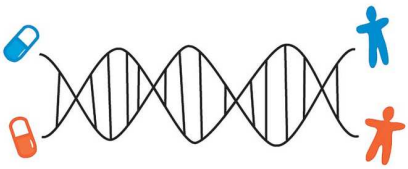


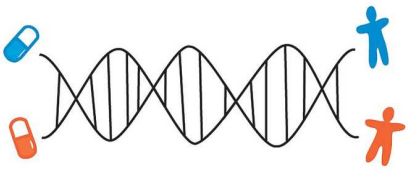
EPEMED
The European Personalised Medicine Association

THE GOVERNMENT
OF THE GRAND DUCHY OF LUXEMBOURG
Ministry of the Economy and Foreign Trade

INTEGRATED BIOBANK OF LUXEMBOURG

Official Program Opening & Welcome

Mars Di Bartolomeo
Minister of Health - Luxembourg
Alain Huriez
Chairman EPEMED
Chief Executive Officer TcLand Expression



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Key Note Address
The Personalised Medicine Opportunity in Europe

Isabel de la Mata,
Principal Adviser - Public health and risk assessment,
Health and Consumers Directorate-General /
EU Commission

Luxembourg Personalised Medicine Initiative

Bob Phillips
Luxembourg Speaker Chief Executive Officer IBBL
(Integrated Biobank of Luxembourg)

Luxembourg – Small is Beautiful (Big Dreams and Practical Projects)

Think Big

- Luxembourg is leader in early adoption of new advances in personalized healthcare
- Strive to:
  - Prevent the preventable
  - Cure the curable
  - Manage chronic disease when necessary

Act Small

- Small projects that can be easily replicated anywhere
- Partner with the most innovative companies and research institutes
- Share our experiences

2008 – Luxembourg Creates New Research Program in Personalized Medicine

Luxembourg

- Luxembourg Centre for Systems Biomedicine
- Integrated Biobank of Luxembourg – IBBL
- Lung Cancer

U.S. Partner

- Institute for Systems Biology (Seattle)
- TGen – Arizona Research Centre
- Program in Personalized Medicine – Consortium of several U.S. centres

First Pilot Study: Search for blood biomarkers for lung cancer

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Evolution of Personalized Medicine Consortium (PMC)

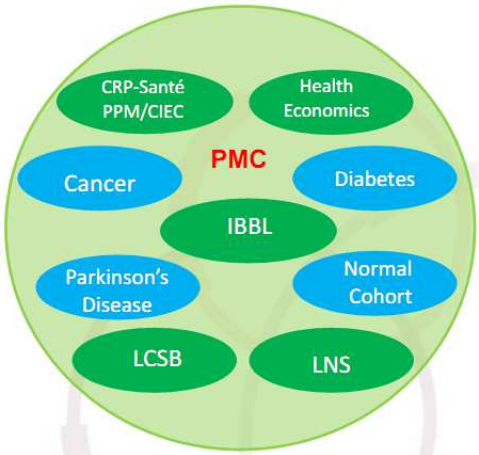
- September 2010 – agree to support a major coordinated initiative in personalized medicine focused on four priority research areas:
  - Cancer (lung, colon, and breast)
  - Type 2 diabetes
  - Parkinson's disease
  - Large population cohort
- Agree to apply a systems biology approach
- Creation of a Personalized Medicine Consortium to bring together all of the key stakeholders under one umbrella
- Build capacity in scientific excellence in priority areas
- Establish international collaborations
- Establish Luxembourg as a leader in the adoption of new advances in personalized medicine

Organization of PMC

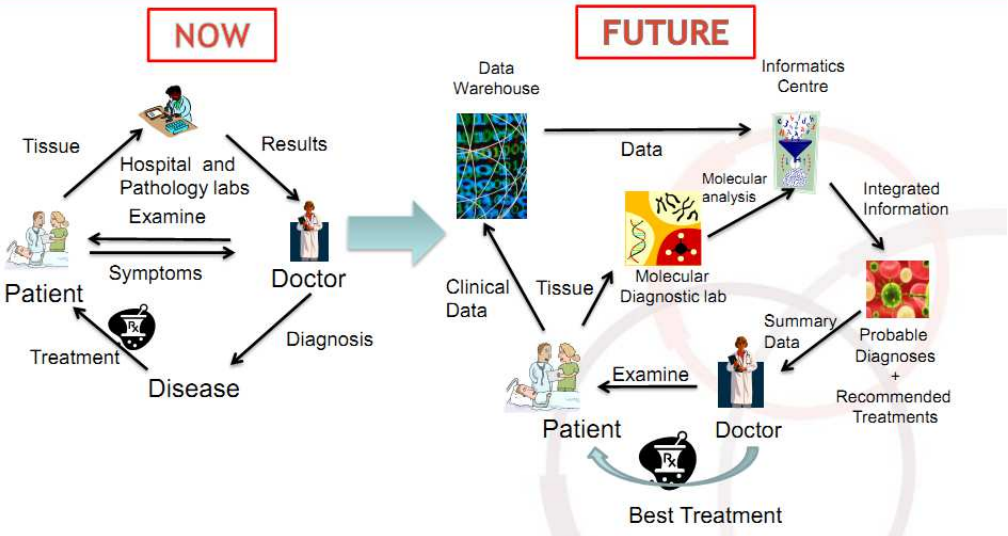
Composition of PMC

- Leaders of each program in personalized medicine
- Leaders from each major partner
- CIEC
- Health economics
- Laboratoire National de Santé

- IBBL accepts responsibility for the administrative budget of PMC and for coordination
- PMC meets monthly
- Decisions made by consensus



Transition Will Require Radical Change



Overview of PMC Strategy

- Cancer – time to introduce molecular diagnosis into regular clinical practice
- Defects in energy metabolism are common in cancer, diabetes and Parkinson's disease
  - Trying to understand the gene-environment interactions that lead to these defects
  - Systems approach to identify specific subtypes of disease
  - For diabetes and Parkinson's disease focus on families

Mission and Vision of IBBL

- IBBL Vision:

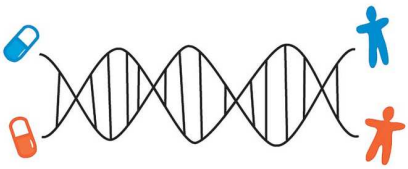
  To be an international centre of excellence in biobanking and accelerate the introduction of personalised healthcare for the benefit of Luxembourg.
- IBBL Mission:

  With the help of the people of Luxembourg, we provide high quality specimens and data, catalyse partnerships and support research that translates today's discoveries into tomorrow's healthcare solutions.

