QIAGEN

Personalized Healthcare

QIAGEN Analyst and Investor Day 2010

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Vice President Personalized Healthcare

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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 - BRAF - 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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Outline

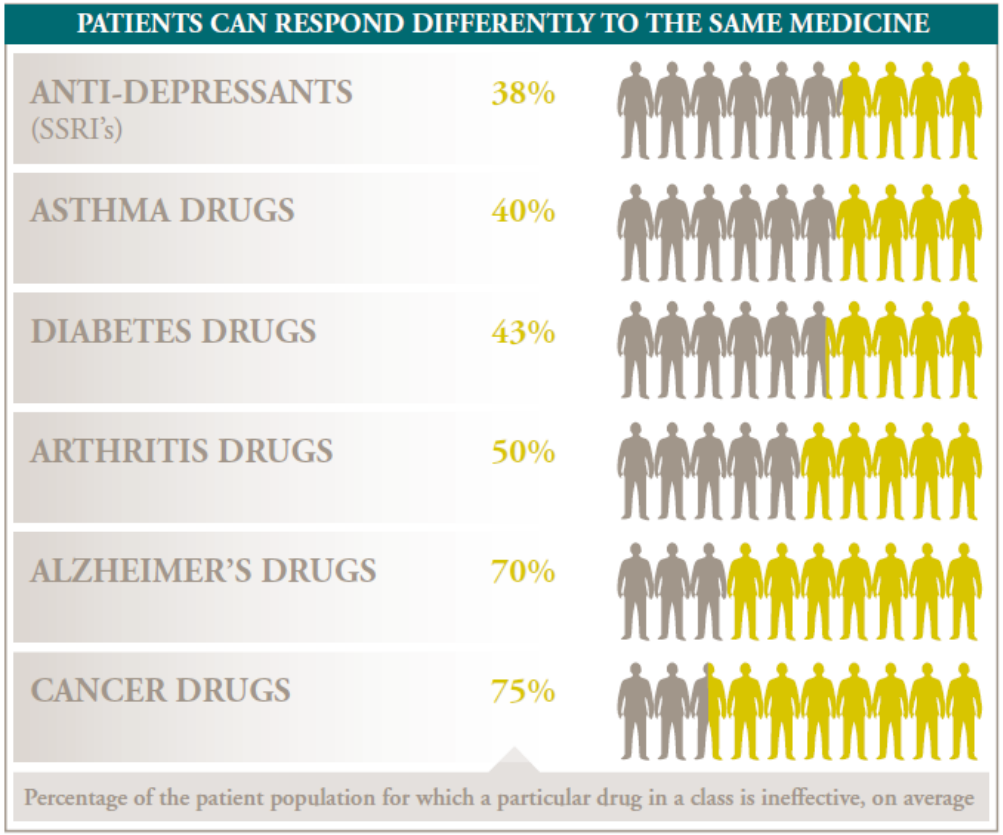
- Current trends in Personalized Healthcare
- Three sectors of Personalized Healthcare
  - Pharma
  - Providers
  - Patients
- QIAGEN's focus in PHC

