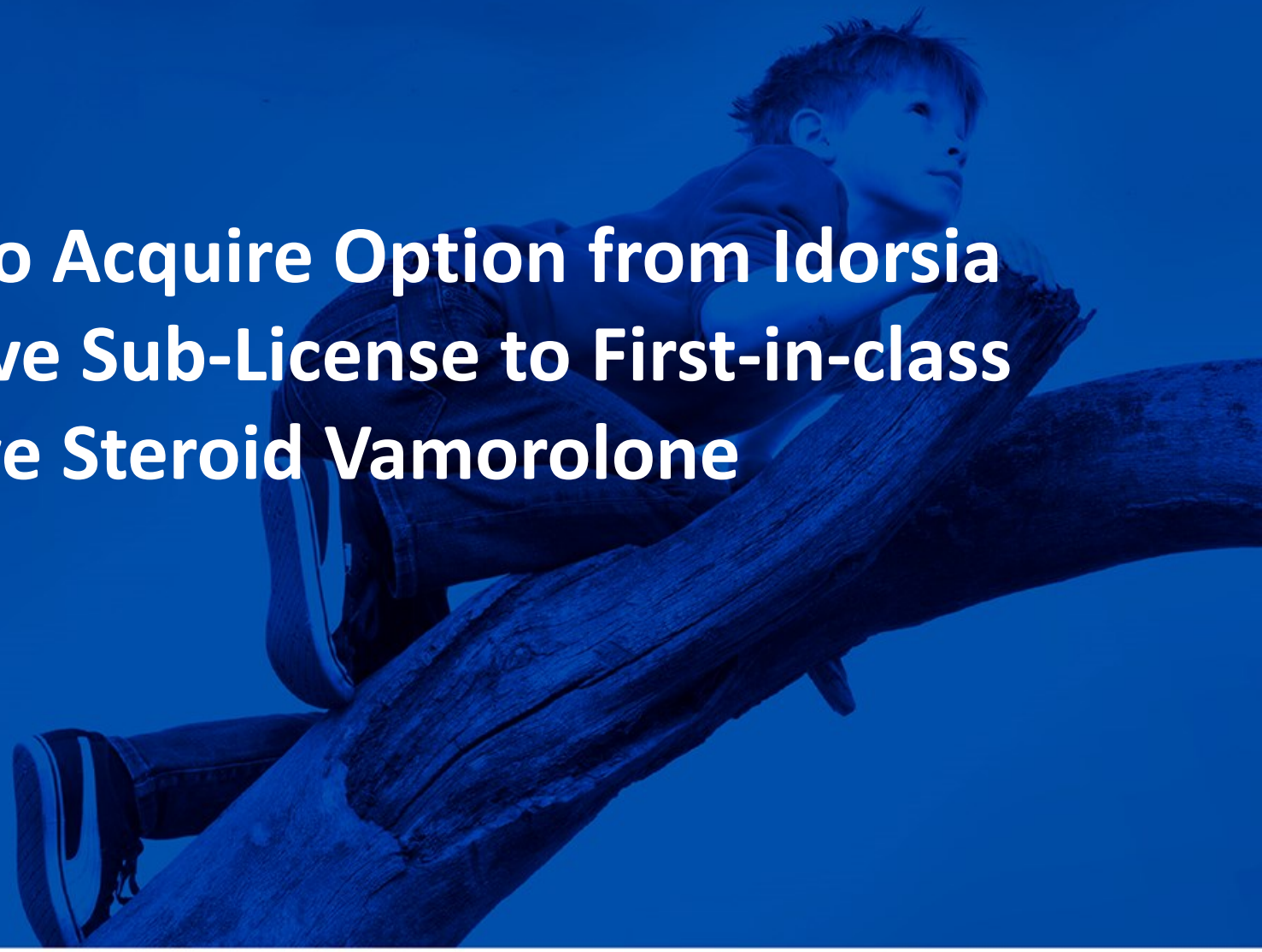
Santhera to Acquire Option from Idorsia for Exclusive Sub-License to First-in-class Dissociative Steroid Vamorolone



21 November 2018

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Todays announcements

Santhera will hold a webcast tomorrow, November 21, 2018 at 13:00 CET, 12:00 GMT, 07:00 EST. Details at the end of statement.

