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Our mission

We are focusing on the development of treatments for neuro-ophthalmological, neuromuscular and pulmonary diseases that have a high unmet medical need.
Strategic milestones achieved in past 18 months

• **Growing revenues from product sales of Raxone® (idebenone) in LHON**
  – FY 2018: income from product sales of CHF 31.7 million, at upper end of guidance
  – Raxone business for LHON reached profitability (including ongoing clinical post-authorization program)

• **In-licensed POL6014 for the treatment of CF and other pulmonary diseases: February 2018**
  – Obtained orphan drug designation for POL6014 for CF in Europe
  – Started Phase Ib, multiple ascending dose (MAD) study in patients with CF

• **Acquired option to exclusive license for vamorolone: November 2018**
  – Complementing DMD pipeline with late-stage product with excellent strategic fit
  – Idorsia became largest shareholder of Santhera

• **Prepared for regulatory filing for Puldysa® (idebenone) in DMD in Europe**
  – Collected new data on long-term efficacy of *idebenone* on respiratory function outcomes and data on clinical relevance of observed treatment effect
  – Intend to file for Conditional Marketing Authorization in Q2 2019
Capabilities from development to commercial sales

4 Clinical Science
3 Bio. Stats
7 Medical Affairs
4 Drug Safety & PV
14 Clinical Operat.
5 Reg. Affairs
50 Market Access
Com. Operat.
2 Non-Clinical
10 Supply Chain
Mark.-ting
2 Patient Advoc.
Technic. Dev.
Management
Human Resources
Administration and Finance
Legal Compliance, Quality Assurance
Geographical presence and headcount

Headcount
N = 130

Status: Q1 2019

- Swiss HQ
- EU Clusters
- North America
## Our product pipeline

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GC: Glucocorticoid; AAT: Alpha-1 antitrypsin deficiency; NCFB: Non-cystic fibrosis bronchiectasis; PCD: primary ciliary dyskinesia

*Raxone® (150 mg idebenone) is approved in the Europe, Israel for the treatment of visual impairment in adolescent and adult patients with LHON*
Raxone® (idebenone) in Leber’s Hereditary Optic Neuropathy (LHON)
Neuro-ophthalmological Diseases

Chaz, patient living with LHON
Raxone® is the first and only approved treatment for LHON

- LHON, a rare mitochondrial disease resulting in progressive and severe vision loss
- Most common in males with a disease onset between 15 – 35 years of age
- Within 1 year > 90% of patients experience vision loss in both eyes
- Raxone® approved in EU, Norway, Iceland, Liechtenstein, Israel and Serbia

Raxone® is the first and only available treatment in LHON and can lead to stabilization or recovery of vision
Raxone® sales up 38% in 2018 – continued growth in 2019

Raxone® is sold in more than 20 European countries and Israel
Commercial success with Raxone® in LHON

In-house clinical development led to EU approval in October 2015

• Raxone® is the 1st and only treatment available for LHON
• Reached profitability in 2018
• Anticipated peak sales potential for Europe: CHF ~50 million p.a.
• Interventional Phase IV study (LEROS) to assess the long-term efficacy and safety of Raxone® in LHON fully recruited (Q1 2019)
• Protection through Orphan Drug Status in Europe until Q4 2025
• Expansion of marketing authorizations to countries outside Europe
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*Raxone® (150 mg idebenone) is approved in the Europe, Israel for the treatment of visual impairment in adolescent and adult patients with LHON*
Pipeline synergies between *idebenone* and *vamorolone* for the treatment of patients with DMD

- Combination of *vamorolone* and *idebenone* addresses medical need of DMD patients at all disease stages
- *Vamorolone* and *idebenone* could be used in all patients (not restricted to certain mutations)
- Combination therapy to be evaluated
Idebenone in Duchenne Muscular Dystrophy (DMD) Neuromuscular Diseases

Anthony, patient living with DMD
Medical need for effective treatment of respiratory illness in advanced patients with DMD

• Increasing respiratory muscle weakness in DMD leads to:
  – Decreased lung volumes and flow rates
  – Decreased ability to cough effectively and clear airways from mucus
  – Increased risk of airway infections
• There are no approved pharmacological therapies for treating respiratory decline
• ~35,000 patients combined in US and Europe
Placebo-controlled DELOS trial showed that idebenone slowed loss of respiratory function over 12 months

- **Idebenone** slowed loss of expiratory respiratory function (peak expiratory flow, PEF%p) and met the study primary endpoint \(^1,2\)

- Consistent treatment effects were seen for inspiratory function (inspiratory flow reserve, IFR) and global respiratory function (forced vital capacity, FVC%p) \(^1,3,4\)

- **Idebenone** also reduced the risk of bronchopulmonary adverse events (such as airway infections), the need of systemic antibiotic treatment and risk of hospitalization due to respiratory complications \(^5\)

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1) Buyse et al. 2015; Lancet 385:1748-57;
2) Buyse et al. 2018; J Neuromuscular Diseases 5: 419–430;
3) Mayer et al. 2017; J Neuromuscular Diseases. 4:189-98;
4) Buyse et al., 2017; Pediatric Pulmonology 52:508-515;
5) McDonald et al., 2016; Neuromuscular Disorders 26: 473–480

PEF%p: peak expiratory flow percent predicted
FVC%p: forced vital capacity percent predicted
New long-term efficacy data with idebenone on respiratory function outcomes – the real world approach

