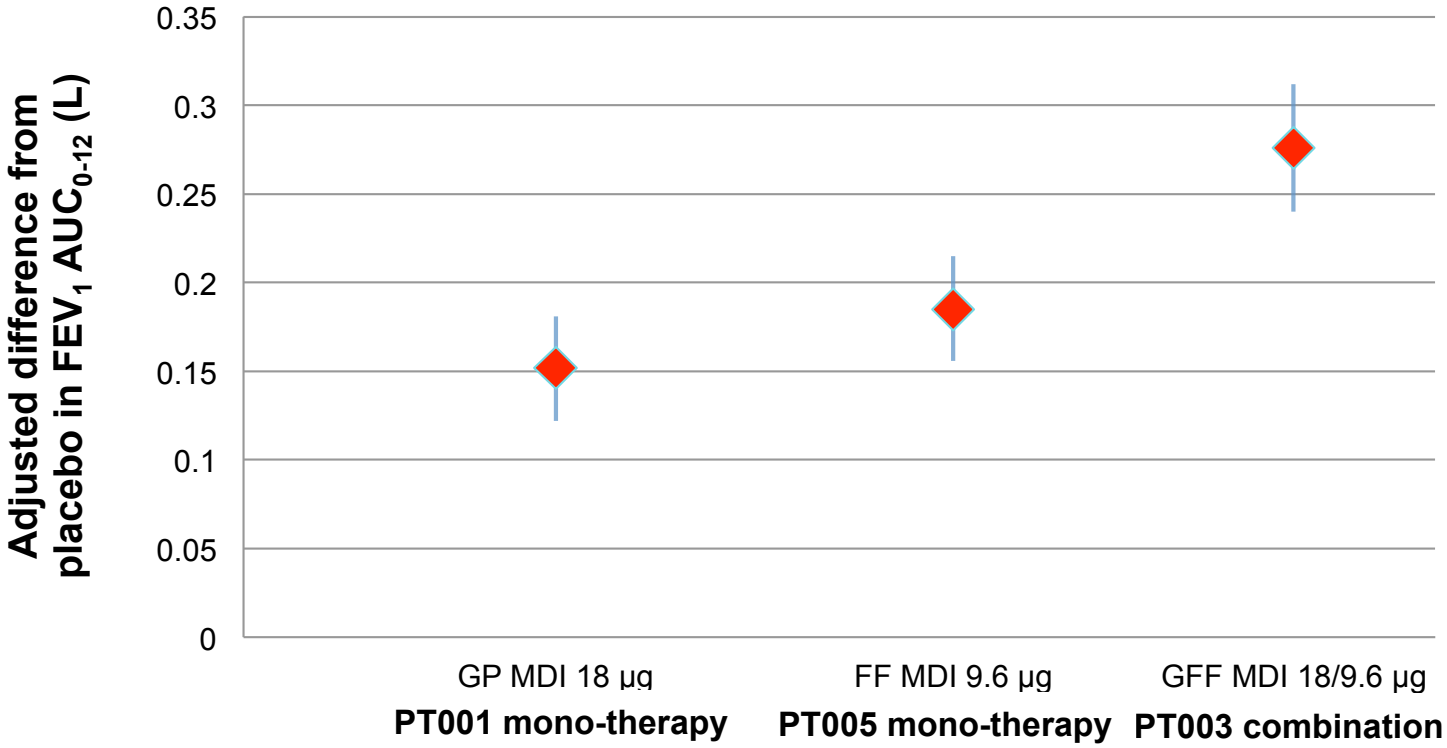


Biologics
Inhaled TLR9
Inhaled IFNβ

PT003
SGRM/MABA

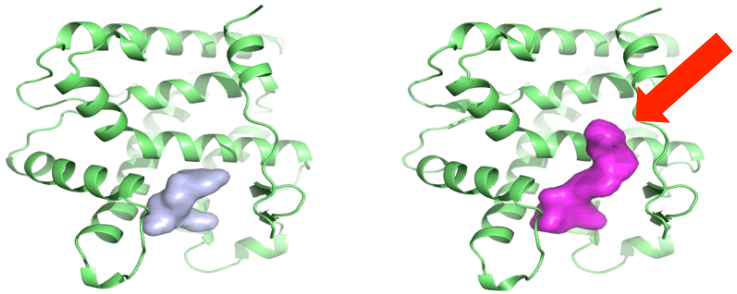
Inhaled p38

PT003 demonstrates incremental benefit of combination therapy ~100mL FEV over monotherapy in Phase IIB



Inhaled SGRM (AZD7594) is a novel, inhaled, non-steroidal anti-inflammatory with potential for improved therapeutic ratio

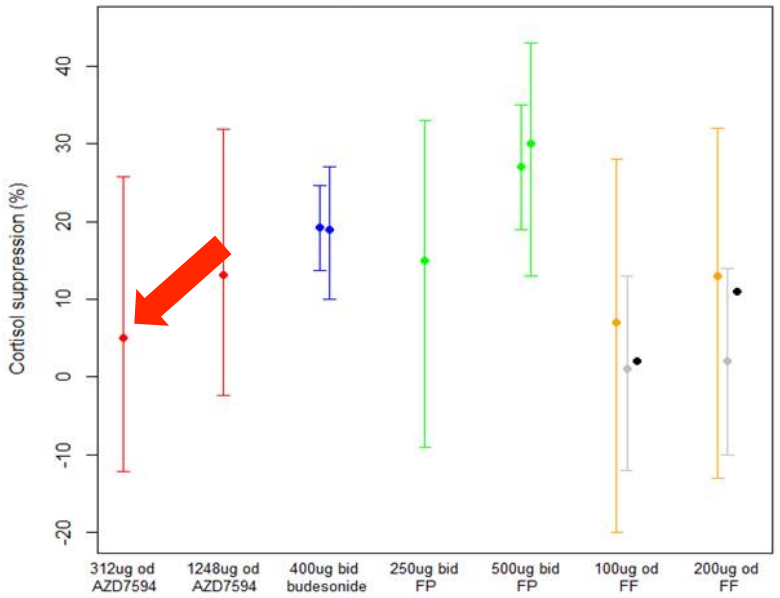
More potent than traditional inhaled steroids



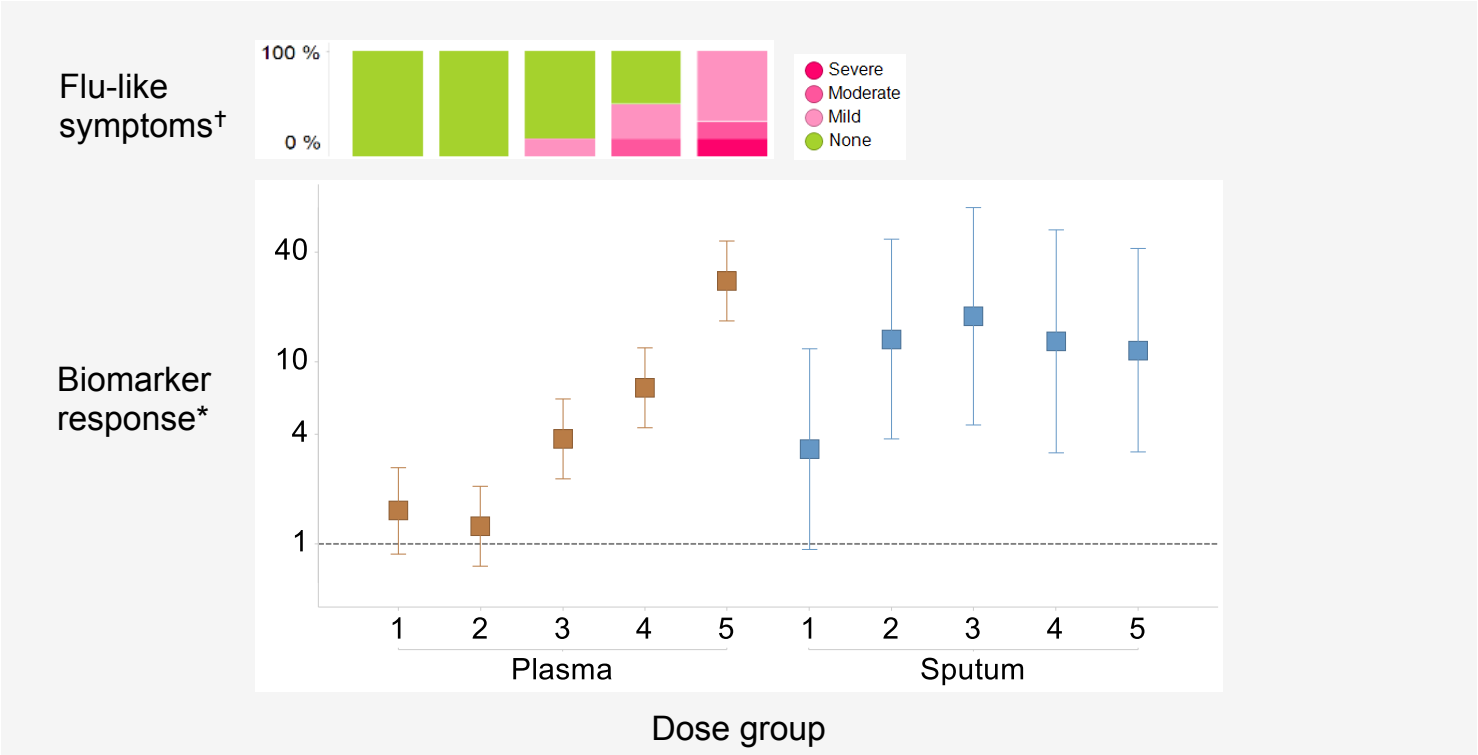
Traditional AZD7594

Exploits water pocket beyond steroid-binding domain

Zero cortisol suppression predicted



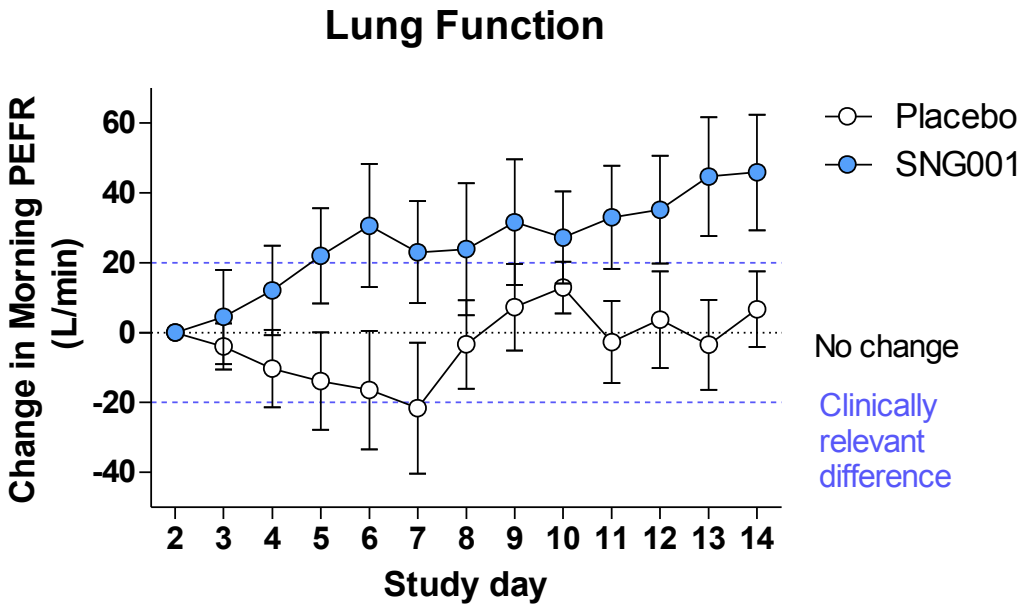
Inhaled TLR9 (AZD1419) in healthy volunteers



*Estimated fold change from baseline versus placebo 24 hr after first dose with 95% confidence interval (ANCOVA)
Subjects reporting one or more incidence of influenza-like symptoms after 4 once-weekly doses

Inhaled IFNβ (AZD9412) may reduce exacerbations on demand in asthma

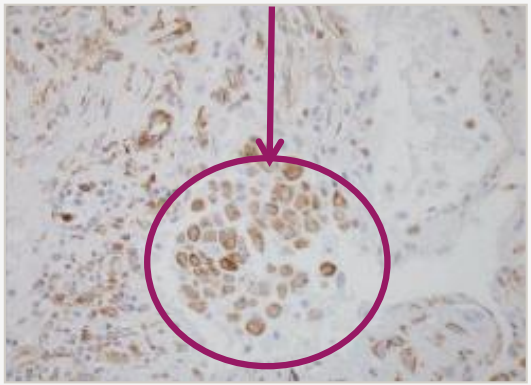
‘Difficult-to-treat’ asthmatics benefit from 14 days of on-demand treatment with AZD9412



