Personalised Healthcare

Drivers, Barriers and Pathways

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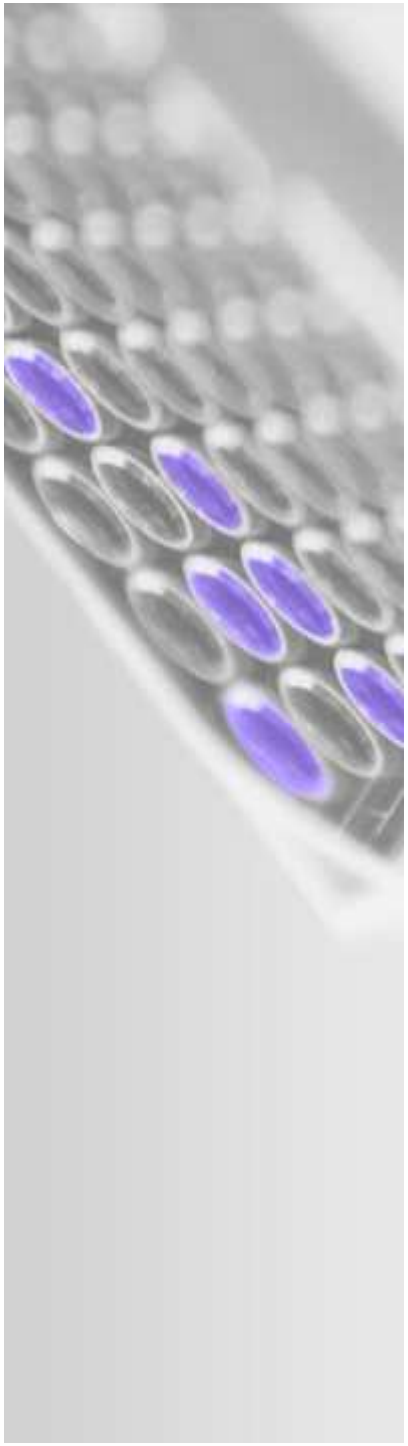
Berlin

June 2010



DxS Diagnostic Innovations

'DxS is a Personalised Medicine Company that meets the needs of the pharmaceutical industry for biomarkers and companion diagnostics to support the development and then sales of cancer therapies.'

- **Founded in 2001** by 2 ex-AstraZeneca managers to exploit Scorpions technology
- Jan 1st 2008 DxS launched its first **companion diagnostic product** to allow the sale of Amgen's cancer drug Vectibix in Europe
- DxS was acquired by QIAGEN in September 2009.

QIAGEN at a glance: A focused market leader

Revenues

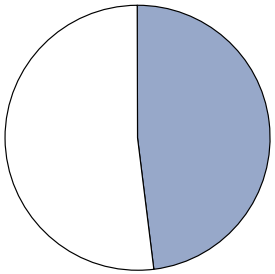
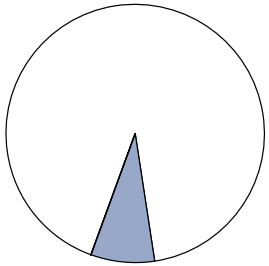
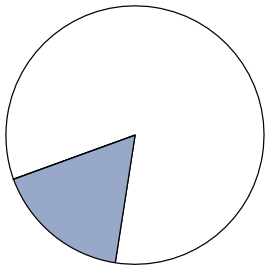
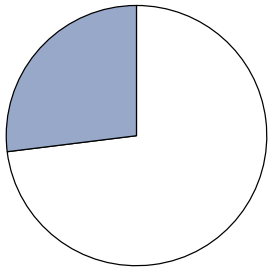
- ~ $1.000 million, Industry-leading growth
- 17% from products under 3 years old
- Molecular Sample & Assay Technologies

Infrastructure and Innovation

Employees	3’040
R&D	$120 million
Presence	Global
Market cap	3,5 B$

(1) All numbers projected 2008

Leading Position - Multiple Growth Drivers

Molecular Diagnostics	Applied Testing	Pharmaceutical Industry	Life Science Research
			
■ Prevention ■ Profiling ■ Personalized Healthcare	■ Veterinary ■ Forensic ■ Bio defense ■ Food	■ Discovery ■ Development	■ Public ■ Private

