Personalised Healthcare

will it deliver?

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AstraZeneca

Personalised Healthcare

It is delivering!

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WARNING!

In this presentation I shall make reference to a number of drugs.

The information I present may not represent the label text for the drugs in your countries (and may not be the approved interpretation of the data by regulatory authorities).

Nothing in this presentation should be construed as promotional material and I am not advocating the use of any test or any medicine outside of the approved label texts.

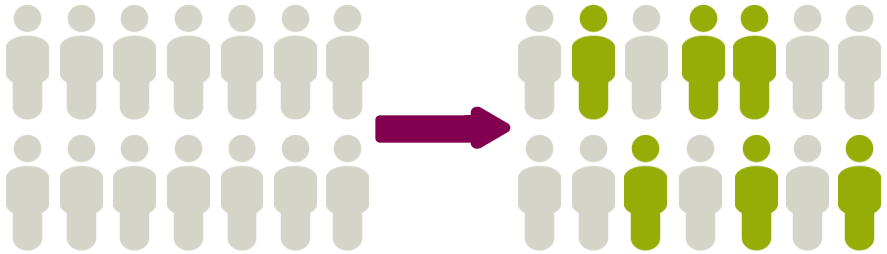
All drugs and diagnostic tests should be used as described in their regulatory authority approved labels.

Topics to be discussed

- What do we mean by “personalised healthcare”?
- Why is there controversy? (PHC perceived as problem)
- Our strategy – (PHC can instead be a simple & pragmatic solution)
- PHC in the industry and in AZ today
- The future

What is Personalised Healthcare?

Delivering the
right treatment
to the right patient
at the right dose



Who could argue with this as a worthwhile objective?

It's basically just good medicine

The why is obvious……..

Patients	**Best treatment**	
Prescribers	**Delivering the best patient outcome**	
Payers	**Right Value**	

Because Personalised Health Care is the right thing to do

In reality, there is little new –

We've always used markers to define patient populations for clinical trials and markers have always been used to define the indication label text, e.g.

- **Blood Pressure for stroke prophylaxis**
- **LDL cholesterol levels for prophylaxis of cardiovascular disease**
- **DEXA scans for osteoporosis**
- **Gail Index for chemoprophylaxis of breast cancer**

We've just got much better at it….
…… especially the use of molecular diagnostics

Drug	Test	Disease
Trastuzumab	Her2 IHC +/- FISH	Breast cancer, gastric cancer
Abacavir (lumaricoxib)	HLA genotyping	HIV infection (osteoarthritis)
Miraviroc	CCR5 tropism	HIV infection
Gefitinib, erlotinib	Mutant EGFR	Non-small cell lung cancer
Crizotinib	ALK "break apart" FISH	Non-small cell lung cancer
Vemurafanib	Mutant BRAF	Melanoma
Panitumumab, cetuximab	Wild-type KRAS	Colorectal cancer, head & neck cancer

Labelling

> 110 genomic markers in current drug labels!

http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm

Well described processes for biomarker “qualification” – i.e. describing the amount of information required about the marker for information to be included in the label

Increasingly well-described processes for the regulatory approval of biomarkers as “diagnostics”

We have:

- **prognostic markers**
- **predictive markers for metabolism, safety and efficacy**
- **markers of pharmacodynamic effect (wanted and unwanted)**

But….. it can look complex (and costly)

Historic pharma industry success based on primary and secondary care blockbusters

- Simple to recognise the patients
- Medicines which are easy to prescribe

Personalised Medicines can look difficult and costly to develop

- Complexity of simultaneous development of drug and diagnostic biomarker
- Complicated clinical trials with sometimes slightly ambiguous results

