Advancing Mitochondrial Medicine

Todd Bazemore, COO
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Key Financials 2016

(IFRS, consolidated, in CHF million)

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
</tr>
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<tbody>
<tr>
<td>Cash &amp; cash equivalents</td>
<td>49.8</td>
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<tr>
<td>Net change in cash &amp; cash equivalents</td>
<td>-27.0</td>
</tr>
<tr>
<td>Operating cash flow</td>
<td>-27.1</td>
</tr>
<tr>
<td>Net sales</td>
<td>19.0</td>
</tr>
<tr>
<td>Operating expenses</td>
<td>-48.6</td>
</tr>
<tr>
<td>Net result</td>
<td>-35.4</td>
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</tbody>
</table>

- Revenue from Raxone increased to CHF 19.0 million (+340% compared to 2015)
- Financing in February 2017 with Convertible Bond: CHF 60 million
- Cash and cash equivalents as of February 2017: CHF 100.8 million
- Current Headcount: 83
Santhera Offices

Montreal

Boston

London  Utrecht

Liestal (Global HQ)

Milan

Munich

partner (EWOPharma)
## Santhera Pipeline

<table>
<thead>
<tr>
<th>Santhera Pipeline</th>
<th>Preclin.</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Filing</th>
<th>Market</th>
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</thead>
<tbody>
<tr>
<td><strong>Raxone® (idebenone 150mg)</strong></td>
<td></td>
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<tr>
<td>Leber’s Hereditary Optic Neuropathy</td>
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<td>LHON EU approval</td>
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<tr>
<td>Duchenne Muscular Dystrophy</td>
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<td></td>
<td>DMD Filed in EU</td>
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<tr>
<td>Primary Progressive Multiple Sclerosis</td>
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<td>PPMS Completion 2017 (at NIH)</td>
</tr>
</tbody>
</table>

**Omigapil**

| Congenital Muscular Dystrophy | | | | | | CMD Completion 2017 (at NIH) |

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LHON | DMD | PPMS | CMD

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Corporate Update | 8 March 2017
Pipeline with Raxone® (idebenone) in three indications with high unmet medical need

- **Primary progressive MS (PPMS):** Phase II study ongoing
- **Duchenne Muscular Dystrophy (DMD):**
  - EU: MAA filed; US: NDA in preparation
- **Leber’s Hereditary Optic Neuropathy (LHON):**
  - Commercial launch in EU

Corporate Update | 8 March 2017
Raxone® in Leber’s Hereditary Optic Neuropathy (LHON)

Leber’s Hereditary Optic Neuropathy (LHON): Commercial launch in EU
LHON – an inherited form of blindness

- Inherited form of blindness:
  - Incidence: ~ 1 in 1 million

- Genetic disease with clear diagnosis and family pattern

- Affects predominantly young males across all ethnic groups

- Rapid loss of central vision caused by functional loss and degeneration of retinal nerve cells

- Raxone® the first and only treatment available
Clinical presentation of LHON

Normal vision

Vision due to LHON

Days, weeks or few months
Raxone® is the first and only approved treatment for LHON

- Authorized for the treatment of visual impairment in adolescent and adult patients with LHON
  - for all disease stages
  - for all LHON mutations
- 10 years market exclusivity due to Orphan Drug Status (until Q3 2025)
- Ongoing discussions with FDA on regulatory path to approval
**Raxone® in Duchenne Muscular Dystrophy (DMD)**

Duchenne Muscular Dystrophy (DMD):
Positive phase III study outcome,
EU: MAA filed as Type II variation
US: NDA filing in preparation
Medical need for effective treatment of respiratory illness in DMD

- Medical complications include ineffective cough, nocturnal hypoventilation, sleep disordered breathing, and ultimately daytime respiratory failure

DMD patients develop cardiac and respiratory complications that typically lead to early morbidity and mortality

Corporate Update | 8 March 2017
Urgent medical need for patients unable to take glucocorticoid steroids

- With increasing age, fewer patients tolerate glucocorticoid steroids (side effects)
- Loss of respiratory function enters critical stage in early teenage years
- There is currently no treatment available for this group of DMD patients
Development program with Raxone® in DMD

**GC non-users**

- **Phase 3**
  - DELOS

**GC users**

|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|

**GC**: glucocorticoid steroids; **PPM study**: prospectively planned matching study
Phase 3 DELOS trial

Efficacy of idebenone on respiratory function in patients with Duchenne muscular dystrophy not using glucocorticoids (DELOS): a double-blind randomised placebo-controlled phase 3 trial