SAMPLE Technologies → ASSAY Technologies

Product and Technology Continuum

QIAGEN's 4 "P" Framework in MDx

	LABORATORY BASED TESTING			POINT OF NEED
	Prevention *Asymptomatic patients* *Goal: Early detection*	**Profiling** *Symptomatic patients* *Goal: Confirm*	**Personalized Healthcare** *Pre-diagnosed patients* *Goal: Guide therapy*	*Rapid turnaround needed* *No laboratory reachable* *Goal: fast result, on spot*
Assay Technologies	Narrow portfolio High volume/<$20/assay	Broad portfolio High value, low volume	Growing portfolio High value, low volume	Emerging segment Instrument <$2k, Assays: $3-30
	Examples - HPV - Chlamydia/NG - 5 additional assays in pipeline - More to come	Examples - CMV - EBV - HBV - HIV - HCV - Influenza	Examples - KRAS - EGFR - B-RAF - PI3K - Pathogen Genotyping	Examples - careHPV - HAI - Influenza
Instruments	High throughput Continuous load	Random access Continuous load	Random access Continuous load	Portable test systems Rapid turn around < 2hrs
	QIA*ensemble*	QIA*symphony*	QIA*symphony*	*TBA*
Assay Design	Fast, typically isothermal amplification or no amp	PCR Pyrosequencing	PCR Pyrosequencing	Isothermal amplification

Focusing on Personalized Healthcare

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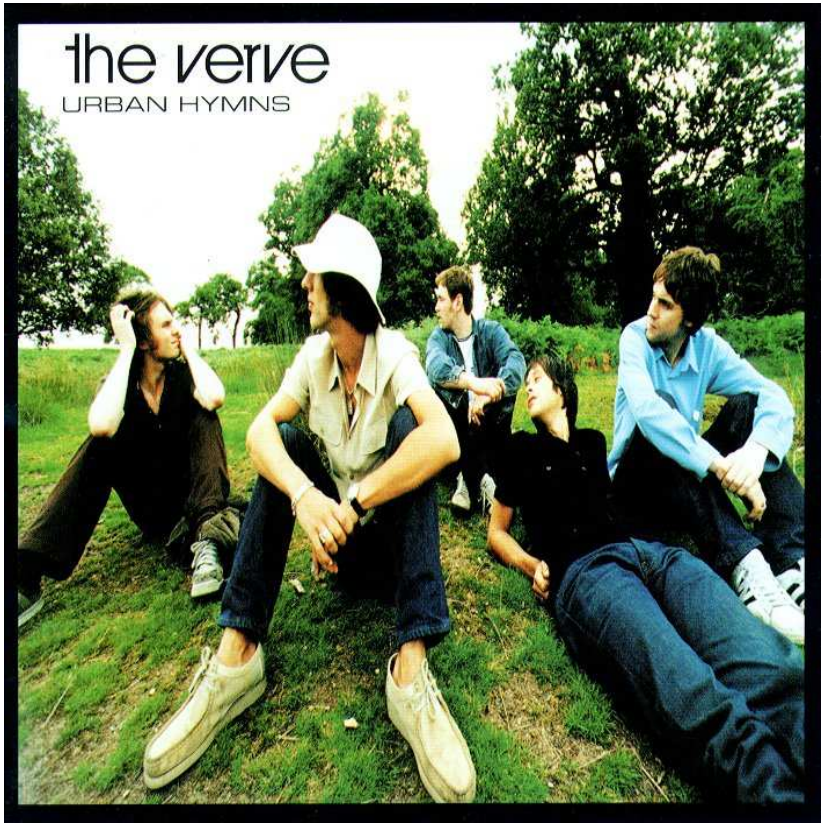
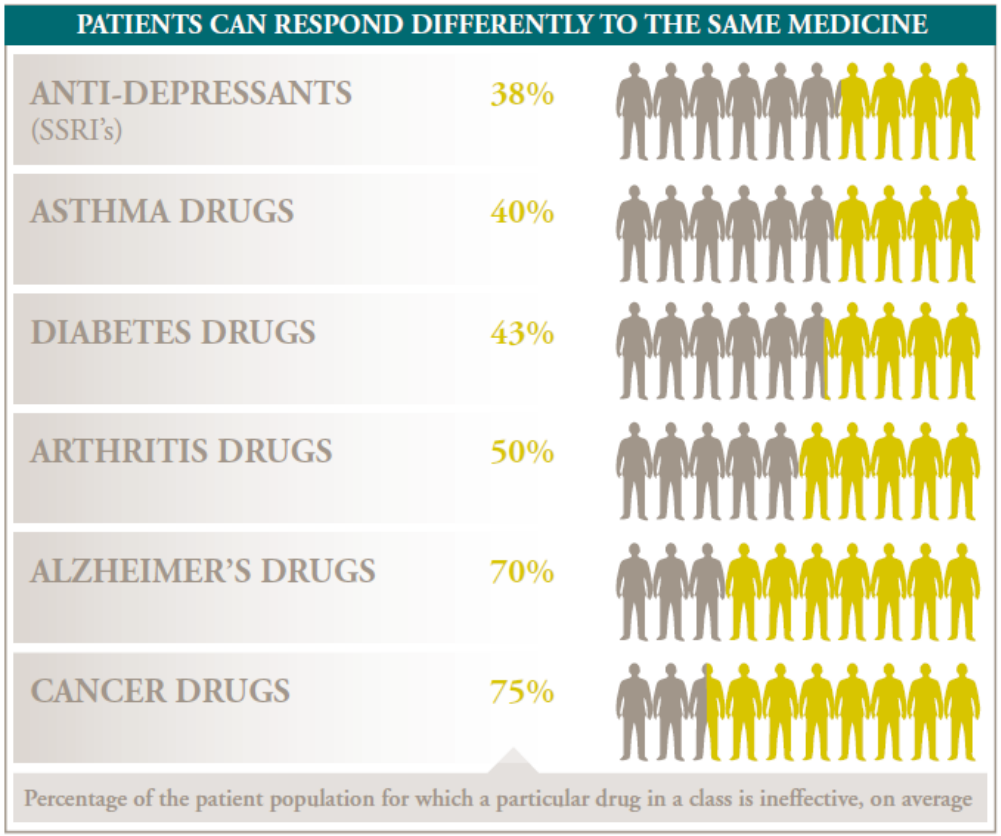
The Problem - Drugs Don't Always Work