Personalized Healthcare

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

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



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

Personalized Medicine in 2010
Three Major Trends

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

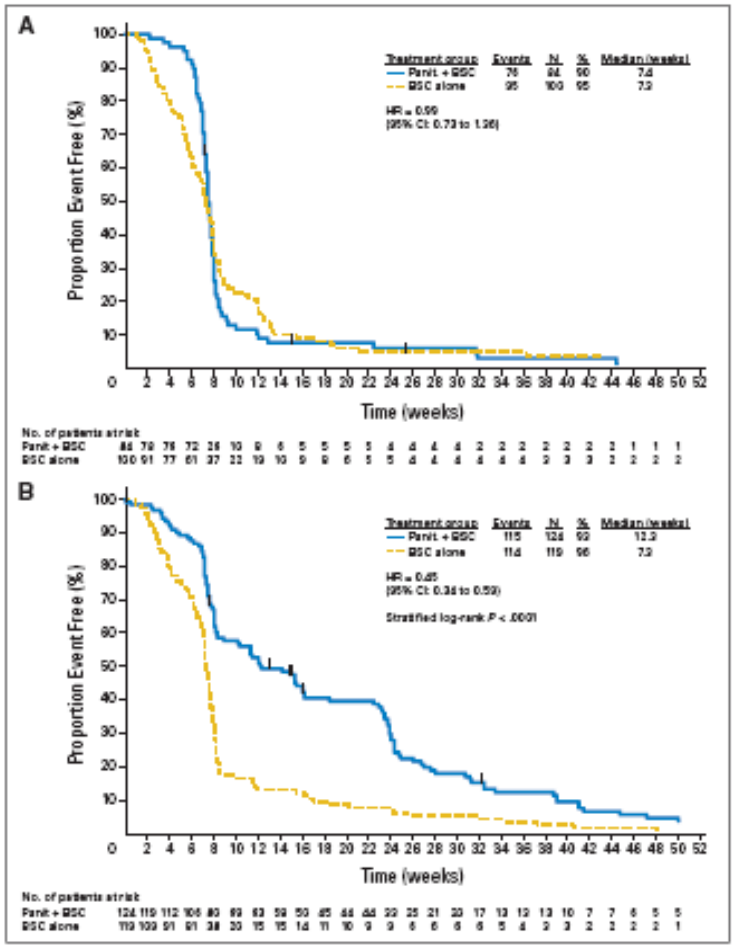
- Advancement in understanding of disease processes lead to target drugs, more closely to specific molecular targets
- Increasing demand for diagnostic tools to identify patients with specific disease sub-types, likely to respond to the therapy

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
- Dx-Rx combination will become an obligate element of NDA/BLA submission and product labeling

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

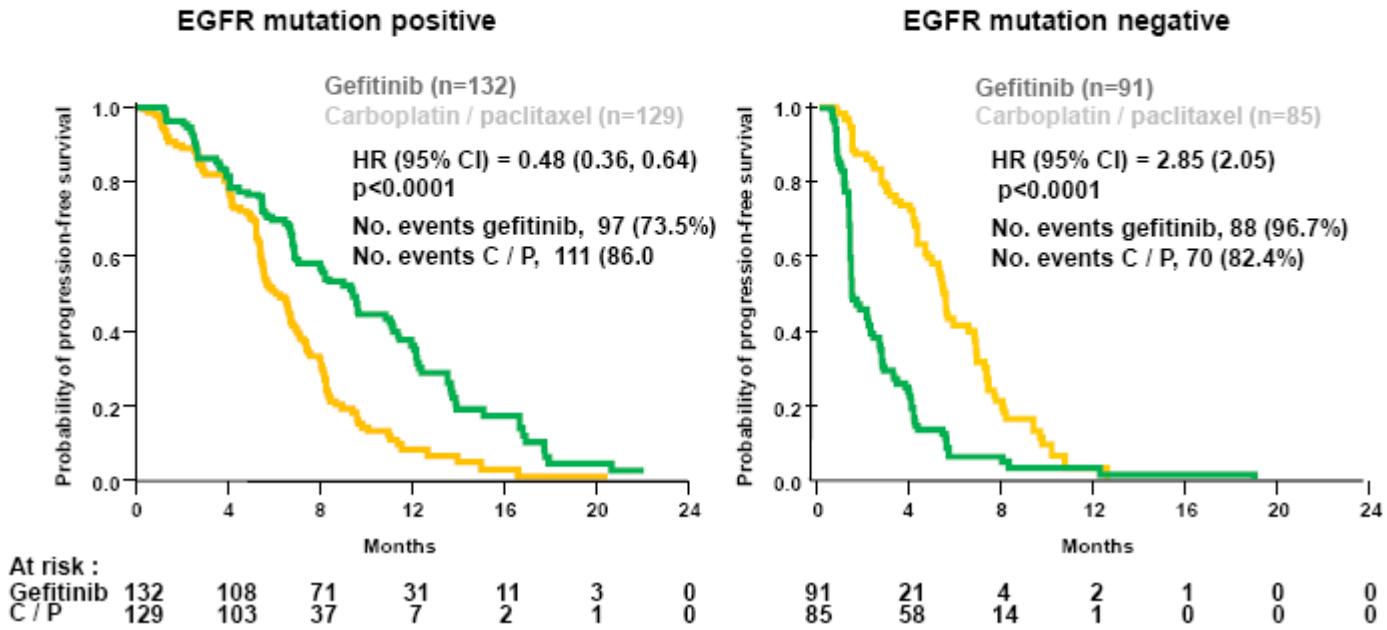
JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

