

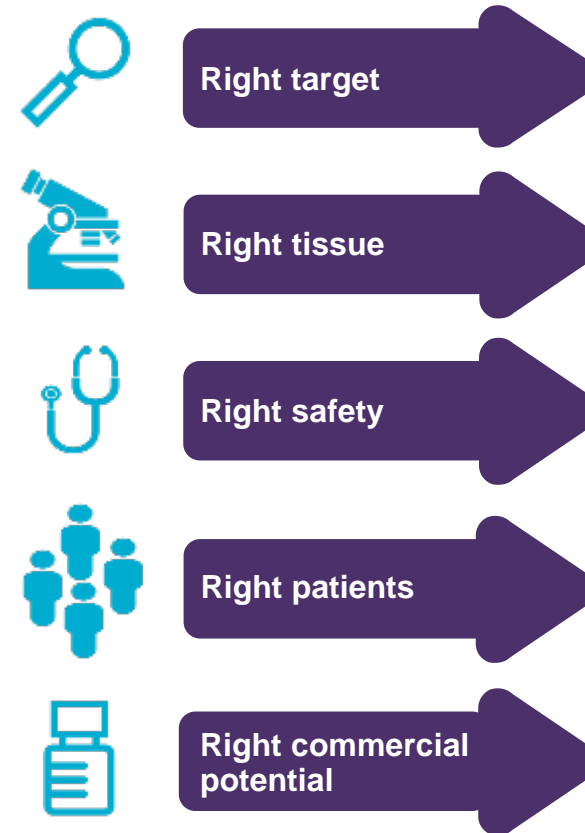


Innovative Medicines & Early Development

Delivering the next wave of scientific innovation

Mene Pangalos, Executive Vice President, Innovative Medicines

AstraZeneca is a place where science thrives



AstraZeneca continues 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



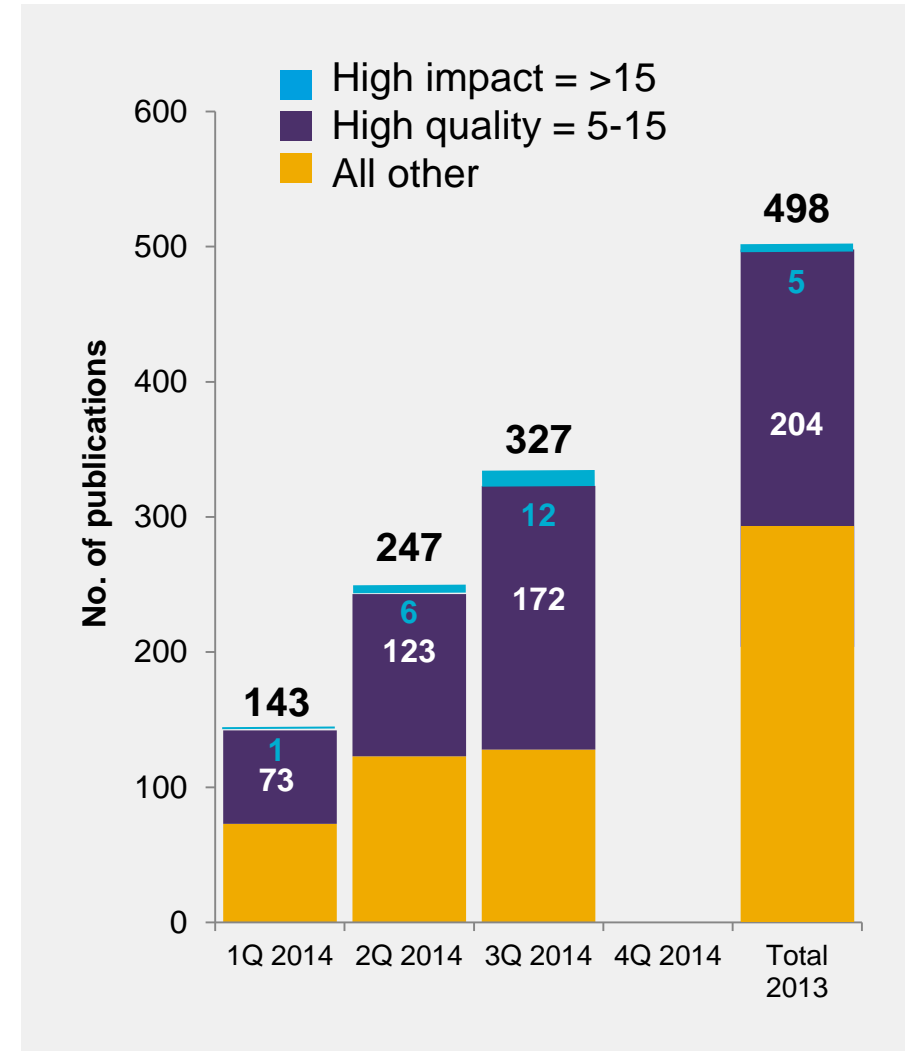
Outi Vaarala
Translational Science
Previously Helsinki University
206 publications including NEJM, Lancet, Diabetes