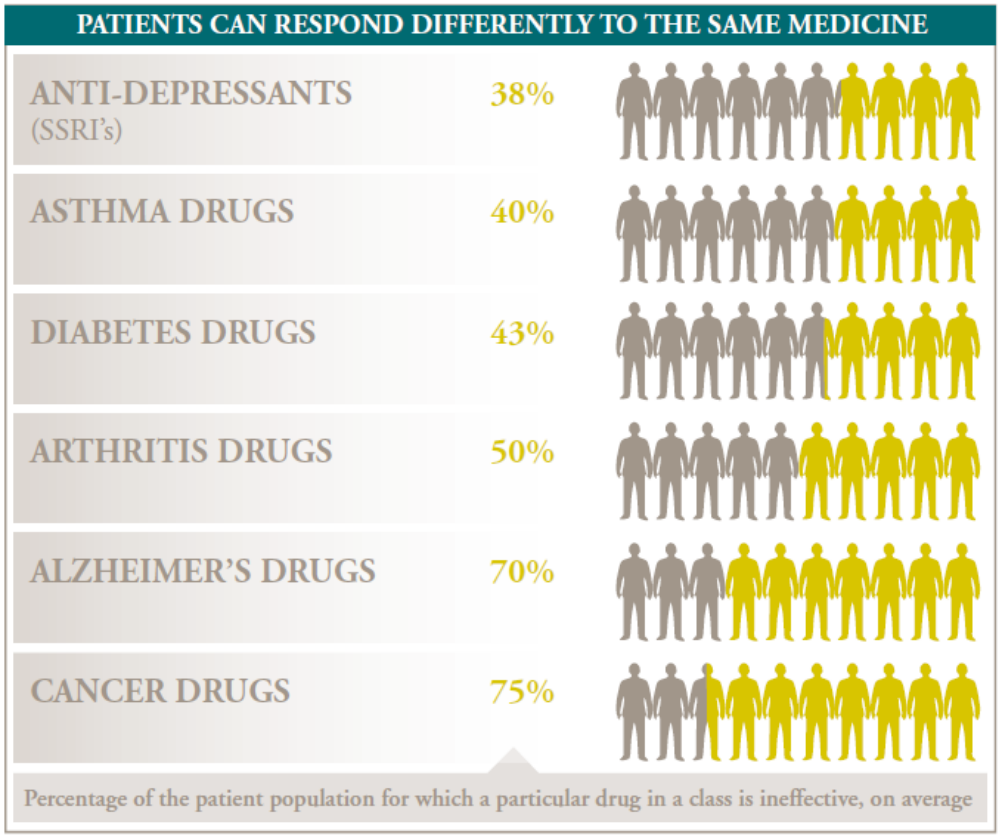




Source of data: Brian B. Spear, Margo Heath-Chiozzi, Jeffrey Huff, "Clinical Trends in Molecular Medicine, Volume 7, Issue 5, 1 May 2001, Pages 201-204.