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

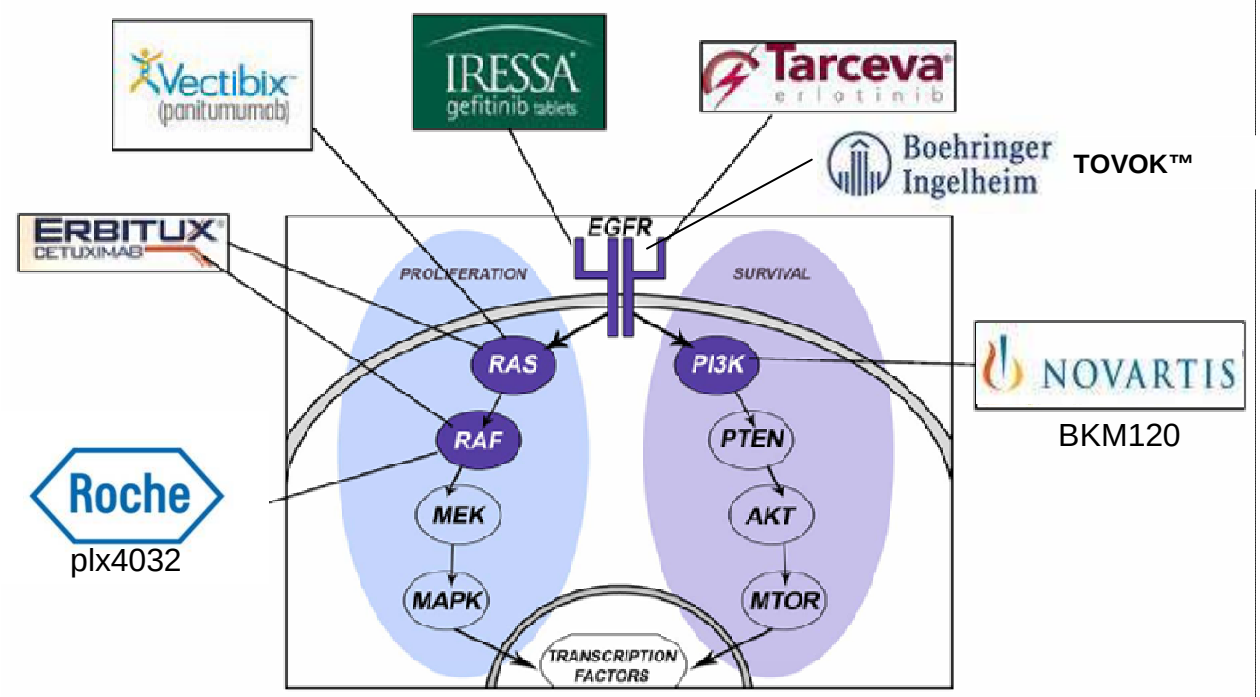
Rafael G. Amado, Michael Wolf, Marc Peeters, Eric Van Cutsem, Salvatore Siena, Daniel J. Freeman, Todd Juan, Robert Sikorski, Sid Suggs, Robert Radinsky, Scott D. Patterson, and David D. Chang

