Quo vadis Medical Industry?

18th December 2014

Karl Branzén
Sweden has experienced the winds of change in the drug industry

- **In the 70s and 80s** Sweden had two big medical/drug corporations - Pharmacia and Astra.

- **Before the end of the 90s** both companies were non-Swedish; after mergers with Upjohn and Monsanto, Pharmacia was finally acquired in 2002 by Pfizer, USA, **AND** Astra decided to merge with Zeneca, UK, in 1999. Today Pfizer has no "Pharmacia" operation in Sweden and AstraZeneca is managed from the UK.

- Some old Pharmacia units are still running under other names, **but at a much smaller scale** **AND** AstraZeneca has scaled down its Swedish R&D operations - closed Lund, minimized Södertälje, but expanded in Göteborg.
and the conclusions for Sweden as well as for the Nordic countries are that ..... 

- Countries outside the Nordic area are more important to the future development of the pharma industry.

- Of the 2300 jobs created by the Nordic pharma industry over the last 2-3 years more than 2000 were created in non-Nordic countries,

- Novo Nordisk is the exception.
Drug industry landmarks

- **1982** - Humulin, Eli Lilly, recombinant human insulin
- **1920s** - First insulin used in humans extracted from pancreas of cadaveric dogs, later extracted from slaughterhouse animals, mostly pigs and cows
- **1985** - Protropin, Genentech, recombinant human growth hormone
- Approval of Protropin coincided with withdrawal of cadaveric growth hormones from the market because of Creuzfelt-Jacob disease (caused by sub-viral particles, prions)
Top 10 selling drugs globally

<table>
<thead>
<tr>
<th></th>
<th>2001</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Classic&quot; chemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small molecules</td>
<td>93%</td>
<td>29%</td>
</tr>
<tr>
<td>Biotech/Biologics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein based</td>
<td>7%</td>
<td>71%</td>
</tr>
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Biotech drugs share of GLOBAL DRUG SALES

<table>
<thead>
<tr>
<th></th>
<th>2001</th>
<th>2012</th>
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<tbody>
<tr>
<td></td>
<td>8%</td>
<td>17%</td>
</tr>
<tr>
<td>(= USD 36 bn)</td>
<td>(= USD 163 bn)</td>
<td></td>
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</tbody>
</table>
### Global drugs sales - USD billion

<table>
<thead>
<tr>
<th>Year</th>
<th>Developed countries</th>
<th>Developing countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>730</td>
<td></td>
</tr>
<tr>
<td>2013-14</td>
<td>1000 (= 1 trillion)</td>
<td>20%</td>
</tr>
<tr>
<td>2017</td>
<td>1200 (=1,2 trillion)</td>
<td>40%</td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td>20%</td>
</tr>
<tr>
<td>2017</td>
<td>20%</td>
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<td>2017</td>
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<td>2017</td>
<td>60%</td>
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<tr>
<td>2017</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>2017</td>
<td>60%</td>
<td>40%</td>
</tr>
<tr>
<td>2017</td>
<td>90%</td>
<td>10%</td>
</tr>
</tbody>
</table>

- **Oncology**: 80% in Developed countries, 20% in Developing countries.
- **Pain**: 60% in Developed countries, 40% in Developing countries.
- **Hypertension**: 60% in Developed countries, 40% in Developing countries.
- **Diabetes**: 80% in Developed countries, 20% in Developing countries.
- **Respiratory**: 90% in Developed countries, 10% in Developing countries.
- **Infections**: 50% in Developed countries, 50% in Developing countries.
- **Cardiovascular**: 60% in Developed countries, 40% in Developing countries.
- **Autoimmunity**: 90% in Developed countries, 10% in Developing countries.
Drug "classification" today

<table>
<thead>
<tr>
<th>Trademarked</th>
<th>Generics</th>
</tr>
</thead>
<tbody>
<tr>
<td>chemicals/small molecules</td>
<td>Biosimilars</td>
</tr>
<tr>
<td>Trademarked biologics/biotechs</td>
<td></td>
</tr>
</tbody>
</table>
Features of the drug market today

- Big Pharma ➔ Giant Pharma
- Growing market share of Biotech drugs/Biologics
- Building a business or being acquired - a key issue
- (Don’t forget the med-tech, diagnostic and other companies)
Creation of Giant Pharma companies - does it pay off?

Megamergers created shareholder value

Of the top 20 companies in 1995 there were 18 remaining in 2012, either as buyers or as merged

Consolidation deals generated greater economic profit

Profits of the pharma sector outnumbered profits of most other industry sectors since 1995
Average number of annual approvals of innovative new drugs by the US FDA

Impact of enhanced FDA review process, 2011-12:

20-year average, 1993-2012 28
Average, 2011-12 35
Personalized Medicine
- a new era for healthcare and industry
The Human Genome Project

- Initiated in 1990
- Formally completed in 2003, when the human reference genome was sequenced
- Mapping of the individual chromosomes completed in the years 2001-2005

... and today, some 10 years later
- New biomedical R&D approaches
- New industrial opportunities AND challenges
- THE HUMAN PROTEIN ATLAS completed in 2014 !!!!
Some interesting quantitative measures