The Solution
Personalized Healthcare

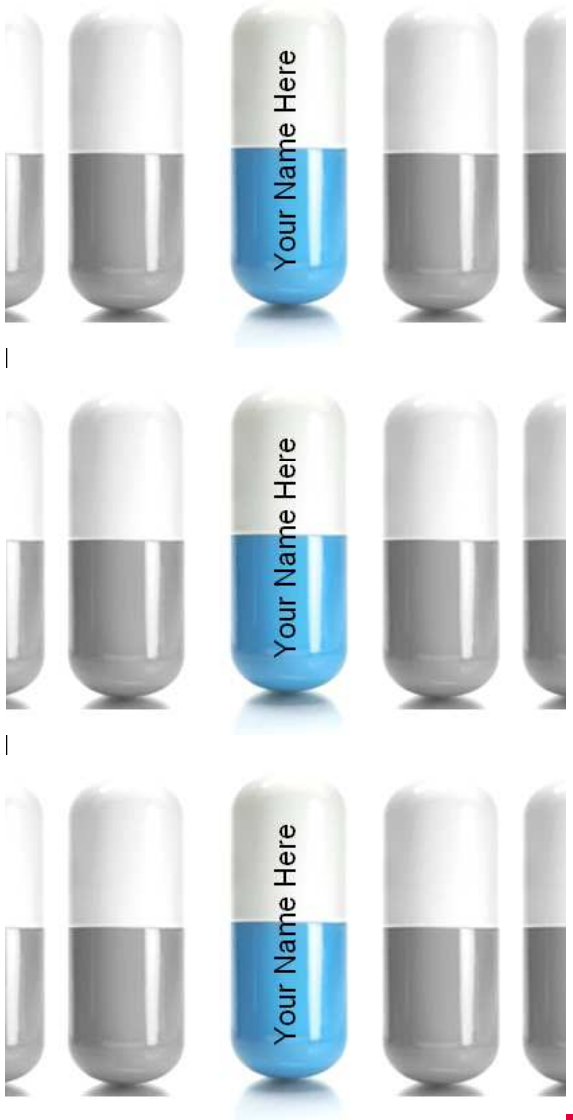
- 90% of drugs work in 30–50% of individuals
- $770B annual global drug sales in 2008 (IMS Health)
- $350B annually spent on ineffective medicines globally
- Many novel therapies are very effective but only in a proportion of the target population
- Identifying a sub-group of patients likely to respond can dramatically increase cost effectiveness of a drug



Personalized Healthcare

The use of a companion diagnostic to predict in advance which patients are most likely to benefit from a particular therapy

Personalized Medicine in 2010
Three Major Drivers



Political - Effectiveness to Cost Effectiveness

- WW acceptance: Money spent on healthcare is finite
- Increased emphasis on health technology assessment (HTA)
  Aim: Increase cost effectiveness of treatments
- Pharmaceutical companies are responding
  Trend: Development of companion diagnostics (CDx) to increase cost effectiveness of drugs