Significant (56%) reduction in moderate or severe exacerbations (p=0.028)

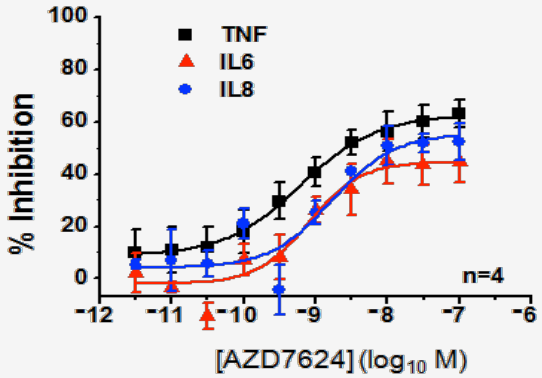
Inhaled p38 inhibitor (AZD7624) could change disease management for steroid-resistant patients with COPD

Phospho p38+ alveolar macrophages in COPD lung

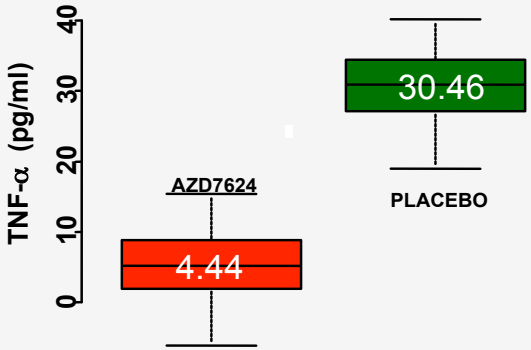


(In-house IHC data)

Inflammatory cytokines in human alveolar macrophages



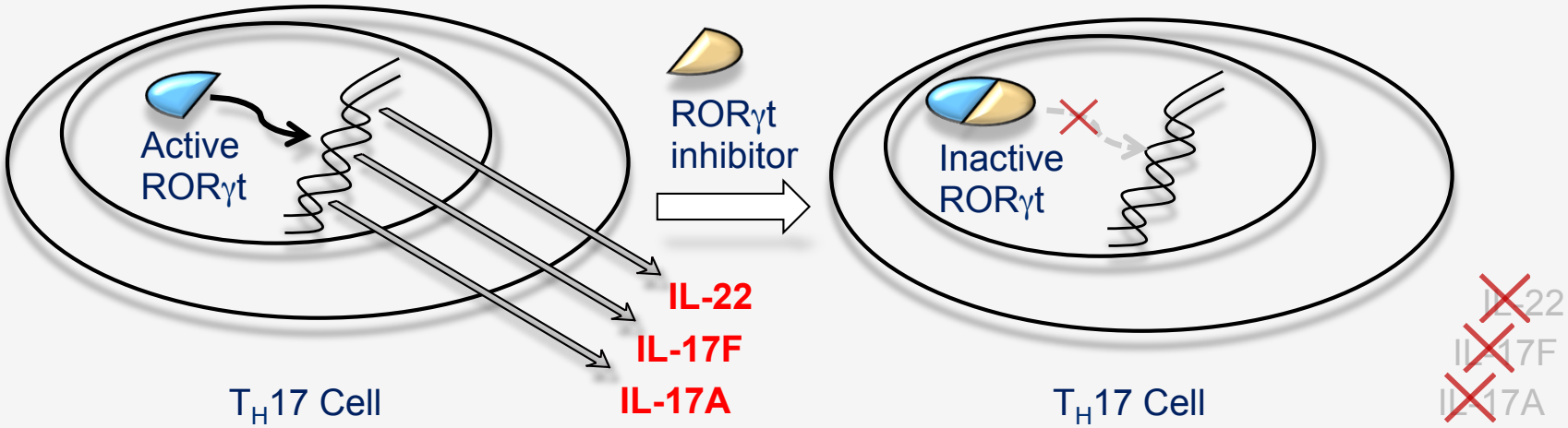
Significant attenuation of LPS-induced TNF-α



Cutting-edge science with leading academics to unlock new treatment possibilities with RORγ

RORγ drives important pathway in inflammatory responses

RORγ inhibitors have the potential to modulate and not just suppress the inflammatory response



Collaboration with ORCA pharmaceuticals and leading academics

- Strengthen our internal program with new RORγ compounds
- Sharing scientific insight

Collaborating with leading academic research groups to shape the future of inhaled, immuno-modulatory treatment

UNIVERSITY OF GOTHENBURG

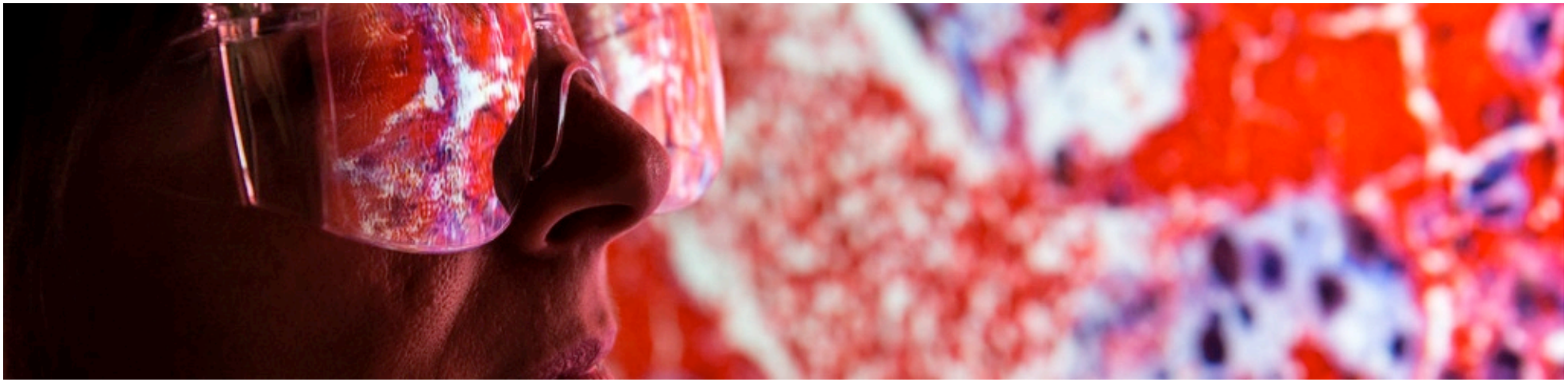
GLAZgoDiscoveryCentre

University of Glasgow AstraZeneca

www.GLAZgoDiscoveryCentre.co.uk 0131 330 6443 OpsManager@GLAZgoDiscoveryCentre.co.uk

