

Personalized Medicine: Is it really the next growth vector for the pharmaceutical industry?

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Summary:

Personalized medicine is seen by many in the pharmaceutical industry as one of the major growth vectors for the future. This breakthrough change could impact the healthcare landscape in depth. To make the dreams become true, science will have to fuel the change. But the industry will have to understand how to handle it and invest on it, regulatory bodies will have to clarify the pathway to market and payers will have to decide whether they will pay or not and on which criteria. But like any life changing technology, ethical considerations will not have to be forgotten.

Key Words: Personalized medicine, theranostic, genomic, reimbursement, diagnostic tests

Médecine Personnalisée: Est-ce vraiment le prochain relais de croissance pour l'industrie pharmaceutique.

Résumé:

La médecine personnalisée est vue par beaucoup dans l'industrie pharmaceutique comme l'un des prochains relais de croissance. Cette « révolution » pourrait changer le paysage de la santé en profondeur. Pour que ce rêve devienne réalité, il faudra que la science apporte son lot de preuves. Mais il faudra aussi que l'industrie comprenne comment l'intégrer et investir, que les autorités définissent les chemins d'approbation et que les payeurs décident comment rembourser ces nouveaux médicaments. Mais comme pour toutes les nouvelles technologies impactant la vie des gens en profondeur, il ne faudra pas oublier les considérations éthiques et morales.

Mots-Clés:

Médecine personnalisée, théranostique, génomique, remboursement, tests diagnostiques

1. INTRODUCTION

Since Hippocrates, western world medicine has worked based on a “trial and errors”. This is actually quite an efficient and powerful way provided 1 – the caring team can learn from it, 2 – the caring team has time for it 3 – the unit cost of the trial remains reasonable compared to the expected benefit. In addition, the way drugs have been historically developed leads to marketed compound that are very beneficial for some patients and inefficient or even deleterious to others. Sometimes, the fraction of people who suffer more than they benefit can be a very tiny minority of others... Inability to carefully balance the two populations (responders and non-responders) may lead to failure in the registration phase or to the withdrawal of the treatment sometimes years after market authorization. In both cases, this often has very tough consequences for the patients (side effect or death) and for the industry (financial and reputation loss).

Over the past fifteen years, the idea of using new technologies to personalize medicine based on genetic or other characteristics. Actually, the human genome and proteome current knowledge is providing an unprecedented understanding of the genetic basis of a number of diseases. This understanding extends to hereditary factors, but also to the mechanisms whereby disease-associated genes are expressed (or blocked) leading to disease onset. It can also potentially uncover important information about individualized variations in the response to therapeutic agents. This ability to assess predisposition to disease as well as response to therapy theoretically allows therapeutic development strategies that could eventually lead to individualized patient management.

In this context, the dream is to shift the current medical practice to a new one where each patient would receive the most appropriate treatment regimen based on selected personal biomarkers. This raises a lot of excitement and expectations from various stakeholders involved in the healthcare world: regulatory authorities, physicians, patients but also business executives and investors... Figures seem to speak for themselves. PricewaterhouseCoopers (PwC) estimated in 2009 the US market for personalised medicine around \$230 billion [1] and forecast it to grow 11% annually reaching the size \$450 billion by 2015. PwC estimates that the core of the personalised medicine market i.e. diagnostic and therapeutic segment to be worth approximately \$24 billion and expects it to grow by 10% annually to reach \$42 billion by 2015 (US market).

After a brief review of history and actual achievements of personalized medicine, we review the perspective of personalized medicine within the classical framework, i.e. the

pharmaceutical industry confronted with two the stakeholders, granting or not market access to new drugs: the regulatory bodies and the payers. Finally we discuss some of the key challenges and key success factors that may impact the move or not from science to the use of personalized drugs in usual clinical practice.