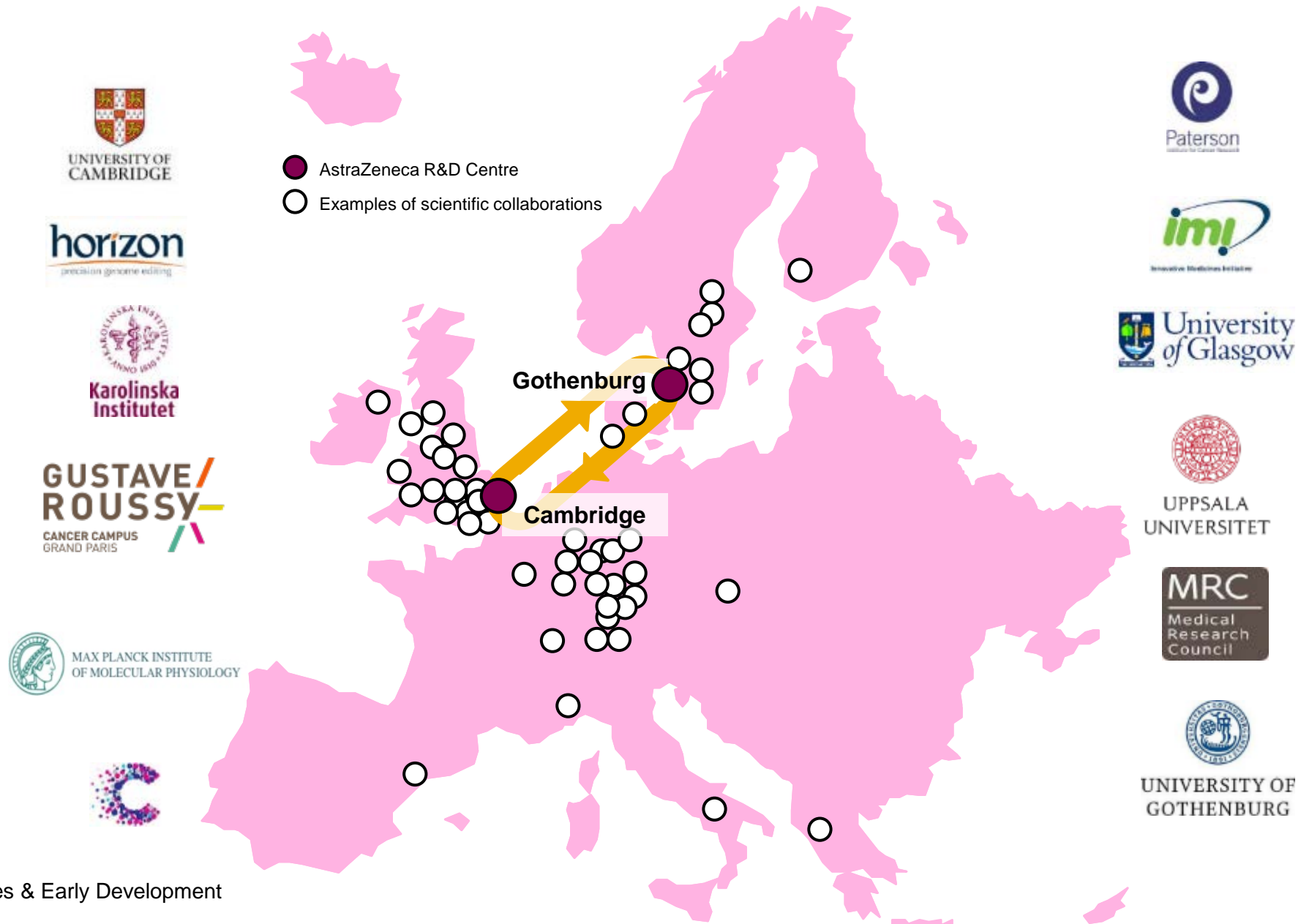
James Matcham
Biometrics
Previously Amgen

