The revolution of molecular diagnostics and personalized medicine

Paris, 17th March 2011
A. Personalized medicine, biomarkers and molecular diagnostics

B. The revolution of molecular diagnostics: benefits for patients and impact on the pharmaceutical industry

C. About Cepton
Scientific progress and increasing economic constraints are forcing physicians to change their approach of medicine

From treating diseases to managing outcomes – A new approach in modern medicine

**PAST**

Treating diseases

“One size fits all”

? | Diagnose | Treat | ?

Better understanding of diseases

Economic pressure

**FUTURE**

Managing outcomes

Personalized medicine

Prevent | Detect early | Diagnose accurately | Select treatment | Monitor / adjust treatment | Detect relapses

Better understanding of diseases

Economic pressure
Personalized Medicine covers Stratified Medicine, Tissue Engineering, Oncological Vaccinations and Gene Therapy

Scope of Personalized Medicine

„One fits all“

Personalized medicine

Risk profiling

Stratified Medicine¹

Heterologous Tissue Engineering²

Autologous Tissue Engineering³

Oncological Vaccinations³

Gene Therapy⁴

1) Drugs only suitable for certain groups of patients
2) Patients receiving stem cells (own, or donated by others)
3) A patient’s own cells are re-implanted after external “treatment”
4) Gene modification – vectors used as carrier into patients’ cells

Source: CEPTON analysis
Stratified medicine and risk profiling rely on molecular biomarkers, hence the name "Molecular diagnostics."

**What does "molecular diagnostics" mean?**

**Molecular target/biomarker**

- *In human body*
- **Probe**
  - *Designed in laboratories*
- **Complex**
  - *Detection or visualization using a specific molecular biology technique*

**What is a "Biomarker"?**

- "a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention"
- *National Institute of Health, 1998*

Biomarkers can be **molecules** (DNA, RNA, peptides, proteins) or even **entire cells**.

- Molecular diagnostics is used to detect and **measure specific molecular target/abnormalities** using **selective targeted probes** and corresponding visualization methods.
- The value if these targets is that they **correlate with disease** or ideally are causative for the disease.

Source: CEPTON analysis
Molecular biomarkers are key in the detection of a disease – however, there is often no direct causality between a biomarker and a disease.

One biomarker may detect several diseases

Examples:
- **AZCP1**: cardiac hypertrophy, hypercholesterolemia, cirrhosis of liver, squamous cell carcinoma
- **CD46**: status epilepticus, rheumatoid arthritis, congestive cardiomyopathy, lung-transplant rejection

Several biomarkers may be necessary to identify a disease

Examples:
- **Breast cancer**: ENPP4, PFKP, THBD, IGFALS
- **AIDS**: PAPPA, TRADD, APRIN, MAP3K5

Less than 20% of measurable proteins in both blood plasma and urine proteomes are biomarkers

Source: NIH, Pacific Symposium on Biocomputing 2009, CEPTON analysis
Each type of biomarker is associated with one or more specific technologies

### Biomarker diagnostics

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Method (common examples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNA(^1)</td>
<td>• PCR(^4) (and variants like LCR(^5), …)</td>
</tr>
<tr>
<td></td>
<td>• Sequencing</td>
</tr>
<tr>
<td></td>
<td>• FISH(^6)</td>
</tr>
<tr>
<td>Epigenetic modification (DNA(^1) methylolation)</td>
<td>• Methylation specific PCR(^4)</td>
</tr>
<tr>
<td></td>
<td>• Differential methylation microarray</td>
</tr>
<tr>
<td>Multiple genes / Genomic profile / SNP(^3) profile</td>
<td>• Microarray (DNA(^1)-Chip)</td>
</tr>
<tr>
<td>Single gene expression</td>
<td>• Quant. Reverse Transcriptase-PCR(^4)</td>
</tr>
<tr>
<td>Gene expression profile</td>
<td>• Microarray (RNA(^2)-Chip)</td>
</tr>
<tr>
<td>Defined protein (Antibody, Enzyme, …)</td>
<td>• Immunochemistry, esp. ELISA(^7)</td>
</tr>
<tr>
<td>Proteomic profiling</td>
<td>• Mass-spectroscopy peptide profiling</td>
</tr>
<tr>
<td>Cell types according to cell surface proteins</td>
<td>• Mass-spectroscopy peptide profiling</td>
</tr>
<tr>
<td>Abundance of protein in tissue</td>
<td>• FACS(^8)</td>
</tr>
<tr>
<td>Abundance of DNA/RNA(^2) in tissue</td>
<td>• Immunohistochemistry</td>
</tr>
<tr>
<td></td>
<td>• Molecular imaging (in vivo!)</td>
</tr>
<tr>
<td></td>
<td>• FISH(^6)</td>
</tr>
</tbody>
</table>

