Medimetrics

Company Overview

- Spin out from Philips - July 2011
  - Private (main investors Philips and ZFHN Heilbronn)
  - Based in the Netherlands, USA & Germany

- Inventor/developer of
  - IntelliCap® technology - world’s first & only electronic oral drug delivery & patient monitoring capsule
  - LiGalli intravaginal ring – JV with LiGalli BV

- Extensive Proof of Technology – in animal and clinical studies
  - Close partnership with Philips for production, development, and technology
  - Projects with 5 of top 10 pharma companies
  - CE Marking

- Medimetrics provides access to the IntelliCap® technology for:
  - Smart Pharmaceuticals
  - Pharma R&D Services
Introduction – Medimetrics Awards

Medimetrics Awards

External Recognition for Innovation

Medimetrics’ Unique Core Competencies
(1) very precise delivery of drugs
(2) connectivity with outside world

Medimetrics Technology

The IntelliCap® acts by real-time wireless drug release guided by the physiology (pH, transit time and temperature) of the gut regions.
Core Competencies

Value based on our Core Competencies -> 2 case studies

- CC1: very precise delivery over a certain time
- CC2: Communication

<table>
<thead>
<tr>
<th>Company</th>
<th>Intarcia</th>
<th>Proteus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product</td>
<td>implantable drug-device combination (only CC1)</td>
<td>Chip on a tablet – to communicate with outside (only CC2)</td>
</tr>
<tr>
<td></td>
<td>valuation 5.5 B USD</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion:
- each of the two core competencies is potentially very valuable
- in contrast to these companies, Medimetrics offers both CC’s into one product!

Prologue

The Health Care Industry is changing dramatically
'Beyond the pill'

Medimetrics can provide 'Outcomes beyond the pill'
Big pharma will take digital health on board

![Graph showing importance of digital health strategy](image)

Big Pharma regard Digital Health Strategy as crucial for future success...

A different species is entering into the Health Care Ecosystem ...

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**Top 9 Companies Leading The Digital Health In 2015**

1. Intel – digital health foundation
2. IBM – personalised medicine
3. Google – digital health alphabet
4. Qualcomm – connecting devices
5. Microsoft – connected health platform
6. Samsung – digital health initiative
7. Apple – digital health revolution
8. Philips – patient relationship management
9. Amazon – digital health retailer

Source = WT Vox : WT VOX is the most trustworthy, authoritative resource in IoT and Wearable Technology landscape and a Top 10 influencer in 2015.
VC funding in digital health companies

The Digital Health Hype Cycle

- The Digital Health Hype Cycle: The key question is not if this cycle is there or not — the key questions are:
  - (1) how to get over the depression of disillusionment?
  - (2) where the plateau of productivity is going to stabilize?

The answer to both questions is to be found in the same area: the health economic benefit that your application is providing...

For instance:
- What is the health economic benefit of Google Glass?
- What is the health economic benefit of electronic health records?
- What is the health economic benefit of e.g. an activity tracker, a Fitbit device or a smartwatch?
- What is the health economic benefit of a smart pill?

We better focus on this question … and the answer is different for each of the applications …
Shift in Pharma Industry Focus

Paradigm Past 30 years
...“The Pill”...

Drug Innovation
- Identify unmet needs for key diseases
- Research fundamental causes
- Develop biological models
- Screen and test molecule drugs
- Select lead molecules
- Develop in the clinic through phase I, II and III
- Prove quality, efficacy and safety
- Commercialize to the customers (patients)

Paradigm Next 30 years
...Provide Outcomes “Beyond The Pill”...

Improved Outcomes
- The “customers” (patients, doctors, payers) expect more active partnership and services
- Doctors > effective personalized treatments with increased precision and feedback on the treatment – support compliance – tracking patient data and response
- Patients > information on the treatment – real time when possible
- Payers > adherence and compliance data – confirmation of health economic benefits – build and track patient (population) history
- Developers > more precise feedback during development

Disruptive innovations tend to become reality slower then expected but
Their impact tends to be higher then expected

Paradigm Shift in the Healthcare Industry

...“The Pill” ...