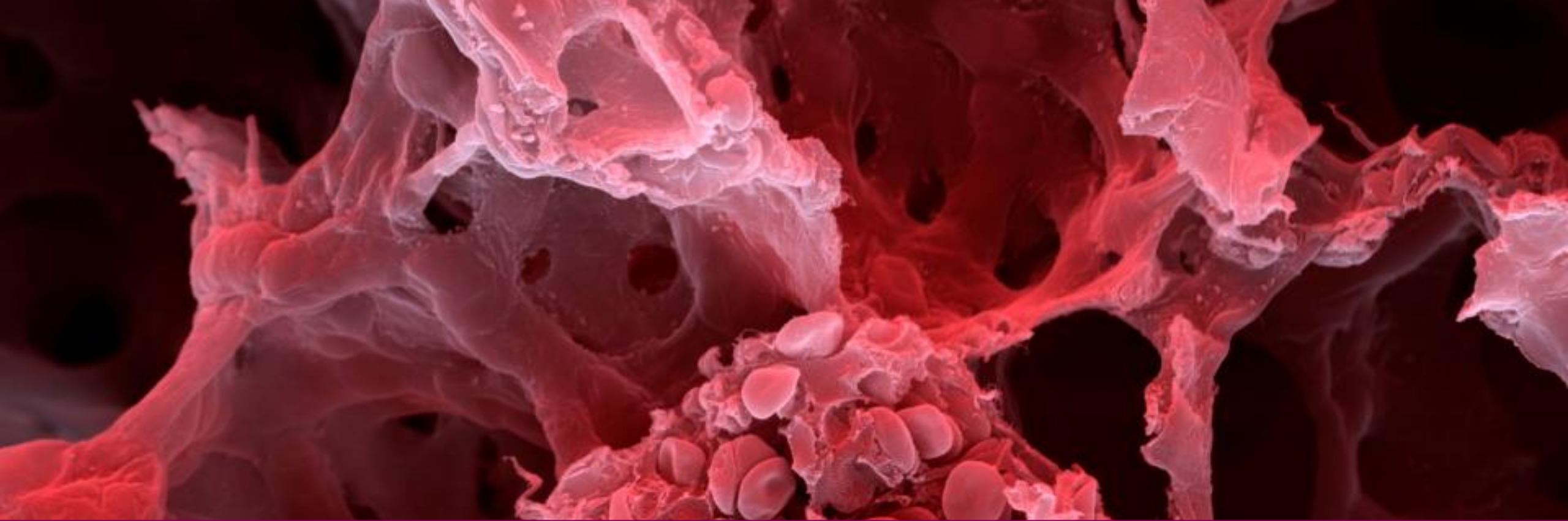


Strengthening scientific reputation through a focus on high quality publications



Connecting Cambridge & Gothenburg to create a scientific powerhouse in Europe





Application of inhaled technology in modifying respiratory disease

Future therapies for respiratory disease supported by advanced inhaled technology platforms



Broad range of inhalation technologies

Improved symptom control

Cutting edge science to modify disease

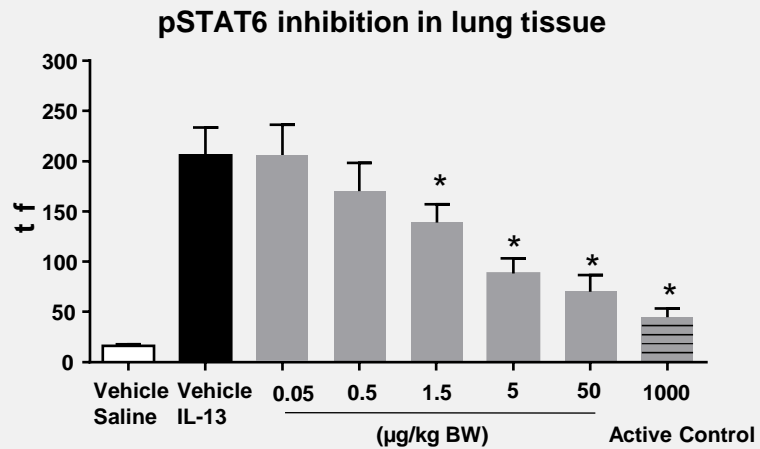
Next-generation treatments for asthma and COPD



Targeted therapies to drive efficacy in asthma

AZD0449: iJAK inhibitor for asthma

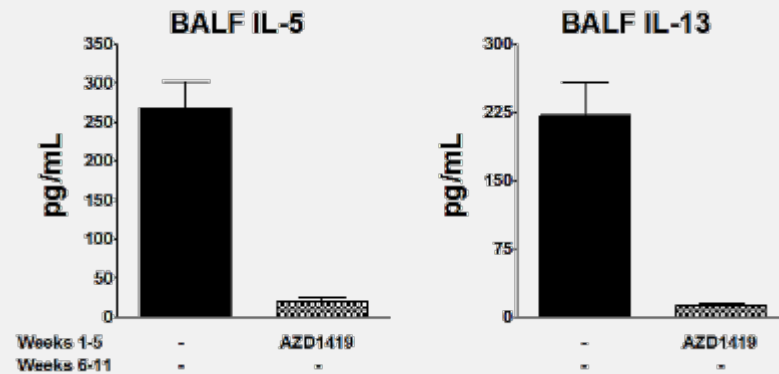
- Well-validated pathway
- STAT signalling critical player
- FTIM 2015
- Collaboration with Rigel



AZD1419: iTLR9 agonist for early-onset asthma

- Sustained correction of Th2 imbalance
- Phase II H1 2015
- Collaboration with Dynavax

5 weeks AZD1419 blocks lung inflammation in mice

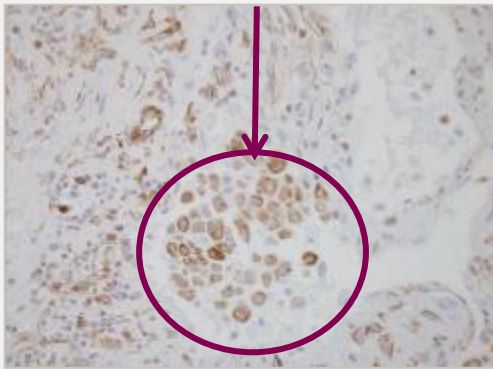


AZD7624: Inhaled P38 inhibitor for patients with COPD

- Well-validated pathway
- Aimed at steroid insensitive patients

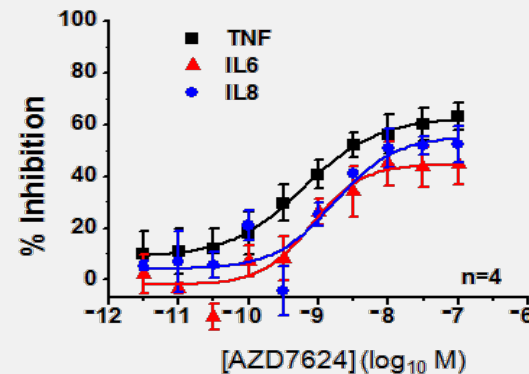
- Direct targeting of immune cells in lung
- Phase II Q4 2014