Santhera Enters into Agreement to Acquire Option from Idorsia for Exclusive Sub-License of First-in-class Dissociative Steroid Vamorolone

- *Vamorolone in clinical development for Duchenne muscular dystrophy (DMD) by ReveraGen BioPharma Inc. – pivotal VISION-DMD Phase IIb study ongoing*
- *Vamorolone has the potential to become standard of care in young patients with DMD*
- *Positions Santhera as a leading company in the DMD space with two late-stage assets addressing the medical need of DMD patients at all disease stages*
- *Idorsia to become the largest shareholder in Santhera with a 13.3% equity stake*

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Santhera Calls Extraordinary General Meeting and Proposes Ordinary Share Capital Increase to Raise Approximately CHF 50 Million

Pratteln, Switzerland, November 20, 2018 – Earlier today, Santhera Pharmaceuticals (SIX: SANN) announced that it has entered into an agreement to acquire the option for the exclusive sub-license to the first-in-class dissociative steroid vamorolone in all indications and all territories except Japan and South Korea from Idorsia Ltd (SIX: IDIA). Santhera plans to raise approximately CHF 50 million gross proceeds through a capital increase to be effected by way of an accelerated book building in order to finance the initial payment of USD 20 million to Idorsia for the rights to vamorolone, to further invest in the development of vamorolone and to fund its ongoing activities.

Vamorolone as innovative treatment addressing an urgent medical need in patients with DMD

- Glucocorticoids (GCs) are recognized standard of care in children and adolescent patients with DMD
- High-dose GCs have severe systemic side effects preventing lifelong treatment
- Regulators and patients/families seek better tolerable alternatives to the current GCs
- *Vamorolone* was discovered and is currently developed by ReveraGen BioPharma
- ***Vamorolone* is a first-in-class, "dissociative steroid" in development as potential replacement of existing GCs as new standard of care**
- ReveraGen has conducted extensive non-clinical studies, Phase Ia and Ib studies and Phase IIa and IIa-extension studies. Based on knowledge obtained from these studies, ReveraGen is currently conducting the Phase IIb - VISION DMD trial, which together with the previous studies could form the basis for approval in DMD
- Time to approval targeted to be 2H 2021 in US and early 2022 in EU

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Excellent strategic fit: *Vamorolone* complements Santhera's late-stage pipeline in DMD

- In 2016 Actelion acquired the option to an exclusive worldwide license for *vamorolone* from **ReveraGen**. This option was subsequently transferred to **Idorsia**
- Santhera acquires from Idorsia the option to an exclusive sub-license for *vamorolone* and ReveraGen consented to this agreement. The option to this sub-license includes all indications for *vamorolone* worldwide, except for Japan and South Korea
- ***Vamorolone*** has an excellent strategic fit to Santhera's pipeline, being complementary to ***idebenone,*** establishing **Santhera** as a leading company in the DMD disease space with two late-stage assets addressing the medical need of DMD patients at all disease stages
- Idorsia has chosen Santhera as its partner for this program due to Santhera's expertise in the DMD field
- Idorsia receives a non-refundable consideration of 1,000,000 shares in Santhera and an upfront cash payment of USD 20 million, a cash payment of USD 30 million upon the exercise of the option by Santhera as well as milestone payments and royalties
- Idorsia, led by CEO Jean-Paul Clozel (founder of Actelion), becomes the anchor shareholder in Santhera with 13.3% equity position (lock-up until *vamorolone* obtains FDA approval in the US).