- Research, manufacturing and sale of drugs, in a physical healthcare world
- During development
  - Statistically proven efficacy, quality and safety
- ... and on the Market
  - Dose with acceptable variability
  - Delivered at a certain place
  - To the patient

Providing Outcomes beyond the pill in the digital healthcare world

- During Development
  - More precise development possible – absorption window mapping – potential cost reduction and treatment optimization
- ... and on the Market
  - Unprecedented precision of drug delivery
  - Adherence and compliance information – has the drug taken correctly – right time, right place and right dose?
  - Communication – realtime feedback on the treatment possible to patients, doctors and ultimately payers – could be with a smart phone or over a computer network

Disruptive innovations tend to become reality slower then expected but
Their impact tends to be higher then expected
Eye opener - Adherence & Health Care Costs

Between $100 and $300 billion of avoidable health care costs have been attributed to nonadherence in the US annually, representing 3% to 10% of total US health care costs.\(^7,\)\(^8\)

- Medimetrics perspective
- Increased adherence is just one of the factors that the Medimetrics core technology enables, aside from:
  - increased precision of place, time and dose
  - potential increase of safety/efficacy
  - potential increase of cost-effectiveness

Exact costs can be calculated for each indication and molecule to make the business case.

Non-adherence in patients

Source: Manhattan Research, 2004
Medimetrics Business

Medimetrics Core Technology:
Personalized Electronic Drug Delivery and Digital Monitoring

- Absorption
- Microbiome
- Monitoring

Services

- Multi dose
- Unit Dose

Smart Pharmaceuticals

IntelliCap® Services for Drug Development

Medimetrics operates the system during a study for:
- Modified Release development
- Compound characterization
- Clinical or pre-clinical use

Unique combination:
- Control location
- Control time
- Control amount
- Control release profile

Benefits for Pharma R&D:
- Save 3-6 months development time
- Get decision making data earlier
- Ranking/prioritizing of your drugs
- Increase your success rate
Project Example - Targeted Delivery

Does my drug have sufficient distal / colonic absorption?

**PROTOCOL**

1. IntelliCap® delivers compound as bolus into distal small intestine (dSI) and into ascending colon (AC)
2. Analyze PK data to determine precise regional absorption

**RESULT**

- BA decreases in distal GI tract
- Use data to assess MR feasibility

**REFERENCE**

Bio-Images Research Ltd. LA Hodges, UK PharmSci 2013

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Gut Health & The Microbiome

A new direction for drug targets and treatments

- Humans possess an extended genome of millions of microbial genes located in the intestines
- The gut microbiome has been connected to
  - Colorectal cancer
  - Cardiovascular disease
  - Diabetes and obesity
- The gut microbiome represents a new frontier for health and disease
- Sampling of small intestines demonstrated with Nizo
**Precision Medicine & Medimetrics**

**Precision Medicine in the digital era**

- **Smart Pharmaceuticals** (based on Intellicap and LiGalli ring)
- **Smart Diagnostic Procedures** (based on smart sampling and microbiome & metabolome)

**Medimetrics Business Lines**

- Absorption
- Microbiome
- Monitoring
- Services
- Multi dose
- Unit Dose
- Smart Pharmaceuticals

**Medimetrics Core Technology**

- Marketed as "Personalized Electronic Drug Delivery and Digital Monitoring"
- This "core technology" and its broad applicability is also our Unique Selling Point
Smart Pharmaceuticals to develop with IntelliCap

Drugs that could benefit well from the IntelliCap

<table>
<thead>
<tr>
<th>Product</th>
<th>Company</th>
<th>2014 Sales (USD Billion)</th>
<th>Peak Sales (USD Billion)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sovaldi (sofosbuvir)</td>
<td>Gilead</td>
<td>9.1</td>
<td>15.4</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Tecfidera (dimethyl fumarate)</td>
<td>Biogen</td>
<td>3.1</td>
<td>4.6</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)</td>
<td>Celgene</td>
<td>2.2</td>
<td>9.75</td>
<td>Myeloma Cancer</td>
</tr>
<tr>
<td>Gilenya (fingolimod hydrochloride)</td>
<td>Novartis</td>
<td>2.2</td>
<td>4</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>Harvoni (sofosbuvir + ledipasvir)</td>
<td>Gilead</td>
<td>1.5</td>
<td>10.1</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Zivo (linezolid)</td>
<td>Pfizer</td>
<td>1.4</td>
<td>Peak sales achieved in the past</td>
<td>Hospital-acquired pneumonia infection, Vancomycin-resistant infection</td>
</tr>
<tr>
<td>Afinitor (everolimus)</td>
<td>Novartis</td>
<td>1.3</td>
<td>2.51</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>Dalacin (daclatasvir)</td>
<td>Bristol Myers Squibb</td>
<td>0.32</td>
<td>Peak sales not available in secondary research</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Nexavar (sorafenib)</td>
<td>Bayer</td>
<td>0.5</td>
<td>0.9</td>
<td>Liver Cancer</td>
</tr>
<tr>
<td>Stivarga (regorafenib)</td>
<td>Bayer</td>
<td>0.11</td>
<td>Peak sales not available in secondary research</td>
<td>Colorectal Cancer</td>
</tr>
</tbody>
</table>

