Measuring brain vascular status at the time of precision medicine

Company Presentation

Feb 2018
**We are scientists, engineers and doctors**

| Luciole Medical is a Swiss medical technology company developing brain oxygenation monitoring systems. We are located in Zürich. |

**ETH is the leading science institute where Albert Einstein studied**

| The company has developed a unique proprietary technology making the measurement of the true oxygen content and blood flow of the brain tissue possible. |

**One platform, two products**

| The platform has one product (minimally invasive probe) with CE mark in Europe and anticipate to obtain the CE mark for the second product (patch) in the coming year. |

**We provide physicians with information to act**

| As well recognized the acute insufficient oxygen availability in the brain can have severe consequences. The chronic or temporary reduced/sub-acute oxygenation is often undetected and has serious consequences on the brain such as cognition impairment. |

**and...we are on a mission!**

| We want our technology and products to help doctors and save patients!! |
Why is it important to measure the oxygenation of the brain?

| The human brain represents 2% of the body weight... consumes 15% to 20% of the oxygen of the body |
| 3% of the population have an aneurism in their brain |
| 25% of patients undergoing cardiac surgery have post op. cognitive dysfunction |
| It is proven that impairment of circulation (and thus oxygenation) plays a role in degenerative disease: CVD is Cerebral Vascular Dementia |
| The brain is a complex and highly regulated organ, one parameter is not sufficient to capture the whole picture of what is going on and to initiate the best treatment |

Precision Medicine and A.I.
Important medical need and commercial opportunity

Traumatic and acute compromised oxygen supply
- Traumatic Brain Injury: 1.7 mio in the US per year, 55’000 deaths, USD 60 bn in costs
- Brain bleeding (aneurism) 9 to 20 per 100’000 people
- Secondary Vasospasm

Deaths, coma
- Neurological: paralysis, speaking impairment
- Cognitive issues

Hospital conditions: surgery
- Cardiac anesthesia
- Anesthesia monitoring

25% of cardiac surgery patients have serious post operative cognitive issues

Emerging opportunities
- Role of the low blood perfusion in the development of Vascular dementia
- Monitoring of various degenerative brain conditions
- New parameters: water content and ICP

Increased demand from medical community
A unique versatile multimodal monitoring system

- **Implantable** single use probe
- **Intensive Care Unit**
- **For patient in coma after haemorrhage or severe trauma**
- **One probe replacing up to three conventional probes**

- **Adhesive patch** applied to the skin on the skull
- **Delivers brain blood flow, brain blood volume and oxygen**
- **For patient during surgery or conscious.**
- **Can be used together with probe**

- **Pocket sized NIRS\(^1\) control unit emitter**
- **RheoControl Unit allows for modular expansion up to 6 devices per patient**
- **USB Plugged in medical monitors**

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**Our USP**

The platform is the only one able to measure the content in oxygenated and deoxygenated haemoglobin allowing the doctors to:

- Rapidly identify the ischemia
- Understand the origin (flow, anaemia, ..)
- Design, implement and follow the best treatment

\(^1\) Near Infrared Spectroscopy
Two large growing market segments represent a multi billion opportunity

14
Million general anaesthesia patients annually

4
Million cardio-anaesthesia patients annually

3
Million critical care patients annually

### Anaesthesia
- Initial focus market for RheoPatch is the cardiac anaesthesia market, representing 4 million patients annually:
  - Cardiopulmonary bypass surgery
  - Other cardiac surgery
  - General anaesthesia in high risk and elderly patients will follow, representing 14 million patients annually
  - Currently, 1 million of all cardiac anaesthesia patients qualify for monitoring with RheoPatch

### Critical care
- Validation market for RheoSens and RheoPatch:
  - Subarachnoid haemorrhage
  - Traumatic brain injury
  - Severe stroke
  - Critical care market represents 3 million patients annually
  - Currently, 2 million of critical care patients qualify for RheoPatch and 0.5 million for RheoSens