AstraZeneca
What science can do

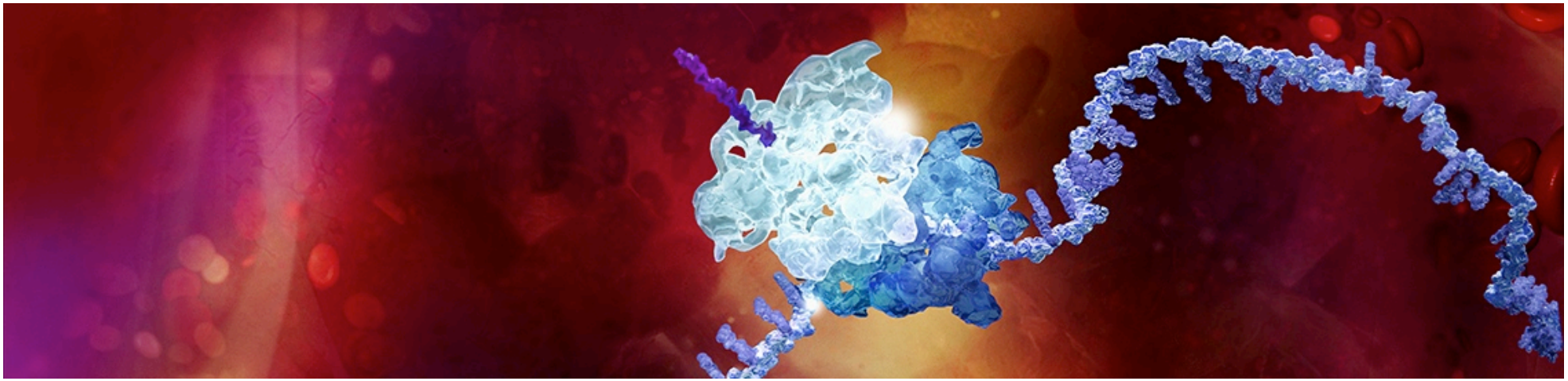
Lab tours



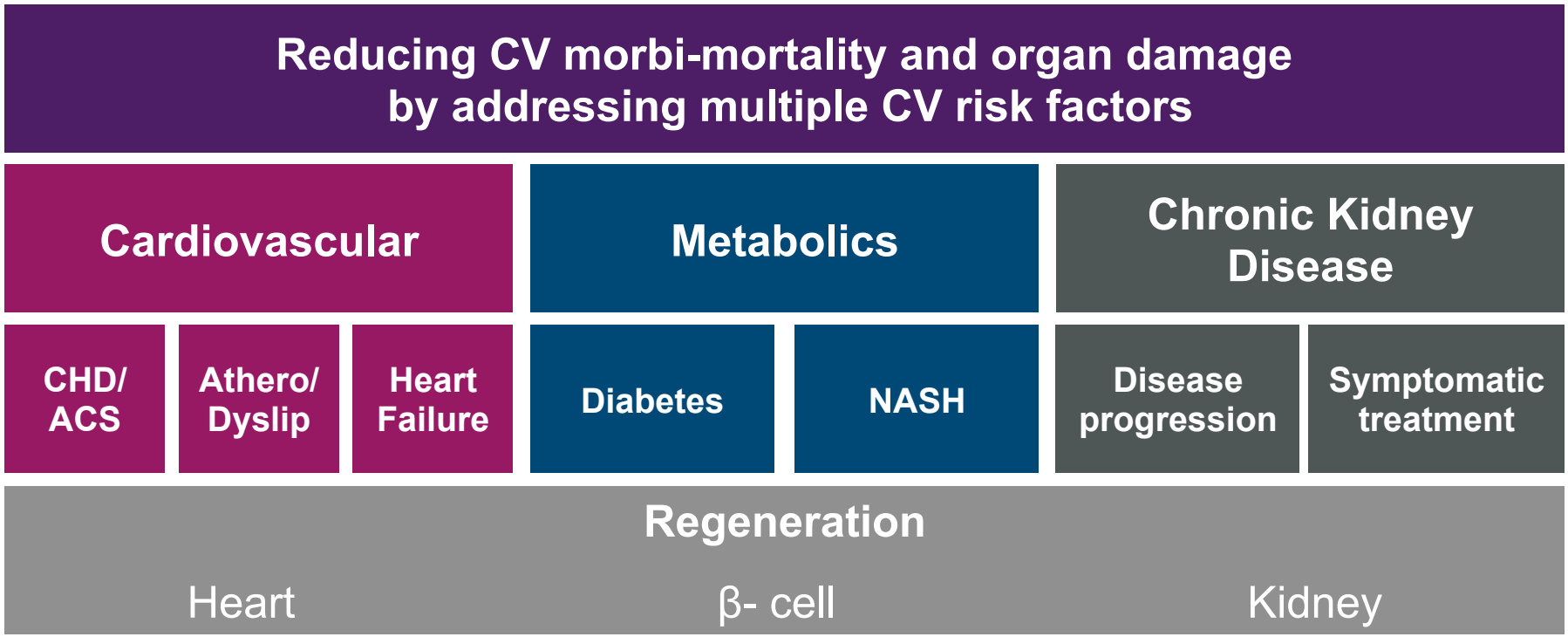
AstraZeneca
What science can do

CVMD Pipeline Update

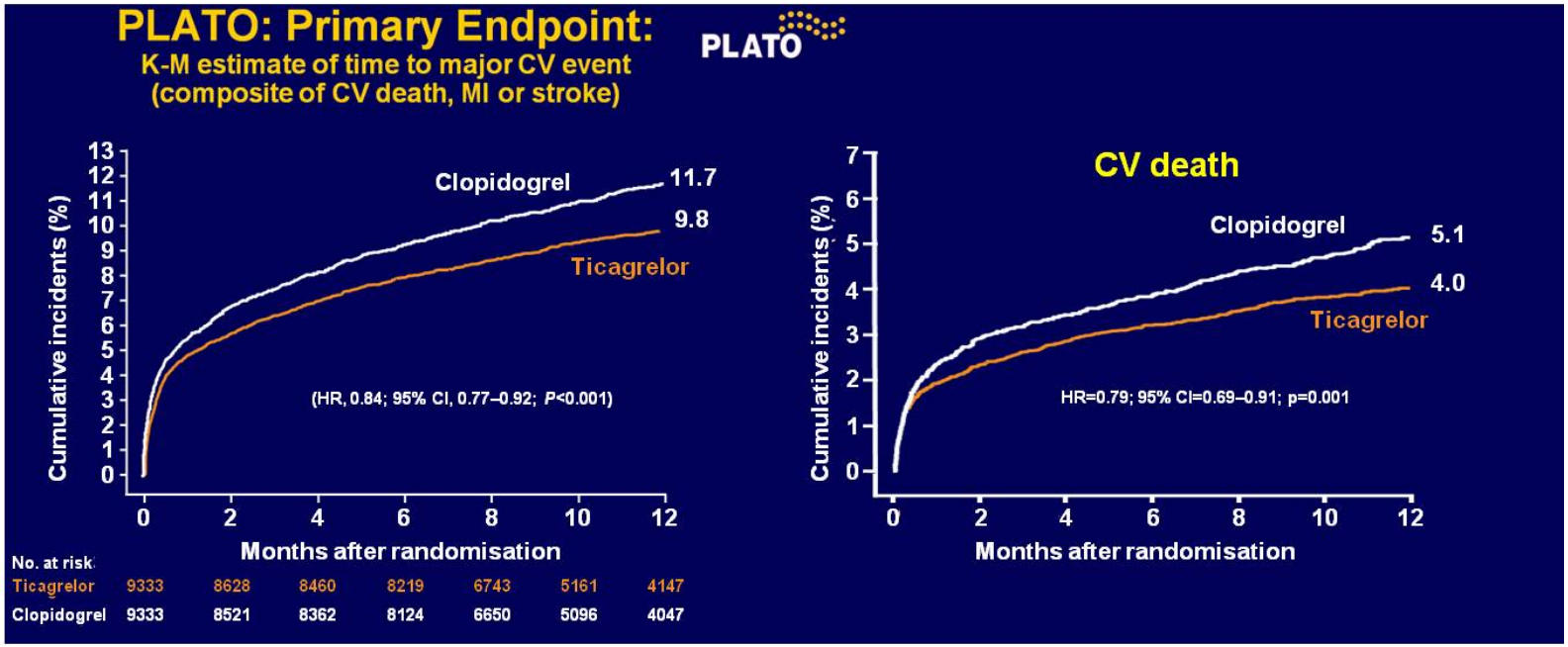
Elisabeth Björk,
VP, Head of Cardiovascular & Metabolic Disease GMD



CVMD strategy built on three pillars



Brilinta: PLATO results displayed unique clinical profile



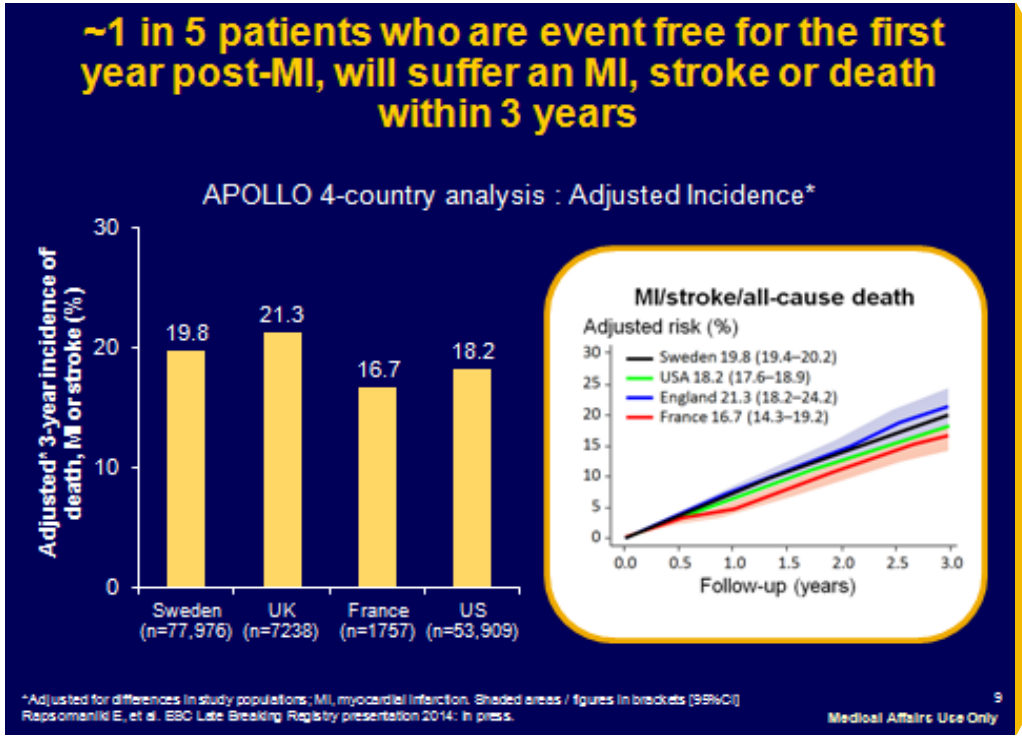
- Continuous benefit for one year
- Mortality benefit
- Potential unique benefit beyond P2Y12 inhibition driven by ENT1

K-M, Kaplan-Meier
Wallentin L, et al. N Engl J Med. 2009;361:1045-1057

Beyond 12 months

Patients remain at a significant risk

APOLLO; late-breaking registry presentation at the 2014 European Society of Cardiology



Patients who are event free in first year after their index event will suffer a **MI, stroke or death in the subsequent three years**

PEGASUS-TIMI 54 study of BRILINTA® / *BRILIQUE*™ meets primary endpoint in both 60mg and 90mg doses

PEGASUS-TIMI 54 study

- Investigated 60mg and 90mg ticagrelor vs. placebo in patients (low-dose aspirin) aged 50 and older with a history of heart attack and one additional CVD risk factor[1]
- Designed to better understand the management of patients more than 12 months after their heart attack, who remain at high risk for major thrombotic events

PEGASUS-TIMI 54 study, epidemiology[2]

Definitions: ACS - Acute Coronary Syndrome; MI - myocardial Infarction; STEMI - ST Segment Elevation myocardial Infarction; NSTEMI - Non-ST Segment Elevation myocardial Infarction; and ASA - Aspirin **Notes:** 1. Bonaca MP, Bhatt DL, Braunwald E, et al. Design and rationale for the Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 PEGASUS-TIMI 54) trial. Am Heart J. 2014;167:437-44. 2. Markets include Australia, China, EU5, Japan, Russia and United States only. **Source:** Kantar Health (2010), GRACE Registry (2007), National Health & Wellness Survey (2013), medical literature, internal data

Outstanding collaboration with TIMI Study Group

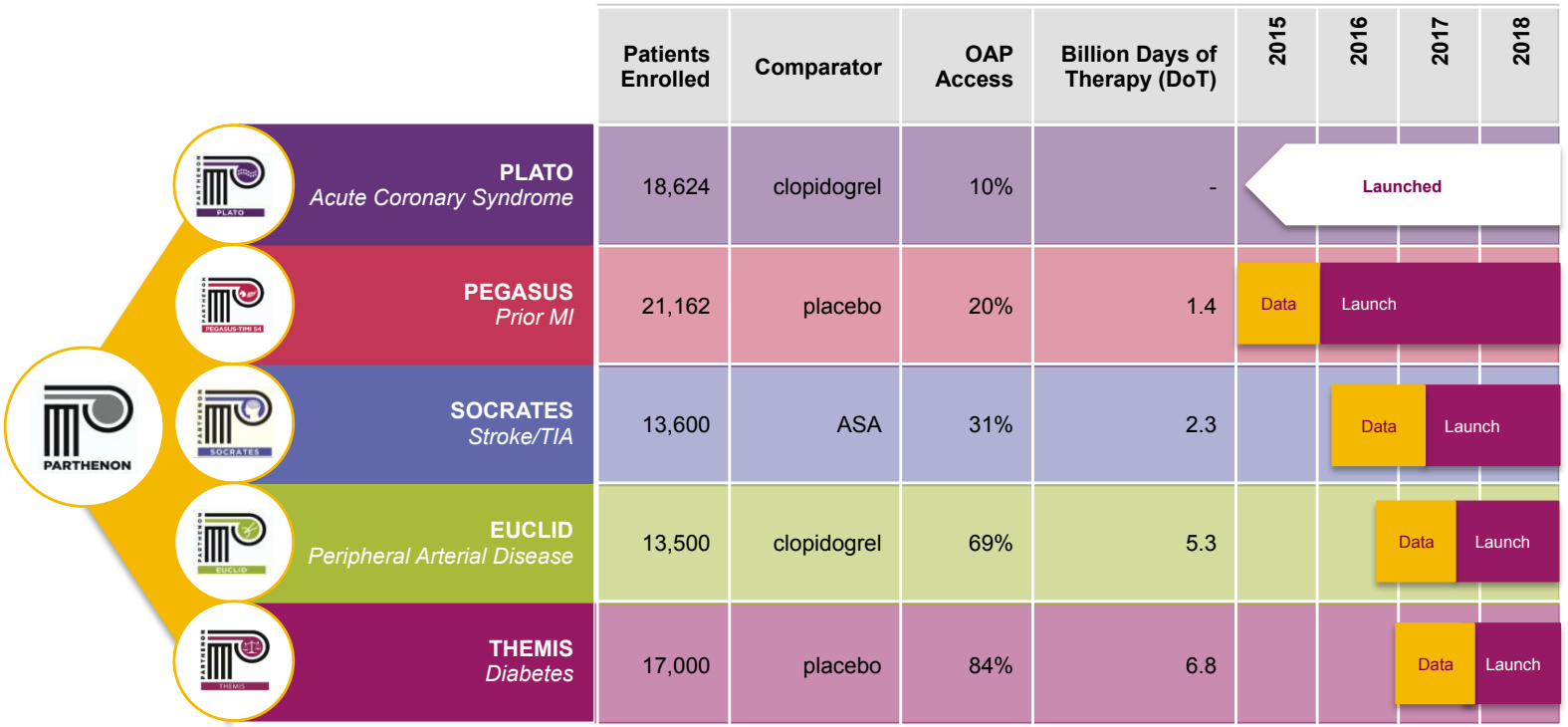
Publication, regulatory, prepare to launch

Study metrics	Publication, regulatory	Towards launch
• 21,000 patients in 31 countries • >210,000 patient visits • <0.1% patients lost to follow-up	• FDA and EMA submissions complete • Parallel presentation and publication ACC/ NEJM[1]	• Regulatory submission • Pre-launch planning • Disease and risk education

1 The New England Journal of Medicine

PARTHENON Programme

Potential for four launches in four years



	Patients Enrolled	Comparator	OAP Access	Billion Days of Therapy (DoT)	2015	2016	2017	2018
PLATO *Acute Coronary Syndrome*	18,624	clopidogrel	10%	-	Launched			
PEGASUS *Prior MI*	21,162	placebo	20%	1.4	Data	Launch		
SOCRATES *Stroke/TIA*	13,600	ASA	31%	2.3		Data	Launch	
EUCLID *Peripheral Arterial Disease*	13,500	clopidogrel	69%	5.3			Data	Launch
THEMIS *Diabetes*	17,000	placebo	84%	6.8			Data	Launch

Key Facts

4 in 4
Number of launches in consecutive years

>4.2x
Increase in access to OAP market volume

>5.5x
Increase in access to billion Days of Therapy (DoT)

SOCRATES - next *Brilinta* study, to read out in H1 2016

AIS = Acute Ischemic Stroke

...a complete blockage of a cerebral artery, leading to more severe and permanent disability and even death

Stratified according to symptoms and disability at presentation using the NIHSS 42-point scale

Minor stroke (NIHSS≤5 = 53% AIS population) eligible for enrolment in SOCRATES

TIA = Transient Ischemic Attack

...a temporary blockage or reduction in cerebral blood flow leading to milder, transient symptoms