IBBL - Integrated Concept

- Tissue bank
- Data repository
- Technology hub
- Research
- Personalized Medicine Consortium (PMC)

Questions and Comments



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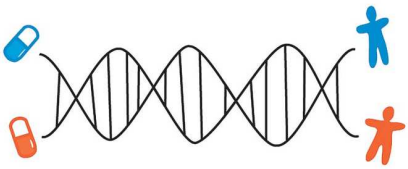
European Innovation in Diagnostics

SESSION'S CHAIR:
Peter Collins
Vice President of Diagnostics, GlaxoSmithKline

PANEL OF COMPANIES WITH INDIVIDUAL CASE STUDIES OF SUCCESS IN EUROPE
Werner Kroll
Global Head Research & Innovation
MDx
Novartis Institutes for BioMedical Research Inc.
Peter Payne
Chief Business Officer,
TcLand Expression
Richard Watts
Senior Director of Business Development
Companion Diagnostic Partnerships, Qiagen
Iain Miller
Global Head, Personalized Healthcare Strategy and Partnerships
GE healthcare

European Innovation in Diagnostics
Format of Session

- Introduction and role: what innovation are they involved in
- What incentives are there Dx Innovation in Europe?
  each panel member to deliver their view
  opportunity for audience response/questions – 10 minutes
- How can Europe be a leader in the delivery of Dx Innovation?
  each panel member
  audience response/questions
- Summary and Conclusions



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European Innovation in Diagnostics

SESSION'S CHAIR:
Oliver Bayliss
Principal Sales Director
Oracle Health Sciences Business Unit.

Loic Kubitza
Director
PriceWaterhouse Coopers
Kristin Pothier
Partner
Health Advances

www.pwc.com/lu

Economics of developing companion diagnostics – Insights from *Diagnostics 2011*

Loïc Kubitza
Director, PwC Luxembourg

EPEMED Conference
Luxembourg, 8 December 2011

pwc

A new study on diagnostics and personalised medicine was released on 6 December 2011

The PwC Pharmaceuticals, Life Sciences and Healthcare practice conducted two recent studies on the diagnostics sector and its increasing role in the development of personalised medicine. These studies are complemented by another PwC report on the challenges and opportunities of personalised medicine for players within and beyond the health industry.

Dec 2011

The ***Diagnostics 2011*** study covers:

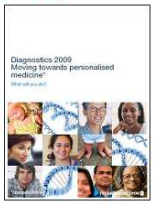
- M&A activity in the IVD sector
- Pharma's business models for in-house IVD capability
- Companion diagnostics partnerships with the pharmaceutical industry
- Diagnostics for early detection
- Ten significant events for personalised medicine
- Case studies

Dec 2009

The ***New Science*** report covers:

- The importance of collaboration as a key to success as new approaches, relationships and ways of doing business are required to best leverage opportunities in identifying new products, services and information
- In-depth discussion about how personalised medicine is redefining the industry and disrupting business models
- Key observations and how to capitalise on the opportunity personalised medicine presents

Jul 2009



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- M&A activity in the IVD sector
- In-licensing activity by IVD majors
- Regulatory requirements for biomarker testing
- Companion diagnostics partnerships with the pharmaceutical industry
- Ten significant events for personalised medicine
- Case studies

Content

1. Demand for diagnostics
2. Pharma's interest in diagnostics
3. The economics of companion diagnostics innovation
4. The challenge to Pharma

Demand for diagnostics

1

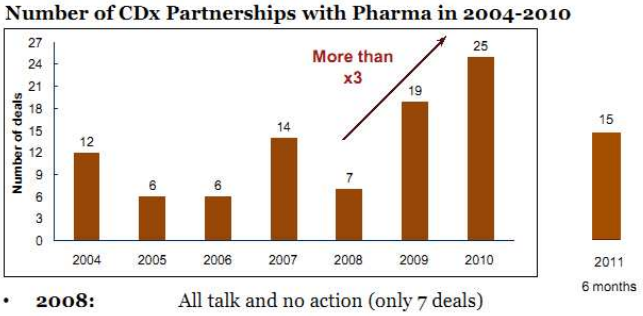
4 symptoms suggest strong demand for Dx

1. CDx partnerships with Pharma
2. Revenue projections
3. M&A
4. Venture funding

Symptom #1: CDx partnerships with Pharma

More than tripled in 2010 compared with 2008

Number of CDx Partnerships with Pharma in 2004-2010



- **2008:** All talk and no action (only 7 deals)
- **2009-2010:** Pharma has started to "walk the talk" (deals almost tripled in 2009): A larger number of Pharma companies are taking more seriously the need for co-development programs (Drug + Biomarkers + CDx)
- **2011:** Strong growth continues (15 deals in first half-year)

PwC Source: PwC analysis using data from Windhover and other publicly available sources 6

Symptom #1: CDx partnerships with Pharma

Analysis by type of partner and disease during 2009-2010

Pharma partner

- **Big Pharma** continues to dominate
  - Leading the way: GSK, Roche and Pfizer
- But some **Medium-sized and Niche** Pharma are active as well
  - For example: OSI (now part of Astellas), Merck KGaA, Aeterna Zentaris, Biogen Idec, Clovis Oncology, Daiichi Sankyo, Merz, Optherion and Transgene

Diagnostic partner

- **Medium-sized and Niche** IVD specialists continue to dominate (e.g. Qiagen, Almac, Dako and MDxHealth)
- But a larger number of **top-9 IVD** players (Roche, Abbott, bioMérieux) have been active partners for Pharma

Disease areas

- **Cancer** continues to dominate
- But **neurology, infectious and other** diseases are making an appearance

PwC Source: PwC research using publicly available sources 7

Symptom #1: CDx partnerships with Pharma

2011 so far and outlook for 2012-1015

- **2011:** Start of 2011 was lively ... at least **15 IVD partnerships** with Pharma were reported in **first half-year**. Here a **selection** of a dozen partnerships ...

Dx Partner	Pharma Partner	Deal Subject	Disease Area	Deal Date
Roche	Clovis Oncology	Dev PCR based CDx for CO-1686 (precln for advanced NSCLC), to id activating EGFR mutations eg EGFR T790M	Cancer - Lung	Jun-11
Roche	Merck & Co	Dev assays for investigational cancer products and expand use of AmpliChip p53 to select and stratify patients for trials	Cancer - Unspecified	Jun-11
Foundation Medicine	Celgene	Dev cancer genomics test to recruit patients suitable for Celgene drug candidate trials. The test will use NGS	Cancer - Unspecified	May-11
MolecularMD	ARIAD Pharma	Dev and sell CDx for pan-BCR-ABL inhibitor, ponatinib, to id T315I mutation in CML and to id Philadelphia + in ALL	Cancer - Leukemia	Mar-11
Invivoscribe	Novartis	Dev and sell a test to id FLT3 mutated AML patients for use with midostaurin, in Phase III for newly diagnosed patients	Cancer - Leukemia	Feb-11
bioMérieux	Ipsen	Id Rx-Dx co-dev opportunities in hormone-dep't cancers, initially for prostate, breast, neuro-endocrine and pituitary	Cancer - Prostate and	Feb-11
Biocartis	J&J	Janssen Pharma to co-dev and sell assays on Biocartis MDx platform in fields of neurological and viral diseases	Neurology - Unspecified	Jan-11
Opko Health	BMS	Investigate blood-based technology to id individuals with early stage cognitive impairment likely to progress to AD	Neurology - Alzheimer	Jan-11
MDxHealth	Pfizer	Id and dev a biomarker predicting response to PF-01367338, the PARP-inhibitor candidate for ovarian and breast cancer	Cancer - Ovarian and	Jan-11
Zinfandel	Takeda	Study diabetes drug Actos as AD prevention treatment using TOMM40 test to id high risk adults for trials	Neurology - Alzheimer	Jan-11
Beckman Coulter	Transgene	Dev test to measure activated NK to select patients for immunotherapy TG4010 for pivotal Phase IIb/III trials	Cancer - Lung	Jan-11
Foundation Medicine	Novartis	Dev and optimise cancer genome panel test for Novartis' needs. If pilot successful, will consider further collaboration	Cancer - Unspecified	Jan-11