### Additional applications
- RheoPatch:
  - Sleep apnea (30m patients in the EU, US, Japan)
  - Transient ischemic attack (1m eligible patients annually)
  - Traditional pulse oximetry market (over $2bn market)
  - Telemedicine/e-health
  - Prediction software
  - Asthma/chronic obstructive pulmonary disease
  - Post-cardiac arrest care

- RheoSens:
  - Osteosynthesis
  - Muscular compartment syndrome
  - Reconstructive surgery
  - Oral surgery
  - Organ transplantation

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<tr>
<th></th>
<th>Europe</th>
<th>US</th>
<th>Japan</th>
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<tbody>
<tr>
<td>Cardio-anaesthesia</td>
<td>1.5</td>
<td>0.6</td>
<td>4.0</td>
</tr>
<tr>
<td>General anaesthesia</td>
<td>1.9</td>
<td>6.6</td>
<td>5.3</td>
</tr>
<tr>
<td>Critical care</td>
<td>1.0</td>
<td>0.4</td>
<td>3.0</td>
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1) No. of patients per year in millions
## Basis for success

<table>
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<th>Basis</th>
<th>Details</th>
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<tr>
<td>First class unique product with clear path to market</td>
<td>Luciole Medical solved scientific problems in NIRS and made the technology fit for use</td>
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| Large growing market with undisputed medical need | - Two differentiated market segments  
- Potential for competitive pricing and low reimbursement hurdle |
| Largely de-risked | clinically, regulatory pathway, industry confirmation, partially commercially |
| Attractive valuation and low cash burn | Turn around opportunity with no liability: execution play |
| Short term value generation | Key data points to generate concrete short term value creation and exit opportunities |

**Attractive acceleration opportunity**
Luciole Medical has an experienced leadership team with strong execution skills

New talents will join upon financing

Luciole Medical is an award winning company

Strong scientific position:
- 18 peer reviewed publications in renowned journals

Luciole Medical has received the Certificate for a Quality Management System in Oct 2014

Board

- Philippe Dro, PhD, MBA
  CEO & Chairman of the Board
  Former CEO of GlycoVaxyn
  Former CEO of EndoArt
  Co-founder of Axovan

- Bruno Reihl, PhD
  Member of the Board
  Former CTO and deputy CEO at Disetronic
  Former CEO of Raumedic
  Founder of several companies

- Markus H. Muser, PhD
  Member of the Board
  Over 25 years experience in engineering and medicine, inventor of several patents
  Co-founder and co-owner of AGU Zürich

Key Team Members

- Jürg Fröhlich, PhD, CSO
  Electromagnetics in biomedical applications and Biomedical Photonics
  Former Associate Director, ITIS Foundation, Zurich
  Visiting Senior Research Fellow NUS, Singapore
  Co-Founder of Fields at Work GmbH, Zurich (Spin-Off ETH Zurich)
  Co-Founder of Pomic Medical AG, Zurich

- Dirk Baumann, PhD, Head Development
  Manages the development of software, algorithms and hardware
  Internship at the University of Fairbanks, Alaska
  Research Assistant / Phd Student ETH Zurich
  Former Research Engineer at A*STAR, Singapore
  PostDoc Biomedical Photonics ETH Zurich

- Medidee SA
  Medidee is a QA/regulatory boutique with expertise both in EU and US
  The company is actively involved with supporting Luciole Medical. A QA manager will be hired upon closing of Series A

Advisors

- Prof. Emanuela Keller, MD, Founder
  Head of the Neurocritical Care Unit, Dep. of Neurosurgery, University of Zürich
  Prof. Javier Fandino, MD
  Division of Neurosurgery, Kantonsspital Aarau

- Prof. Daniel A. Rüfenacht, MD
  Prof. of Neuroradiology, Klinik Hirslanden, Zürich
  Prof. Jose I. Suarez, MD
  Baylor College of Medicine, Neurosensory Centre of Houston
Investment case: Cutting edge technology at pre commercial stage with large upside potential