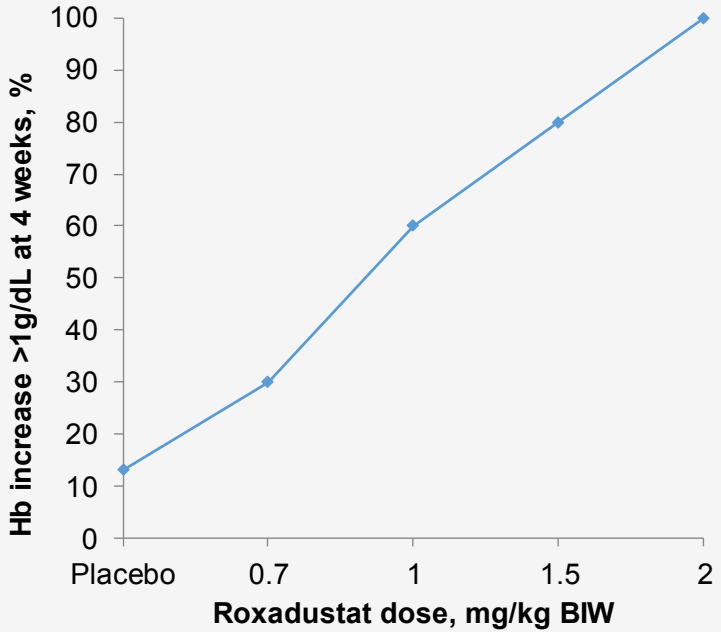
Stratified according to risk level using the ABCD2 9-point scoring system

High-risk TIA (ABCD2≥4 = 77% TIA population) eligible for enrolment in SOCRATES

Roxadustat (CKD): Potential to be first oral erythropoietic anaemia treatment

- Oral HIF-prolyl hydroxylase inhibitor
- Favourable efficacy and safety profile in Phase II
- >7,000 patient Phase III ALPINE programme **designed to demonstrate CV safety** in patients with dialysis and non-dialysis dependent chronic kidney disease (CKD)
- Top-line data post-2016

Hb correction in pre-dialysis CKD patients

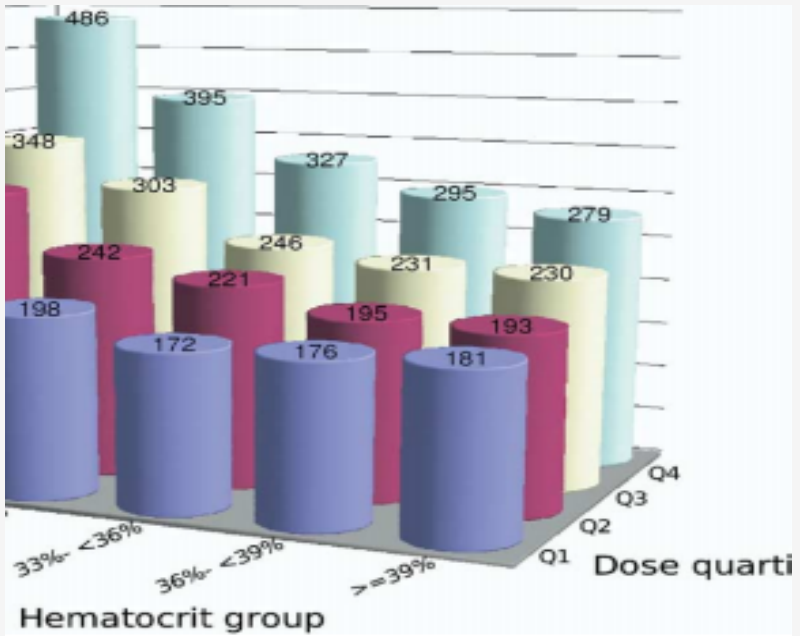


Source: FibroGen Registration Statement

Roxadustat (CKD): Potential for reduced cardiovascular risk vs. rEPO

- Higher doses of rEPO predict mortality regardless of hematocrit
- Mechanism for increased CV risk with rEPO is uncertain, but may involve
  -supra-physiologic EPO levels
  -rapid rate of Hb rise
  -high Hb targets
  -effects on blood pressure
- Phase III programme designed to avoid these concerns through the novel mechanism of action and intermittent dosing

USRDS: Unadjusted 1-year mortality by epoetin dose & hematocrit

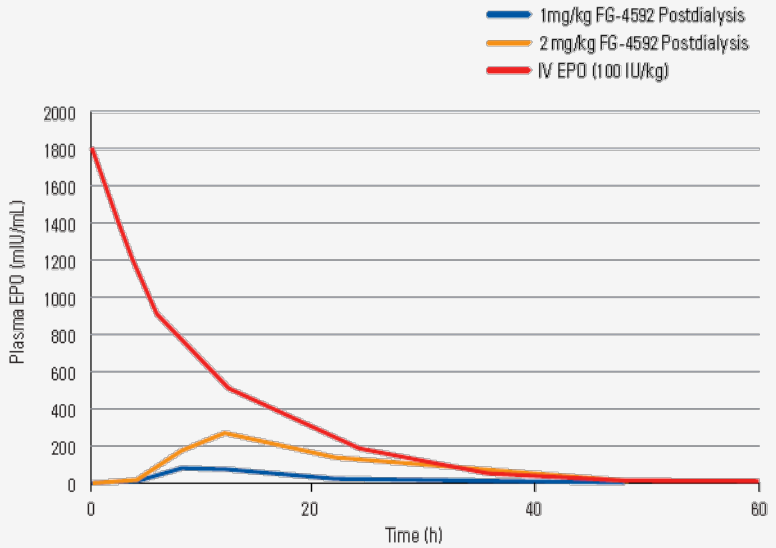


Zhang et al. Am J Kidney Dis 2004;44:866-87

Roxadustat (CKD): Stimulates erythropoiesis similar to the body's normal co-ordinated response to hypoxia

- rEPO infusion produces supra-physiological EPO concentrations, whereas roxadustat induces endogenous EPO concentrations within physiological range
- In addition, roxadustat induces expression of the EPO receptor as well as proteins that promote iron absorption and recycling

Median plasma EPO concentration at two oral doses of roxadustat postdialysis compared with reported EPO levels following IV administration of rhEPO [100 IU/kg]*



Source: FibroGen Registration Statement-

* Data from IV EPO taken from Figure 1 in MacDougall, et al. J Am Soc Nephrol 1999;10(11):2392-95. Provenzano et al. Nat. Kidney Foundation Conf 2011 (Poster #189)

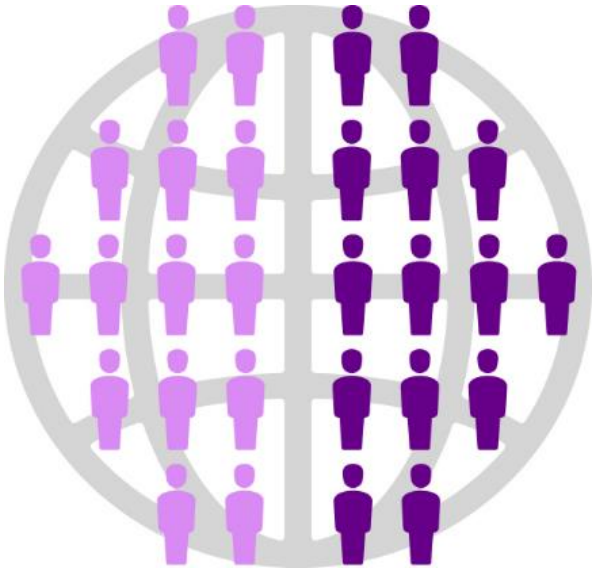
Diabetes: Strategy to transform patient care

Shift treatment paradigm to early combination therapy and accelerate achievement of treatment goals

Develop a science-led life cycle management strategy

Expand into new areas of unmet need, including expansion into Type 1 diabetes with *Forxiga*

The real world picture of glycaemic controls shows…



… 50% of type 2 patients uncontrolled and above the 7% HbA1c goal, supporting the need for more effective treatment options and strategies

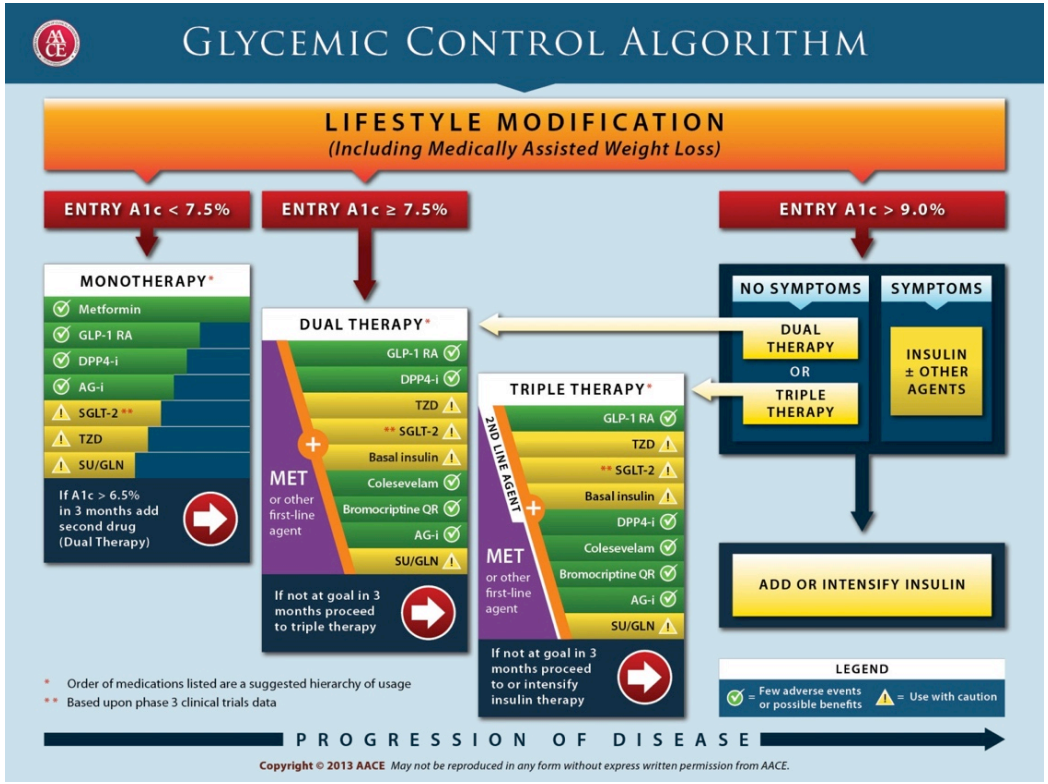
Why ?

- Disease progression
- Modest doses of moderately effective oral agents cautiously added in sequence resulting in…