  - **Rx partners:**
    - Big Pharma dominates scene but presence of parties not commonly involved in past: Takeda, J&J
    - Medium or niche therapeutics players: Clovis, Ipsen, Celgene, Transgene, ARIAD
  - **Dx partners:**
    - Top-9 IVD: Roche is keeping a strong momentum; bioMérieux is present as in 2009-2010; Beckman Coulter made a rare appearance
    - New niche players: Foundation Medicine, MolecularMD, Biocartis, Opko Health, Zinfandel
  - **Disease:** Several neurology partnerships alongside a majority of cancer deals

- **2012-2015:** **Pharma**'s demand for CDx deals will remain strong ... the same drivers will continue and intensify over the next few years
  IVD players will face strong economic challenges to sustaining innovation ...

PwC Source: PwC research using data from publicly available sources 8

Symptom #2: Revenue projections

Strong growth is expected in certain segments of IVD sector

IVD market sales by segment

Market Segments	2009 ($bn)	2014E ($bn)	CAGR 2009–2014E	Market Dynamics
Professional Diagnostics	29	36	5%	Driven by testing efficiency and unmet medical needs. Serum work area is largest segment.
Diabetes Monitoring	8	9.5	3%	Market growth declining due to pricing pressure.
Molecular Diagnostics	3	6	11%	Fastest-growing market segment. HPV and other cancer and genetic testing are key growth drivers.
Tissue Diagnostics	2	3	9%	Driven by continued lab automation and new cancer tests
Total	42	53	5%	

Segments most relevant to CDx

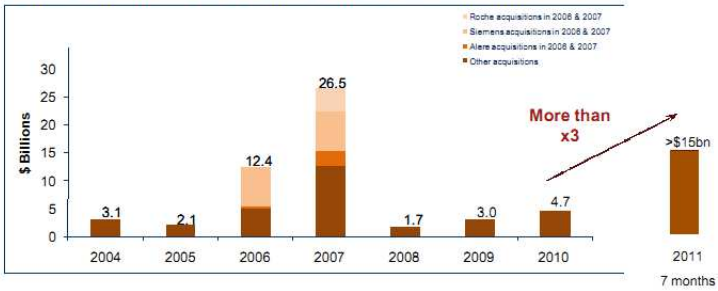
- **Overall:**
  - 5% growth
- **Molecular and tissue diagnostics:**
  - Small (12% of total IVD market) BUT
  - Growing fast (11% and 9% growth forecasted to 2014) AND
  - Attracting significant investor interest

PwC Source: Presentation by Roche at the American Association for Clinical Chemistry meeting of July 2010 9

Symptom #3: IVD M&A

Value will more than triple in 2011

Value of disclosed M&A deals in the IVD Sector 2004-2010



- **2009-2010:** M&A deal values increased gradually following trough of 2008
- **2011:** After 7 months, selected deals drove the value of M&A to $15bn

 Source: PwC analysis using data from Thomson Financial, Windhover, Mergermarket, Zephyr and other publicly available sources

Symptom #3: IVD M&A

Top 10 deals of 2010: strong interest from non-IVD players

Top 10 M&A Deals in IVD Sector in 2010

Value ($m)	Target	Bidder	
1,094	Sebia	Cinven	1
925	Genzyme Genetics	Labcorp	2
587	Clarient	GE Healthcare	3
265	Genzyme Diagnostics	Sekisui Chemical	2
255	Epocal	Alere (Inverness)	4
217	Standard Diagnostics	Alere (Inverness)	4
215	Home Diagnostics	Nipro	3
130	Diagnostic Hybrids	Quidel	5
112	Innogenetics	Fujirebio	2
105	Helixis	Illumina	5

5 themes:

1. Return of the LBO
2. Domino effect of business portfolio restructuring
3. Industry convergence
4. Consolidation of POC testing
5. Addition of complementary products

Value of IVD M&A deals in 2010

- Deal value rose 57% to $4.7bn in 2010, following a small number of higher-value deals

Analysis of top 10 deals in 2010

- 5 themes
- Appetite from non-IVD bidders:
  - Financial (Cinven)
  - ClinLabs (LabCorp)
  - MedTech (GE)
  - LS Research (Illumina)
- But … no Pharma bidders

 Source: PwC analysis using data from publicly available sources, including Thomson, Mergermarket, Zephyr and Windhover

Symptom #3: IVD M&A

Selected deals of 2011: Novartis is the only Pharma bidder

Selected M&A Deals in IVD Sector in Jan-Jul 2011

Value ($m)	Target	Bidder
330	Genoptix	Novartis
6,800	Beckman Coulter	Danaher
344	Celera	Quest Diagnostics
119	PVT	Roche
355	Cellestis	Qiagen
80	Rules Based Medicine	Myriad Genetics
3,500	Phadia	Thermo Fisher Scientific
1,100	Prometheus Labs	Nestlé
32	Stanbio Laboratory	EKF Diagnostics
101	Ipsogen	Qiagen
1,973	Immucor	TPG
266	mtm Laboratories	Roche

Note: Includes selected CLIA labs

- Genoptix is a CLIA lab – not an IVD business
- We have included selected CLIA lab deals in the list of M&A deals in the IVD sector:
  - CLIA labs represent half the channel to market for *in vitro diagnostics* in the US. Thus, CLIA labs are an important way of operating an *in vitro diagnostics* business in the US.

Value of IVD M&A deals in 2011

- >$15bn – After 7 months, the value of announced deals is more than $15bn
- Gen-Probe – In Jun 2011, press reported potential acquisition by Novartis but in July deal seemed off. Market cap was $4bn at 3 Jun 2011.

Analysis of selected deals in 2011

- Appetite from non-IVD bidders continues:
  - Existing sectors: ClinLabs (Quest), LS Research (Thermo Fisher), ...
  - New sector: Food (Nestlé)
  - Pharma: Novartis is the only Pharma bidder ... showing the way for other Pharma bidders in future?