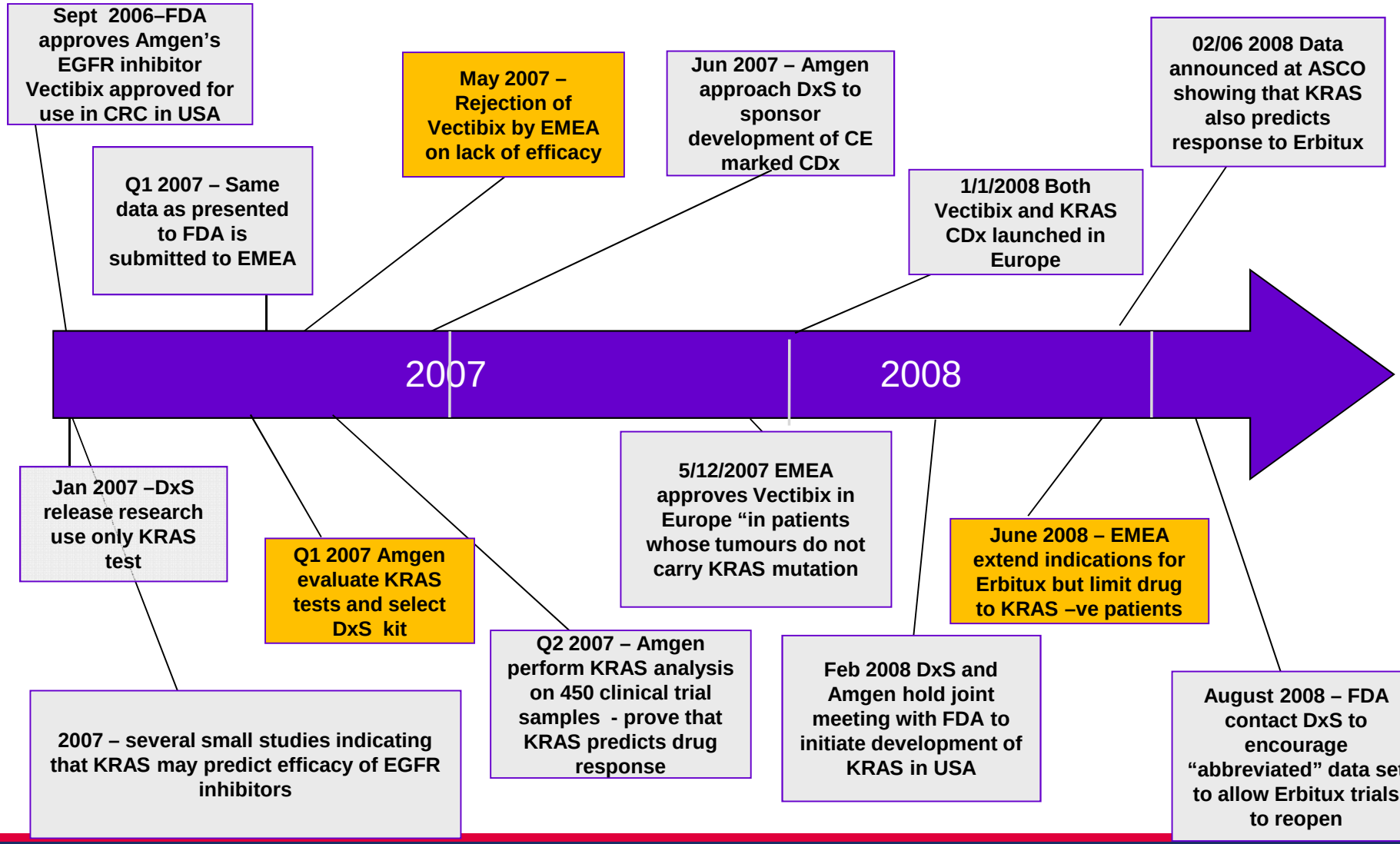
Scientific - Therapies to Targeted Therapies

- Advancement in understanding of disease processes lead to target drugs, more closely to specific molecular targets
- Increasing demand for diagnostic tools to identify patients with specific disease sub-types, likely to respond to the therapy
- Omic analysis becoming increasingly feasible