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Overview of the key terms of the transaction

Asset

- Option to sub-license *vamorolone* in all indications worldwide, excluding Japan and South Korea

Upfront Consideration to Idorsia

- USD 20m in cash payable at closing (expected before year-end)
- 1m newly issued shares; Idorsia to become anchor shareholder with 13.3% position in Santhera

Upon option exercise (positive Phase IIb data)

Milestone and Royalty Payments to Idorsia

- USD 30m paid upon option to sub-license being exercised
- Regulatory and commercial milestones of up to USD 80m (approval in US and EU for DMD)
- One-time sales milestone payments of USD 130m in aggregate
- Regulatory milestone payments for three additional indications up to USD 205 million in aggregate
- Tiered single-digit to low double-digit royalties on the annual net sales of *vamorolone*

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Specific details of the offering

Extraordinary General Meeting (EGM) to vote for ordinary capital increase

- Proposed increase of share capital: up to 3.5 million shares at nominal value of CHF 1
- Number of shares outstanding after the share capital increase (incl. shares issued to Idorsia) : approximately 11 million

Planned capital raise:

- Targeted proceeds of approximately CHF 50 million by accelerated bookbuilding
- Price determined by the bookbuilding procedure

Use of proceeds:

- To finance USD 20 million upfront payment to Idorsia
- For ongoing commercialization, clinical development programs (including vamorolone) and other operating activities

Transaction advisor:

- **Centerview Partners** acted as strategic advisor to Santhera
- **UBS** is sole Global Coordinator & Bookrunner; **Mirabaud Securities Limited** acts as Co-Manager

Vamorolone – a breakthrough treatment for patients with DMD

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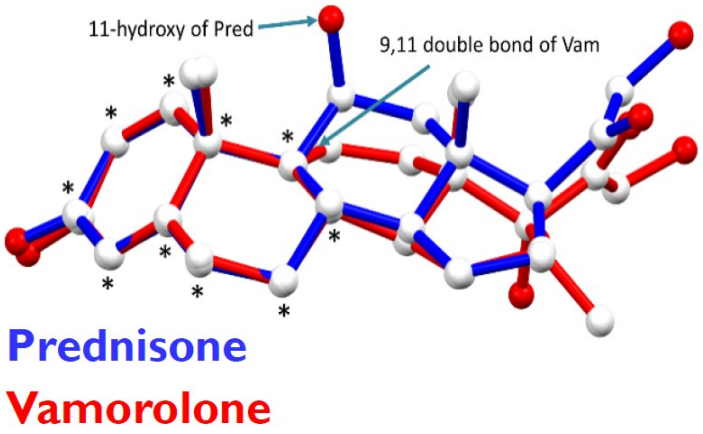
Vamorolone – revolutionizing mode of action

- Discovered and developed by ReveraGen BioPharma
- **First-in-class dissociative steroidal anti-inflammatory drug**
- Close analog to prednisone, a standard glucocorticoid (GC)
- Different pharmacological properties allow dissociation of beneficial effects from GC-class side effects



- *Vamorolone* binds to glucocorticoid receptor (GR) and
  - activates anti-inflammatory (NFκB), "non-genomic" pathway as *vamorolone*/GR monomer
  - does not activate gene transcription, "genomic" pathway; does not form *vamorolone*/GR dimers
- Differential activation of GR-mediated pathways results in therapeutic (anti-inflammatory) activity but shows reduced activation of pathway associated with GC-class side effects
- *Vamorolone* is antagonist for mineralocorticoid receptor adding to favorable safety profile compared to GCs

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Vamorolone – pharmacology

Effects of *vamorolone* in animal model for DMD:

- Retains GC-type anti-inflammatory efficacy and reduces dystrophy, improves muscle strength and motor function
- Superior safety profile with respect to loss of stunting growth, bone symptoms, cardiac side effects

Effects of *vamorolone* in Phase I trial of healthy volunteers:

- *Vamorolone* was well tolerated at all dose levels (up to 20mg/kg/d)
- Biomarker studies suggest mitigation of GC-class side effects (bone fragility, metabolic disturbance, immune suppression)
- Suppression of the adrenal axis, a safety concern of standard GCs, was 10-fold less than with prednisone

Phase 1 trial of vamorolone, a first-in-class steroid, shows improvements in side effects via biomarkers bridged to clinical outcomes

Eric P. Hoffman[a,b,*], Valerie Riddle[c], Maxime A. Siegler[d], Daniel Dickerson[e], Miroslav Backonja[e], William G. Kramer[f], Kanneboyina Nagaraju[a,b], Heather Gordish-Dressman[g], Jesse M. Damsker[a], John M. McCall[a]

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Vamorolone – safety and efficacy in patients with DMD

Phase IIa study (VBP15-002): complete

- 2-week, open label, 4-dose study
- 48 DMD pts at age 4- <7 y
- *vamorolone* was safe and well tolerated up to 6.0 mg/kg/day (~10x standard GC dose)
- improved safety of *vamorolone vs* GCs by reduction of insulin resistance, beneficial changes in bone turnover, reduction in adrenal suppression
- preserves anti-inflammatory efficacy and decreases GC-associated safety concerns

Phase IIa trial in Duchenne muscular dystrophy shows vamorolone is a first-in-class dissociative steroidal anti-inflammatory drug

Laurie S. Conklin[a,b,1], Jesse M. Damsker[a,1], Eric P. Hoffman[a,c], William J. Jusko[d],

Phase IIa-Extension study (VBP15-003) : complete

- 6-months, open-label, multiple dose study
- all 48 pts from VBP15-002 study enrolled; 46 completed
- timed function tests compared to standard GC and natural history data
- dose-dependent efficacy in timed function tests (comparable to standard GC)
- improved safety signal (biomarkers: insulin resistance, bone formation, adrenal suppr.)

All patients of VBP15-003 study now enrolled in long-term open, label extension study VBP15-LTE (ongoing)

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Vamorolone – pivotal Phase IIb trial (VBP15-004), ongoing

The Vision-DMD trial	
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**
Randomization	1:1:1:1 randomization (*vamorolone* 2.0 mg/kg/day : *vamorolone* 6.0 mg/kg/day : prednisone 0.75 mg/kg/day : placebo)
Dosing	**Orally** at daily doses of **2.0 mg/kg** and **6.0 mg/kg** versus **prednisone** 0.75 mg/kg/day and placebo
Treatment	**24 week treatment period #1** (weeks 1-24), a 4-week transition period (weeks 25-28), a **20-week treatment period #2** (weeks 28-48), and a 4-week dose-tapering period (weeks 49-52); one visit per month
Protocol	Developed under FDA and EMA scientific advice; “pivotal” trial
Study start/end	Start: August 2018; estimated end: 2H 2020
Primary outcome	Muscle function measured by **Time to Stand Test** Body weight as measured by body mass index (**BMI**) z-score
Secondary outcomes	Safety, cardiac function, efficacy: 6MWT, NSAA, run/walk test; other secondary outcome measures
Study conduct	Approximately 30 sites in US (recruiting), EU, Canada, Australia, Israel