Clinical inertia

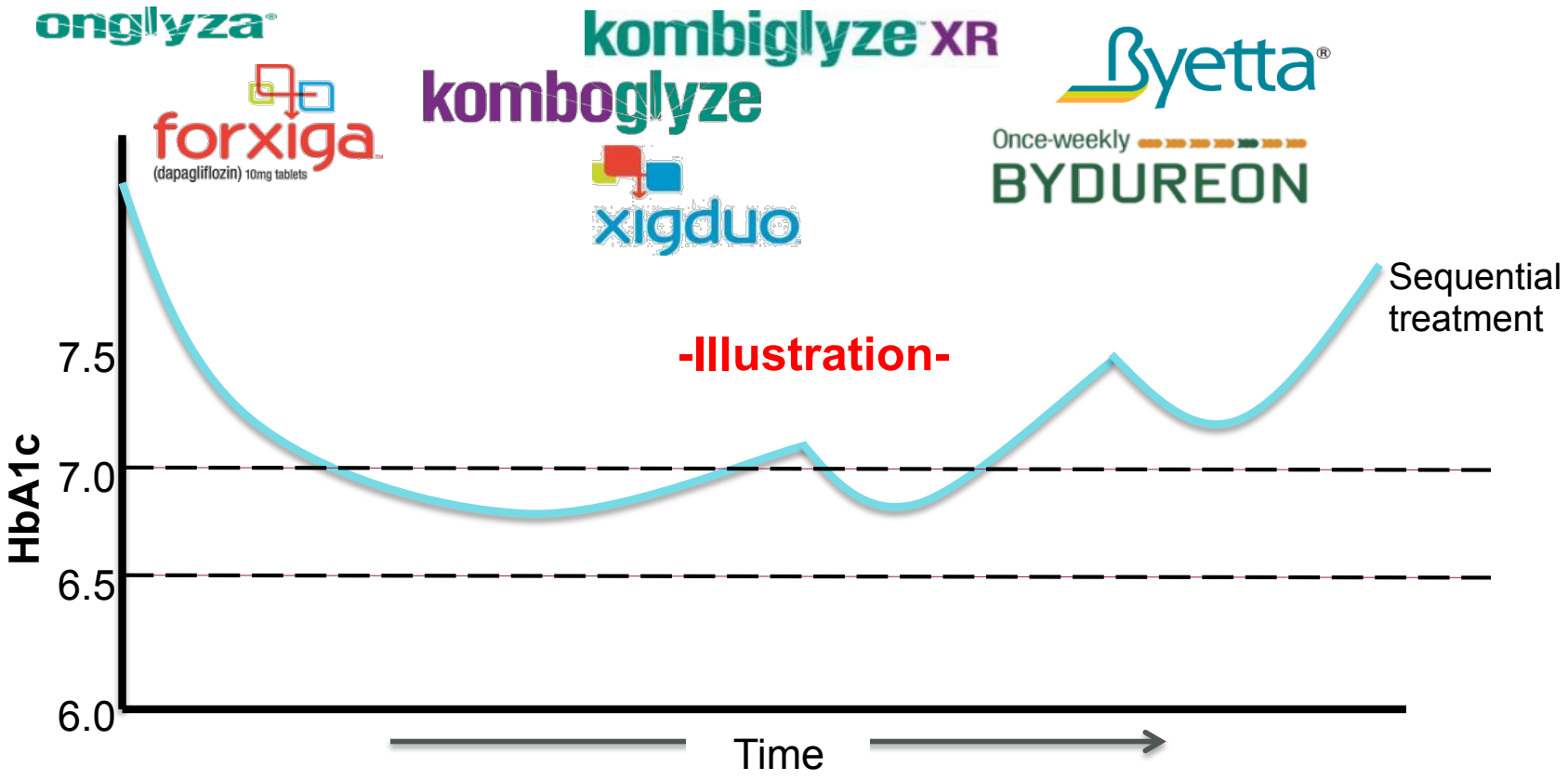
Cook MN, et al. Diabetic Med 2007;24:350-358
Inzucchi SE, et al. Diabetes Care 2015;38:140-149
Khunti K, et al. Diabetes Care 2013;36:3411-3417

New guidelines more aggressive with earlier combinations

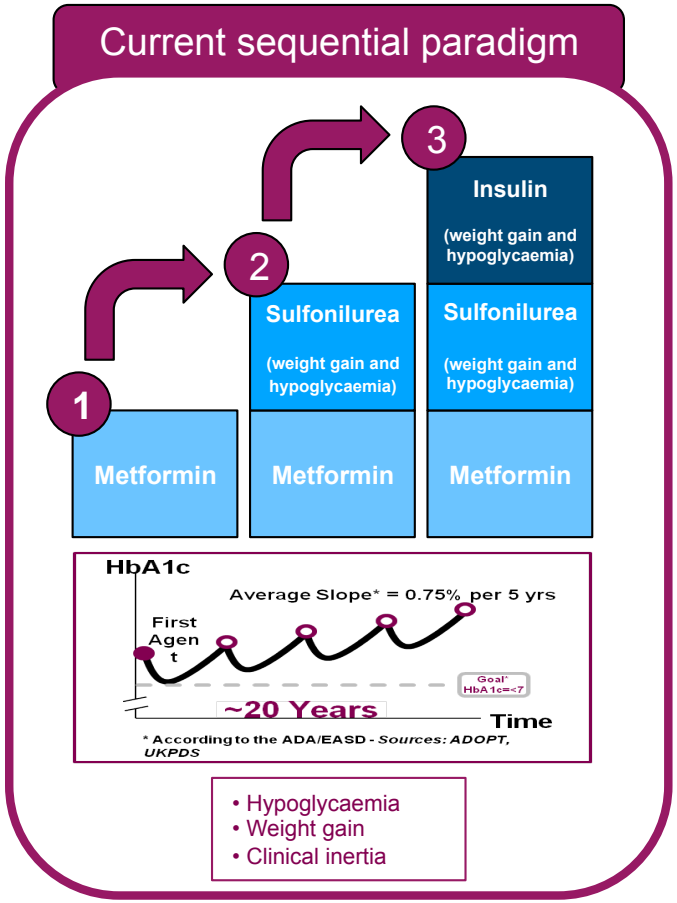


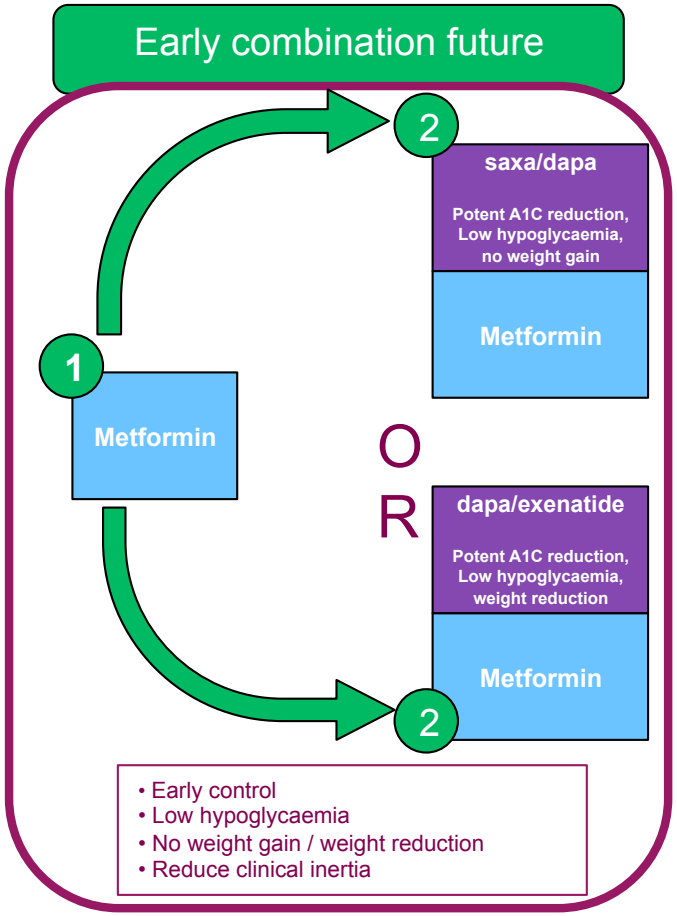
Note: AACE guidelines were published March 2013, SGLT-2 recommendation was based on Ph3 data.

Helping patients along disease progression



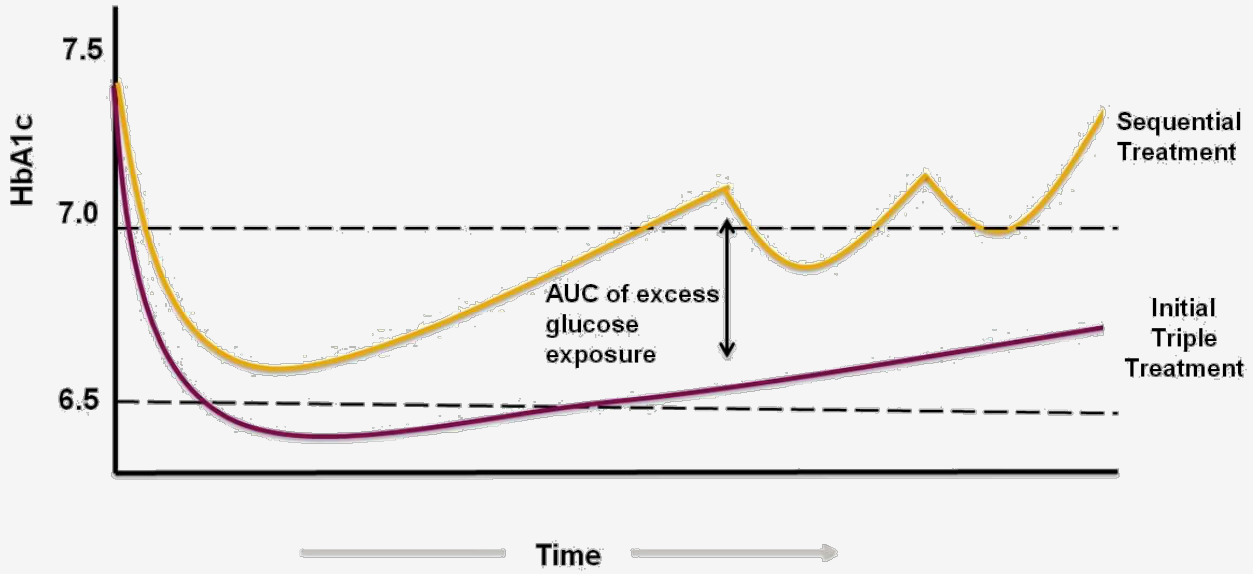
AstraZeneca's portfolio: Makes early combination possible





Potential of early combinations to slow disease progression

Illustrative



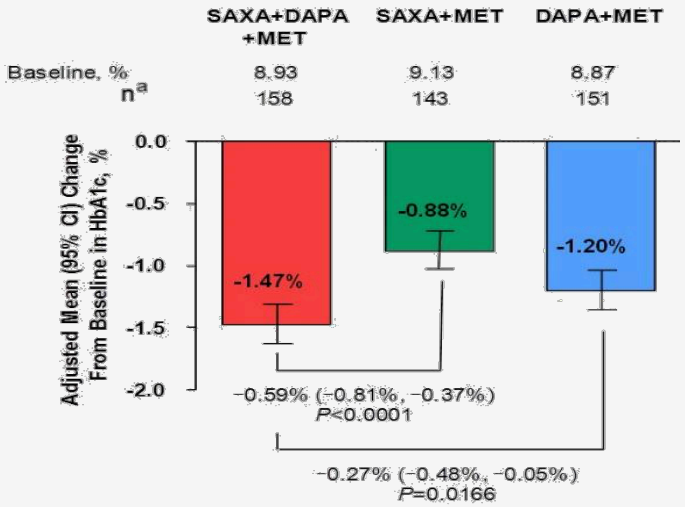
Oral combinations: Saxa/dapa & saxa/dapa/metformin

Portfolio well-positioned to enable early combination treatment

- Saxa/dapa added to metformin in poorly controlled T2DM
  - HbA1c reduction 1.5%
  - HbA1c <7% in 41% of patients
- Regulatory submission for saxa/dapa FDC under review (US)
- Saxa/dapa/met FDC development ongoing. Regulatory submission expected post 2016

Significant reduction in HbA1c with low rates of hypoglycemia

Adjusted mean change from baseline in HbA1c at 24 weeks



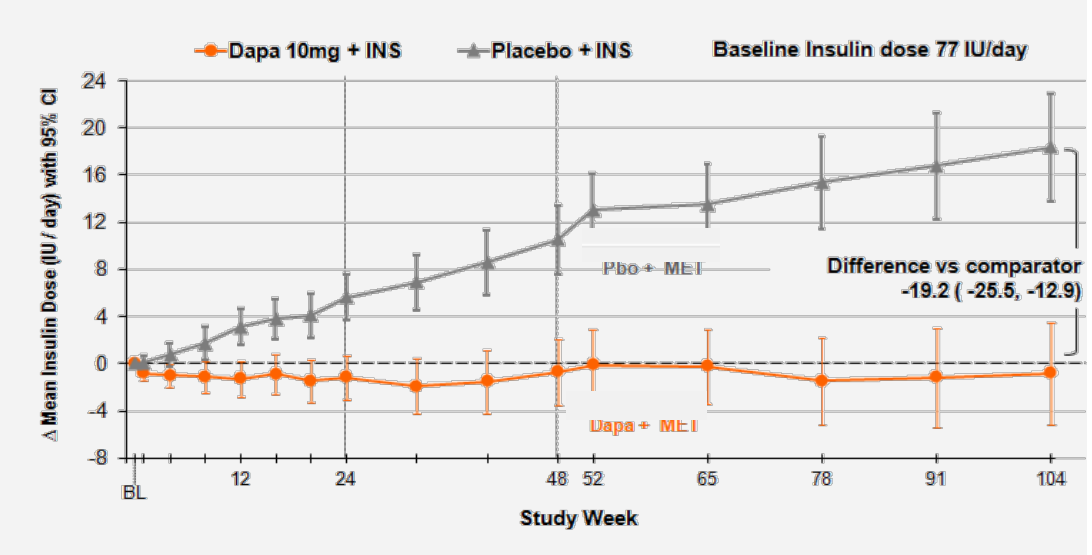
[a] Number of randomized patients with non-missing baseline values and Week 24 values.