2. HISTORICAL PERSPECTIVE

2.1. *Definition*

The concept of personalized medicine emerged practically started in the late 90's with the Human Genome Project. Already in 2002, Kain and al, gave one of the first compelling definition [2]. In 2007, during BIO Meeting, Paul Keckley¹ gave an holistic one: "Any of the ways in which understanding meaningful differences between individuals helps guide the use and interpretation of diagnostics, as well as choices in therapies and prevention" [3]. In that same panel discussion, Mara Aspinall² summarized it even more: "A technology that enables physicians to improve care through tailoring". Lately, McKinsey & Company gave a more precise definition: "The management of a patient's disease or disposition by using molecular knowledge (genomics, DNA modification, proteomics, metabolomics) to achieve the best possible medical outcome for that individual" [4].

However, a number of definitions can be and has been indeed given of personalized medicine. One could object that surgery where, by definition, the surgeon applies a therapeutic procedure specific to one patient, qualify as personalized medicine. Some consider that traditional Chinese medicine or homeopathy also as a way to specifically adapt treatment to individual patients in a "personalized" way.

Without entering further in the debate, we will use the definition established in [3] but will exclude all individualized invasive procedures such as surgery, grafts, stem-cell based therapies, or portable / implantable device-monitored therapies. They are all very effective or promising concepts but bare different challenges than targeted therapies driven by a better molecular understanding of the disease or of the patient genetic background. We will also concentrate on the curative aspects of personalized medicine i.e. drug / diagnostic combination also called

¹ Executive Director, Deloitte, Director of Vanderbilt Center for evidence-based medicine.

² President of Genzyme Genetics

theranostics³. Genotype screenings leading to disease predisposition assessment will be only touched slightly as the business model behind is far from being well established and is not, so far, to much on the plate of the pharmaceutical industry.

2.2. *Personalized medicine quick history.*

Historically, a number of therapeutic improvements have been brought to patients either by luck (e.g. Penicillin, Sildenafil...) or more recently through the use of more and more powerful screening capabilities leading to testing chemically synthesized or extracted drugs in a variety of models. However, a better understanding of disease physiopathology also significantly helped improving care. For example, as early as 1972, receptor hormones for estrogen were identified as valuable markers for selecting women patients with breast cancer who would benefit from hormonal treatment. In addition, Table 1 provides a summarized historical perspective of the evolution in the understanding of blood disorders over the past century. Medicine came from a “one size fits all” treatment for all patients suffering for a “Disease of the Blood” to a very fine-tuned understanding of the different sub-types of leukemia / lymphoma leading to a number of treatments best suited for each individual patients based of specific diseases characteristics. Does it matter? Probably yes if we remember that in the same period of time, survival rate has moved from 0 to 80%+.

³ The term was used first by the CEO of PharmaNetics, John Funkhouser in 2004 is the fusion of the words therapeutics and diagnostic (source: wikipedia)

Table 1: Improvement in the understanding of blood disorders [5]

80 Years Ago	"Disease of the Blood"	
70 Years Ago	Leukemia or Lymphoma	
60 Years Ago	Chronic Leukemia Acute Leukemia Preleukemia	Indolent Lymphoma Aggressive Lymphoma
Today	38 Leukemia types identified: Acute myeloid leukemia (III 2 types) Acute lymphoblastic leukemia (2 types) Acute promyelocytic leukemia (2 types) Acute monocytic leukemia (2 types) Acute erythroid leukemia (2 types) Acute megakaryoblastic leukemia (2 types) Acute myelomonocytic leukemia (2 types) Chronic myeloid leukemia Chronic myeloproliferative disorders (5 types) Myelodysplastic syndromes (6 types) Mixed myeloproliferative/myelodysplastic syndromes (3 types) ...	51 Lymphomas identified: Mature B-cell lymphomas (III 4 types) Mature T-cell lymphomas (15 types) Plasma cell neoplasm (3 types) Immature (precursor lymphomas (2 types) Hodgkin's lymphoma (5 types) Immunodeficiency associated lymphomas (5 types) Other hematolymphoid neoplasm (7 types) ...