Gunnar M Buysse, Thomas Voit, Ulrike Schara, Chiara S M Straathof, M Grazia D'Angelo, Günther Bernert, Jean-Marie Cuisset, Richard S Finkel, Nathalie Goehmans, Craig M McDonald, Christian Rummey, Thomas Meier, for the DELOS Study Group

Patients:

- Age 10-18 years
- No selection for mutational status
- Patients had to be off chronic steroids
- 92% of patients were non-ambulatory
- Established respiratory function decline

Randomized treatment:

- Raxone (900 mg/d): N=31
- Placebo: N=33
- Mean Age: 14.3 y
- Treatment duration: 12 months
Raxone® delays the loss of respiratory function

Corporate Update | 8 March 2017
Fewer patients on Raxone® experience bronchopulmonary disease (e.g. airway infections)

<table>
<thead>
<tr>
<th></th>
<th>Raxone®</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Subjects (%)</td>
<td>6 (19.4%)</td>
<td>17 (51.2%)</td>
</tr>
<tr>
<td>Events</td>
<td>7</td>
<td>28</td>
</tr>
</tbody>
</table>

Duration of bronchopulmonary disease

| Total Days     | 82      | 222     |

Hazard Ratio* 0.28; p=0.0026

*proportional means regression analysis

McDonald C. et al., 2016; *Neuromuscular Disorders* 26:473-480
Summary of DELOS outcome

- The Phase 3 trial met its primary endpoint
- Supportive evidence for efficacy from secondary endpoints
- Demonstrated a consistent treatment effect for idebenone (Raxone®) on expiratory and inspiratory function
- Provides supportive evidence for efficacy in clinically relevant responder analyses (e.g. peak cough flow, FVC)
- Demonstrates clinically relevant impact of Raxone® treatment on bronchopulmonary disease, antibiotic use and hospitalization
SIDEROS – a new trial with Raxone® in patients with DMD using concomitant glucocorticoids (GCs)

GC non-users
- DELPHI
- DELPHI-E
- CINRG DNHS

GC users


Phase 3
- DELOS
- PPM Study
- SIDEROS

GC: glucocorticoid steroids; PPM study: prospectively planned matching study
Glucocorticoids (GCs) delay the onset but not the rate of pulmonary function decline

- GCs delay time to clinically important threshold of pulmonary function decline by ~2 years
- Once this threshold of decline is reached, the rate of decline is similar to that seen in patients not using GCs

Source: CINRG Natural history data base
N= 334 patients; data is mean ±SEM
The SIDEROS trial

To assess the efficacy of idebenone (Raxone®) compared to placebo, in slowing the loss of respiratory function in patients with DMD receiving glucocorticoids (GCs)

- SIDEROS study started to enroll patients
- 60 study centers in US and EU participating

Corporate Update | 8 March 2017
Regulatory objective

- Based on DELOS data obtain early approval for DMD patients not using steroids

The **intended indication** is for patients in whom respiratory function has started to decline and who are currently not taking glucocorticoids.

The indication would include patients who previously were treated with glucocorticoids or in whom glucocorticoid treatment is not desired, not tolerated or is contraindicated.

- In EU: Marketing Authorization Application (MAA) under review by CHMP
- In US: Possibility for Accelerated Approval to be further evaluated with FDA
- Combined data from DELOS and SIDEROS would allow label to treat respiratory function decline in all DMD patients (irrespective of mutational type or glucocorticoid use)
Raxone® in primary progressive MS

Primary progressive MS (PPMS):
Phase II study in collaboration with NIH
Phase II study in PPMS with Raxone®

- Primary progressive MS
  - affects 10-15% of total MS population
  - no approved treatment available
  - associated with mitochondrial pathology

- Phase II trial (IPPoMS) in collaboration with NIH ongoing
- Study is fully recruited; outcome expected in late 2017
- Santhera has exclusive license to granted use patent
Omigapil in CMD

- **Congenital muscular dystrophy (CMD)**
  - Ultra-rare severe muscle disease with onset in infancy or childhood
  - Several genetically and clinically different sub-forms

- **Phase I clinical trial: CALLISTO**
  - In CMD patients (20 patients, 3-month treatment, different dose levels)
  - Pharmacokinetic, safety and clinical endpoints (exploratory)

- **Regulatory / Funding**
  - Orphan Drug designation (EMA / FDA); Fast Track designation (FDA)
  - Private / public funding and FDA Orphan Drug grant
Future opportunities for Santhera in advancing mitochondrial medicine

Source: Foundation for Mitochondrial Medicine
Advancing Mitochondrial Medicine