1) Desoxyribonucleic acid 2) Ribonucleic acid 3) Single nucleotide polymorphism 4) Polymerase chain reaction 5) Ligase chain reaction 6) Fluorescence in-situ hybridization 7) Enzyme-linked Immunosorbent Assay 8) Fluorescence-activated cell sorting

© CEPTON
### PCR, Micro-Arrays and FISH are the most widely used technologies in molecular diagnostics

<table>
<thead>
<tr>
<th>Description</th>
<th>Benefits</th>
<th>Weaknesses</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polymerase Chain Reaction (PCR)</strong></td>
<td>Chain amplification of a segment of DNA or RNA by polymerization</td>
<td>• Low quantity of raw material (exponential amplification)</td>
<td>• Too much information to make the interpretation easy for physicians • Risk of samples contamination</td>
</tr>
<tr>
<td><strong>Micro-Arrays</strong></td>
<td>Hybridization of a sample of DNA by DNA fragments placed on a coated quartz grid</td>
<td>• Numerous tests can be performed simultaneously (1 million) • Possibility of quantification of sample components</td>
<td></td>
</tr>
<tr>
<td><strong>Fluorescent in situ hybridization (FISH)</strong></td>
<td>Identification of a target molecule by a system of coupled antibody / fluorescent site</td>
<td>• Useful technique for cells not in process of division • High sensitivity that allows its use for early detection of pathological processes</td>
<td>• Complex • 5 -10% error (false positives)</td>
</tr>
</tbody>
</table>

¹ Hepatitis B & Hepatitis C Virus

Source: Business Insights, Desk research, CEPTON analysis

© CEPTON
However, new technologies keep emerging in this very innovative, not yet mature field

Examples of more recent in vitro technologies

<table>
<thead>
<tr>
<th>Description</th>
<th>Benefits</th>
<th>Prospects</th>
<th>Examples</th>
</tr>
</thead>
</table>
| Biobarcode™ Nanosphere | Detection of proteins by amplification of a DNA sequence with a gold coated nanoprobe | • Higher sensitivity than FISH, ELISA and mass spectrometry  
• Cheaper than mass spectrometry  
• Practicable by hospital employees | • Diagnosis of ovarian, prostate and pancreas cancers  
• Diagnosis of neurological degeneration (Alzheimer’s disease) | • Diagnosis of thrombophilia & hypercoagulation problems  
• Cystic fibrosis diagnosis |
| DNA methylation | Observation and quantification of DNA methylation | • Detection of tumors before they actually exist  
• Prognosis of tumor aggression  
• Prognosis of response to treatment (in some cases) | • Classification of prostate, breast and colorectal cancers  
• Response to cancer treatments  
• Detection of lung cancer | • Colorectal cancer detection by blood analysis |
Biomarkers have been used in laboratories & in hospitals for a long time – However they are now developing at a much faster pace

**History of biomarkers**

- **1848**
  - Birth of the word *Pharmacogenetics*
  - Biomarker of diabetes: glucose
  - Biomarker of cancer: alpha-fetoprotein & carcinoembryonic antigen

- **1848**
  - 1959
  - 1960

- **1980**
  - Biomarker of cancer: CA125 (ovarian cancer) & PSA (prostate cancer)
  - 1986

- **1998**
  - 1997
  - Birth of the word *Pharmacogenomics*

- **2005**
  - 2007
  - 2010

- **2010**
  - Couple Herceptin/Herceptest
  - Couple Erbitux or Vectibix/KRAS Test
  - Couple Selzentry/Trofile

Source: CEPTON analysis
A. Personalized medicine, biomarkers and molecular diagnostics

B. The revolution of molecular diagnostics: benefits for patients and impact on the pharmaceutical industry

C. About Cepton
Biomarkers may be used in a variety of situations, from drug discovery to patient monitoring, with different objectives.