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

Progression-free survival in EGFR mutation positive and negative patients



Therapies Addressing Epidermal Growth Factor Receptor



Diagnostic Solutions for the EGFR Pathway are Highly Relevant For Many Current and Future Therapies in Oncology

Source: QIAGEN

EGFR = Epidermal Growth Factor Receptor

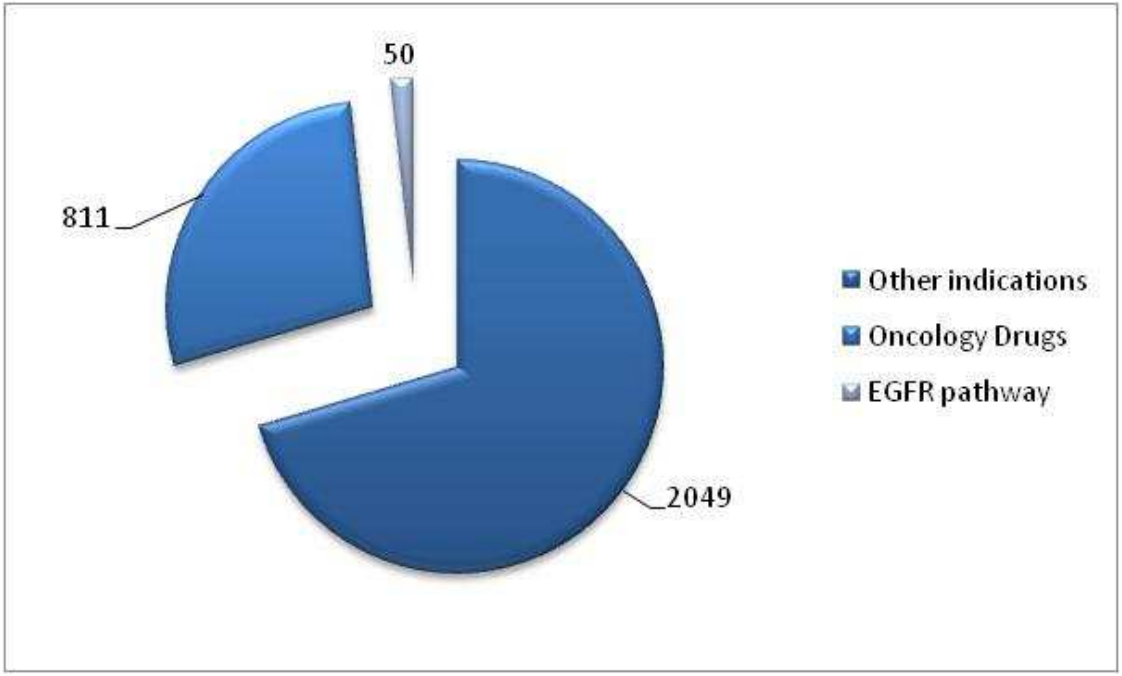
Molecular Diagnostics – Personalized Healthcare
New Partnerships in Companion Diagnostics

Exclusive Licence for Biomarker PI3K from John Hopkins University

- QIAGEN to develop RT-PCR and Endpoint-PCR assays for companion diagnostic use with certain cancer treatments
- Provides QIAGEN pharma partnering opportunities to develop and market tests for new cancer drug candidates
- Expands opportunity to develop a series of personalized healthcare diagnostics based on proprietary platform

NOVARTIS ONCOLOGY	BKM120
sanofi aventis	XL147
Genentech A Member of the Roche Group	GDC0941
gsk GlaxoSmithKline	GSK1059615
ONCOTHYREON	PX-866
Calistoga Pharmaceuticals	CAL101

CDx Market Potential
EGFR Pathway Represents Just a Fraction



Drugs targeting the EGFR pathway represent <2% of drugs in development

New Wave of Safety Biomarkers

Drugs with pharmacogenetic safety markers			
Drug	Company	Safety marker	Prediction
Abacavir	GSK	HLA B5701	Rash
Antibody flucloxacillin		HLA B5701	Liver injury
Allopurinol		HLA B5801	Severe adverse events
Carbemazapine		HLA B1502	Serious adverse events
Warfarin		VKORC1	Dose
Warfarin		CYP2C9	Dose