<table>
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<tr>
<th>Technology &amp; Products</th>
<th>Unique new generation platform providing vascular and metabolic information for diagnostic, treatment and monitoring</th>
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| Medical Need & Market | Very large unmet medical need: monitoring of cerebral oxygenation in various medical conditions:  
- ICU market: USD 500 million per year  
- Anesthesia: USD 1+ bn  
- Emerging new indications and markets |
| Stage of Development  | With human data, CE mark and early manufacturing capabilities, the company is largely de-risked. Building of relationship with industry already started, interest confirmed. Ready for commercialization (EU) and regulatory activity in large territory (US) |
| Financing need and Terms | Financing round in preparation for early 2018  
Target is a total of CHF 5 to 8 million  
Invested so far: CHF 10 million (7 in equity/3 grants) |
| Clear value creation path | Shape the company as solid innovative play becoming an attractive acquisition target:  
- Sale and Pipeline  
- 2010 Acquisition of Somanetics by Covidien for USD 250 mio |
Additional Information:

Clinical Case*
Management of a Patient in Hypoxia consecutive to a Subarachnoid Hemorrhage due to Aneurysm Rupture

*Case was handled in Zürich University Hospital, dept. of Neuro Intensive Care by Pr. E. Keller, founder
Clinical case: subarachnoid hemorrhage

- Only 1/3 of patients survive with mild or no disabilities
- 1/3 of patients develop cerebral vasospasm leading to ischemia & secondary infarctions
- Death or severe disability in all patients with vasospasm refractory to treatment

Vasospasm ➔ ischemia ➔ infarctions due to:
1. Low oxygen supply (O₂ ↓)
2. Low oxygen carrier (hemoglobin; anemia)
3. Low blood flow (CBF)
4. High oxygen demand of brain cells
Ischemia in Intensive Care Unit: What does it mean?

Day 0: ruptured aneurysm: bleeding in the brain

Consequences:
After several days the patient is developing vasospasms that can lead to severe damages. This ischemia can’t be detected as the patient is in coma.

brain vessels constricted ➔ imminent ischemia
Clinical case: treatment cascade of SAH with vasospasm

1. Correct anemia ➔ increase of oxygen carrier (hemoglobin) concentration
2. Treat fever ➔ decrease oxygen demand
3. Artificial hypertension ➔ increase blood flow
4. Balloon dilatation of large cerebral vessels ➔ increase blood flow
5. Intraarterial vasodilators ➔ increase blood flow
6. Therapeutic hypothermia ➔ decrease metabolism (“hibernating”)

➢ Precision medicine: The ORIGIN of ischemia is to be identified to decide which treatment(s) is specifically adapted to the each patient
Every patient is unique, and the evolving field of precision medicine aims to ensure the delivery of the right treatment to the right patient at the right time. In an era of rapid advances in biomedicine and enhanced understanding of the genetic basis of disease, health care providers increasingly have access to advanced technologies that may identify molecular aberrations specific to an individual patient that subsequently can be targeted for treatment. Known as biomarker tests for molecularly targeted therapies, these complex tests have the potential to enable selection of the most beneficial treatment for the molecular underpinnings of an individual patient’s disease. Such tests are key to unlocking the promise of precision medicine (see Box 1-1).

**ABSTRACT**

**Introduction:** Precision medicine provides individualized treatment of diseases through leveraging patient-to-patient variation. Aneurysmal subarachnoid hemorrhage carries tremendous morbidity and mortality with cerebral vasospasm and delayed cerebral ischemia proving devastating and unpredictable. Lack of treatment measures for these conditions could be improved through precision medicine.

**Areas covered:** Discussed are the pathophysiology of CV and DCl, treatment guidelines, and evidence for precision medicine used for prediction and prevention of poor outcomes following aSAH. A PubMed search was performed using keywords cerebral vasospasm or delayed cerebral ischemia and either biomarkers, precision medicine, metabolomics, proteomics, or genomics. Over 200 peer-reviewed articles were evaluated. The studies presented cover biomarkers identified as predictive markers or therapeutic targets following aSAH.