### Possible roles of biomarkers

<table>
<thead>
<tr>
<th>Type</th>
<th>Research</th>
<th>Preclinical and Clinical</th>
<th>Patient monitoring</th>
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<tbody>
<tr>
<td></td>
<td>Mechanistic</td>
<td>Pharmaco genomics</td>
<td>Safety</td>
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<td>Effectiveness</td>
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<td>Diagnosis</td>
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<td>Stratification</td>
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<td>Prognosis</td>
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<td>Stage</td>
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</tbody>
</table>

#### Objective

- **Disease mechanism**
  - Determination of genetic variations in drug response
    - Sulfatide in cerebrospinal fluid for Alzheimer’s disease
    - HER2+ for response to Trastuzumab in breast cancer
  - Determination of drug’s toxicological effects on *in vivo/in vitro* systems
    - Proteins in urine for nephrotoxicity
  - Measure of treatment effectiveness / Clinical POC
    - ERCC1 and XPF for response to chemotherapy
  - Detection of disease
    - Troponin for myocardial infarction
    - PCA3 for prostate cancer
    - YKL-40 for rheumatoid arthritis
  - Determination of patient’s response to treatment
    - KRAS mutation for response to Panitumumab in colorectal cancer
    - HER2+ for response to Trastuzumab in breast cancer
    - EGFR for response to Gefitinib in lung cancer
  - Determination of disease evolution
    - SLAK serum factor for lung cancer
    - HbA1c for diabetes
    - Circulating Tumor Cells for cancer
  - Distinction of disease stages
    - GCC for colorectal cancer

### Companion diagnostics

Sources: Biotech Perspectives October 2007, Eurasanté, CEPTON analysis 1) Proof of Concept
Discovery biomarkers can significantly speed up the drug discovery process by reducing time to POC

Discovery biomarkers - The new innovation cycle

Benefits from the new approach

- Clinical constraints are anticipated at an early stage of Research
- The waste of resources is reduced as more failing Projects are « killed » earlier
- Projects entering Phase II-b have a higher chance of making it to the market

Sources: Nature Reviews, drug discovery, Vol 9, March 2010, p. 203, CEPTON analysis
### Development biomarkers reduce lead times in clinical phases, improve probability of success and stratify patients to optimize efficacy

Examples of development biomarkers

<table>
<thead>
<tr>
<th>Objective</th>
<th>Examples</th>
</tr>
</thead>
</table>
| **Safety** | Predict or anticipate toxic side-effects  
 Detect damage earlier |
| **Surrogate endpoints** | Measure the effect of a specific drug or therapy that may correlate with a real clinical endpoint |
| **Pharmacogenomics** | Determine genetic variations in drug response  
 Stratify for better selection of patients in clinical trials |

- **Examples**
  - Kidney’s protein biomarkers which are specific to a kidney’s region, thus enabling to better & earlier detect damage through urine analysis  
    - clusterin  
    - Kim-1  
    - ß2 microglobulin
  - **Circulating Tumor Cells** (CTC), detectable in patients suffering from metastatic breast cancer  
  - **Prostate Specific Antigen** (PSA), present in high quantities in patients suffering from prostate cancer
  - Sulfatide in cerebrospinal fluid for response to AD1 treatment  
  - Her2/neu for response to Herceptin®  
  - **KRAS mutation** for response to Erbitux® and Vectibix®

Source: CEPTON analysis 1) Alzheimer’s Disease
Efficacy data of Vectibix® shows increased progression-free survival only in patients carrying the KRAS wild-type

Commercial biomarkers - Example of KRAS mutation

- Patients with mutant KRAS do not benefit from targeted therapy
- Survival without disease progression (PFS²) is significantly increased in wild-type KRAS group
- Side-effects in non-responders are avoided

1) Best supportive care  2) Progression-free survival

Herceptin® has been a real success story for Roche – first example of a combined drug and "Companion" diagnostic kit commercialization

Commercial biomarkers – Herceptin® (trastuzumab) case

- HER2\(^1\) normally expressing cell
- HER2 over-expression causing increased cell proliferation
- HER2 antibodies binding to receptors thereby inhibiting tumor growth

✓ HER2+ is predictive of Herceptin® response
✓ Testing for HER2 over-expression is mandatory

Source: Roche company website (pictures) / CEPTON 1) Human epidermal growth factor receptor 2
Despite Roche’s diagnostic capabilities, even for Herceptin® there are diagnostic tests from other providers