Over the recent years, a number of drugs have been developed which target specific disease forms characterized by gene mutations, hormone sensitivity or marker expression on the cell. Cancer can stand as a golden example for such a refinement procedure. Thus, so far, most of these drugs have been developed in oncology but it is expected that some other conditions can benefit from these types of targeted drugs. In some cases (e.g. Herceptin®), the drug has been commercially launched together with a co-developed companion diagnostic. In this case, the kit is referenced by regulatory authorities in the product label and can then only be prescribed upon a positive test result. These targeted drugs can help the physician answer a number of questions such as which drug should I use (e.g. Herceptin®), how much of the drug do I need (e.g. Campto®), is the drug working (e.g. Gleevec®), is my disease cured (e.g. Campath®)? Table 2 illustrates some examples of currently commercially available drugs.

Table 2: Some personalized medicine drugs commercially available in 2010

	Brand / Drug Name	Indication	Mutations / Expression
Drug Selection	Tamoxifen [®]	Breast Cancer	ER/PR ⁴
	Herceptin [®]	Breast Cancer	HER2 ⁵
	Gleevec [®]	Leukemia, CML	BCR-ABL ⁶
	Erbix [®]	Colorectal Cancer	EGFR ⁷
	Tarceva [®]	Lung Cancer	EGFR
Dose Selection	Warfarin	Atrial Fibrillation / DVT	CYP2C9 ⁸ & VKORC1 ⁹
	Campto [®]	Colorectal Cancer	UGT1A1 ¹⁰
Drug Efficacy	Gleevec [®]	Leukemia, CML	Quant BCR-ABL
	Gleevec [®]	Leukemia, CML	BCR-ABL mutations
Disease Progression / Cure	Campath [®]	Leukemia, CLL	Minimal Residual Disease

These drugs are today considered by many as “personalized medicine drugs”. However, there is an ambiguity. These compounds are not targeted to patient per se but more to the specific mechanism responsible for one given form of a disease. This is probably a first early form of personalization.

3. STAKEHOLDER PERSPECTIVE

The move toward personalized medicine is a breakthrough and is potentially disruptive to the whole value chain of healthcare. This raises a number of questions: How broadly applicable is

⁴ Estrogen and progesterone receptors

⁵ Human epidermal growth factor receptor 2

⁶ Breakpoint cluster region – Abelson

⁷ Epidermal Growth Factor Receptor

⁸ Cytochrome P450 2C9 gene

⁹ Vitamin K epoxide reductase complex 1

¹⁰ UDP-glucuronosyltransferase 1A1

personal medicine? Is there sufficient scientific evidence to support it? Is the screening technology reliable enough and economically relevant? Will testing improve medical outcome (e.g., lower risk, improve efficacy) or jeopardize outcomes in some cases (e.g., over-reliance on testing, reduced physician oversight)? How evaluate the difference between what is possible and what is payable? Can we apply our existing ethical principles to personalized medicine?.

On top of these general considerations, each healthcare stakeholder has a different perspective. We focus here on the pharmaceutical industry and two of its historical partners, regulatory bodies and payers. But doctors, patients, investors... also have their own perspective on this topic that could deeply impact their life and / or practice.

3.1. *Pharmaceutical companies*

Over the past years, the pharmaceutical industry has been facing unprecedented pressure [6, 7, 8]. Its full business model is under threat as the industry has to fight many battles at the same time [9]. On one side, patent protection loss and launch of generic drugs are dramatically reducing income. On the other side the number of New Chemical Entities (NCE) submission has constantly decreased of the past years leading naturally to a low level of approval. In the US, the number of NCEs approvals dropped from close to 60 in 1996 to 25 in 2009 [10]. Unfortunately, at the same time, the cost of developing drugs has boomed forcing pharmaceutical companies to invest more and more in R&D [11]. Although profits are under challenge by the combination of decreased revenue and increasing costs, the pharmaceutical industry remained over the years one of the most constantly profitable industry of all. But this strength is also a challenge as it makes it under constant pressure from the investors demanding higher earning per shares and double digit growth despite an overall economy stalling at 1 or 2% yearly growth.