Phospho p38+ alveolar macrophages in COPD lung

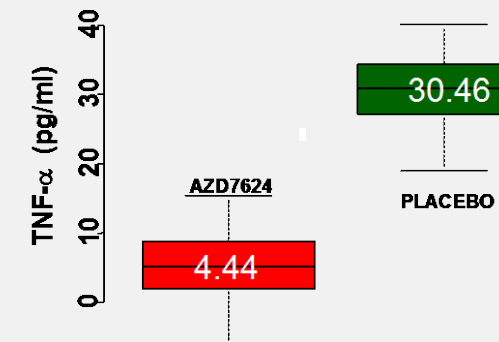


(In-house IHC data)

Inflammatory cytokines in human alveolar macrophages



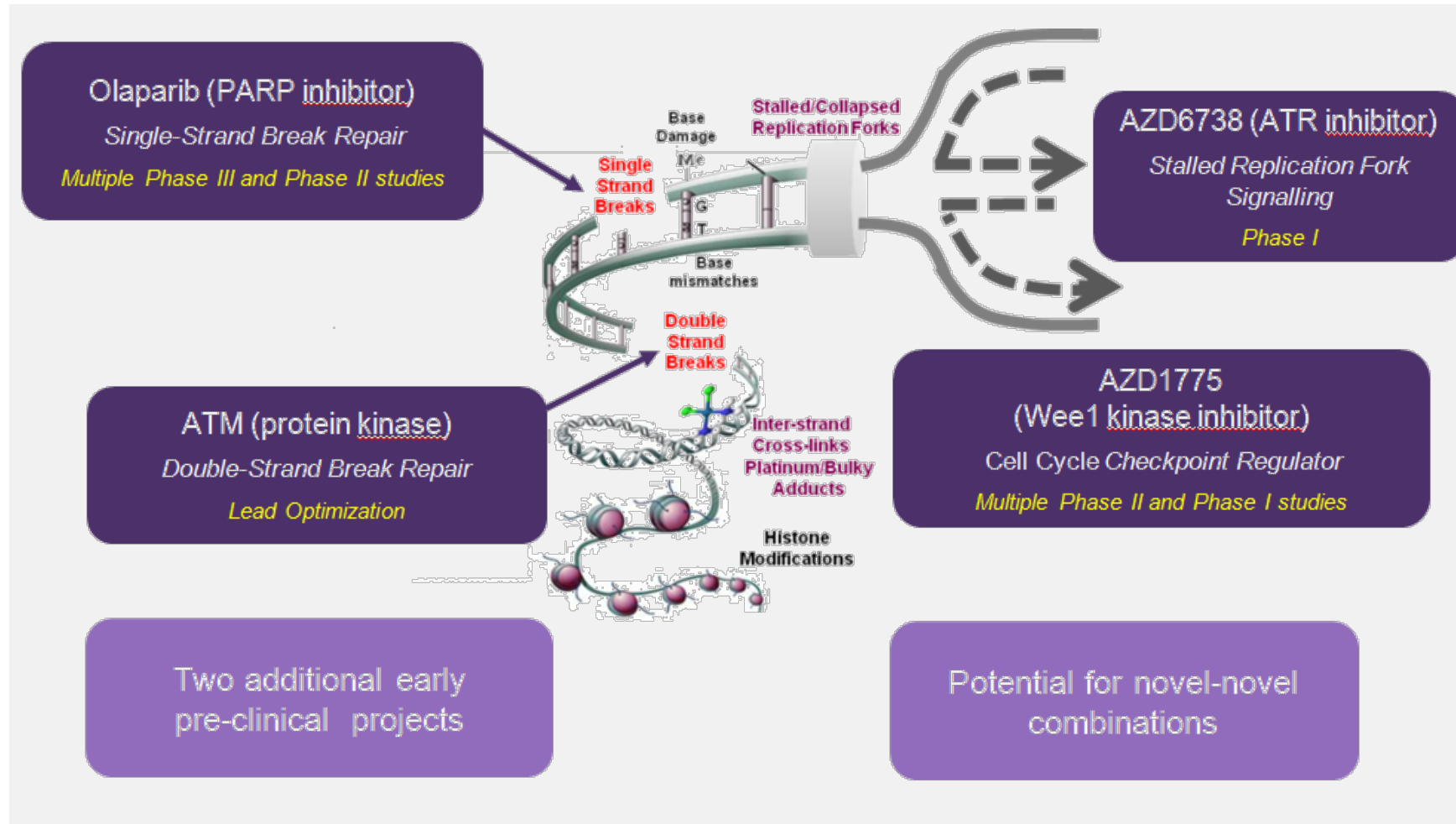
Significant attenuation of LPS-induced TNF- α





Leading in DNA damage response (DDR)

Leading “first in class” DDR portfolio

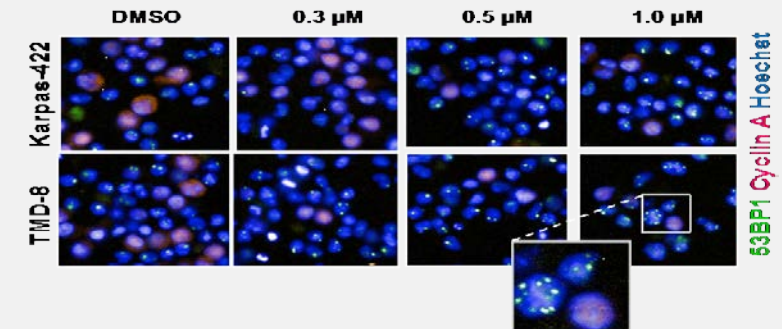


AZD6738:

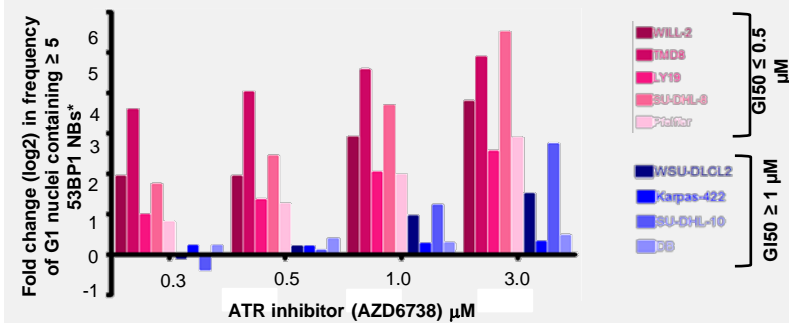
First-in-class ATR inhibitor for ATM-low NSCLC

- Leads to tumour cell death
- Potent and selective inhibitor
- FTIM Q4 2013
- Combination with carboplatin 2015

AZD6738 increases 53BP1 replication stress nuclear bodies



Increased 53BP1 nuclear bodies are a marker of AZD6738 sensitivity



*Relative to DMSO treated cells

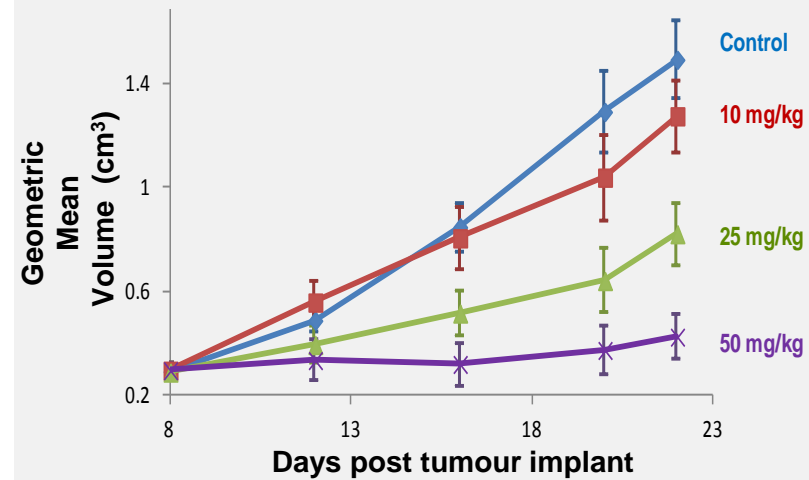


AZD6738:

First-in-class ATR inhibitor for ATM-low NSCLC

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AZD6738 in ATM-low colorectal model



Breadth of portfolio allows combinations with strong scientific rationale

Breast cancer

Lynparza & AZD1775 in TNBC

Gastric cancer

Lynparza & AZD6738 in ATM-deficient GC

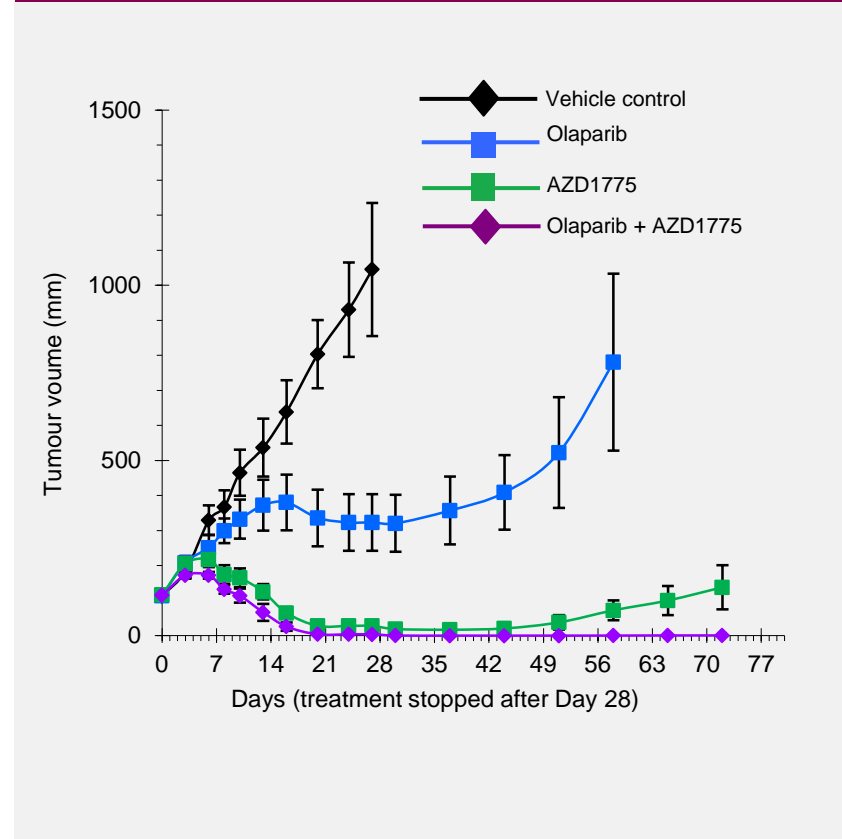
Lung cancer

Lynparza & AZD1775 in NSCLC and SCLC

Ovarian cancer

Lynparza & AZD1775 in platinum-resistant ovarian cancer

AZD1775 combination with Lynparza in a TNBC PDX model

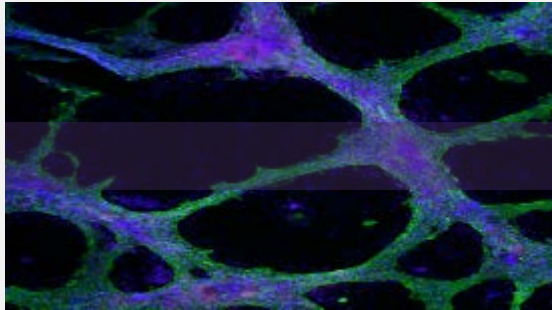


A microscopic image of biological tissue, possibly a cross-section of a vessel or organ, showing a complex network of fibers and cells. The image is overlaid with a gradient from dark red at the top to dark purple at the bottom. The text is positioned in the lower-left quadrant of the image.