### Commercial biomarkers – Herceptin® (trastuzumab) case

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Company</th>
<th>CDx Name</th>
<th>Company</th>
<th>Indication</th>
<th>Reg. agency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selzentry®/Maraviroc</td>
<td>Pfizer</td>
<td>Trofile®</td>
<td>Monogram Bioscience</td>
<td>HIV</td>
<td>FDA</td>
</tr>
<tr>
<td>Ziagen®/Abacavir</td>
<td>GSK</td>
<td>HLA-B*5701</td>
<td>Many LDTs²</td>
<td>Infectious disease</td>
<td>EMEA</td>
</tr>
<tr>
<td>Erbutix®/Cetuximab</td>
<td>Merck/BMS</td>
<td>EGFR1 pharmDx™</td>
<td>Dako</td>
<td>Colorectal cancer</td>
<td>FDA/EMEA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TheraScreen® K-RAS</td>
<td>Qiagen/ Roche</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vectibix®/Panitumumab</td>
<td>Amgen</td>
<td>EGFR1 pharmDx™</td>
<td>Dako</td>
<td>Colorectal cancer</td>
<td>EMEA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TheraScreen® K-RAS</td>
<td>Qiagen/ Roche</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herceptin®/Trastuzumab</td>
<td>Roche</td>
<td>HercepTest™</td>
<td>Dako</td>
<td>Breast cancer</td>
<td>FDA/EMEA</td>
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<tr>
<td></td>
<td></td>
<td>Pathway®</td>
<td>Roche</td>
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<tr>
<td>Tykerb®/Tyverb®/Lapatinib</td>
<td>GSK</td>
<td>HercepTest™</td>
<td>Dako</td>
<td>Breast cancer</td>
<td>EMEA</td>
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<tr>
<td></td>
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<td>Pathway®</td>
<td>Roche</td>
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<tr>
<td>Tarceva®/Erlotinib</td>
<td>Roche</td>
<td>EGFR1 pharmDx™</td>
<td>Dako</td>
<td>NSCLC</td>
<td>EMEA</td>
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<tr>
<td>Iressa®/Gefitinib</td>
<td>AZ/Teva</td>
<td>EGFR1 pharmDx™</td>
<td>Dako</td>
<td>NSCLC</td>
<td>EMEA</td>
</tr>
<tr>
<td>Epitol®/Tegretol®/Carbamazepine</td>
<td>Novartis</td>
<td>HLA-B*1502</td>
<td>Many LDTs²</td>
<td>Neuropsychiatric disorders</td>
<td>EMEA</td>
</tr>
</tbody>
</table>

### Examples

**HER2**² normal expression

**HER2** over-expression

**Examples**

- HER2 antibodies binding to receptors, inhibiting tumor growth

Source: CEPTON / PWC

1) Human epidermal growth factor receptor 2

2) Laboratory developed tests

© CEPTON
Biomarkers may also be used to reduce overall treatment costs, as exemplified by MammaPrint® in stage I and II breast cancers

Commercial biomarkers – Cost effectiveness study example

**Description**

- Nucleic acid test determining the tumor’s fingerprint by comparing a sample of the tumor with the 70-gene signature of breast cancers
- **Designed for Stages I & II**
- Performed before or during surgery determining whether hormone therapy will be enough to curb cancer
- Avoidance of ultrasound, biopsy and possibly usual treatment for stage I & II breast cancers

- **Better quality of life** during treatment and after treatment
- Cost effective if it avoids heavy treatments for more than 15% of stages I&II cancers

<table>
<thead>
<tr>
<th>MammaPrint®'s result</th>
<th>Oncologist's assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT enough</td>
<td>HT enough</td>
</tr>
<tr>
<td></td>
<td>- 0.65 k€</td>
</tr>
<tr>
<td>HT not enough</td>
<td>HT not enough</td>
</tr>
<tr>
<td></td>
<td>Does not exist</td>
</tr>
<tr>
<td></td>
<td>- 0.65 k€</td>
</tr>
</tbody>
</table>

**Cost comparison of breast cancer treatment**

<table>
<thead>
<tr>
<th>With MammaPrint®</th>
<th>Without MammaPrint®</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 k€</td>
<td>16.7 k€</td>
</tr>
<tr>
<td>4.1 k€</td>
<td>4.9 k€</td>
</tr>
<tr>
<td>9.1 k€</td>
<td>4.1 k€</td>
</tr>
<tr>
<td>2.4 k€</td>
<td>3.4 k€</td>
</tr>
<tr>
<td>1.9 k€</td>
<td></td>
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</tbody>
</table>

1) Hormonal Therapy
Source: Agenda, Doctissimo, INCA, Bulletin du Cancer, MedCost, CEPTON analysis
The biomarkers market is expected to increase sharply in the near future, driven by oncology and cardiology.