In order to please investors but also to ensure its sustainability, the pharmaceutical industry is betting on some new options. Among them, is personalized medicine and its promises. This is seen by a number of executives and analysts as one solution to fix some of the more hurting strategic issues. First, it could significantly improve R&D productivity. Adequately identified biomarkers could allow a reduction of development risks and costs and potentially increase the clinical utility of drugs. During the research process it could improve research target identification and validation. In the clinic, it could accurately predict and increase compound success rates allowing efficient portfolio management by dropping the wrong assets. By better

defining the target population for clinical trials, it could help improving the design and therefore reducing their length and cost. Ultimately, this streamlining clinical development would also results into an increased likelihood of registration by offering regulatory bodies submissions with an increased quality of claims (e.g. screen respondent and not respondent populations).

On top of improving development, companies also see some benefit in terms of enhancing corporate protection against liability and their financial consequences. In 2004, following the Vioxx[®] registration suspension by the FDA, Merck & Co share price dropped roughly 40% in 6 weeks (From \$ 44.92 on Sept 29, 2004 to \$ 26 on Nov 9, 2004 [12]). In addition, the company had to establish a \$ 4.85 Billion fund for the case settlement [13]. Other legal costs and reputation loss were never disclosed or measured but they are most probably very significant. If available with the drugs, diagnostics tools could increase drug safety and decrease adverse events in two means. This would enable doctors to prescribe the right drugs at the proper doses based on metabolism and genetic makeup, not on average effect derived from clinical trials and statistics. In addition, this would also allow doctors to avoid prescribing the drug to patients that could be subject to side effects. Topol and al (2010) just disclosed results of a study tending to show that genetic testing might have helped identify people who would become depressed or suicidal while taking weight loss drug Acomplia[®] [14]. These side effects pushed EMEA to withdraw the drug from the market in October 2008. It was not even approved by the FDA. The authors argue that having these genetic tests available might have helped keep the drug on the market [15].

Through pharmacogenomic¹¹ techniques, personalized medicine is expected to help drive future drug profitability through enhanced marketability and pricing. Companies expect that they can indeed demonstrate efficacy versus competitors, command a price premium based on value, demonstrate efficacy for intended target market....

Beyond science and potential industry benefits, what does the emergence of personalized medicine means to pharmaceutical executives? It is likely that a number of them will have to acquire new competences and skills. Scientists and project managers will have to improve their ability to include the potential companion diagnostic in their project and development plans and work with their diagnostic counterparts to make things effectively happen. This will require interdisciplinary development of drugs and diagnostics by teams that historically have been pretty

¹¹ Pharmacogenomics can be defined as the branch of pharmacology which deals with the influence of genetic variation on drug response in patients by correlating gene expression or single-nucleotide polymorphisms with a drug's efficacy or toxicity.

much siloed. Partnerships will have to be build between pharmaceutical and diagnostic companies. In both industries, deals structures, deals amounts, intellectual properties constraints, benefits and liabilities are different. Business Development executives will have to learn how to close deals and moreover manage alliances in this uncommon environment. Marketers will also be impacted and will have to adapt. As explained by Dunn in 2009 [16] there are a number of differences in marketing attitudes and habits: target audience, sales force sizes and types, and very critically size of the promotional budget (very large for pharmaceuticals, small for diagnostics). Like for their scientific colleagues, marketers with have to cope with the fact that personalized medicine does blur a number of boundaries. Dunn makes it clear. “Now, however, drugs and diagnostics will not only be co-developed, but also co-marketed, requiring marketers to possess both pharmaceutical and diagnostic expertise”.