Personalised Medicines can look complicated to sell

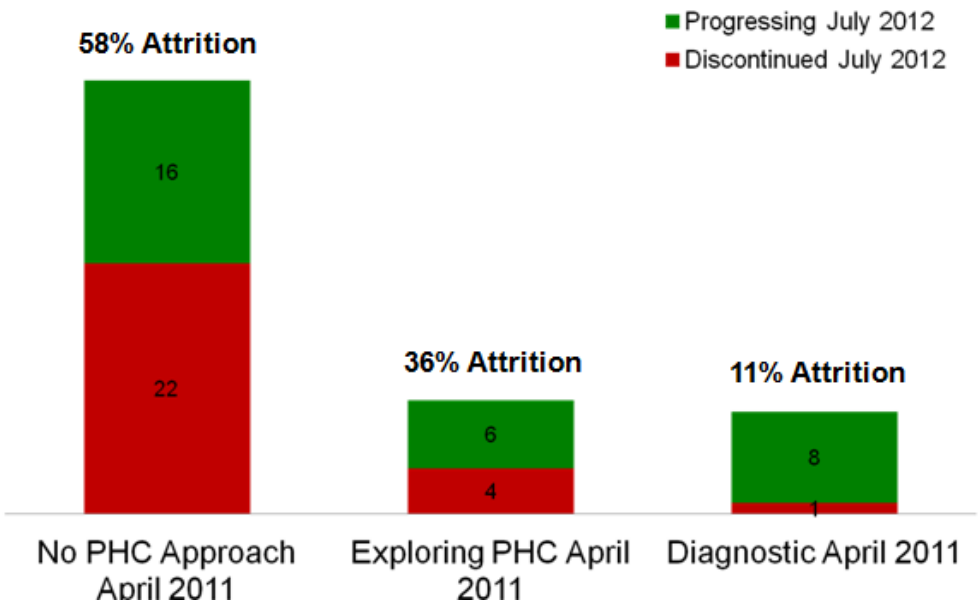
- Increased cost for payer due to testing
- Testing adds a barrier to prescription
- Testing reduces the number of accessible patients

Problems and Solutions

Low probability of R&D technical success

- Perhaps only 2-5% for small molecule candidates
- Perhaps 10+% for large molecules (but declining)

Impact of PHC Approach on Project Survival



Problems and Solutions:

R&D costs

- Somewhere between $1B and $4B to bring a drug to the market if we include all the actual costs
- The industry spends approximately $140B per year on R&D and develops around 30 NMEs

Clinical trials costs can be extraordinary

- $100k per patient are not unusual
- Regulatory submissions run from say 800 patients for oncology to 20 000 for some CV products, averaging around 5000.

Careful choice of patients can reduce trials sizes substantially

Problems and Solutions:

Downward pressure on prices

- Imposed reductions by governments and pricing authorities
- Generic Competition

Improved Value Proposition for Payers

- Fewer patients to be treated
- Increased benefit per patient

Simple, pragmatic solutions

1. Patient stratification tools must be easy to use and fit within the normal care pathway

2. Low Tech or already existing tools are good!

3. The tools don't need to perform perfectly – the target patient population should be enriched sufficiently to create a clinically relevant improvement in benefit to risk for the patient

- **Sensitivity, specificity and cut-offs can be adjusted as appropriate to the consequences**
  - **High sensitivity when the benefits are great and there no alternatives (few false negatives)**
  - **High specificity when reasonable alternatives exist or the treatment has significant AEs (few false positives)**

How AstraZeneca is approaching PM

Embed Personalised Health Care at the heart of Discovery and Development

Leverage translational science to develop drugs

Develop partnerships with diagnostic companies

Develop, validate and deliver registration-ready biomarkers and companion diagnostics

Support lifecycle management to help existing treatments achieve their potential

AstraZeneca's Strategy

Focussed effort through a *substantive* centralised group

- ***All*** LO projects to have RUO biomarkers (segmentation and drug effect) – invented by the Discovery project teams
- A new Personalised Healthcare Function has the expertise, and internal & external lab facilities to convert the RUO into an IUO for use in the first clinical studies
  - with line of sight to an eventual marketable diagnostic product
- Conversion of the IUO into a regulatory approved IVD occurs with external partners