- Long-term efficacy data are desirable to inform about patient benefit in this chronic disease
- **SYROS**: prospectively planned collection of long-term respiratory function data from patients previously enrolled in the DELOS trial
- Long-term respiratory function data were collected from 18 patients treated with idebenone in Expanded Access Programs (EAPs)
SYROS primary endpoint: Annual rate of decline in FVC%p is slowed by switching from Off-Idebenone to On-Idebenone

- Annual rate of decline of FVC%p reduced by ~50% when switching from Off-Idebenone to On-Idebenone
- SYROS primary endpoint confirms and supports efficacy outcome seen in DELOS trial

FVC%p: forced vital capacity percent predicted
EAP: expanded access program
“Off-On”: off-idebenone before EAPs and on-idebenone during EAPs
Data from random coefficient regression model
SYROS: Idebenone treatment showed persistent effect on respiratory function for up to 6 years

- *Idebenone* treatment showed a persistent effect in slowing decline in FVC%p for up to 6 years
- Annual decline in FVC%p in patients on *idebenone* was consistently smaller than in untreated patients from a matched external control group (from CINRG Duchenne natural history study)
Estimated time to market

**Protection and regulatory status**
- Orphan drug protection: USA (7y) and EU (10y)
- Fast track designation in USA

**Competitive positioning and sales potential**
- **Idebenone** targets treatment of older patients
- First treatment of respiratory complications

NDA: new drug application; MAA: marketing authorization application
Vamorolone
in Duchenne Muscular Dystrophy (DMD)
Neuromuscular Diseases

Partnership with

Prednisone
Vamorolone
**Vamorolone** – revolutionizing mode of action

- Discovered and developed by **ReveraGen**
- **First-in-class dissociative steroidal anti-inflammatory drug**
- Different pharmacological properties allow dissociation of beneficial effects from GC-class side effects

<table>
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<th>Promoter Type:</th>
<th>Drug effect relative to Prednisone: Blue = beneficial effect, Red = negative side effect</th>
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<tr>
<td>NF-κB</td>
<td>Anti-inflammatory Anti-inflammatory Anti-inflammatory inactive / weak</td>
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<td>GRE</td>
<td>Activates Activates inactive / weak inactive / weak</td>
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<td>MRE</td>
<td>Activates inactive / weak Antagonist Antagonist</td>
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GR: glucocorticoid receptor  
MR: mineralocorticoid receptor  
GC: glucocorticoid

Data from Heier et al. (2018); DOI 10.26508/lsa.201800186
The Vision-DMD trial by ReversaGen

**Design**
Phase IIb randomized, double-blind, parallel group, placebo- and active-controlled study with double-blind extension

**Participants**
120 **ambulant** boys ages **4 to <7 years**, **not taking steroids**

**Design**
1:1:1:1 randomization
(vamorolone 2.0 mg/kg/day : vamorolone 6.0 mg/kg/day : prednisone 0.75 mg/kg/day : placebo)

**Treatment**
24 **week treatment period #1** (weeks 1-24),
4-week transition period (weeks 25-28),
**20-week treatment period #2** (weeks 28-48)

**Protocol**
Developed under FDA and EMA scientific advice; “pivotal” trial

**Timeline**
Start: August 2018; estimated end: 2H 2020

**Primary outcomes**
Efficacy: Muscle function measured by **Time to Stand Test**
Safety: Body weight as measured by body mass index (BMI)

**Sites**
Approximately 30 sites in US, EU, Canada, Australia, Israel
Estimated time to market

Protection and regulatory status
- Orphan drug protection: USA (7y) and EU (10y)
- Method of use patent until 2029 (by country)
- Fast track designation in USA

Competitive positioning and sales potential
- *Vamorolone* to become standard of care
- Efficacy comparable/superior to standard GCs avoiding severe side effects

NDA: new drug application; MAA: marketing authorization application
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POL6014 in Cystic Fibrosis (CF)
Pulmonary Diseases
Cystic fibrosis, a rare inherited lung disease

- CF is a progressive, genetic disease leading to thick mucus in the lung (airway obstruction)
- This results in persistent lung infections, chronic inflammation and loss of respiratory function

- The disease is diagnosed in young children, about 70,000 patients live in US & EU
- Current treatments do not specifically address the chronic, underlying inflammation
Targeting *elastase* to treat chronic lung inflammation

- Inflammation causes excessive production of neutrophil elastase (hNE)
- POL6014 is a reversible, competitive and selective inhibitor of hNE
- POL6014 presents an opportunity for a pipeline in a product
- Phase Ib, multiple ascending dose (MAD) trial in CF patients is ongoing
- Preparation for a Phase II efficacy trial is under way
Summary

• Santhera established as specialty pharma company with focus on drugs for rare diseases

• Commercial success with Raxone® in rare neuro-ophthalmological disease (LHON)

• Positive data (including new long-term data) allow for filing of conditional marketing authorization for Puldysa® in patients with DMD in Europe

• Pipeline in DMD expanded with option to acquire vamorolone with the potential to replace standard glucocorticoids with better safety profile

• In-licensed POL6014, a first-in-class drug candidate for the treatment of CF (synergistic to existing treatment options)
Implemented strategies for further growth

**Grow** sales of Raxone® for the treatment of LHON and expand commercial reach

**Progress** pipeline assets and advance towards regulatory approval

**Advance licensing / partnering strategy** for high-quality, late-stage rare disease assets with a short time to market
THEIR FUTURE
OUR FOCUS