Some companies have been anyway putting personalized medicine at the center of their growth strategy. Roche was one of the first ones to do so and recognized early the value it can bring to the company (and to the patients). In 2008, they declared personalized healthcare central to the group’s strategy seeing it as a key enabler “to increase their (our) success rate in drug development and bring more clinically differentiated medicines”. [17]. In 2008, Solvay Pharmaceuticals (Abbott since Feb 2010) invested € 210 M to acquire Belgian company Innogenetics. The rationale for this significant investment is very clearly explained in the company annual report [18]: “For Solvay Pharmaceuticals, this strategic acquisition is another major step towards anticipating future trends in personalized medicine. In the future it will become increasingly common practice to measure patients’ personal parameters before administering prescription medication, with medicines prescribed only to patients who are likely to respond to them. While this evolution will not take place overnight, this approach is already being applied in certain cancer treatments”. Even if most companies do not go that far, lots of experiments are made: joint ventures, cross-licensing, new business units, etc. This is an example of “co-opetition” that the industry has to explore and is slowly and somehow shyly starting to do.

3.2. *Regulatory Authorities*

Regulatory authorities are more than ever under pressure by all the other healthcare stakeholders. On one hand they are somehow held responsible for increasing the hurdles to registration leading to a dramatic reduction in NCE approvals. On the other hand, they are under

tremendous pressure from patients and politicians to minimize the risk related to drugs. Vioxx® and more recently the Avandia® controversies showed clear examples of difficulties regulatory bodies are coping with. Regulatory bodies do have an interest in seeing drug / diagnostic combination more and more approved as it can improve certainty on drugs efficacy, avoid side effect, potentially lead to faster approvals.

For example FDA has clearly stated their interest in promoting the use of theranostic. Already in 2005, the FDA released "Drug-Diagnostics Co-Development Concept Paper" representing their initial thoughts on this topic [19]. This is still a reference paper in which the authors made clear that the companion diagnostics development should occur as early as possible in the drug development process. In 2006 EU (European Commission and EMEA) and FDA agreed on what should be guiding principles for joint FDA / EMEA voluntary genomic data submission. [20]. Since then, both agencies have been putting a lot of efforts and initiatives in trying to setup guidelines to clarify use of genomic data as well as the pathways for test clarifications as the current diversity in regulatory pathways for the commercialization is one of the major issues. Resolution of these issues will be a major driver for development of personalized medicine.

3.3. Payers

When it comes down to covering healthcare cost, the notion of “payers” embraces a multitude of realities with which the industry is not always easy with. The patient is often the ultimate payer through its taxes or insurance fee but there is a number of bodies who actually pay for the drugs. It can be private payers such as insurance, complementary health insurance or public payers such as European social security systems, or American Medicare / Medicaid. In any case, these bodies have limited budget and have to decide what they will pay for or not. Currently, personalized medicine is hardly hitting the ‘top 10 priority’ list of most payers. However, today they can already save costs if they identify cost saving tests (e.g. HER-2, BCR-ABL, c-KIT...) and avoid “cost creating” tests (e.g. most risk markers) as illustrated in Table 3.

Table 3: Example of tests and their cost benefits

Personalized medicine test	Purpose	Test benefits	Estimated Cost Savings
HER2 testing / (trastuzumab)	Disease differentiation in breast cancer	Candidates to drug	\$8000–30,000 [21]
Hepatitis C genotyping	Disease differentiation in Hep C	Treatment duration	\$7,500 [22]
UGT1A1 testing (irinotecan)	Side effect prediction	Prevent adverse events	TBD

However, should all the promises been delivered, personalized medicine and companion diagnostics could enable payers to increasingly focus on outcomes. They could indeed benefit from a variety of improvements. Tests can help them having more clarity on the indications, assess the superior performance vs. competition to secure pricing and /or reimbursement with a premium or understand value creation for them through the assessment of potentially compelling economic data generated by pharmaceutical companies. From a pure economic standpoint, they can directly generate savings from avoiding severe adverse events but also avoiding drug prescription to non responders.

Although a number of arguments plea for a better reimbursement of tests and drugs with a companion diagnostic, there is actually quite some skepticism from the payers and, so far, payer adoption has been slow. One can assume that they would cover these technologies in a manner similar to the way they list drugs for their formularies. Actually specific drivers for reimbursement have been identified [23].