CI, confidence interval.

Rosenstock J, Hansen L, Zee P, Li Y, Cook W, Hirshberg B, Iqbal N. Dual Add-On Therapy in Poorly Controlled Type 2 Diabetes on Metformin: Randomized Double-Blind Trial of Saxagliptin+Dapagliflozin vs Saxagliptin and Dapagliflozin Alone. 127-LB, American Diabetes Association, 2014.

Forxiga / Xigduo:
Insulin doses remained stable over two years

- Dapagliflozin showed sustained reductions in HbA1c in when used in combination with insulin
- Patients on dapa +insulin lost weight -3kg vs insulin alone
- Insulin doses remained stable over the study period

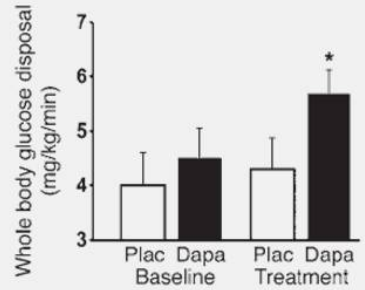


Forxiga + insulin maintained HbA1c and induced weight loss vs. insulin alone

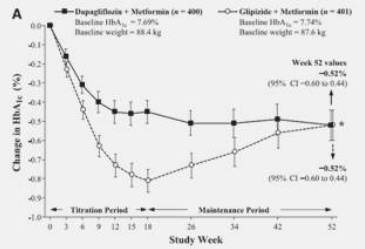
Ann Intern Med. 2012;156(6):405-415.
Study 006 Clinical Study Report, Figure4, Table 11.2.6.1.1

Visualising diabetes impact via differentiated technology

Functional data



Source: Merovci et.al JCI 2014



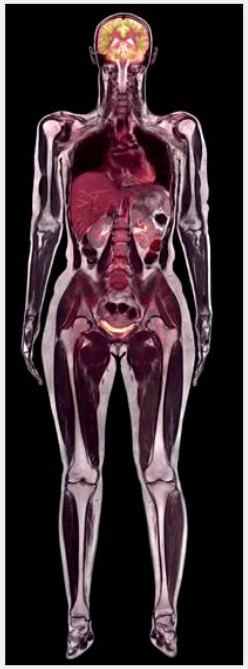
Source: Nauck et.al Diabetes Care 2011

Glucose disposal and HbA1c

Body composition and ectopic lipids

Automated body composition analysis (DAPA-12)

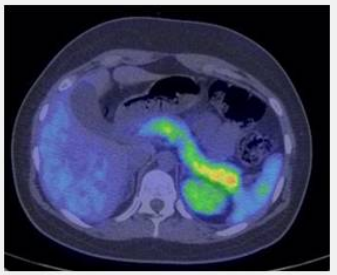
Tissue-specific insulin sensitivity



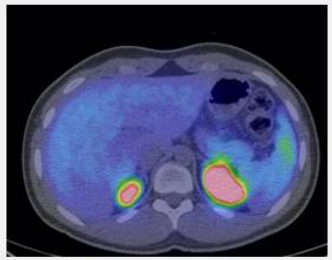
FDG (fluor-dioxyglucose) uptake during insulin clamp

Beta cell mass

Healthy control

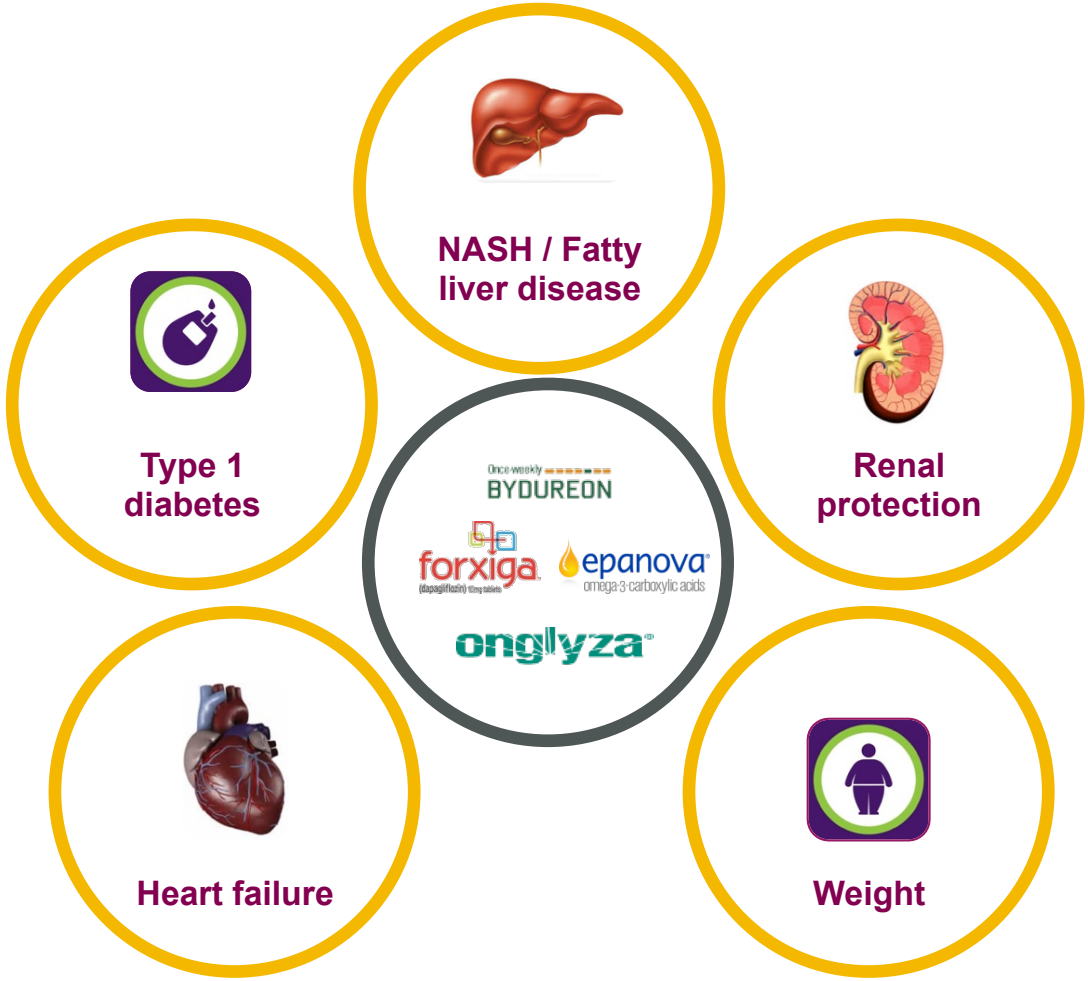


T1D patient

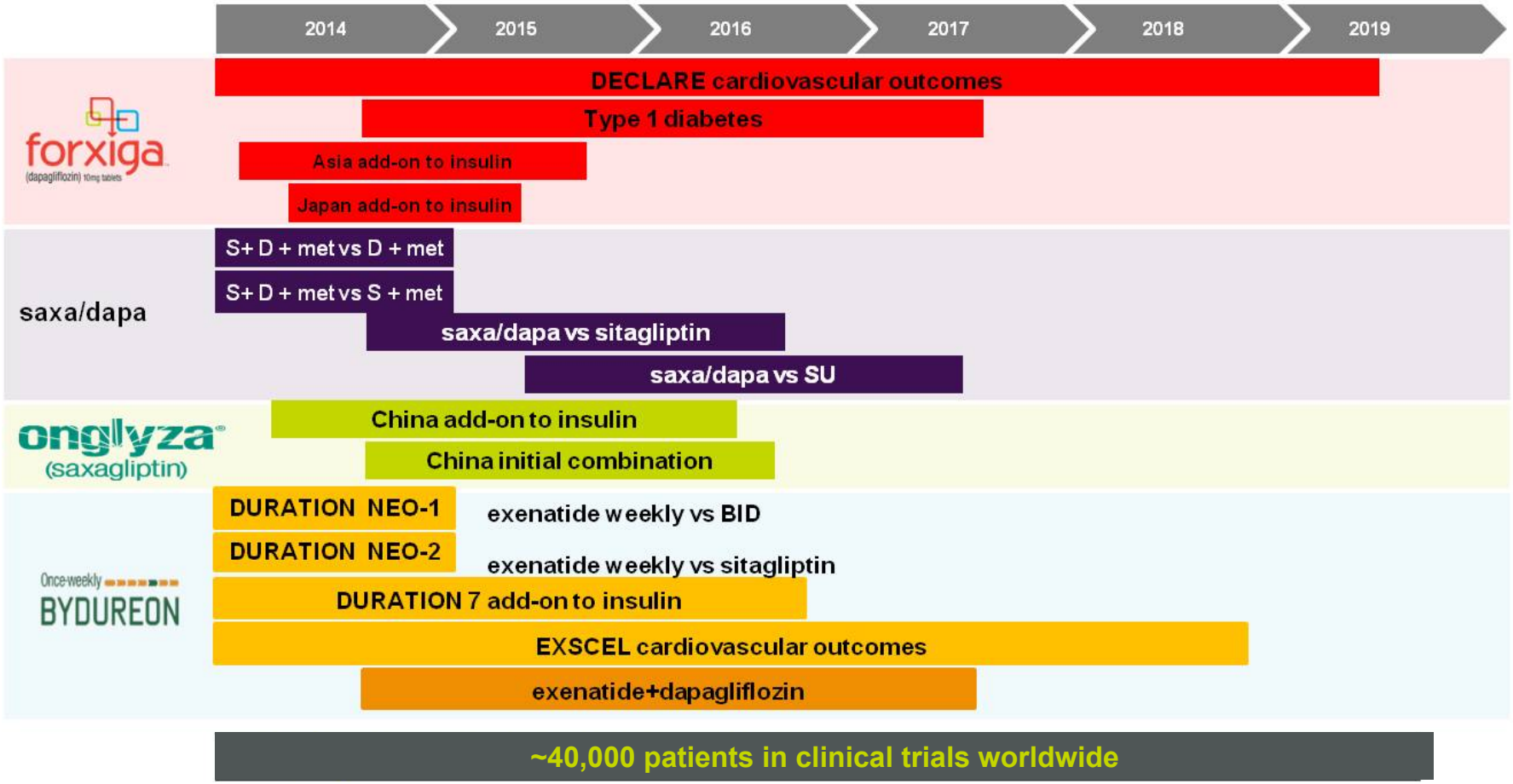


^{11}C-5-HTP or ^{68}Ga-Exendin-4

Science-driven innovation into new areas of unmet need



Diabetes: R&D commitment



Summary

Strategy of reducing morbidity, mortality and organ damage

Transform atherosclerosis through *Brilinta* PARTHENON trials

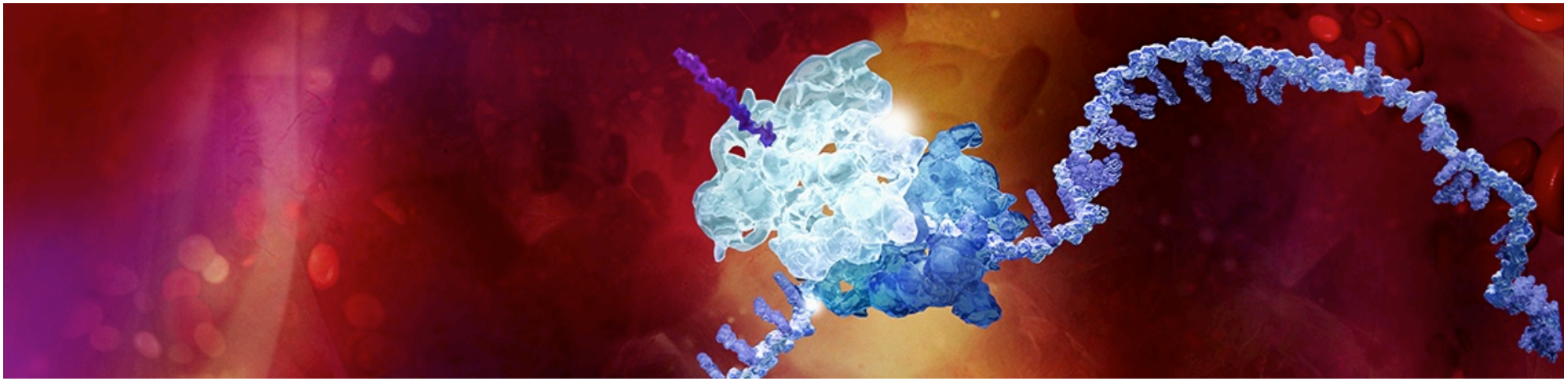
Opportunity to change the lives of CKD patients