### Trend in biomarker sales, 2007-2015

<table>
<thead>
<tr>
<th>Year</th>
<th>Patient monitoring</th>
<th>Clinical Trials</th>
<th>Drug Discovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>2.4</td>
<td>0.5</td>
<td>2.7</td>
</tr>
<tr>
<td>2012</td>
<td>13</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>2015</td>
<td>22</td>
<td>5</td>
<td>13</td>
</tr>
</tbody>
</table>

CAGR 07-15: 19%

### Top 3 research fields

- **Oncology**
  - hLAP -protein-: diagnosis, therapy management and monitoring of germ cell tumors
  - P53 -protein-: cancer diagnosis
  - ERCC1 and XPF -proteins-: prognosis of response to chemotherapy

- **Cardiovascular diseases**
  - sPLA2 -protein-: diagnosis and prognosis of coronary disease and heart attack
  - NT ProBNP -protein-: diagnosis of congestive heart failure, prognosis of 6-month-survival

- **Neurology, Autoimmune diseases, Infectious diseases**
  - Sulfatide in cerebrospinal fluid -lipid-: AD diagnosis
  - YKL-40 -protein-: diagnosis of rheumatoid arthritis
  - CPS1 -protein-: diagnosis of sepsis disease

Source: BBC Research, Global Business Intelligence, Biopharmaceutiques April 2010, Eurasanté 2005, CEPTON analysis
Tomorrow, biomarkers will be everywhere in the healthcare value chain; however, the road is still long

Main barriers to the development of molecular diagnostics and biomarkers

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Impact on players</th>
</tr>
</thead>
<tbody>
<tr>
<td>More complex clinical trials</td>
<td>Increased R&amp;D costs and lead times</td>
</tr>
<tr>
<td>• More patient groups</td>
<td></td>
</tr>
<tr>
<td>• More complex monitoring</td>
<td></td>
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<tr>
<td>• More data to manage</td>
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<tr>
<td>• Need for co-development of diagnostic tools</td>
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</tr>
<tr>
<td>Fragmented regulatory and HTA(^1) processes</td>
<td>Uncertainty about the future business model of molecular diagnostics</td>
</tr>
<tr>
<td>• Different requirements between EMEA and FDA</td>
<td></td>
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<tr>
<td>• HTA process managed at sub-national level in EU</td>
<td></td>
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<tr>
<td>Slow and uncertain reimbursement processes</td>
<td></td>
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<tr>
<td>• Based on decentralized HTA processes (2-5 years lead times)</td>
<td></td>
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<tr>
<td>• Little recognition by payors of the value of information provided by diagnostics</td>
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</tbody>
</table>
Collaborations are the prevalent approach to develop and commercialize companion diagnostic tests

Strategies to approach companion diagnostics

Collaboration with Genzyme genetics on BCR/ABL testing for CML drugs

Collaboration with Monogram Biosciences for HIV drugs
Monogram’s Trofile Assay is used to test CCR5 for Maraviroc

Collaborated with University of North Carolina for breast cancer studies on Gemzar

Partial control with limited Rx/Dx integration (Veridex and OrthoClinical Diagnostics)

Most integrated Rx/Dx – close cooperation between Rx and Dx to validate novel Oncology markers for personalized medicine test

Partial control with limited Rx/Dx integration (Abbott Dx & Vysis)

Roche model of Rx-Dx integration

Research

1. Molecular Biology & biomarker relevance

Translational Medicine

2. Biomarker screening & development expertise
3. Biomarker strategy & clinical stratification strategy

Clinical Development

4. Assay development & technical support
5. Alignment of Rx / Dx platforms
6. Clinical development of assay

Strategic Marketing

7. Commercialization model
8. Companion diagnostic registration strategy
In the long term though, the impact of molecular diagnostics on pharma will be huge, both in scientific and economic terms.

Biomarkers: benefits for patients and impact on healthcare industries

**Benefits for patient**
- Earlier POC\(^1\) in man
- Better understanding of disease mechanisms

**Impact on healthcare industries**
- Biomarkers speed up drug discovery process
- Biomarkers improve productivity of clinical trials and reduce failure rate
- Biomarkers bring medical value and improve cost-effectiveness of treatments

Source: CEPTON analysis 1) Proof of Concept
Content

A. Personalized medicine, biomarkers and molecular diagnostics

B. The revolution of molecular diagnostics: benefits for patients and impact on the pharmaceutical industry

C. About Cepton
CEPTON is a Spin-Off of one of the most renowned global consulting firms operating from 4 locations with a team of ~20 permanent consultants.