- Novartis submitted lumiracoxib (Prexige, COX2 inhibitor) and a safety genetic marker (DQA1*0102) to predict liver toxicity for the management of osteoarthritis pain to the European regulatory authorities in December 2009. FDA discussions planned.
- Exanta, an AstraZeneca oral direct thrombin inhibitor which was withdrawn from development in 2006 due to liver toxicity. This was shown to be associated with HLA alleles DRB1(*)07 and DQA1(*)02 but AZ has not announced any plans to try to use a pharmacogenetic test to rescue this drug.

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

Understanding the Customers' Needs
Key to Commercial Success

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

Deliver Companion Diagnostics
Seven Critical Issues

Clinical
- Sufficient data to demonstrate the clinical utility

Technical
- Assays need to be reliable, robust, and compatible with diagnostic lab operations

Regulatory
- Approval needed for the drug, the diagnostic, and (in USA) the instrument

Availability
- Needs to match the distribution of the drug – global if there is a pharma partner

Reimbursement
- Who will pay for the test and how much

Legal
- Are all technology and gene licenses in place

Commercial
- Different models needed depending on level of drug company involvement

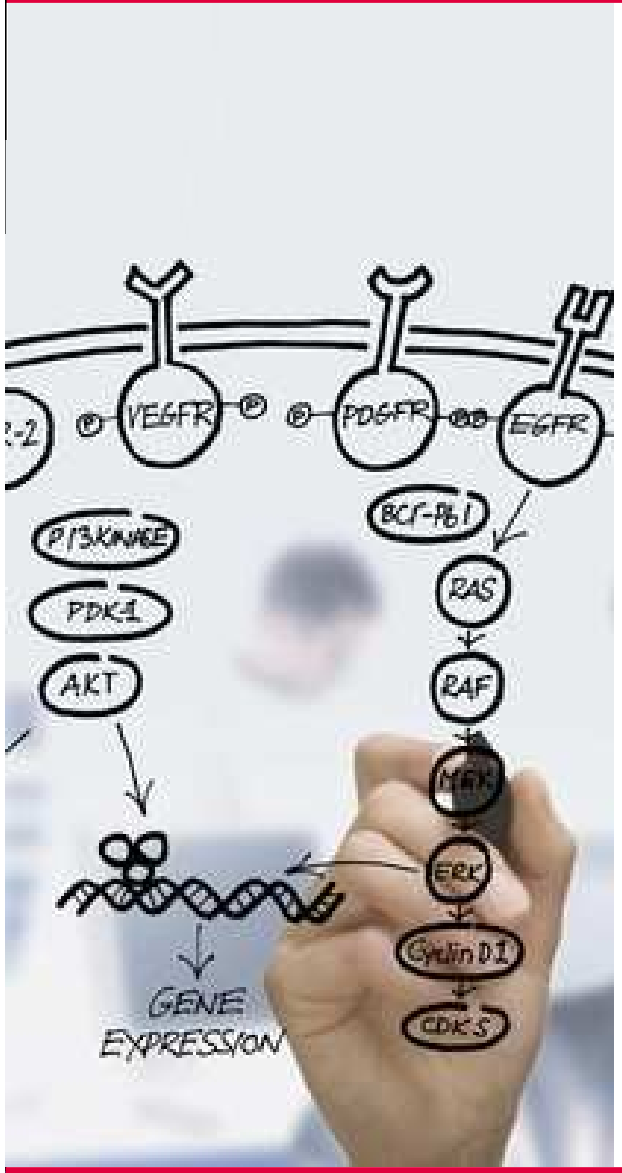
The Economics of Companion Diagnostic Development

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
- A standalone clinical trial for the companion diagnostic can easily run over $20M
- 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.