115 FTEs

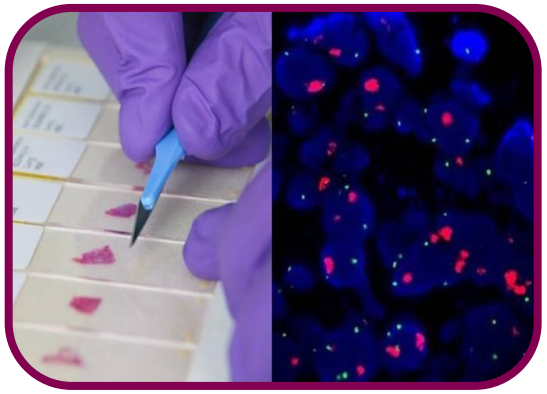
Technology platform agnostic

but, skilled in molecular biology and imaging

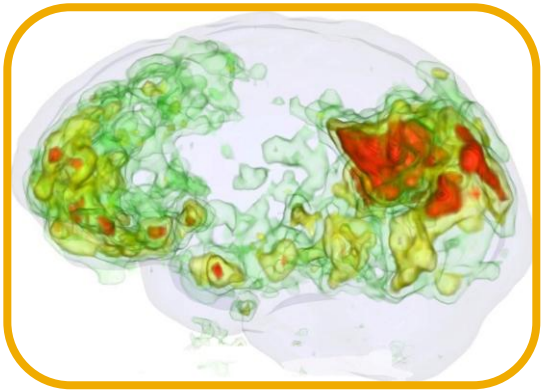
RUO = research use only **IUO = investigational use only** **IVD = in vitro diagnostic**

Personalised Health Care in AZ

Tissue Diagnostics

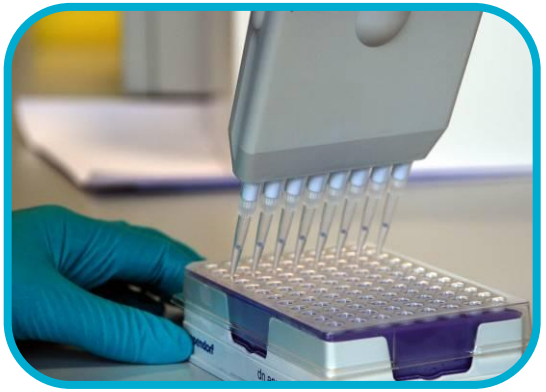


Imaging Biomarkers



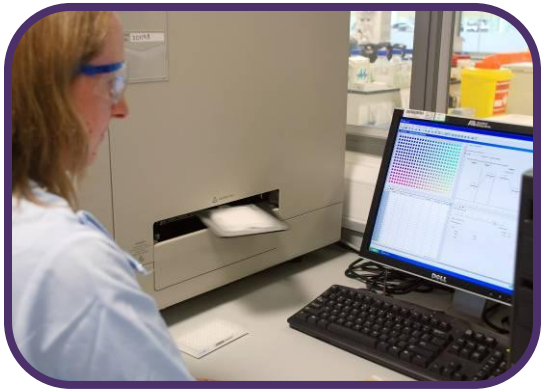
Molecular Diagnostics

Protein Biomarkers



Clinical Decision Tools

Pharmacogenomics



Partnerships, collaborations and Strong Science at the core of PHB strategy

Collaborations

Approx 50% biotech and 50% Academic

Roche Diagnostics

Karolinska Institutet

Dako

AmoyDx

agendia
decoding cancer.