CEPTON globally

- Founded in 2006
- Strategy Consulting Firm
- 6 partners in 4 international offices
- ~20 consultants with industry specific experience
CEPTON - high value advice with small teams, senior team members and Partners dedicated to project work

- Small effective teams of **senior experts** and dedicated Partners

- CEPTON Managers and Partners all have **15+ years of experience** either in well-known Consulting firms or in the pharmaceutical Industry

- **Junior** consultants only on specific request – Partners and Managers are directly involved in projects

- Focus on **international** industry know-how and specifically adapted methods

- Integrating the client’s organization and existing data by relying on proven **project management skills**

- Fostering **implementation** even as interim managers
We focus on selected industries in which we have gathered long term relations and know-how

Our Focus

<table>
<thead>
<tr>
<th>Industry</th>
<th>Strategy Consulting</th>
<th>Mediation &amp; Senior Advice</th>
<th>Interim Management</th>
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<tr>
<td>Pharmaceuticals</td>
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<td>Medical Devices</td>
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<td>Biotechnology</td>
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<td>Automotive</td>
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<td>Process Industries</td>
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Our offerings cover a spectrum of essential top executive questions and solutions

CEPTON Offerings

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<th>Strategic Management</th>
<th>Performance</th>
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<td>Corporate Strategy</td>
<td>Launch Readiness (MAXXIMizing®)</td>
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<tr>
<td>Therapeutic Area Strategy</td>
<td>Marketing &amp; Sales Force Effectiveness</td>
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<tr>
<td>Regional Strategy</td>
<td>Cost optimization</td>
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<td>Portfolio-Management</td>
<td>R&amp;D efficiency</td>
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<td>Reorganization</td>
<td>Restructuring</td>
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<td>Post Merger Integration</td>
<td>Business Development support</td>
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<td>Turnaround Management</td>
<td>Due Diligence (commercial)</td>
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<td>Change Management</td>
<td>Acquisition Screening &amp; Valuation</td>
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Transformation

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<th>Transactions</th>
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<tr>
<td>Due Diligence (commercial)</td>
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<td>Acquisition Screening &amp; Valuation</td>
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<tr>
<td>Carve Out Preparation</td>
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</table>
Even since Cepton was founded early 2006 many interesting and fast growing clients have been served

Selected references of Cepton clients since 2006

Source: Cepton
Jean Reboullet  
Managing Partner France

Year of birth: 1961  Nationality: French

<table>
<thead>
<tr>
<th>Professional experience</th>
<th>Key projects</th>
<th>Industry competence</th>
<th>Education</th>
<th>Languages</th>
</tr>
</thead>
<tbody>
<tr>
<td>since 2006  CEPTON Founding Partner – Paris Office</td>
<td>- Optimization of R&amp;D organizations in several mid-sized pharma</td>
<td>- Pharmaceuticals</td>
<td>- 1985  Sup’Aero (85) – Best French equivalent of a Master in Science in Aerospace</td>
<td>- French</td>
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<tr>
<td>2004-2005 Schlumberger Business Consulting: Director ECA area</td>
<td>- Sales force optimization and marketing excellence in pharma</td>
<td>- Process industry</td>
<td></td>
<td>- English</td>
</tr>
<tr>
<td>1999-2004 Roland Berger Strategy Consultants: Partner then Senior Partner</td>
<td>- Launch readiness for several pharma products: onco blockbuster, allergy tablet, antibiotic…</td>
<td>- Oil &amp; Gas</td>
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<td>1997-1999 AT Kearney: Principal</td>
<td>- Several Therapeutic Area strategy design</td>
<td>- Private Equity</td>
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<tr>
<td>1990-1997 Arthur D. Little: Consultant then Associate Director since July 93</td>
<td>- Development strategy for Biotech start ups</td>
<td>- Automotive</td>
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<tr>
<td>1987-1990 Touche Ross – Braxton Associates: Consultant</td>
<td>- Several marketing optimization programs in chemical and process industry</td>
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<tr>
<td>1985-1987 Aérospatiale – Design Engineer</td>
<td>- Strategic planning in process industry</td>
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</table>
## Marc-Olivier Bévierre
**Partner France**