PwC Source: PwC analysis using data from publicly available sources 12

Symptom #4: Venture funding for IVD

Overall numbers modest but strong investor interest for specific cases

IVD Private Placements (excluding PIPEs) in 2009-2011 YTD

	2009	2010	11m 2011
Number	43	29	21
Amount ($m)	553	591	392
Selected US	• $48m Tethys Bioscience (D) • $45m Complete Genomics (D) • **$40m Integrated Diag. (A)**	• $109m Pacific Biosciences (F) • $39m Complete Genomics (E) • $35m CardioDx (D)	• $60m CardioDx (E) • $32m HTG (D) • $31m Crescendo Biosc. (C)
Selected EU	• $50m Curetis (A) • $23m Agendia (E) • $15m Biocartis (A)	• $40m Biocartis (B) • $26m Oxford Immunotec (D) • $18m Horizon Discovery (C)	• **$96m Biocartis (C)** • **$15m Transmedi (B)** • $8m Population Genomics (B)

- Investors are willing to invest **large amounts in specific IVD companies**, even in early Series
- Three "European" cases to highlight:
  - Biocartis – More than $150m raised from 3 Series (A, B and C)
  - Integrated Diagnostics – US but with Luxembourg connection (BioTech Cube)
  - Transmedi (Genclis) – Cancer early detection, based in Nancy (near Luxembourg)

PwC Source: PwC analysis using data from Windhover and publicly available sources 13

Pharma's interest in diagnostics

2

5 reasons for Pharma to be interested in Dx

1. Regulatory pressure
2. Payer pressure
3. Time to market
4. Drug response
5. Niche-buster revenues

Sticks

Carrots

5 reasons for Pharma to be interested in Dx

1. Regulatory pressure	• Regulators are asking for companion test when expect significant response improvement in sub-population • E.g. Omapro by ChemGenex for CML adults (FDA, April 2010)
2. Payer pressure	• Payers encourage diagnostics as effective tools for cost-control • E.g. Potential annual savings of $600 million are expected in the US from KRAS testing to predict response to EGFR inhibitors (e.g. Erbitux)
3. Time to market	• Halving TTM is possible through patient stratification • E.g. 47% and 55% saving in development time for Zelboraf (vemurafenib) (Roche/Plexxikon) and Xalkori (crizotinib) (Pfizer) vs cancer average
4. Drug response	• 80% possible vs 25% average response rate for cancer • E.g. 81% for Zelboraf (Roche / Plexxikon) for metastatic melanoma in a preliminary study. Drug and CDx approved in Aug 2011.
5. Niche-buster revenues	• Potential billion dollars revenues are not ruled out, based on high market shares within targeted population • E.g. $1.5 billion peak by 2020 for crizotinib for lung cancer

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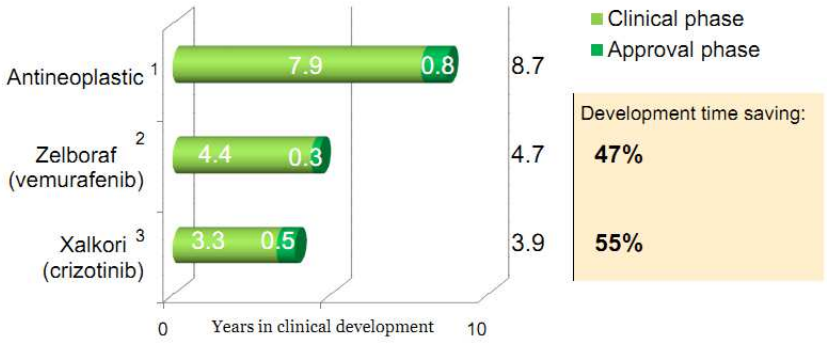
2 promising Rx-Dx cases

Approved by FDA in Aug 2011 with development time halved vs average



Source: bioMérieux presentation, Jun 2011, updated by PwC in Sep 2011 based on company press releases

1. Kaitin K. Clin Pharmacol Ther., Mar 2010; 87(3):356-61
2. Zelboraf for melanoma: FDA submission in May 2011; approval in Aug 2011 (Rx: Roche / Daiichi-Sankyo; Dx: Roche)
3. Xalkori for lung cancer: FDA submission in Jan 2011; approval in Aug 2011 (Rx: Pfizer; Dx: Abbott)

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4 business models for Pharma

Examples of in-house IVD capability and options to grow CDx activity

Model	Model (1): Dx Division	Model (2): Dx BU in Pharma Division	Model (3): Dx BD Group in Pharma Division	Model (4): Lx Division
Description of in-house Dx capability	• Standalone Dx business in separate division • CDx are part of scope but non-CDx are main source of business	• Capability to develop own Dx within Pharma division • CDx are the main (but not exclusive) focus of the Dx capability and the CDx tests are mainly for own Rx products (but scope to license out non-core applications)	• Capability to license-in Dx technology • Dx focus is exclusively on CDx to support own Rx products	• Standalone life sciences research products business • Some of the technology could be adapted to Dx use in future
Company examples	• Roche • Abbott (current) • J&J	• Novartis	• AZ • Lilly • GSK	• Merck KGaA (Millipore)
Options for growth of CDx activity	• Adapt Dx capability to CDx needs • Pursue CDx partnerships in-house as well as with external partners • Acquire new technology	• Grow Dx development capability • Grow Dx licensing-in capability • Acquire new technology	• Add to licensing-in capability • Grow biomarker discovery capability • Shift to Model (2) by adding assay development capability	• Adapt technology from research use to clinical use with focus on CDx applications • Acquire technology for clinical use

Notes: BU = Business unit; Dx = Clinical diagnostics; CDx = Companion diagnostics; Lx = Life sciences research products (non-clinical)

PwC Source: PwC analysis following discussion with industry contacts 18

1 break-up scenario

What if a Pharma with a large IVD division considers breaking up?

What may be driving break-up?

- The drivers may not be related to the value of Rx-Dx synergies:
  - **Releasing value through separation** – The focus may be on releasing greater value for shareholders by providing greater visibility for the specific dynamics of each division
    - The focus may be on helping equity research analysts see more value
  - **Carving out CDx-relevant technologies may be difficult** – Not all technologies within a large, broad-spectrum, stand-alone IVD businesses are relevant to supporting a Pharma pipeline/portfolio. Some of the CDx-relevant technologies may have dual ambitions (CDx and standalone Dx)
    - In some cases, decision makers may find it easier to:
      - › separate completely the existing IVD and Pharma divisions, and
      - › rebuild a CDx-focused business from scratch within Pharma division

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1 scenario for future: IVD M&A by Pharma

The option has not really been exercised … but is still there

- Pharma has not acquired a high-value IVD business recently (if we ignore the Genoptix acquisition by Novartis) …
- But … the time may come soon when the practice of Rx-Dx co-development will become so prevalent that some Rx players will consider the M&A route
- **What IVD business profile will attract M&A by Pharma?**

- **Top 5 IVD company?** Unlikely …
  Their presence across most of the traditional IVD market segments will not be relevant
- **Niche IVD player?** More likely …
  A focus on relevant molecular or tissue diagnostic technology will be attractive

The economics of companion diagnostics innovation

3

Major challenges to sustained Dx innovation remain despite strong demand for Dx …

3 key challenges	Current situation	Illustration
Pricing	• Pricing is **cost-based** in most cases • Some cases of **value-based pricing** exist but (1) mainly driven by Lab developed tests in US and (2) not replicated in Europe	• In the US, one rare example of value-based pricing is Genomic Health's Oncotype DX ($4,000) • This model has not been widely replicated in Europe (although it is starting in Ireland)
Reimbur-sement	• Takes **4-7 years** post marketing • HTA process is different in **each territory** in EU • Fix: Several cases of **Rx partner subsidizing the CDx**	• 4 years is seen as a minimum for Germany • AstraZeneca **sponsors** EGFR mutation testing in the UK NHS
Share of Deal Value	• Long-standing **perception** of low entitlement to value for Dx • History of **< 2% of HC spend** whilst influencing **> 60% of HC decisions**	• Senior CDx deal makers from Dx sector refer to **1% share of Rx-Dx project value for Dx partner**

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Impact on economics of Dx innovation