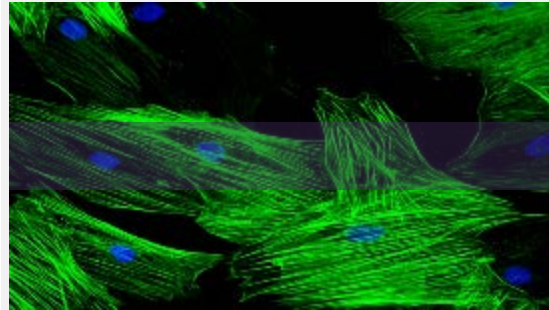
**Pioneering research in
oligonucleotide therapeutics**

Collaborating with the best partners to harness cutting- edge science in oligonucleotide platforms

Messenger RNA



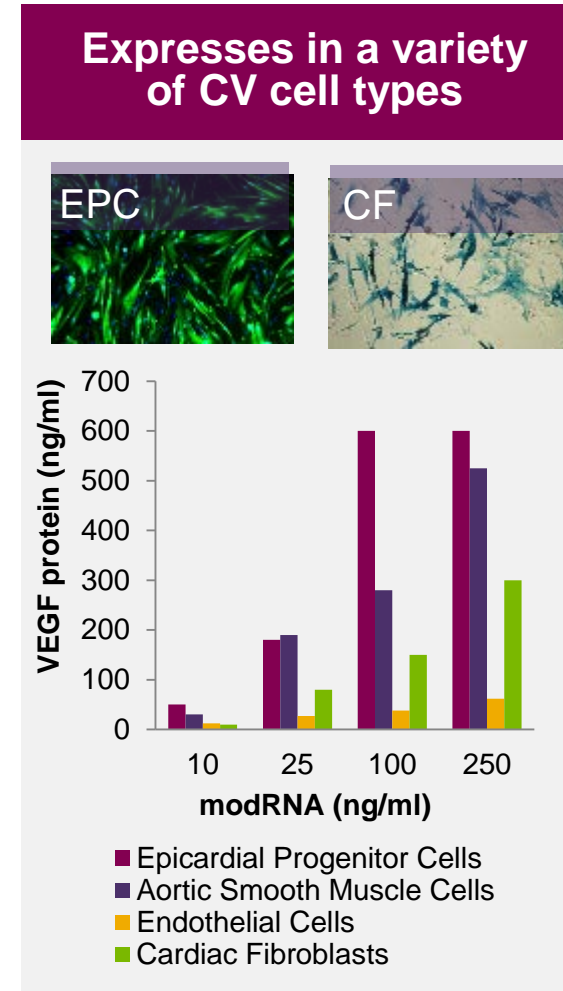
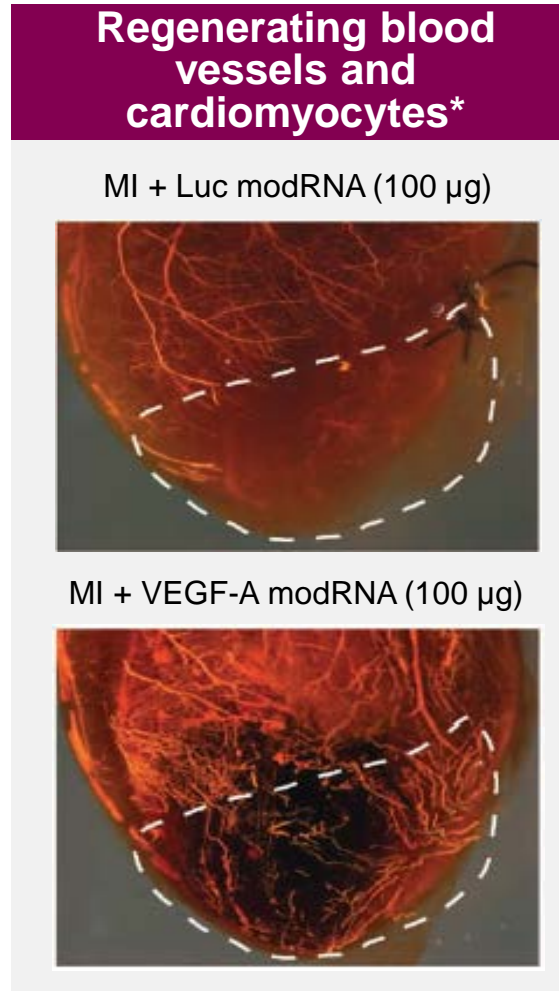
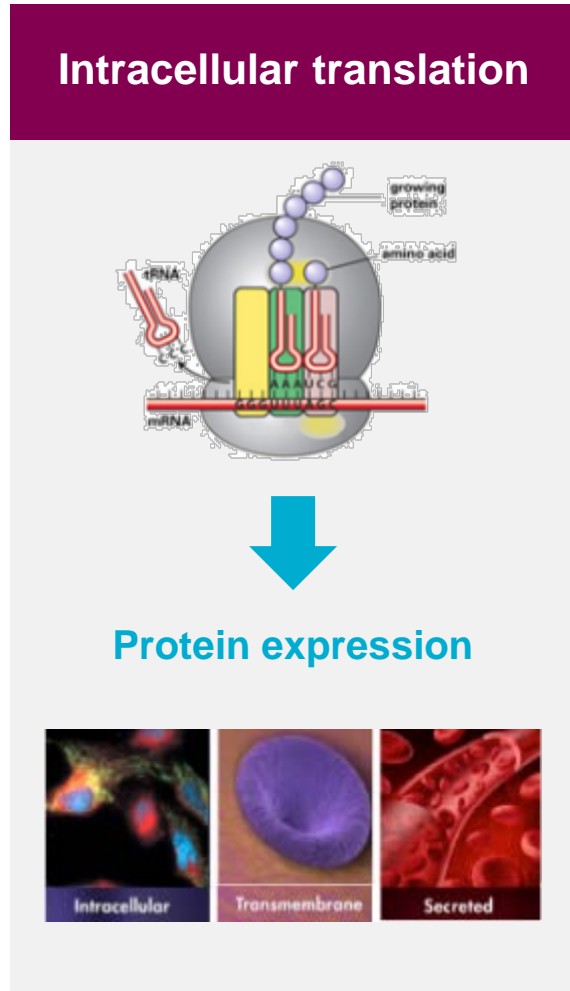
Micro RNA