**Expert commentary:** The biomarkers reviewed here correlate with CV, DCL, and neurologic outcomes after aSAH. Though practical use in clinical management of aSAH is not well established, using these biomarkers as predictive tools or therapeutic targets demonstrates the potential of precision medicine.
Clear need for neuromonitoring

ischemia = dysbalance

\[ O_2 - \text{delivery} \]

given by:
- \( O_2 \) content (~Hboxy)
- hemoglobin (carrier of \( O_2 \))
- blood flow (CBF)

\[ O_2 - \text{consumption} \]

given by:
- cell metabolism
- \( O_2 \) need (~Hbdeoxy)

Luciole System measures
- CBF
- Hboxy

Luciole System measures
- SbtO_2

Luciole System measures
- Hbdeoxy
Sbto2: a good indicator of hypoxia

Reason for ischemia?

1. Low hemoglobin?
2. Low O₂ content/delivery?
3. Low CBF?
4. High O₂ need?

ischemia with ptiO₂ < 15-20mmHg
The system can detect ischemia earlier than other measures.

SbtO₂ is the earlier indicator for ischemia (> 1 min.) than ptiO₂.

Start treatment earlier with Luciole System.
Cerebral Blood Flow measures gives origin of ischemia
Continuous measure of Hboxy, Hbdeoxy indicates cause of ischemia

\[ \text{SbtO}_2 = \frac{\text{Hboxy}}{\text{Hbtotal}} \]

\[ \text{Hbdeoxy} \uparrow \Rightarrow \text{O}_2 \text{ need} \uparrow \]

\[ \text{Hboxy} \downarrow \Rightarrow \text{O}_2 \text{ delivery} \downarrow \text{ due to CBF} \downarrow \]

due to blood pressure drop \downarrow
Initiate and monitor the best therapeutic action(s)

- **SbtO₂ = Hboxy/Hbtotal**

- **Treatment: 1.** Increase blood pressure to increase blood flow & O₂ delivery (monitor impact on CBF & Hboxy)

- **Treatment: 2.** Induce hypothermia to decrease O₂ need (monitor impact on CBF & Hbdeoxy)

- **Hboxy ↓ → O₂ delivery ↓ due to CBF ↓**

- **Hbdeoxy ↑ → O₂ need ↑ due to blood pressure ↓**
Control effectiveness of treatment: reduction of metabolism

Induction of hypothermia

Hbdeoxy ↓ ➔ O₂ need ↓
Control effectiveness of treatment: increase of $O_2$ delivery

- Induction of hypothermia
- Artificial increase of blood pressure
- $Hboxy \uparrow \Rightarrow O_2$ delivery $\uparrow$

Artificial increase of blood pressure
Conclusions

- Oximetry values obtained with the Luciole System are valuable
  - SbtO$_2$ values behave similarly to ptiO$_2$ values
  - Hboxy and Hbdeoxy values are in close relationship with clinical events

- Luciole System allows detection of brain ischemia earlier
  (SbtO$_2$ reacts earlier than ptiO$_2$)

- Multiparameter monitoring with the Luciole System, delivering CBF, SbtO$_2$, Hboxy and Hbdeoxy allows
  - to identify the exact cause of ischemia
  - to enable causal treatment of ischemia
  - to control the effectiveness of treatment
  - to explore new neuroprotective therapies
Thank you!

Luciole:  pronounced: lysjɔl ("Lüssiol")
French word for Firefly (Eng.); Glühwurm (Ger.), Lucciola (Ita.)

Flying insect of the family of Lampyridae having the property to emit fluorescent light between 510 and 640 nm wavelength and showing a moving green dot in the night.

Similar to the technology used by the company (NIRS) to measure oxygen saturation of brain tissue.

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www.luciolemedical.ch

Luciole Medical is the successor company of NemoDevices AG