Despite its critical importance for adoption of the Rx, the companion Dx typically faces a challenging NPV equation

	Key factors impacting business economics	Potential combined effect
Pricing	• **Low pricing** … due to cost-based approach in most cases	• Pressure on potential to achieve a positive NPV by Dx companies • Risk of discouraging investment in emerging Dx ventures • Pressure on sustainability of innovation effort by emerging Dx companies • Delay patient's access to important new heath technology
Reimbur-sement	• **Slow market adoption curve** … due to delay in obtaining reimbursement (4-7 years post marketing) • **High sales and marketing costs** … due to complexity and diversity of HTA process in each territory in EU	
Share of Deal Value	• **Limited updside for Dx when Rx succeeds** … due to low recognition of Dx value by Rx	

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Potential actions to address economic challenge

Regulators, Payers and other stakeholders need to help Dx originators gain stronger recognition – in concrete economic terms – for the value contributed by Dx to patients, healthcare budgets and the Rx partner

Actions proposed by Dx industry members

Pricing

- Pricing should reflect the **value** of the test (clinical benefits as well as cost savings) rather than its **cost**

Reimbur-sement

- HTA models and review processes should be optimised and harmonised to **reduce the diversity** of HTA demands across territories
  - The EC is sponsoring EUnetHTA initiative to explore options
  - Concrete improvements need to come through in practice

Share of Deal Value

- CDx originators are asking Rx partners to provide a **royalty on sales of the Rx** or at least agree a form of **value-added fee** based on success of Rx
  - Dx partners feel it would be fair to increase Dx share of Rx-Dx deal values because value of Rx is **critically** dependent on CDx contribution
  - Rx are resisting this model: if the Dx partner wants a share of Rx rewards then he should share into the Rx development costs

What if stakeholders do not take action?

- Not taking action would **damage the survival prospects of many emerging IVD players**, specifically those that are most innovative:
  - Diagnostics innovation could be handed over too cheaply to Pharma
  - Continued investment into diagnostics ventures could be discouraged
  - Patients' access to important new health technology could be delayed

Slow geographic expansion is a specific consequence of long and complex HTA procedures

Emerging US Dx companies have been slow at entering the European market

Perceived Barriers

- Market fragmentation
- Cannot decide what country to focus on
- Afraid of pricing and reimbursement complexity
- Overwhelmed by cost of establishing sales distribution, commercial support and expertise
- Too complicated and expensive to focus on at an early stage
- Could be taken advantage of by large companies

Source: Barriers adapted from workshop with a dozen US based CEOs moderated by Doug Dolginow and Noel Doheny at Luxembourg House in New York, 20 October 2010

Implications

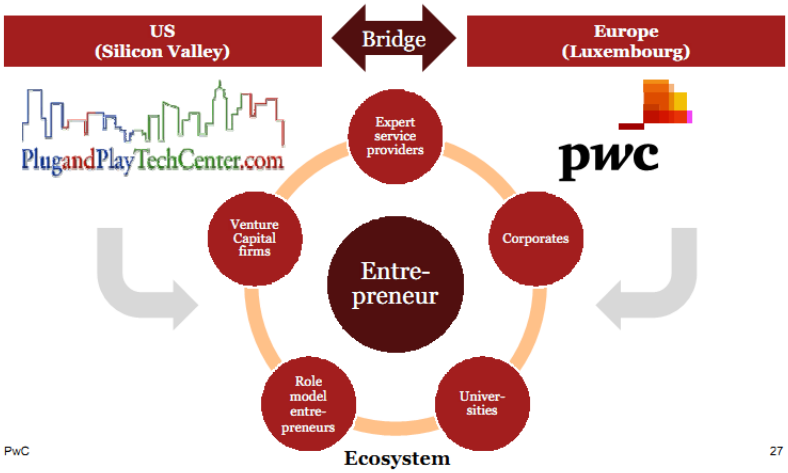
- Avoid EU and international to focus on the US
  - investment needed for success is considered too large
- EU revenues generally planned for out-years (years 5-10)
  - EU considered opportunistic at best
- Occasional discussions with large companies about distribution agreements

Problem: Lost revenue potential for emerging innovative Dx companies

Case for an Accelerator to help promising, "local" US Dx companies go "global"

PwC 26

The PwC Accelerator aims to (1) *build a dynamic* ***ecosystem*** *around the entrepreneur to support both its business and financial development and* ***(2)*** *offer a direct* ***bridge between the US and Europe*** *through its* ***partnership with Plug&Play***



Ecosystem

PwC 27

The challenge to Pharma

4

Is Pharma taking all necessary action to adapt its R&D to personalised medicine?

- Need to analyse Pharma's pipeline to answer this question …
- **Hypothesis:** Pharma is not moving as fast as it should if we consider the proportion of pipelines where an Rx-Dx co-development approach may be relevant

Key messages

- **Trends suggest there is significant demand for / interest in CDx / Dx**
  - Rising CDx partnerships with Pharma
  - Strong revenue growth projections for molecular and tissue diagnostics
  - Rising IVD M&A deal values
  - Willingness to invest significant funds into selected Dx ventures
- **Pharma, in particular, has strong reasons for being interested in Dx**
  - *5 reasons:* regulatory pressure, payer pressure, time to market, drug response, niche-buster revenues
  - Pharma has not been using M&A to access CDx technology but this could change
- **Despite the strong demand for, interest in, and importance of Dx, the economics of Dx innovation are challenging**
  - *3 factors depressing the economics:* the low pricing, slow reimbursement and low value recognition of Dx
  - *Key stakeholders must take action to improve the economics of Dx innovation:* otherwise, they could damage the survival prospects of many emerging IVD players

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THE GOVERNMENT
OF THE GRAND DUCHY OF LUXEMBOURG
Ministry of the Economy and Foreign Trade

INTEGRATED BIOBANK OF LUXEMBOURG

EPEMED – European PM Association and closing of morning session

Alain Huriez
Chairman, EPEMED
Chief Executive Officer TcLand Expression

2nd annual EPEMED conference 7-8 December 2011 Luxembourg

HEALTH ADVANCES

Economics of Life Science Innovation and Personalized Medicine

EPEMED

December 8, 2011

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Strategy Consulting for Industry Leaders: Diagnostics and Life Sciences Practice

Clinical Diagnostics | Life Sciences | Personalized Medicine

- Health Advances is a healthcare strategy firm focused on commercialization strategies in the therapeutics, diagnostics, device, and life sciences industries.
- The Diagnostics and Life Sciences Practice, led by Kristin Pothier, works across the industry from single innovative biomarker companies to large IVD, therapeutic, and life science companies.
  - Personalized medicine is a major initiative in this practice. This initiative, led by Gary Gustavsen, assists therapeutic, diagnostic, and life sciences companies in several ways:
    - Commercialization strategy for products and services
    - Platform and menu prioritization
    - Health economics studies
    - Partnering strategy and acquisition diligence

The Definition of Personalized Medicine

The application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, and help determine a person's predisposition to a particular disease or condition.

– US Congress

Getting more than 7 minutes with my PCP.

– Biotech Industry Executive

The tailoring of medical treatment to the individual characteristics of each patient . . . to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment.