Year of birth: 1964   Nationality: French

### Professional experience

<table>
<thead>
<tr>
<th>Year</th>
<th>Experience</th>
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<tbody>
<tr>
<td>since Oct 2008</td>
<td>CEPTON Partner</td>
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<tr>
<td>1991-2008</td>
<td>16 years of experience in the Pharma Industry in different positions</td>
</tr>
<tr>
<td>2004-2008</td>
<td>Director of Strategy &amp; Business Intelligence, J&amp;J Pharma France</td>
</tr>
<tr>
<td>1997-2004</td>
<td>3 positions in Marketing &amp; Sales management, both local and International (Novartis, J&amp;J)</td>
</tr>
<tr>
<td>1991-1995</td>
<td>Medicinal Chemist in Drug Discovery (Novartis, Basel)</td>
</tr>
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</table>

### Key projects

- 5-year Strategic Plan of a medical device and drug manufacturer with a special focus on the development of the Homecare business
- Reorganization of clinical trials management processes in a top 5 Pharma
- Design and financial assessment of strategic scenarios for relaunch of a major OTC brand in France, Italy and Germany
- Performance assessment and improvement of a major diabetes BU in Germany (350 reps)
- European launch of a new tablet product in allergy - Support in marketing, sales readiness and medico-marketing for product launch preparation
- Re-Launch of a Meningitis C vaccine in France: business case, marketing plan

### Industry competence

- Pharmaceuticals
- Animal Health pharmaceuticals
- Biotechnology

### Education

<table>
<thead>
<tr>
<th>Year</th>
<th>Degree</th>
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</thead>
<tbody>
<tr>
<td>1996</td>
<td>MBA INSEAD</td>
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<tr>
<td>1991</td>
<td>Ph.D. Organic Chemistry</td>
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<tr>
<td>1988</td>
<td>Engineer Ecole Polytechnique</td>
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</tbody>
</table>

### Methodological competence

- Business case / Financial modelling
- Sales & Marketing Management
- Strategic Marketing
- Market Research
- Sales Force Effectiveness
- Pharmaceutical R&D management
- Portfolio management
- Due Diligence in Life Sciences
- Business Planning & Forecasting
- Chemical Synthesis & Processes

### Languages

- French (mother tongue)
- English (fluent)
- German (fluent)
- Spanish (proficient)
# Francis Turina-Malard
**Partner**

**Year of birth:** 1969  
**Nationality:** French

## Professional experience

<table>
<thead>
<tr>
<th>Year</th>
<th>Position/Company</th>
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<tbody>
<tr>
<td>since 2008</td>
<td>CEPTON Partner</td>
</tr>
<tr>
<td>2007-2008</td>
<td>CEPTON Senior Manager</td>
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<tr>
<td>2004-2007</td>
<td>Microsoft – Program Manager Customer &amp; Partner Satisfaction</td>
</tr>
<tr>
<td>2002-2004</td>
<td>Keyrus IT – Organization &amp; HR Director, member of the Board</td>
</tr>
<tr>
<td>2000-2002</td>
<td>Keyrus IT - Founder of the Consulting Department</td>
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<tr>
<td>1998-2000</td>
<td>The Boston Consulting Group – Consultant</td>
</tr>
<tr>
<td>1994-1998</td>
<td>Aerospatiale (Space) – Project Manager</td>
</tr>
</tbody>
</table>

## Key projects

- Modeling of organizational scenarios and outsourcing strategy of DMPK teams - Pharma
- Set-up of a framework, governance & tools to improve productivity of Research – Pharma
- Business case on the evolution of the International clinical studies organization for the French affiliate of a big Pharma
- Diagnosis & definition of an action plan with medical & marketing teams to reach excellence in local medico-marketing studies
- Definition of a global IS Strategy to support Marketing & Sales Operations - Pharma player
- Several Mgmt seminars on Organization, growth & culture - different activity sectors
- Global change management program for the WW Leader of the Software industry
- Corporate structuring, Organization and HR Strategy & Management of a Group during growth phase (150 to 1000p.)
- More than 4 years as Project Manager on International multi-cultural environment

## Industry competence

- Pharmaceuticals
- High-Tech + IT
- Automotive
- Process Industry

## Education

1993  
Telecom Bretagne (French Engineering School – one of the top 2 schools in the Telecom field)

## Languages

- French (mother tongue)
- English (bilingual)
- German (good working knowledge)
- Spanish, Italian (basic)
# Dr. Michael C. Müller
Managing Partner Germany