Five Ways to Demonstrate Clinical Utility



1. **Stand alone**
   Diagnostic company can identify a way to gain IP on an assay and generate sufficient returns to pay for the investment in discovery and clinical development

2. **Partnership (Piggy Back)**
   Drug industry requires a companion diagnostic to effectively market its therapies and works with a partner to make this happen

3. **FDA assent**
   FDA are eager to promote personalized medicine and have relabeled a number of drugs to include a reference to personalized medicine e.g. Warfarin, Irinotecan, or 6MP

4. **One-stop shop**
   Integrate Drug and Diagnostic Delivery

5. **Short cut**
   Introduce tests based on early data – prior to rigorous demonstration of clinical utility

Features of CDx Business Models

	Stand alone	Partnership	FDA Assent	Short cut	One-stop shop
Costs	High - Dx co-funded clinical	Revenue generating	Low – no clinical	Medium – minimal clinical	High – part of drug development
Revenues	High – Dx driven	Medium - Rx driven	Low – Dx driven	Low - medium	Low – not significant
Marketing	Independent	Rx co-supported	Independent if generic	Independent or payor	Rx/Dx partnership
Exclusivity	IP driven	Clinical trial and IP	None or IP driven	None or IP driven	Clinical trial or IP
Risk	High	Low	Low	Medium	High
Regulatory Pathway	LDT or 510K	IVD - PMA	IVD – 510K	LDT	IVR - PMA
Examples	Genomic Health, XDx, etc.	QIAGEN, (DxS), Monogram, Dako	Osmetech Third Wave	Caris, Clarient	Roche
Location	Geographic	Global	USA	USA	Global

Pharma Partnership
The Most Attractive for QIAGEN

- Funding for CDx development
- Clinical utility issue solved
- Drug success guarantees market
- Reimbursement levels increasing
- Co-marketing with Pharma

and…

- QIAGEN has infrastructure
- QIAGEN has platforms, flanking menu, and Sample & Assay Technologies needed

QIAGEN – Best Partner for Pharma

Pharma's Options for Partnered Companion Dx

	QIAGEN	Small Dx Company	Large Dx Company	Reference Laboratory	Specialized, Small Lab
Technology Options	Broad	Limited	Limited (in Mdx)	Broad	Limited
Platform presence	Broad	Limited	Broad	No	No
Independency from Pharma	Fully independent	? Can change fast	Mostly NOT given	Given	? Can change fast
CDx Experience	Yes	Possibly	Selectively	Possibly	Possibly
Global presence	Yes	No	Yes	No	No
Regulatory	Yes	Limited	Yes	Selectively	Limited
Manufacturing	Yes	Limited	Yes	No	No
Menu options	Yes	No	Yes	Yes	No
Access to physicians	Yes	Limited	Rare	Yes	Possibly

Meeting the Needs of Pharma
High Speed and Low Risk

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

Partnering with the Pharmaceutical Industry

Dx pathway

Identify Relevant Biomarkers (GeneGlobe, SABiosciences)

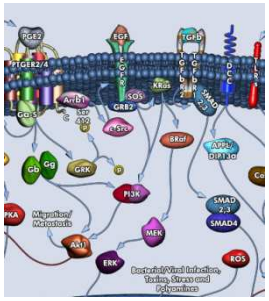
Develop Approved CDx products (DxS)

Sell Companion Diagnostics (QIAGEN)