<table>
<thead>
<tr>
<th></th>
<th>By 2003</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost to sequence 1 Human Genome</td>
<td>USD 10-20 million</td>
<td>USD 3-5 thousand</td>
</tr>
<tr>
<td>Time to sequence 1 Human Genome</td>
<td>3-4 months</td>
<td>1-2 days</td>
</tr>
<tr>
<td>No of disease-causing gene mutations</td>
<td>1474</td>
<td>2972</td>
</tr>
<tr>
<td>FDA-approved drugs with genomic information on Label</td>
<td>46</td>
<td>106</td>
</tr>
<tr>
<td>No of biobanks</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

*Source: National Human Genome Research Institute, NIH - USA*
Sufficient descriptive terms??

Different words, different meanings or not?!?! - What is accepted ??

- Personalized Medicine
- Stratified Medicine
- Precision Medicine
- Personalized Health
- Individualized Health
The Personalized Medicine approach
Patient and clinician

Clinical routine
The Personalized Medicine approach
The Personalized Medicine approach

1. Biobanks
2. Registers
3. -omics
4. IT
5. Basic and Applied Medical Research
6. Bio markers
7. Drug candidates
8. Academic Medical Research and Infrastructure
9. EMR
10. Decision Support
11. Patient and clinician
12. Clinical routine
The Personalized Medicine approach

- Biobanks
- Registers
- EMR
- Rx and Dx Products
- Reimbursement
- Registration
- Clinical trials
- Dx development
- Rx development
- -omics IT
- Basic and Applied Medical research
- Bio markers
- Drug candidates
- Decision Support
- Medical/Clinical Research and Infrastructure
- Clinical routine
- Industrial Product Development Drugs and Diagnostics
- Patient and clinician

Drug candidates

Bio markers

-omics IT
Illustration of the -omics
Personalized Medicine and Cancer

Why has the Personalized Medicine approach become so influential in cancer?

The medical rationale

- A highly heterogeneous disease,
- Patients having the same type of tumor show significant molecular differences in expression and distribution of tumor cell markers,
- Cellular mutations usually accumulate as cancer progresses, leading to increased tumor heterogeneity,
- Currently used cancer therapies are often toxic to normal cells,
- Cancer patients have limited time to try other treatments.
The Cancer market

The business rationale

The total global costs for cancer care have passed

... the 1 trillion USD mark !!! (in 2013)

... which of pharmaceuticals represent approx. 75 billion USD,

... and diagnostics approx. 10% thereof, i.e. 7,5 billion USD,

THUS, the value of the cancer market will be attractive to commercial initiatives and companies will aim to capture novel business
Implementation

How far in the implementation of Personalized Medicine have we come today?

- Genomic technologies, such as Whole Genome Sequencing (WGS) and massive parallel sequencing, are used in high volumes which has lowered costs,
- There are IT-solutions for storage, processing and analysis of huge amounts of data,
- Cancer complexity has generated technologies in support of new biomedical research approaches,
- Regulatory authorities promote registration/launch of combination products, i.e. a drug + a diagnostic, to define target group for the therapy in question (companion diagnostics).
... BUT there are obstacles

- Project driven implementation rather than through administrative decisions

- Some disease areas benefit more than others - at least initially

- Test/diagnostic driven approach rather than treatment and care driven, which may be in conflict with current healthcare priorities

- New infrastructure needed that requires investments and competences - IT solutions will be key

- A new way of working means new types of training and education
Products ”inspired” by Personalized Medicine

- FDA in the US has issued regulations on the use of diagnostic tests to determine patient response to therapy, but EMA in Europe not yet introduced similar regulations,
- Biomarkers as a new and expanding publically funded R&D area,
- Emergence of Consumer Genomics,
- Increasingly sophisticated sequencing equipment,
- Supercomputers and IT-solutions to handle data generated through genomics, proteomics and other -omics.
The ideal regulatory model for the development of combination products
Growing number of Personalized Medicine products

- In 2006 there were 13 drug-diagnostic combinations approved by FDA and available in the US,

- In 2014 there are 113 drug-diagnostic combinations either approved by FDA or in clinical development in the US,

- Since 2010 almost all biopharma companies are investing in personalized medicine research, and close to 50% of all clinical development projects aim to produce a drug-diagnostic combination.
Product examples

Mandatory drug-diagnostic combinations (FDA)

- Herceptin, Roche  HER-2/neu-receptor (breast cancer)
- Gleevec, Novartis  Philadelphia chromosome/BCR-ABL (leukemia)
- Xalkori, Pfizer  ALK (lung cancer)
- Zelboraf, Roche  BRAF V600E (melanoma)
Some conclusions

- Drug development/marketing is big business - giant companies in terms of sales and number of employees have been successful

- Biotech drugs are growing in importance and represent close to 50% of drug development projects

- Drug-diagnostic combinations - the Personalized Medicine approach - will be required by regulatory authorities to motivate the (normally) high price of biotech drugs in all therapeutic areas

- More powerful and sophisticated IT-solutions are required to support medical research and clinical development