**Year of birth:** 1963  
**Nationality:** German  
**Founder Munich Office**

## Professional experience

<table>
<thead>
<tr>
<th>Year</th>
<th>Position/Company</th>
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<tbody>
<tr>
<td>since 2006</td>
<td>CEPTON Managing Partner</td>
</tr>
<tr>
<td>2004-2006</td>
<td>Managing Director Accenture</td>
</tr>
<tr>
<td>1996-2004</td>
<td>Roland Berger Strategy Consultants</td>
</tr>
<tr>
<td></td>
<td>Partner &amp; Head of Global Pharma practice group</td>
</tr>
<tr>
<td>1993–1995</td>
<td>Head of Marketing, Servier Munich</td>
</tr>
<tr>
<td>1990–1992</td>
<td>Clinical Research Director, Sanofi-Winthrop</td>
</tr>
<tr>
<td>1988–1990</td>
<td>Practicing as Medical Doctor</td>
</tr>
</tbody>
</table>

## Key projects

- MAXXIIMizing® launch effectiveness for several products in EU and US for leading pharma companies
- Distribution strategy for global pharmaceutical companies
- Due Diligences of international pharma & biotech companies
- Various TA strategies for leading pharmaceutical companies
- Turnaround of a mid-size US-pharma
- Several M&A projects
- Diverse R&D programs
- Strategic Planning redesign for global TOP 3 company

## Industry competence

- Pharmaceuticals
- Medical Devices
- Consumer Products
- Healthcare Management
- Biotech
- Insurance

## Education

<table>
<thead>
<tr>
<th>Year</th>
<th>Degree</th>
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<tbody>
<tr>
<td>1990</td>
<td>Thesis</td>
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<td>1982-1988</td>
<td>Medical Doctor University of Essen, Bochum and Bonn</td>
</tr>
</tbody>
</table>

## Methodological competence

- Corporate Strategy
- Marketing & Sales Excellence
- Corporate Organization
- Portfolio management
- Distribution strategy
- Cost containment/Restructuring

## Languages

- German (mother tongue)
- English (fluent)
- French (proficient)
- Italian (basic)
Bertrand Kleinmann
Partner France

Year of birth: 1960    Nationality: French

**Professional experience**


**Methodological competence**

- Corporate strategy
- M&A
- Strategic alliances
- Post merger integration

**Key projects**

- Alliance strategy between a Telco and a Transport operator
- European consolidation strategy in engineering
- Alliance strategy between a Technology Firm and a Utility followed by a Beauty Contest
- Organization redesign for a leading global supplier of high performance materials
- Enterprise transformation of a leading pan-European Automotive supplier including program profitability.
- Channel strategy design and implementation for a leading European telecom operator
- Numerous turnaround programs for industrial clients

**Industry competence**

- Telecom, Media & Hi Tech
- Transportation
- Industrials: Automotive, Aerospace, other Capital Goods, Paper, Building Products

**Education**

1984    Ecole normale superieure  PhD in Atomic Physics
1982    Ecole Centrale Paris  MsC

**Languages**

- French
- English
Recently, CEPTON released several publications on trends of the pharmaceutical industry in the specialized French press.

"Pharmaceutiques" is the reference journal of the French Pharmaceutical industry.

March 2009
The future of Healthcare industries in France

April 2010
The new organization of hospitals in France and its impact on healthcare industries

© Cepton
CEPTON also regularly writes papers on the latest developments in the biotech industry

February 2009 ("La Jaune et la Rouge")¹
A review of the latest developments of the biotech industry and its impact on the world economy

CEPTON also issues position papers on selected topics that have particular relevance for the pharmaceutical industry.

Recent position papers of CEPTON:

- A study on the impact of the HPST Act for pharma companies in France, performed in collaboration with a legal firm specialized in Healthcare.

**Strategic outsourcing across the Pharmaceuticals Value chain**

**The new Reality – Future needs for Marketing In the HealthCare Industry**

**Impacts de la loi « Hôpital, Patients, Santé, Territoires » pour les laboratoires pharmaceutiques**

Jeudi 17 septembre 2009
Une étude de J. Reboulet, M.O. Béviere et O. Lambris réalisée entre janvier et septembre 2009

Source: CEPTON
CEPTON released three renowned scientific studies on specific therapeutic areas or geographical regions

Examples of past research studies by CEPTON
CEPTON’s consulting approach is well received in the press
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<td>+49 89 20 18 36 36-9</td>
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<td>United States of America</td>
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