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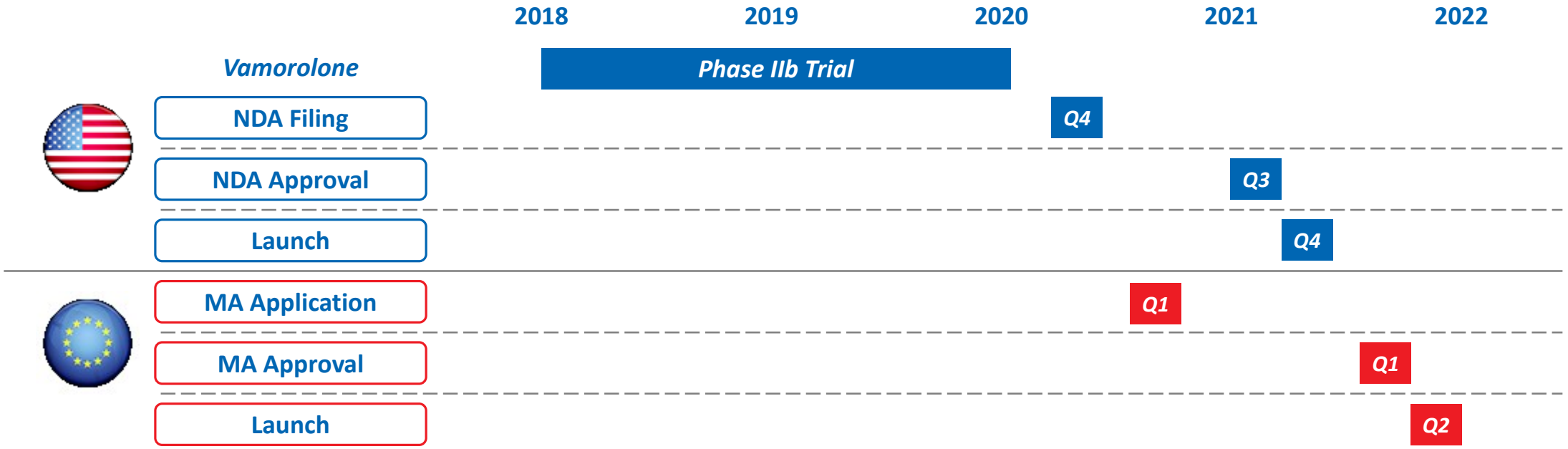
Estimated time to market, protection and sales potential



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
- Sales potential of USD 500m

NDA: new drug application; MAA: marketing authorization application

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Excellent strategic fit – *Vamorolone* complements Santhera's DMD program and strengthens its pipeline

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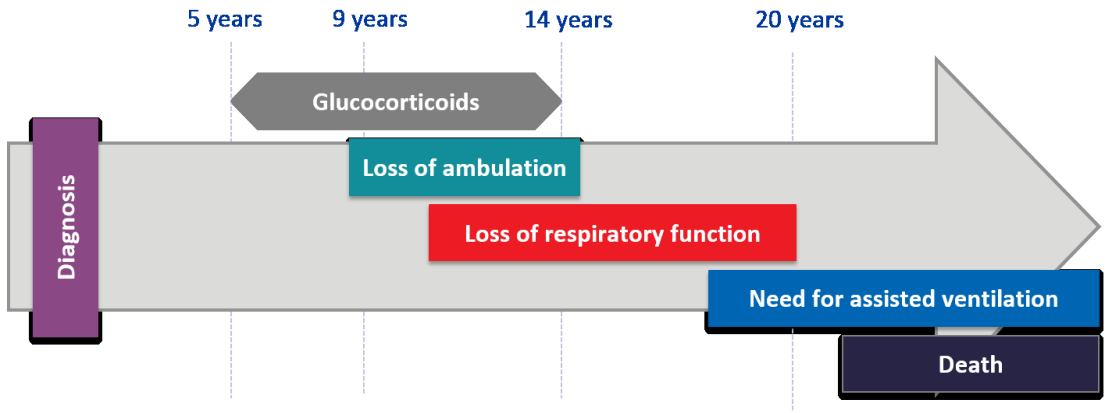
Urgent medical need for new treatments in DMD

- Glucocorticoids (GCs) are recognized standard of care in children and adolescent patients
- Therapeutic goal of GCs is to preserve upper and lower limb strength/function and ambulation
- EMFLAZA (*deflazacort*) approved and marketed in the US by PTC Therapeutics
- High-dose GCs have severe systemic side effects preventing lifelong treatment
- Regulators and patients/families seek better tolerable alternatives to the current GCs