– Personalized Medicine Coalition

A Personalized Approach

Personalized Medicine

The right treatment for the right patient at the right time

Factors Driving Need for Personalized Medicine

- Aging population
- More complex diseases
- Desire to control costs
- Desire to provide better treatment with fewer side effects

Source: Health Advances analysis.

The Paradigm Shift

The biopharma industry has come to appreciate companion diagnostics as a strategic advantage and, in many cases, a necessity.

End of the Blockbuster Era

- End of large "one size fits all" markets (e.g. statins)
- Emergence of niche segments and targeted therapies

Regulatory and Payer Pressure

- Growing emphasis on cost effectiveness

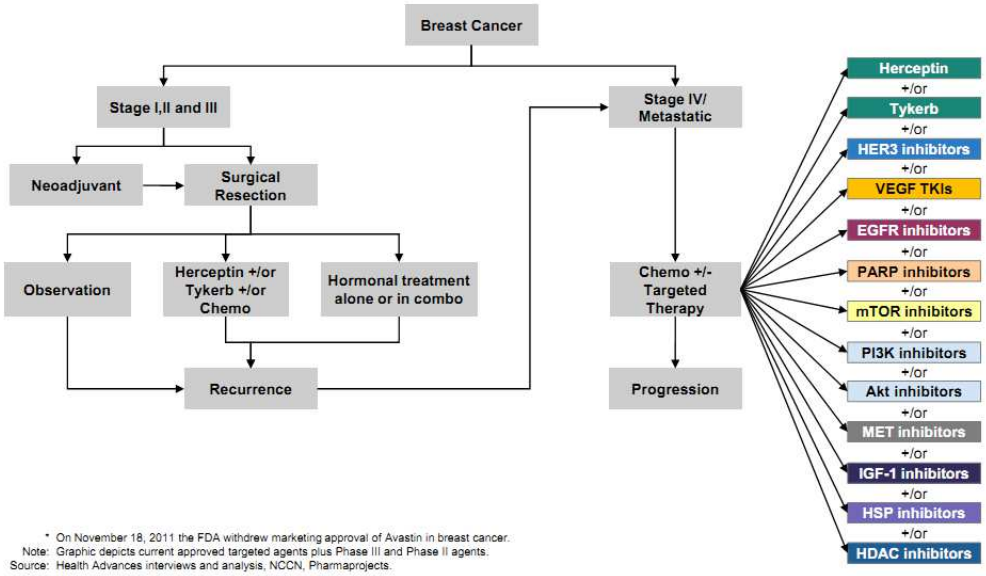
Changing View of Companion Diagnostics

Proof of Concept

- Recent successes prove the value of personalized medicine

Expansion of Targeted Therapies Driving PM: Example

Within a few years, targeted treatment options for metastatic BC will increase dramatically, necessitating novel diagnostics to guide treatment selection.



* On November 18, 2011 the FDA withdrew marketing approval of Avastin in breast cancer.
Note: Graphic depicts current approved targeted agents plus Phase III and Phase II agents.
Source: Health Advances interviews and analysis, NCCN, Pharmaprojects.

Personalized Medicine Applications: Oncology

Personalized medicine has impacted the management of oncology across the continuum of care.

Oncology Continuum of Care

Risk Assessment	Screening	Diagnosis	Staging and Prognosis	Therapy Selection	Monitoring
▪ BRAC*Analysis*®	▪ PreGen-Plus™	▪ CancerTYPE ID®	▪ Onco*type* DX® Breast and Colon	▪ HER2/neu	▪ CellSearch™
▪ COLARIS®	▪ *Early*CDT-Lung™	▪ C-kit	▪ Previstage™	▪ TheraScreen® K-RAS and EGFR Mutation Kits	▪ BCR/ABL
▪ MELARIS®		▪ OVA1™	▪ MammaPrint™	▪ ResponseDX™	
▪ deCODE Prostate Cancer™		▪ *PathFinder TG*®	▪ Prezeon™	▪ VeriStrat®	
		▪ miRview™	▪ Adjuvant! Online	▪ OnDose™	
				▪ ChemoFx®	
				▪ Vysis ALK Break Apart FISH	
				▪ Cobas 4800 BRAF V600 Mutation	

Source: Health Advances analysis.

Personalized Medicine in the EU

EU PM is attractive, but inter-country variability and regulatory/reimbursement challenges are key obstacles.

Opportunities

- Aging population
- Increased incidence of cancer and other diseases
- Strong demand for more targeted, cost effective therapies
- Growing recognition of the value of PM
- Sophisticated clinicians, researchers, and healthcare delivery infrastructure

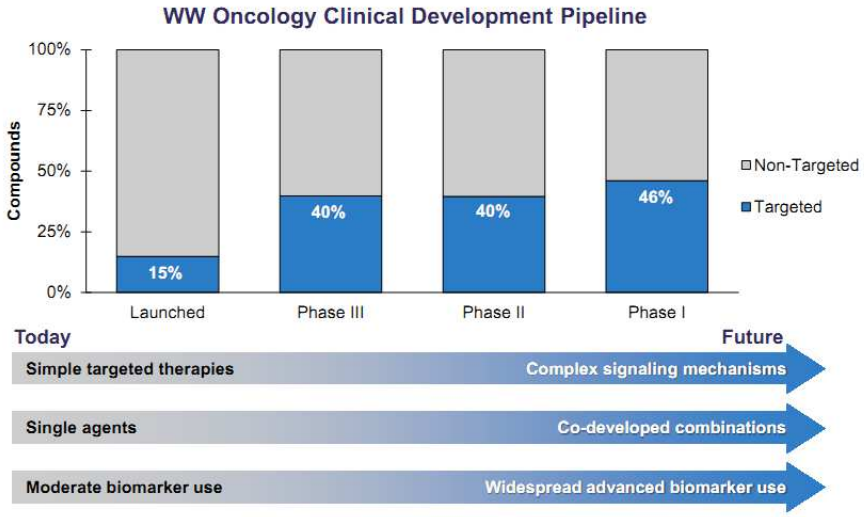
Challenges

- Addressable market(s)
- Economic turmoil and healthcare budget constraints
- Decentralized, complex, and heterogonous regulatory and reimbursement landscape
- Misaligned drug and Dx approval processes
- Frequent reliance on laboratory developed tests (LDTs)

Sources: European Commission; EPEMED; Miller et. al., "Market Access Challenges in the EU for High Medical Value Diagnostic Tests", *Personalized Medicine*, 2011, 8(2).

Oncology Therapy Pipeline

The emphasis on PM and diagnostics in all geographies will only increase, as the pipeline is rich with targeted drugs.



Note: Targeted therapies are defined as affecting specific molecular targets such as EGFR, HER-2, BRAF, etc and are not limited to those with companion diagnostics. Non-targeted therapies include traditional chemotherapeutic agents, hormonal therapies, cell based therapies, non-specific anti-apoptotic therapies, and general immunomodulatory therapies.
Source: Health Advances analysis, Pharmaprojects.

Latest Expansions Beyond Cancer

PM has the ability to transform management of many diseases outside of cancer, and advances are being made in several disease areas.