Regulatory - Passive to Active Regulation

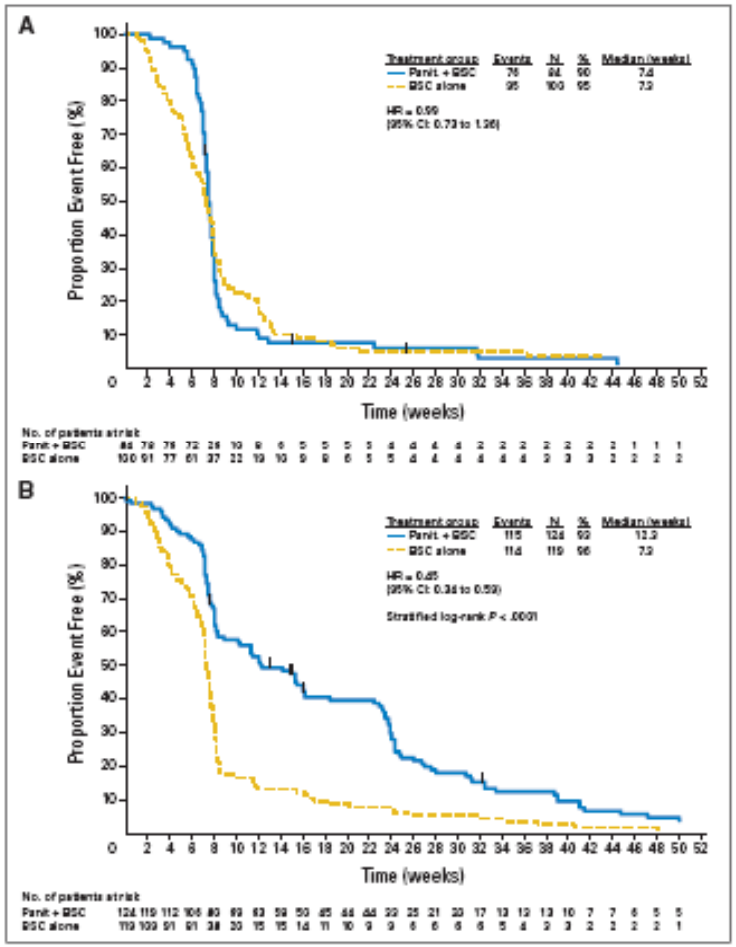
- Regulatory Authorities realized benefits CDx can bring to patients
- Both EMEA and the FDA encouraging pharmaceutical companies to explore the use of CDx during drug development

KRAS time-line



Example: KRAS Test

KRAS Mutations Predict Non Response to EGFR Inhibitor Therapies



KRAS mutant
no benefit

KRAS normal
significant benefit

"Routine use of KRAS mutational testing in colorectal cancer patients could save the health care system more than $600 million in drug costs alone"

ONCOLOGY TIMES

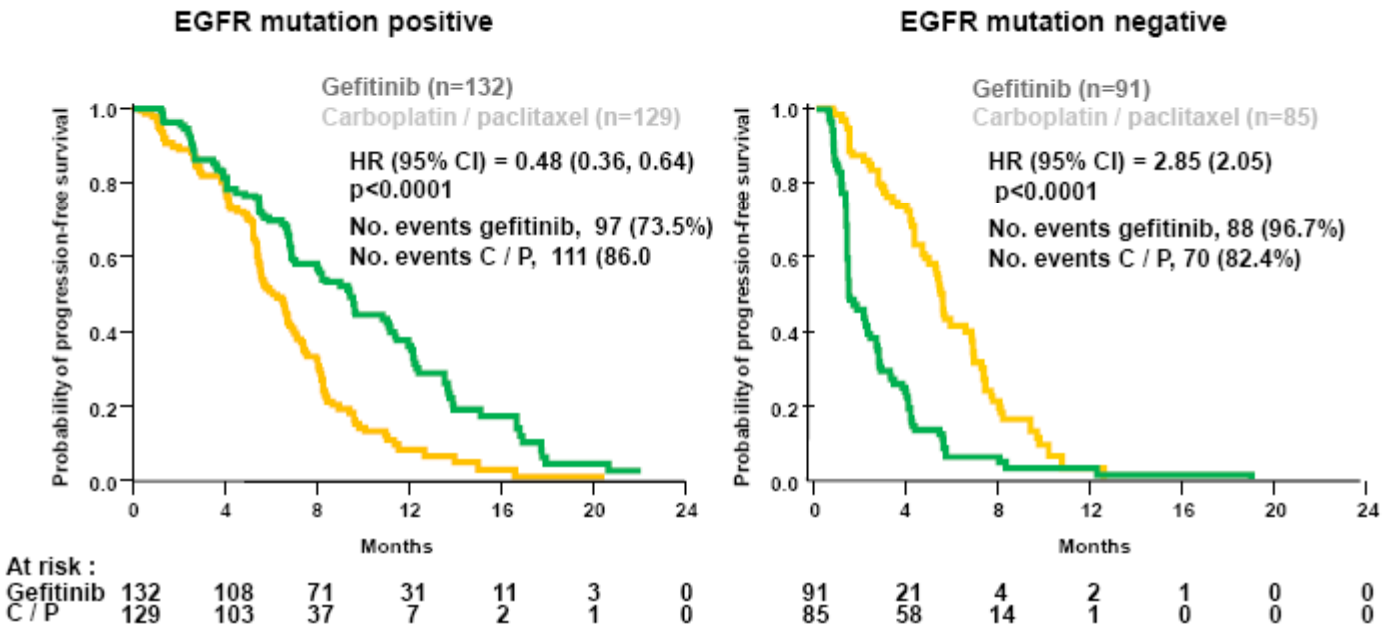
JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Wild-Type *KRAS* Is Required for Panitumumab Efficacy in Patients With Metastatic Colorectal Cancer