**Marketed Product Candidates**

**RESULTS OF MARKET STUDY**

**Product Case Study – IntelliCap Smart Pharmaceutical**

**Breast Cancer – business case (Example)**

**Challenges With BC**

- Monitoring response to treatment is a key element in the management of breast cancer
- Dose adjustments and poor compliance levels
- Occurrence of side effects such as nausea, vomiting, decreased appetite, weight loss, unusual taste in the mouth, nosebleeds, headache, pain or sores in the mouth
- Drugs are given in combination and response monitoring is essential

- Everolimus (Afinitor)
  - Close monitoring for dosing titrations is recommended
  - Low compliance levels

- Palbociclib (Ibrance)
  - Peak Sales: 3.5 bn in 2025
  - Low compliance levels
  - Patient monitoring for side effects and adverse events

**Issue**

- Need for therapeutic drug monitoring to guide subsequent dosing and dose adjustments
- Side effects and monitoring response to therapy
- Low compliance

**Solution**

- IntelliCap can facilitate dose titrations
- IntelliCap can help monitor response to therapy for patients and disease progression

**Potential**

- Scope of improving overall success of therapy by response monitoring
- Cost of pill administration is high for oral drugs
- Scope of improving compliance and dosage monitoring

**HOW**

**Sources:**
2. Drugs.com
4. Ibrance-Breast cancer.org
5. Drake et al; Breast Cancer. 2016; 14:389-400
Partnering for Smart Pharmaceuticals
Technology access, licensing, and production

• Unique drug-device combination products
• Medimetrics offers
  – Product definition brainstorming
  – Partner for development
  – License to intellectual property
  – Device design and production

Example: Intelligent vaginal ring
Partner: LiGalli B.V.
Controlled delivery of drug via the vaginal mucosa, adaptive delivery, sensor integration, wireless data exchange

LiGalli Intra-vaginal ring

Innovative LiGalli i-Ring
• Miniaturized electronic drug delivery & diagnostics device
  – Medication reservoir, delivery pump, electronic microcontroller, sensors, wireless communication
  – 4 week drug residence
  – Stores hundreds of therapeutic doses
  – Programmable and controllable drug delivery
  – Patent protected

First application: Overactive bladder (OAB)
• Unmet medical need
• >$2B market

Empowering female OAB patients to live a normal life
Conclusions

- Digital technologies are transforming healthcare
  - a new phase of integration between pharmaceuticals and devices is being led by digital technologies
  - leading to “Connected Drug-Device Combinations” (“CDDC’s”)
- Medimetrics has a world leading position in electronic drug delivery and monitoring
  - extensive portfolio of patents and publications
- The Medimetrics Technology may be broadly applied to
  - speed oral product development
  - create smart therapeutic products
- Extensive partnering experience
  - top 5 of the top 10 pharmaceutical companies
  - extensive Proof of Technology, in animals and in clinical studies

Extensive Partnering Experience
Services and Smart Pharmaceuticals

Experience with 5 of top 10 pharmaceutical companies
Experience with mid-size companies and biotech companies
Extensive portfolio of patents and publications

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Electronic Drug Delivery

Medimetrics Vision

Our company, Medimetrics is committed to innovating human healthcare.

…We believe that making smart use of the modern digital innovations will bring a revolution in healthcare. We have created a digital device, the IntelliCap®, for smart oral controlled delivery of drugs. This allows drug development in a more intelligent way and enables creation of smart pharmaceuticals....