First, the strength of evidence seems to drive decisions about coverage and reimbursement. However, the strength of evidence varies widely. For disease differentiation kits, associated drug clinical trials have mostly been conducted with the test. A significant amount of data has been generated backing up the concept and its value. Likewise, for drugs in development the test is now often included in the drug clinical development plan [24]. Conversely, disease predisposition tests often probe for conditions for which there is no preventive treatment (e.g. breast cancer). Although often backed up by highly recognized scientific communities, these tests have a low likelihood to be reimbursed as they are not associated with any kind of outcome data in the tested population. Although scientifically reliable, it is unlikely that these data would ever be generated as it would be too costly for any stakeholder to do so with little return on investment. In any case,

it is not necessarily appealing for payers to invest in prophylactic tests that potentially reduce the risk of conditions happening much later in life.

Finally, in addition to the level of evidence payers seem to strongly consider professional society guidelines when taking reimbursement decisions (Table 4). In a number of cases reimbursement seemed associated with a positive recommendation in the therapy guidelines. In the case of Oncotype Dx (a test to decide upon interest of adjuvant chemotherapy in breast cancer) [25] and warfarin testing (a test to adjust drug dose and avoid adverse events) [26], a payer’s policy explicitly referenced both treatment guidelines as well drugs pivotal studies.

Table 4: Relation between reimbursement, evidence and recommendations

Personalized medicine test	Test Included in drug label	Reimbursement	Source of current evidence	Level of evidence	Guidelines recommend
HER2 testing / (trastuzumab)	Yes	Yes	RCT for drug, stratified by test results	Strong	Yes [27]
Hepatitis C genotyping	Yes	Yes	RCT for drug, stratified by test results	Strong	Yes [28]
UGT1A1 testing (irinotecan)	Yes	No	Observational genotype - phenotype	Weak	No

4. LOOKING AHEAD: CHALLENGES AND KEY SUCCESS DRIVERS

Personalized medicine holds a lot of promises for the various stakeholders in the healthcare world. But it can only happen if the industry invests in it. Investors and diagnostic companies can push for it and take their part of the burden (and of the rewards) but the pharmaceutical industry needs to drive it. If the promises are so high, why does the industry is so shy? If a minority is taking big steps, most hadn’t prioritized biomarkers and companion diagnostics and are quite cautious in their approach to investments in the field. The first hurdle is obviously scientific and medical. In a number of therapeutic areas, the clinical need for biomarkers and companion

diagnostics is limited because a number of well known, cheap and safe alternative are available (e.g. hypertension.). From a scientific standpoint, if oncology is more and more explored and understood, in a number of disease areas, understanding of molecular mechanisms is insufficient to select biomarkers at early stages of development (e.g. CNS).

Even if science seems promising, developing itself if the field of personalized medicine adds a number of financials challenges for pharmaceutical companies. First, it is still controversial to know if the identification of biomarkers and subsequently the co-development of companion diagnostics is beneficial to R&D productivity. It may actually do little to it. It may even increase overall costs and delay development. Trials often have to be larger when companion diagnostics are used as they need to be designed with several potential biomarkers candidate (often as of phase II). This relates directly to the questions of the proper level of investments, the measurement of effectiveness and return and adequate portfolio management.

Another key driver for the development of personalized medicine is the clarification of regulatory pathways. FDA and EMEA must improve the clarity and efficiency of regulatory approval processes. These clarifications are essential to help diagnostics and pharmaceutical companies collaborate better and design trials. Leading pharmaceutical, biotechnology, and diagnostics companies should collaborate closely and pro-actively to help shaping the development of the guidelines and standards.