Rafael G. Amado, Michael Wolf, Marc Peeters, Eric Van Cutsem, Salvatore Siena, Daniel J. Freeman, Todd Juan, Robert Sikorski, Sid Suggs, Robert Radinsky, Scott D. Patterson, and David D. Chang

Example: Iressa
Effective in EGFR+ Patients but Appears to Harm EGFR-ves

Progression-free survival in EGFR mutation positive and negative patients



Personalized Healthcare – Seems to Be Good All Round

Stakeholder	Benefit
Patients	Increased effectiveness of therapies
Doctors	Increased safety in treatment decisions
Healthcare providers	Better outcomes for less cost
Pharma companies	Regulatory approval and competitive advantage
Diagnostic companies	New market opportunities

…but Personalized Healthcare has been a challenging business environment

Who is the customer for a CDx product

CDx products have additional benefits

- Patients - better outcomes
- Pharma – sell more drugs
- Providers – spend less money

Diagnostic Tests ordered by Doctors

- Clinical Utility
- Benefit to Patients

Primary customers for products are diagnostic labs

- Pathology (KRAS, EGFR)
- Haematology (Bcr/Abl)
- Molecular
- Clin Chem/ Large Ref labs

Understanding the Customers' Needs

Key to Successful Technologies

Pharma wants to sell drugs

- Focus on meeting the needs of the Pharma industry
  - Custom develop companion diagnostic tests
  - Win regulatory approval
  - Distribute and sell products globally

Providers want to save money

- Focus efforts on meeting needs of national health services pharmacy benefit managers and
- Generate convincing pharmaco-economic data

Patients want better results

- Focus on reducing unnecessary drug usage or selecting best treatment
- Find way of selling benefits to patients and doctors
- Be prepared to invest in marketing

3 levels of customers all with different perspective

Pharma

- Minimise the doctor's inconvenience
- FDA approval
- Rapid and reliable development
- Global distribution

Doctors

- Convincing Clinical Utility
- Clear decisions
- Reimbursement
- Easy access to test

Labs

- Ease of Use – Workflow and Automation
- Cost of the product and the platform
- Single platform, large menu
- Analytical validation
- Technology and Gene IP

The Economics of Companion Diagnostic Development

Demonstrating **“clinical utility”** requires a clinical trial of both the drug and the diagnostic

- A phase III trial of a cancer drug can cost over $100M
- Using typical reimbursement prices the market for a typical cancer drug companion diagnostic is $20-50M per annum

The need to demonstrate clinical utility linked to a specific drug means that diagnostic companies cannot normally develop their own companion diagnostics.

3 routes to overcome clinical utility barrier

Pharma Partnership

- Focus on meeting the needs of the Pharma industry
  - **Eg QIAGEN**

Providers Partnership

- Focus efforts on meeting needs of national health services and pharmacy benefit managers
- **Eg Medco**

Stand Alone

- Focus on reducing unnecessary drug usage or selecting best treatment
- **Eg Genomic Health**

Meeting the Needs of Pharma
Low Risk and High Speed

Requirement	Solution
Regulatory strength and experience with the FDA	QIAGEN are setting the agenda with KRAS and EGFR PMAs
Technology, platform and assays	Own both chemistry and instrumentation
Rapid and reliable development and approval process	Tried and tested process
Access to biomarker IP	Part of the QIAGEN strategy to discover and to license
Route to market for the CDx	Own sales channels
Expertise and experience	World leaders

What does a deal look like?

- Dx industry
  - Low risk Moderate Reward
  - Based on technology and chemistry
- Rx industry
  - High risk High Reward
  - Based on science and clinical innovation

What does a deal look like?