Cardiology

- Heart Failure: Galectin-3, BG Medicine
- Heart Attack/Stroke:CYP2C19, Spartan Bioscience
- Heart Disease: KIF6, Celera

Infectious Disease

- HIV: Trofile, Monogram/Pfizer
- Cholera: rapid pathogen analysis, PacBio
- Latent TB: interferon-gamma Cellestis/Qiagen

Examples of Personalized Medicine Beyond Oncology

Neurology

- MS: STRATIFY-JCV diagnostic, Biogen
- Epilepsy: HLA-A3101 Variant
- AD: TOMM40 / APOE status

Immunology

- RA: Vectra DA, Crescendo
- Lupus, anti ds-DNA GSK/Human Genome Sciences

Source: Health Advances analysis. Examples, not all inclusive.

Return on Investment

There are clearly many reasons why pharma is interested in personalized medicine. However, skepticism still exists as not all therapeutics will benefit from a diagnostic.

Rewards of Companion Dx Over the Therapeutic Lifecycle

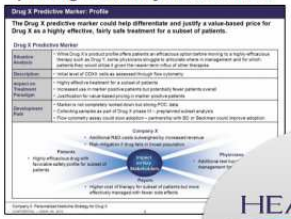
Full economic analysis is needed for all therapeutics to determine a diagnostic's impact and satisfy internal stakeholders

Source: Health Advances analysis.

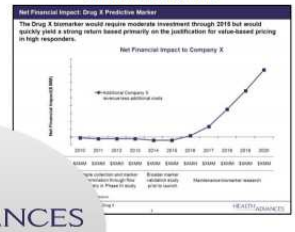
Personalized Medicine Across the Therapeutic Portfolio

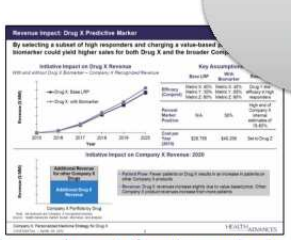
Pharmaceutical companies are considering biomarker impact earlier and earlier in development. Creation of ROI models are imperative across therapeutic portfolios.

Marker impact on treatment paradigm and key stakeholders

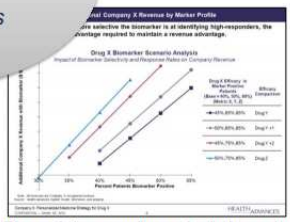


Net financial impact of marker to the company considering additional costs





Revenue impact of marker on the drug based on key assumptions



Financial scenario analysis based on marker characteristics

Source: Health Advances example analysis.

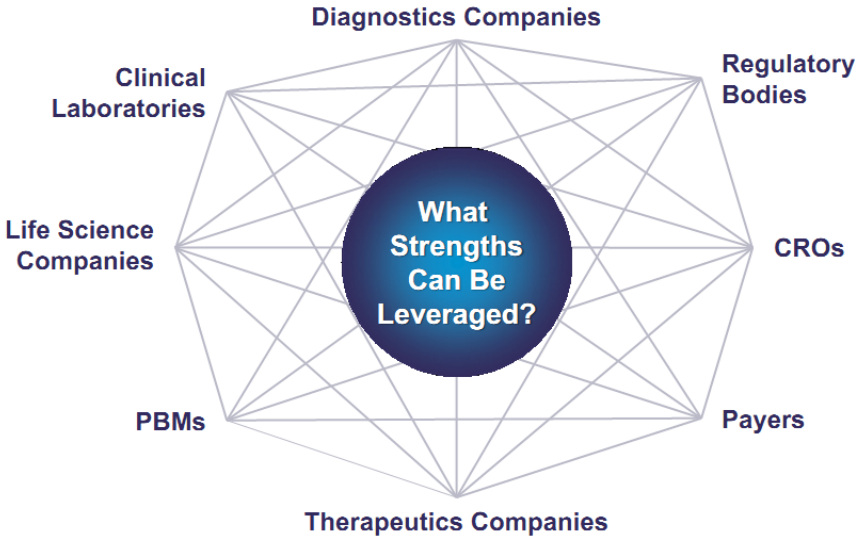
Challenges in Companion Diagnostic Development

Therapeutics companies seeking to commercialize a companion diagnostic face an array of challenges, many of which require assistance from partners.

PM Diagnostic Development Continuum

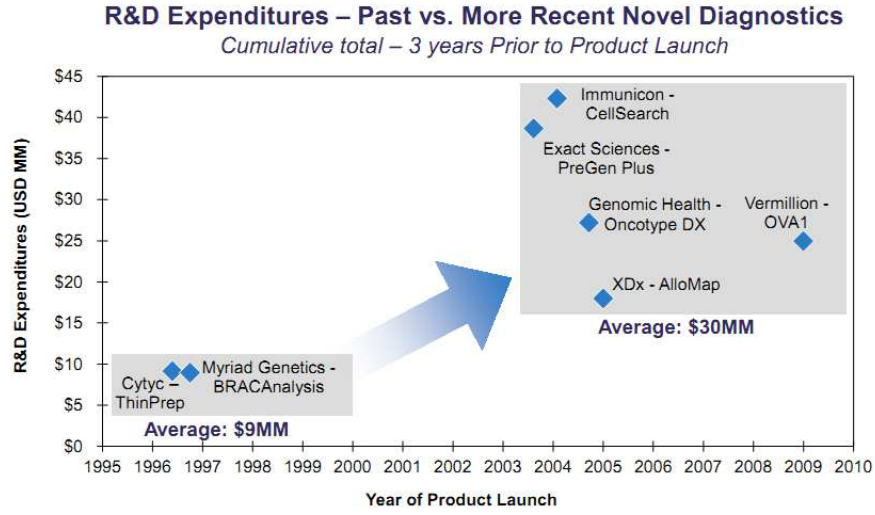
Evolving PM Partnerships

Today, collaborations involve a host of stakeholders leveraging each other's strengths. The ROI for each one must be taken into account so that each stakeholder is satisfied.



Non-Companion Dilemma: Rising R&D Costs

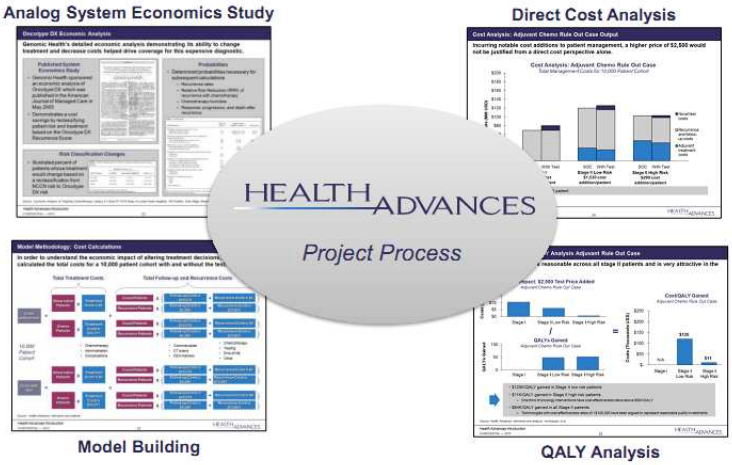
R&D costs for novel diagnostics have risen dramatically, making it more important than ever for diagnostic manufacturers to secure premium prices, especially without a pharma partner.