Payers need also to clarify the way they assess these new technologies. In Europe, although some initiatives have been taken [29,30], so far, none of the biggest Healthcare Technology Assessment organizations (HTA) such as the UK NICE or the French HAS have any serious guidance on reviewing molecular diagnostic tests. Private insurances, governmental payers, diagnostics and pharmaceutical companies can, here also, make coordinated efforts to improve the speed and process of coverage decisions. But in any case, one can expect that better coverage will be related to better evidences. Today, in a number of cases, the impact of tests on patient's outcome is weak if not existing at all. More generous reimbursement for these new technologies is likely to await higher quality of evidences.

In addition to these economics and regulatory issues, there are a number of other questions that start to be raised. Fears and concerns are expressed around personal genetic information and its use from the both the general public and the healthcare professionals: Who should have access to personal genetic information? What happens if genetic information spills over and is used to

discriminate against a person who has been tested? How will professionals be trained to deal with these new data and tools? For example, how can a doctor announce to a given individual that he has an increased risk of a severe debilitating or life threatening disease knowing this is just a risk not a disease that may actually never happen? What will be the psychological impact of such a new? Recent studies conducted in Alzheimer disease concluded that the disclosure of genotyping results to adult children of patients with the condition did not result in significant short-term psychological risks [31]. But further studies should be done in that field to evaluate the psychological and social consequences of such disclosures. The question turns even more accurate when the reliability of the test can be questioned as US investigators recently outlined [32].

These questions have already raised a lot discussions and controversies. In a review published in 2009, Jamie Cuttichia concluded that, conversely to some new technological progresses, personal medicine does not require the construction of new ethic fundamentals [33]. Anyway, business stakeholders such as pharmaceutical and diagnostic companies as well as regulators should keep these questions high on their agenda as the pressure of certain lobbies such as religious or political groups could severely slow the development of personalized medicine and the subsequent market.

5. CONCLUSION

For the last decade, pharmaceutical industry has been going through a serious storm. Companies have to cope at the same time with revenue losses because of generic competition and price pressure and difficulties to find new growth vectors because of the dearth of new compound and barriers to reimbursement. In that context, personalized medicine has been seen by many experts and analysts as one the way forward to generate new revenue by increasing the reel and perceived value of their products. But in order to make these dreams becoming reality the pharmaceutical industry needs, at least, two things. First, science needs to deliver its promises. The industry must join forces with other stakeholders such as academia and biotech to fuel research in the field. This is potentially a new frontier and the effort will have to be sustained on the long term to, eventually, see science deliver. Second, the industry needs to determine the best business model to apply: It has to get strategically organized to leverage these disruptive technologies but more importantly it will have to get out of its ivory tower and also unite forces

with diagnostic companies, regulatory bodies and payers to create a substantial business pond. The industry is now at a clear strategic inflexion point and can decide to give personalized medicine a chance to improve patients' life. But, even if well combined science and business make it successful, this will only be sustainable if the industry does not disrespect the fears and questions raised by the general public especially from an ethical standpoint. As very well explained by Frueh and Gurwitz [34] already in 2004, this will not happen without significant efforts in training and education of healthcare professionals, regulatory and policy makers, patients and citizens...