- Sources of power in the Rx/Dx negotiations
  - Exclusivity (technology or IP)
  - Urgency – drug rescue or planned programme?
  - Patent Extension
  - Dx Co capabilities and competitive situation
- Negotiation around costs and revenues
  - Fee for Service Model – more common
    - Rx Co funds Dx development
    - Dx Co ensures CDx is broadly available at reimbursable levels
  - Revenue Sharing model – less common
    - Dx Co funds Dx development and shares in risk of Rx failure
    - Dx Co shares in value of drug

Medco

Medco is a pharmacy benefits manager in the USA

They fill American's prescriptions by mail order

The wired pharmacy has allowed them to improve their service in two ways

- Drug-drug interactions
- CDx tests eg Warfarin eg Plavix/Effient

Medco introduce these tests on a pharmaco-economic basis

How do we apply this thinking to European health services?

Genomic Health

Genomic Health is a US diagnostics laboratory

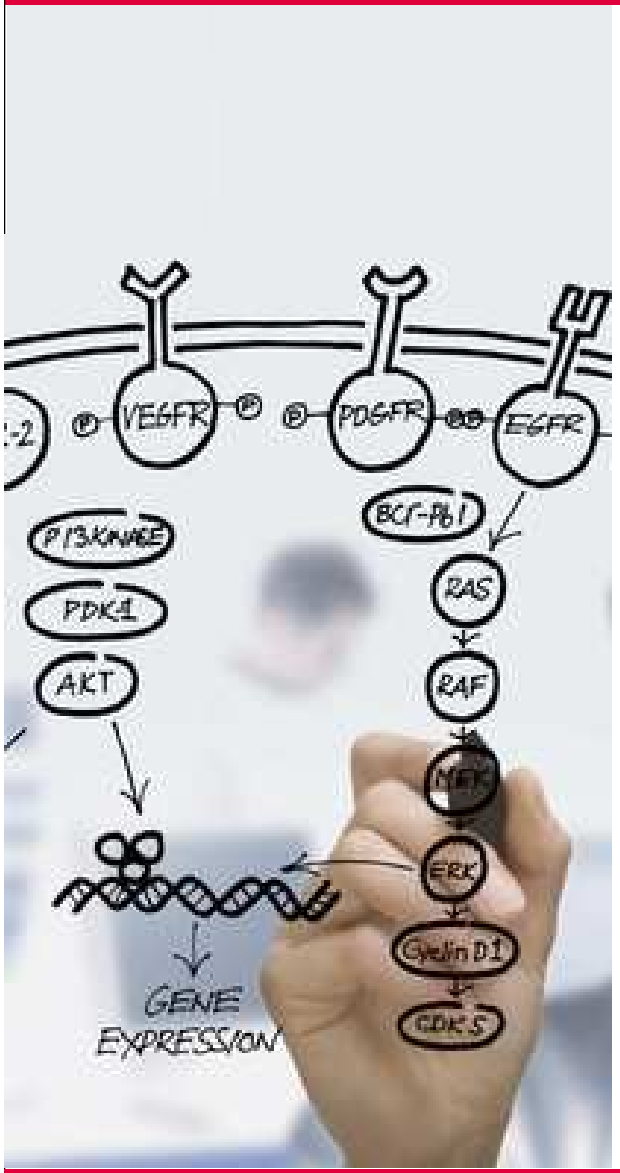
They have introduced a PHC assay called OncotypeDx which gives a breast cancer patient a recurrence score

A high recurrence score would suggest that chemotherapy may be of value, a low recurrence score would suggest less value

The key to their business model is the price of the assay - $3500

This justified the scientific and market investment to date - $100M

Numbers of Analytes



General consideration – for a diagnostic is it best to use a technology that only identifies known and understood changes (eg mutation/SNP detection) or is it preferable to be able to detect known and unknown changes (eg sequencing)

How many analytes will comprise a companion diagnostic?

1-30 – real time PCR

20-100 – arrays, bead arrays, sequencing

100 – 1000 – clonal approaches

Will nextgen sequencing ever be used for diagnostic testing?

Drivers Barriers and Pathways

Drivers

- Political, technical and regulatory

Barriers

- Cost of development compared to value of the market

Pathways

- Pharma partnership
- Provider partnership
- Stand alone, high price

Questions

- How complex will the new generation of diagnostics be

Thank you !