Used by pharma on preclinical and clinical samples

Used by pharma on clinical trial patients

Used by diagnostic labs on samples of „real“ patients



Drug development Phase I and II

Drug development Phase II and III

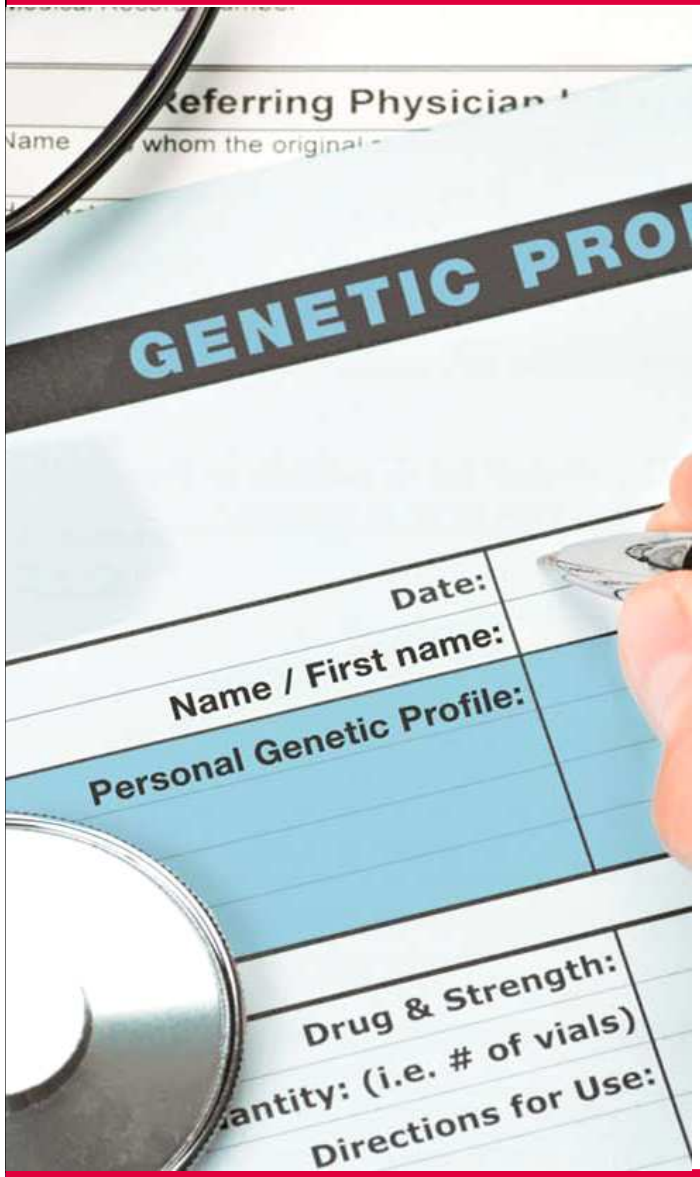
Sell Drugs

Rx pathway

CDx co-development agreement in place

Coordinated submissions to FDA

QIAGEN with Unique Value Proposition



QIAGEN's value proposition for Pharma partners:

- A significant supplier to Pharma discovery and development
- Owner of vast technology portfolio in molecular sample and assay technologies
- Full infrastructure for pharma co-developments
- A leader in molecular diagnostics
  - Own diagnostic platforms with installed base
  - Regulatory depth
  - Sales channel strength
  - Intellectual property – platform and content
  - Global reach
- Independence

Molecular Diagnostics – Personalized Healthcare

New Partnerships in Companion Diagnostics

Development Agreement with Pfizer Inc

- EGFRvIII companion diagnostic for Phase II immunotherapy vaccine against Glioblastoma multiforme (GBM)
  - GMB is most common and most aggressive primary brain tumor in adults
  - GMB occurs in ~25,000 patients annually
  - EGFRvIII mutated in 25-40% of GMB tumors
- RT-PCR assay to identify tumors with mutated EGFRvIII

QIAGEN in the Wider Personalised Healthcare Market

Pharma Partnership	Provider Cost Saving	Patient Outcomes
Global leader in companion diagnostics	Provide reagents	Monitor opportunities
Full infrastructure for partnerships	QIAGEN not active in reference lab market	Sensitive to changes in reimbursement practice
Highest priority	Seek partnerships to productise lab tests	

Summary

QIAGEN is currently the world leader in the provision of companion diagnostics

The opportunity exists to maintain this lead as the market expands, thereby creating a substantial companion diagnostics business

The challenges for the future are all about managing growth and delivering on expectations

Thank you !