Antisense oligonucleotides



Exclusive agreement with Moderna to harness pioneering messenger RNA technology



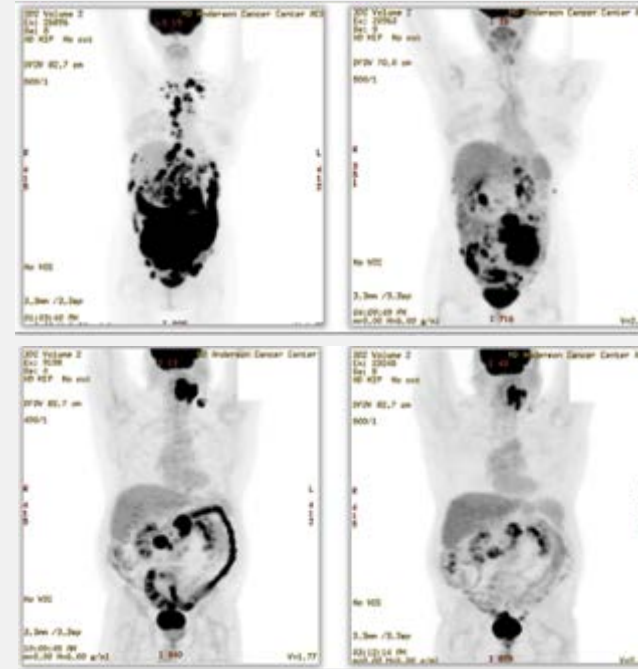
* Lior Zangi et al. Nature Biotechnology (2013)



Collaboration with Isis Pharmaceuticals to harness pioneering antisense therapeutics

- Antisense approach
- Potential to inhibit validated but 'undrugable' targets
- Gen 2.5 chemistry shows improved potency
- Progress:
 - STAT3RX (AZD9150) – Phase I in DLBCL and HCC
 - AR (AZD5312) – Phase I ongoing
 - 3 discovery projects underway

STAT3: Durable partial responses seen in 2 DLBCL patients in Phase I



STAT3 inhibition seen in tumour microenvironment & leukocytes



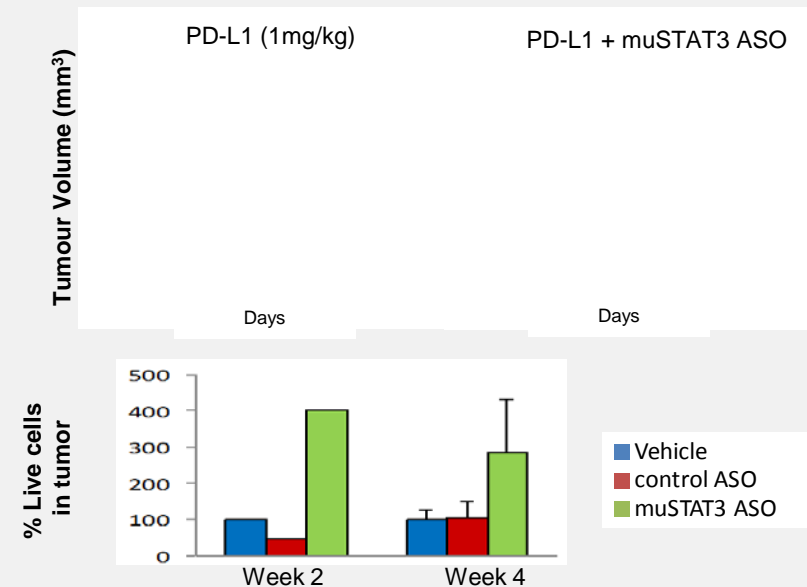
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Increased responses for combination of STAT3 ASO with PD-L1 mAb

STAT3 ASO / PD-L1 combination gives increased responses in CT-26 colorectal tumour model



Increased effector T-cells in tumour post STAT3 inhibition



A microscopic image of biological tissue, possibly a cross-section of a bone or cartilage, showing a complex, porous structure. The image is overlaid with a color gradient that transitions from dark red at the top to a deep purple at the bottom. The text is positioned in the lower-left quadrant of the image.