BANNER INSTITUTE

NKI-AVL

QIAGEN

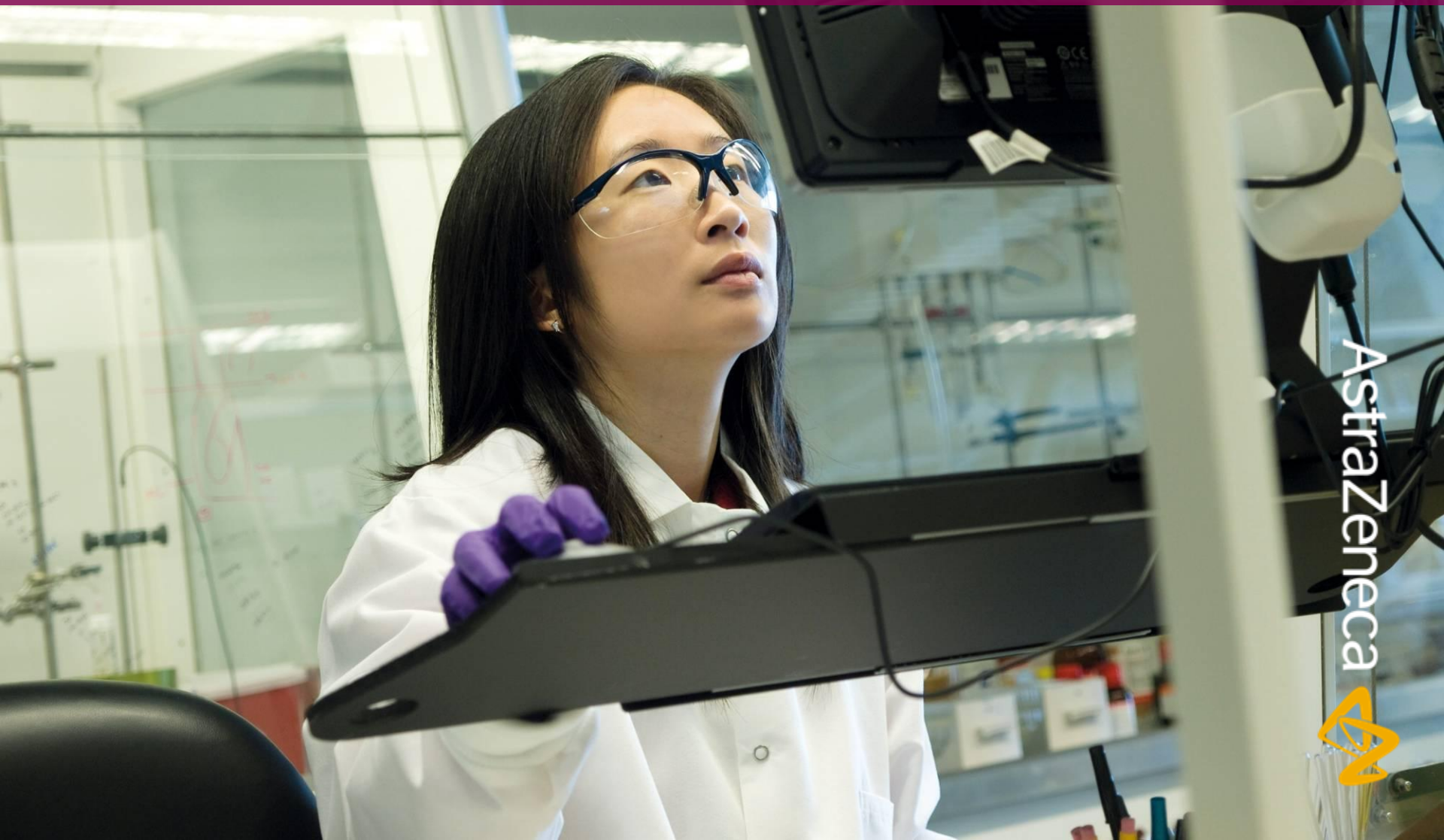
Strong Scientific Reputation

- PHB scientists hold **5 full professorships**, mostly in world-leading Universities
- 13 important reviews and white papers published by PHB scientists on Personalised Healthcare & Biomarkers
- 7 scientists leading and participating in international Pharma consortia
- 4 scientists service on national and international science bodies
- 16 scientists gave invited talks at major meetings in 2012
- Translational Science Centre at Karolinska Institute (TSC@KI)

What has been the impact in AZ?

1. More than two thirds of drug candidates have patient stratification as a key part of their development strategies
2. Most drugs approaching phase 3 have companion diagnostics planned or already in active development
3. We have a drug in some markets requiring tumour genetic testing (IRESSA)
4. We use stratification data to support pricing negotiations

And the future?



As biomarker testing becomes ever more common….. each marker with it's own drug

Non Small Cell Lung Caner

- Histopathology (adenocarcinoma)
- Genetic mutations: EGFR, KRAS, EGFR+r, etc.
- Amplifications (FISH): FGFRx, ROS1
- Translocations: ALK, RET
- Protein Expression (IHC): EGFR, c-MET

How much tissue can be biopsied?

Practically how many tests can be performed?

Panel Testing is inevitable

- *Precompetitive Alliances between companies and academe*)
- *Next Generation Sequencing*

Personalised Health Care
is the right thing to do!