Leveraging Diabetes portfolio - addressing unmet need through early combination therapy and expansion into new populations

AstraZeneca
What science can do

What Science Can Do

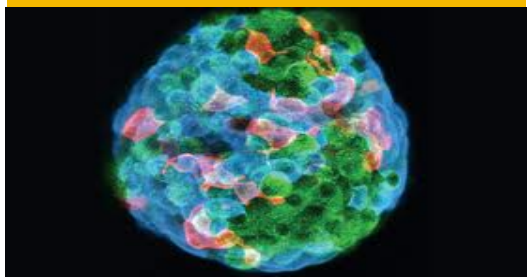
Marcus Schindler, PhD
VP, Head of Cardiovascular & Metabolic Disease iMed



3 strategic research areas in CVMD Innovative Medicines

1 Heart failure

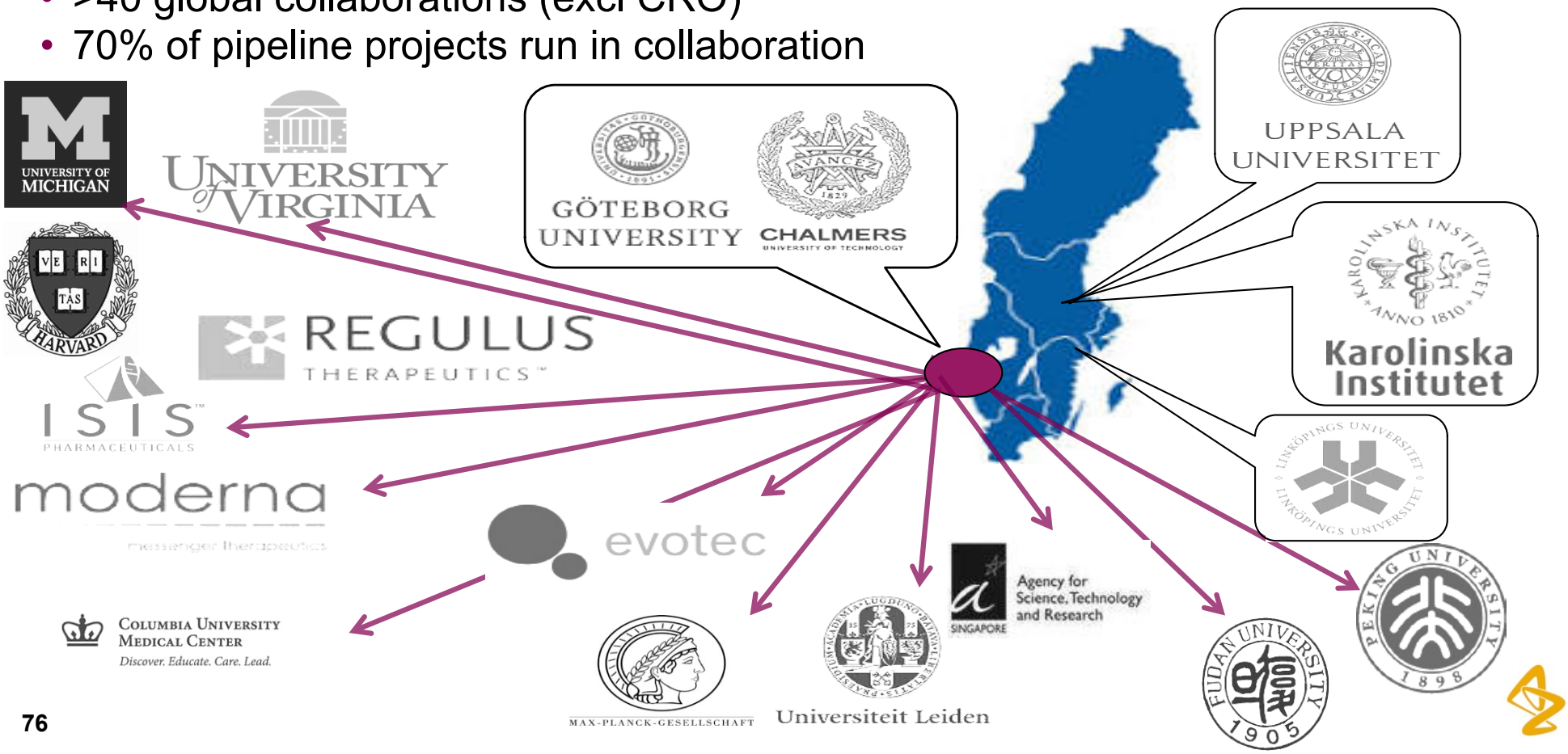
2 Diabetes



3 Chronic kidney disease

Redefining pharma/academia collaborations

- >40 global collaborations (excl CRO)
- 70% of pipeline projects run in collaboration



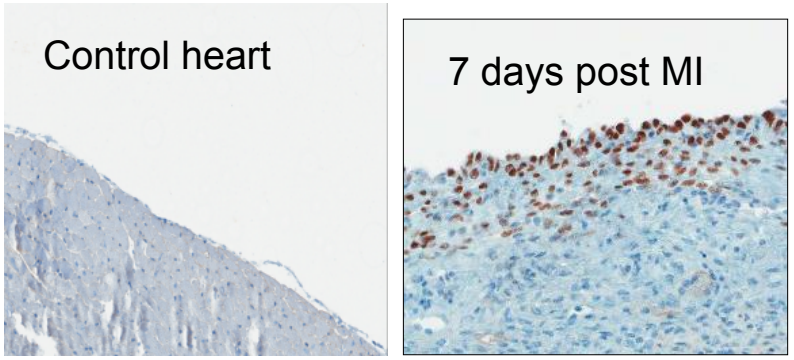
Heart Failure Strategy

To identify and develop small or large molecules that enhance endogenous regenerative capacity of the heart for the treatment of post-MI cardiac dysfunction and heart failure by

- **Activating resident stem cells in the heart: Epicardial progenitor cells or Cardiac stem cells**
- **Reprogramming of cardiac fibroblasts into cardiomyocytes or cardiac stem cells**
- **Proliferation of existing cardiomyocytes and new vessel formation**
- **Improve function of dysfunctional cardiomyocytes and blood vessels**

EPDCs activation post-MI

Wt-1staining

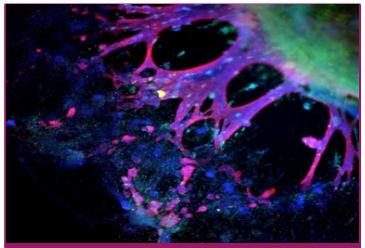


Our Partnerships to deliver HF strategy

Understanding heart failure patient populations

SciLifeLab

University of Virginia



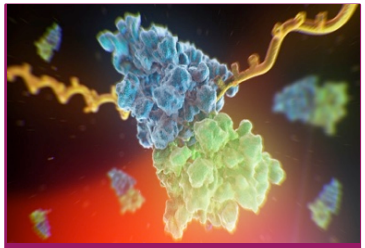
Access to human stem cells & iPS derived cells for TV and phenotypic screening

Cellular Dynamics international

Universiteit Leiden

Sahlgrenska akademin
Vid Göteborgs universitet

SIBS



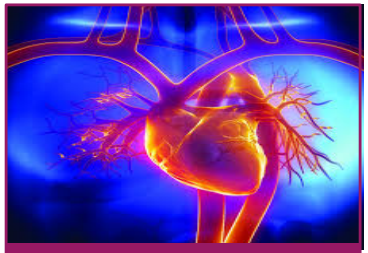
Access to modRNA expertise for local tissue protein production

moderna
messenger therapeutics

Karolinska Institutet

Access to novel expertise in drug targeting

University of Virginia



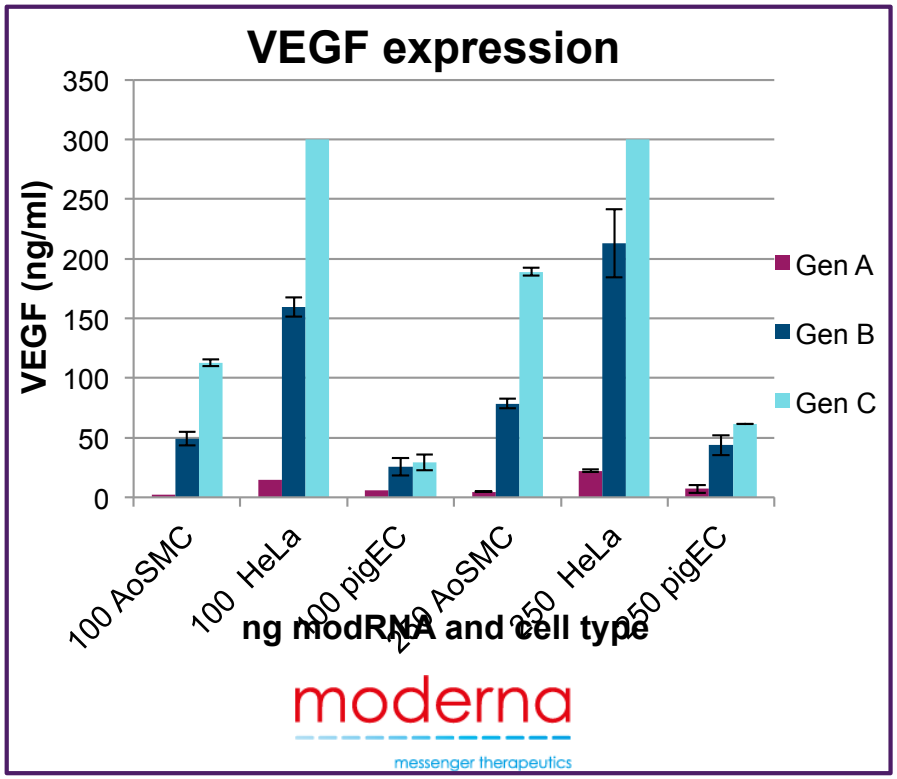
Established translational imaging platform

University of Virginia

Sahlgrenska Universitetssjukhuset

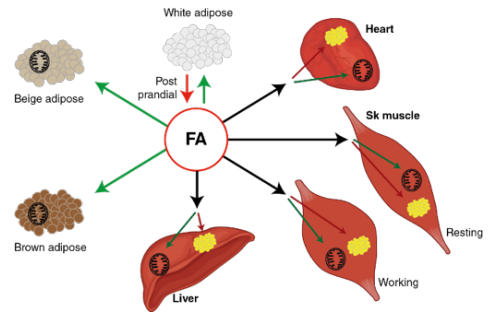
Exclusive agreement with Moderna to harness pioneering messenger RNA therapeutics technology

- Entirely new modality for producing proteins using modified mRNA
  - Exclusivity in CVMD and selected targets in Oncology
- Five-year collaboration – flow of up to 40 targets
- Ability to generate intracellular, transmembrane and secreted proteins in situ
  - Synthetic molecules
  - "Right" tissue for expression ensures correct post-translational modification



Stopping diabetes from progressing remains an unmet medical need despite SoC

Route 1: Improving insulin sensitivity is key



Partitioning fatty acids into the right tissues: white and brown fat for storage and oxidation

Novel target identification and validation platforms:

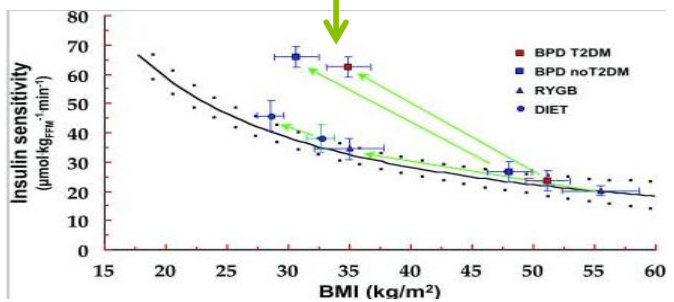
- Phenotypic screens in human adipocytes
- Adipose targeting
- Assessment of whole body and tissue specific glucose, fatty acid and triglyceride metabolism

Perelman School of Medicine University of Pennsylvania

Sahlgrenska Academy University of Gothenburg

University of Virginia

Insulin sensitivity beyond normal levels after BPD



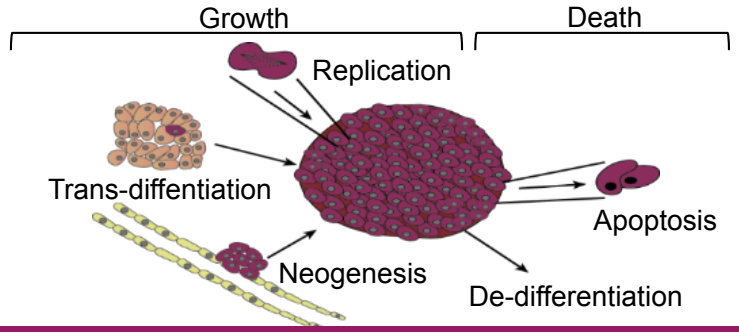
Factors regulating differences in insulin sensitivity in obese subjects pre-post bariatric surgery.