Source: Corporate SEC filings, Health Advances and BIO report 2011

Non-Companion Dilemma: Proving Economic Value

Diagnostic companies have to build thorough system economic models to help justify premium prices to payers. Analysis in preparation for multiple stakeholders, including commercial and government payers, PBMs, and IDNs, is essential.



Source: Health Advances example analysis.

Summary

- Personalized medicine is here to stay, but attention to developing the value proposition and the data surrounding return on investment is essential to gaining traction with key stakeholders.
  - Data needs do not stop at scientific and clinical underpinnings; the economic and market data is essential to developing a sound commercial strategy.
- The economics vary by stakeholder.
  - Therapeutics companies must thoroughly analyze return on investment for any and all potential companions or complementary diagnostics across their portfolios.
  - Diagnostic companies must develop robust system economic arguments to justify premium pricing, with focus on immediate, direct cost savings for commercial payers and nearer term cost savings for an IDN or, in ex-US markets, a national plan.
- Alignment of economic incentives and stakeholder needs, backed by strong clinical, economic, and market data, will be critical for partnerships to thrive in the evolving landscape.

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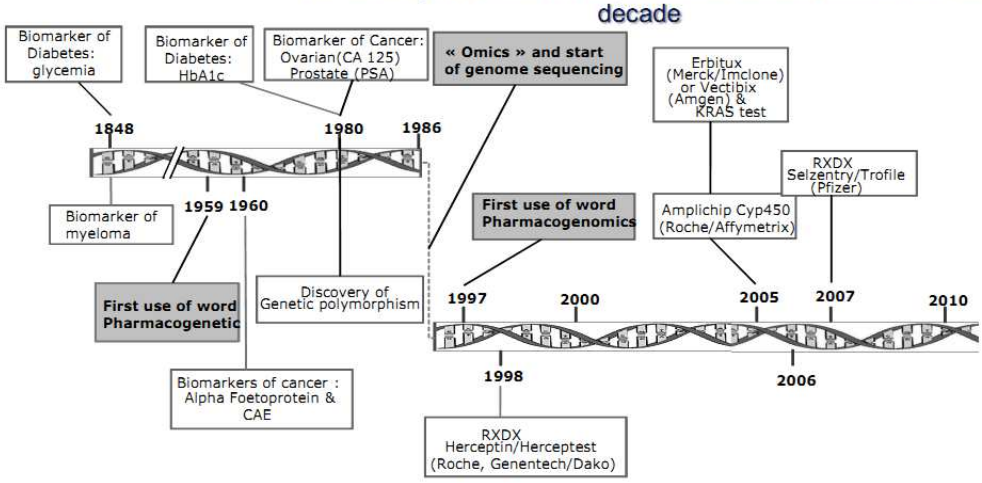
EPEMED
The European Personalised Medicine Association

2nd annual EPEMED conference

7-8 December 2011
Luxembourg

EPEMED
The European Personalised Medicine Association

Biomarkers and PM are included in medical practices since the 19th century but their development has accelerated in the last decade



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Market drivers in Personalised Medicine

Regulatory Agencies

Greater integration of Rx /Dx for more efficient and safer clinical trials

Increased vigilance on drug approvals and increased approval of genetic tests that influence safety and efficacy of drugs

Payors/PBM

Payment for performance

Payors/PBM are pushing for Rx-Dx integration especially diagnostics that reduce healthcare expenditures - Ex: Medco Research Institute

Leadership role in Healthcare Innovation

Establish clinical utility and cost effectiveness

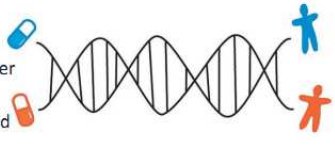
Pharma companies

Potential for higher price due to better efficacy

More effective clinical trials – reduced groups with better results

Dx facilitates better Rx sales by enabling **better market penetration, differentiation and expansion**.

CDX: Life Cycle management tool, defence strategy against biosimilars threat



Patients & Clinicians

Increasing influence of patient advocacy groups

Personalized medicine reduces unnecessary therapies, leading to fewer side effects

Diagnostic Industry

Research progress in biomarker discovery translating into more Dx tests

New emerging companies focusing on Dx

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The 27 Member States of the EU

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Personalised Medicine in EU: Overview

Very few value-based reimbursement initiatives for innovative Dx

Many barriers and levels of complexity

Heterogeneous region in terms of regulation & reimbursement

Differences regarding centralised & de-centralised systems in the individual states

Differences in HTA (Health Technology Assessment) systems between and within countries

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The European Challenge

EPEMED White paper: Market access challenges in the EU for high medical value diagnostic tests

Iain Miller†1,2, Joanna Ashton-Chess1,3, Herman Spolders1,4, Vincent Fert1,5, Joseph Ferrara6, Werner Kroll1,7, Jon Askaa8, Patrick Larcier3, Patrick F Terry1,9, Anne Bruinvels10 & Alain Huriez1,3

*Ref: **Personalized Medicine (2011) 8(2), 137–148***

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European Opportunities for PM

Quality of the scientific research and medical practices

European Commission recent initiative:
(recommendations provided by EPEMED)

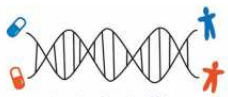
European Perspectives in Personalised Medicine
Square-Brussels Meeting Centre
Brussels, Belgium 12-13 May 2011

Recast of IVD directive ***(input provided by EPEMED)***

EMA initiatives (innovation task force, scientific advices for qualification of biomarkers, EMA "reflection paper on methodological issues associated with PGx biomarkers***…(input provided by EPEMED***)

High level quality Biobanks (IBBL, IMIDBB,…)

EC grants (FP7 health 2011), IMI programs



Luxembourg, December 8, 2011
Personalised Medicine in Europe :
What will it take to succeed ?

European associations (EPEMED, EDMA, EBE ..)

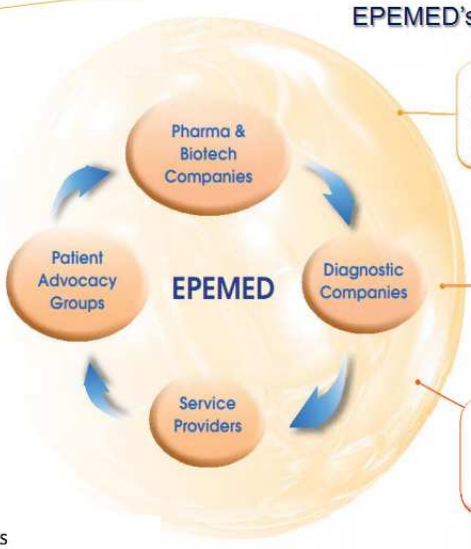
E P E M E D

The European Personalised Medicine Association

EPEMED's Value Proposition

Key Value Points for Members

- Forum to share best practices
- Publications, white papers, conferences, education & promotion on Personalised Medicine subjects
- Privileged access to European decision makers
- Input to policy makers on relevant legislation



Members include clinicians, diagnostic & pharmaceutical companies, service providers as well as patient advocacy groups.

EPEMED will form alliances with other organisations involved with personalised medicine in Europe and worldwide.

EPEMED is keen to welcome members from throughout Europe and beyond with an interest in personalised medicine.

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Thank you for your attention

For more information or to download recent studies or webinars, please visit www.epemed.org

Contact: contact@epemed.org