REFERENCES

- [1] PricewaterhouseCoopers: The new science of personalized medicine (October 2009)
- [2] Jain, K. K. Personalized medicine. *Current Opinion in Molecular Therapeutics*. 2002. 4(6): 548-558
- [3] BIO International Meeting Proceedings, 2007
- [4] McKinsey & Company, Personalized Medicine: Impact on the Healthcare Landscape, 2007
- [5] Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EJ, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2002, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2002/, based on November 2004 SEER data submission, posted to the SEER web site 2005.
- [6] IMS, Success in a period of Global Uncertainty Presentation, 2009
- [7] Price Waterhouse Coopers, Pharma 2020: Challenging business models: Which path will you take?, 2009
- [8] Erisant & Young, Progressions 2010, 2010
- [9] Rambeaux E, Pharma Strategic Challenges: Now, I know.... Pharmabrand Summit, Monte Carlo, June 2010.
- [10] CDER data on Dec 2009,
<http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM192786.pdf> (accessed 08 / 10)
- [11] Adams C, Van Brantner V, Spending on New Drug Development (March 14, 2008). Available at SSRN: <http://ssrn.com/abstract=869765> (accessed 08 / 10)
- [12] Yahoo Finance:
<http://uk.finance.yahoo.com/echarts?s=MRK#chart3:symbol=mrk;range=20040112,20041201;indicator=volume;charttype=line;crosshair=on;ohlcvalues=0;logscale=on;source=undefined>
(accessed 08 / 10)
- [13] <http://www.yourlawyer.com/articles/read/17610> (accessed 08 / 10)
- [14] Topol E. *and al*, Rimonabant for prevention of cardiovascular events (CRESCENDO): a randomised, multicentre, placebo-controlled trial, *The Lancet*, 376, 9740, 517-523
- [15] Reuters, <http://www.reuters.com/article/idUSTRE67B5BB20100812>, (accessed 08 / 10)
- [16] Dunn K., Personalized Medicine: Implications for Pharma. *Pharmaceutical Executive*, Dec2009, Vol. 29 Issue 12, p90-91

-
- [17] Roche Business report 2008, p 30 - 33
- [18] Solvay Annual Report 2008, p 26
- [19] US Food and Drug Administration
<http://www.fda.gov/downloads/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm116689.pdf> (accessed 08 / 10)
- [20] US Food and Drug Administration
<http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/EuropeanUnion/EuropeanUnion/EuropeanCommission/ucm114343.htm> (accessed 08 / 10)
- [21] McKeage K, Lyseng-Williamson KA. Trastuzumab: a pharmacoeconomic review of its use in early breast cancer. *Pharmacoeconomics* 2008;26:699–719.
- [22] Younossi ZM, Singer ME, McHutchison JG, Shermock KM. Cost effectiveness of interferon alpha2b combined with ribavirin for the treatment of chronic hepatitis C. *Hepatology* 1999;30:1318–24.
- [23] Meckley L.M., Neumann P.J. Personalized medicine: Factors influencing reimbursement. *Health Policy* 94 (2010) 91–100
- [24] National Institutes of Health. ClinicalTrials.gov, www.clinicaltrials.gov [accessed on 7/2010].
- [25] Technology Evaluation Center. Gene expression profiling of breast cancer to select women for adjuvant chemotherapy. *Assessment Program* 2007;22.
- [26] Cigna HealthCare. Cigna healthcare coverage position: subject pharmacogenetic testing for warfarin metabolism, <http://www.cigna.com/customer-care/healthcare-professional/coverage-positions/medical/mm-0484-coverage-position-criteria-pharmacogenetic-testing-for-warfarin-metabolism.pdf>; 200.
- [27] Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote J, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *Archives of Pathology & Laboratory Medicine* 2007;131:18.
- [28] Strader DB, Wright T, Thomas DL, Seeff LB. Diagnosis, management and treatment of hepatitis C. *Hepatology* 2004;39:1147–71.
- [29] http://www.ulpmmed.ustrasbg.fr/medecine/cours_en_ligne/e_cours/1ercycle/epidemiologie/EVALUATION_EXAMENS_STRATEGIES_DIAGNOSTIQUES.pdf

[30] http://www.has-sante.fr/portail/jcms/c_433375/comment-evaluer-a-priori-un-programme-de-depistage

[31] Green C.R. et al. N Engl J Med 2009;361:245-54.

[32] Corbett Dooren J, Wilde Matthews A. DNA-Test Results Mislead Consumers, Investigators Say. Wall Street Journal: July 23rd, 2010.

[33] Cuticchia, A : Applying Existing Ethical Principles to Personal Medicine. The Internet Journal of Law, Healthcare and Ethics. 2009 Volume 6 Number 1

[34] Frueh FW, Gurwitz D. From pharmacogenetics to personalized medicine: a vital need for educating health professionals and the community. Pharmacogenomics 2004; 5:571-9.