Target identification in patients

- Biliopancreatic diversion in obese patients
- Proteomics

Università Cattolica del Sacro Cuore

Route 2: Improve functional β-cell mass



Increasing β-cell mass : address multiple mechanisms with strong emphasis on human translation

Novel target identification and validation:

- Phenotypic screens of human β-cells
- Human islet transplantation models
- Beta-cell targeting
- Gut insulin production

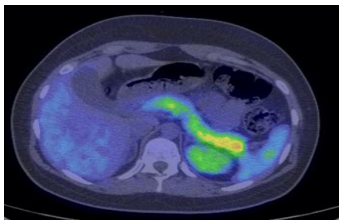
Columbia University Medical Center
Discover. Educate. Care. Lead.

Universitas Osloensis MDCCCXI

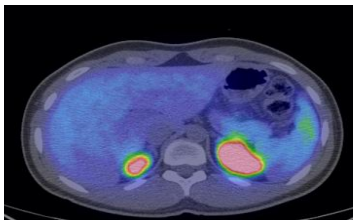
Uppsala Universitet

University of Virginia

Healthy Control



T1D Subject



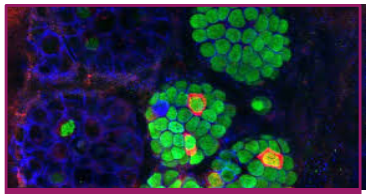
β-cell mass imaging : "Imagine" to monitor decline and restoration

Direct β-cell measurements in man

- PET based imaging in humans
- β-cell specific probe development

Uppsala Universitet

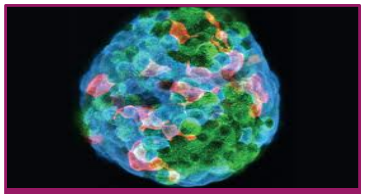
Partnerships to help deliver diabetes therapies



Generation of insulin producing cells in the gut

Columbia University

ISIS Pharmaceuticals



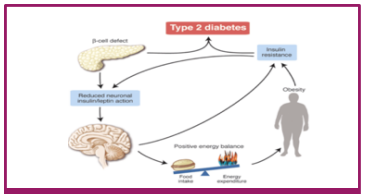
Preservation of pancreatic β-cells

Uppsala Universitet

University of Virginia

Joslin Diabetes Center

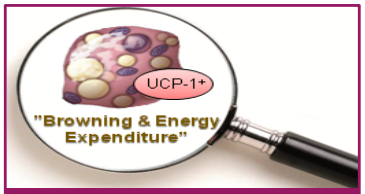
moderna



Body weight reduction and insulin sensitisation by appetite control

University of Eastern Finland

University of Cambridge



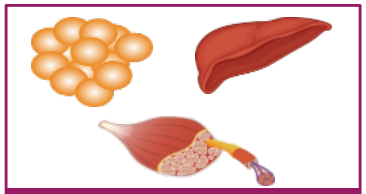
White Brown and Beige fat

Sahlgrenska Academy
University of Gothenburg

moderna

University of Virginia

Perelman School of Medicine
University of Pennsylvania



Insulin sensitizers

REGULUS THERAPEUTICS

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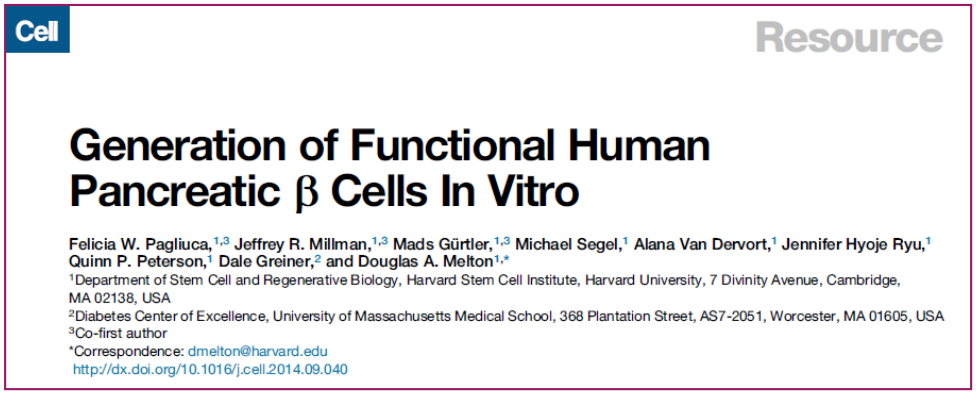
Next generation human beta cell lines



Cell

Resource

Generation of Functional Human Pancreatic β Cells In Vitro

Felicia W. Pagliuca,[1,3] Jeffrey R. Millman,[1,3] Mads Gürtler,[1,3] Michael Segel,[1] Alana Van Dervort,[1] Jennifer Hyoje Ryu,[1] Quinn P. Peterson,[1] Dale Greiner,[2] and Douglas A. Melton[1,*]

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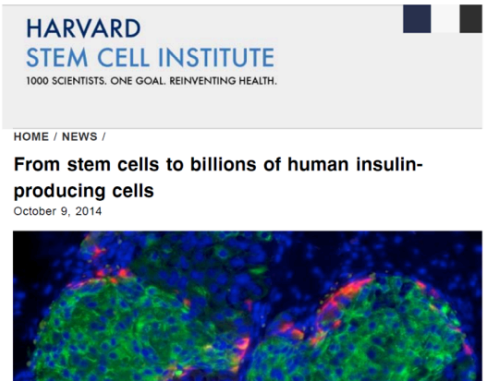
http://dx.doi.org/10.1016/j.cell.2014.09.040

Cell. 2014;159:428-439



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From stem cells to billions of human insulin-producing cells

October 9, 2014

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AstraZeneca Announces Five-Year Collaboration with HSCI

April 3, 2015
Wednesday, 25 March 2015

AstraZeneca today announced that it has entered into a five-year research collaboration with the Harvard Stem Cell Institute (HSCI) to adapt a technique that creates human beta cells from stem cells for use in screens of AstraZeneca's compound library in the search for new treatments for diabetes. The collaboration also aims to better understand how the function of beta cells declines in diabetes and research findings will be made available to the broader scientific community through peer-reviewed publications.

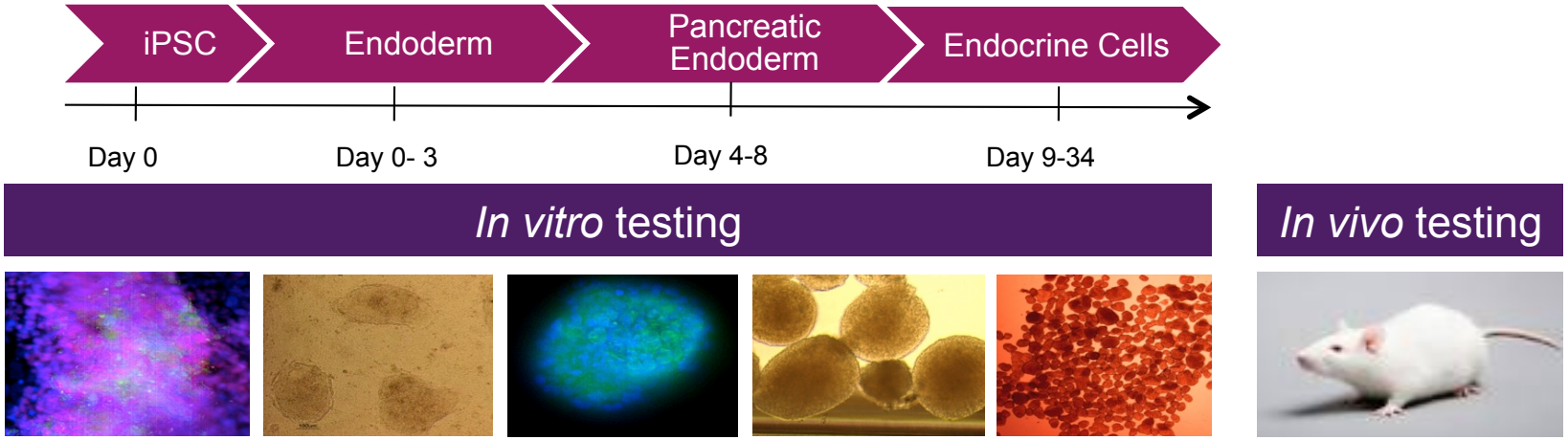
How this collaboration enables leading science

Very limited supply of human islet cells from organ donors for HTV, hypothesis generation, etc

No existing human (or rodent) cell models to study the role of α- and δ-cells in diabetes

No existing models to study human (or rodent) β-cell dedifferentiation

No existing human islet cell models to study mechanisms with gene editing



(Melton Lab at Harvard US.
Pagliuca, F.W. et al 2014)

Our vision: “Treatment modalities for all targets”

Messenger RNA

- Harnessing cutting edge mRNA technology to enable the body to produce its own healing proteins.
- Moderna collaboration provides access to groundbreaking chemistry enabling mRNA to elude the body’s innate immune response – and be translated into active, native protein with therapeutic effects.

moderna
messenger therapeutics

Micro RNA

- More than 500 microRNAs identified in the human genome - over one-third of human genes are believed to be regulated by microRNAs.
- Collaboration with Regulus enables AZ scientists to explore how microRNAs can be harnessed to effectively regulate disease pathways and produce therapeutically beneficial effects.

REGULUS
THERAPEUTICS™

Antisense oligonucleotides

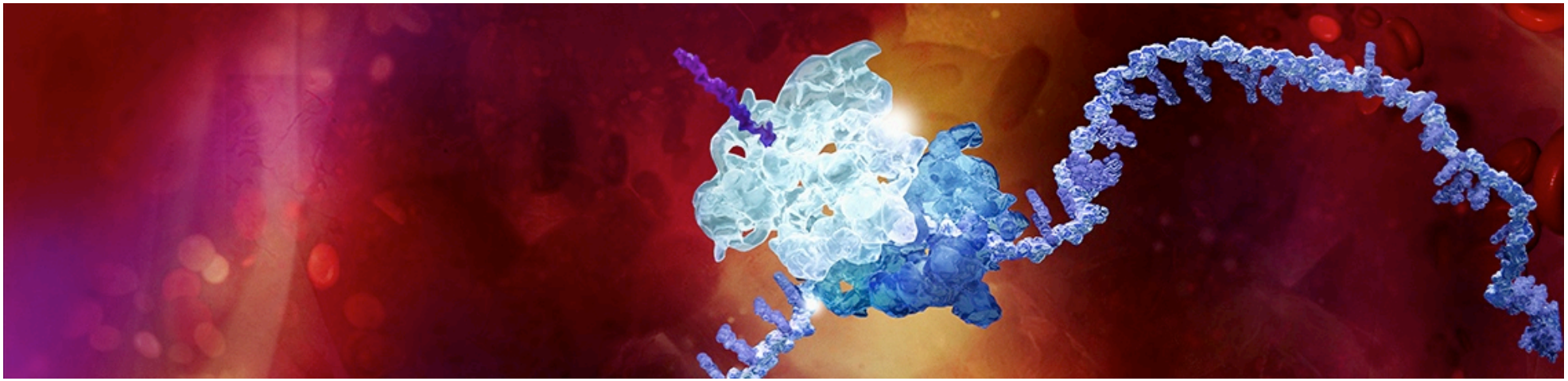
- Antisense oligonucleotides both knock down specific target mRNA and modulate microRNA regulation in tissues throughout the body.
- Strategic alliance with Isis Pharmaceuticals will accelerate the discovery and development of novel generation antisense therapeutics against five cancer targets and CVMD target.

ISIS™
PHARMACEUTICALS

What science can do

AstraZeneca
What science can do

Q&A



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