**Building a world-class Personalised
Healthcare capability**

Establishing a leading position in personalised patient care – across all therapy areas

90M

Dollars invested in diagnostic partnerships

1st

Circulating tumour DNA-based diagnostic approved for *Iressa*

>70%

Percentage of clinical pipeline with a PHC approach

50%

Percentage of launches by 2020 with companion diagnostic

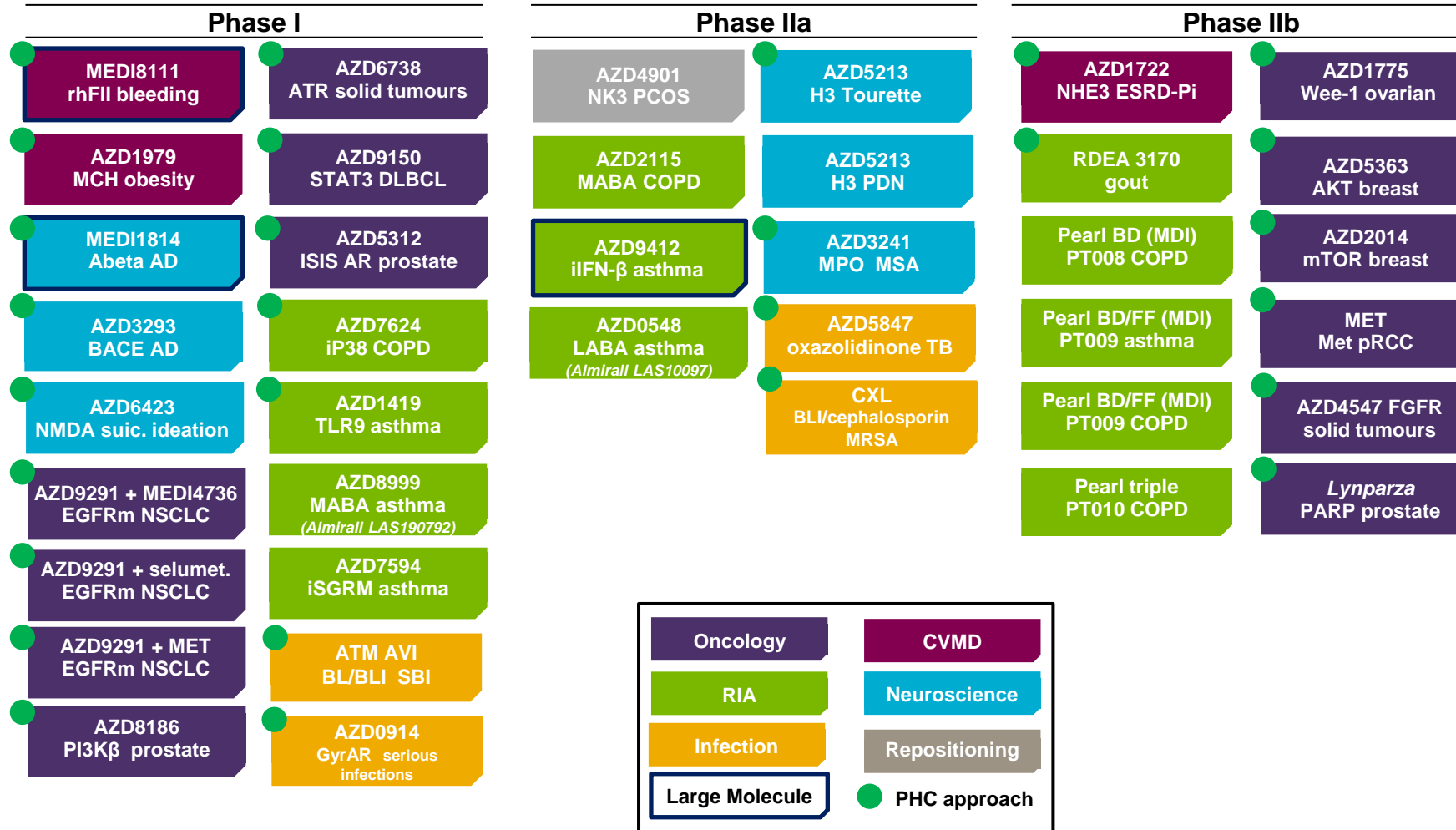
2nd

Rank in companion diagnostic partnerships and biomarker publications

~30

Launches planned with companion diagnostic over next 5 years

Following the science will ensure maintaining a healthy and sustainable pipeline



*AZD6244, ARRY-142886



IMED approach supports delivery of sustainable pipeline



Reduced IMED spend by 39% (and headcount by 42%) since 2010



Back-up programmes reduced from 48% to less than 2% since 2010



Cost per candidate drug \$50-60m (industry benchmark \$80-110m)



Probability of success increased from ~6% to ~16% since 2010



5 Phase III programmes delivered since 2012



Being **open for**
collaboration in an environment
where the **best scientists**
thrive will deliver a **sustainable**
flow of scientific innovation





Innovative Medicines & Early Development

Delivering the next wave of scientific innovation

Mene Pangalos, Executive Vice President, Innovative Medicines