Disease progression and clinical milestones in patients with DMD



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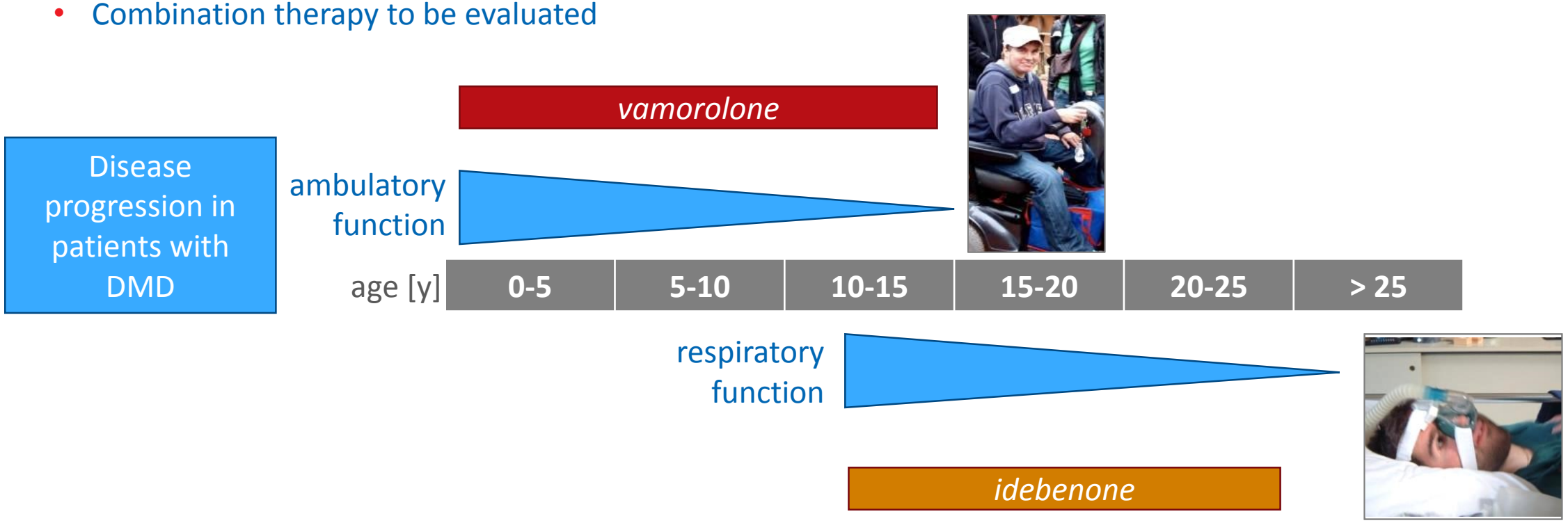
Pipeline synergies between *vamorolone* and *idebenone*

- Combination of *vamorolone* and *idebenone* addresses medical need of DMD patients at all disease stages
- *Vamorolone* and *idebenone* can be used in all patients (not restricted to certain mutations)
- Combination therapy to be evaluated



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Santhera's *pro forma* pipeline post-transaction

Santhera Pipeline	Drug	Preclin.	Phase I	PoC	Pivotal	Filing	Market
Neuro-ophthalmological Diseases							
Leber's Hereditary Optic Neuropathy	Idebenone						***Raxone®***
Neuromuscular Diseases							
Duchenne Muscular Dystrophy (GC non- users)	Idebenone				completed		
Duchenne Muscular Dystrophy (GC users)	Idebenone				ongoing		
Duchenne Muscular Dystrophy	Vamorolone				ongoing	ReveraGen BioPharma	
Congenital Muscular Dystrophy	Omigapil		completed				
Pulmonary Diseases							
Cystic Fibrosis	POL6014		start Q4-18				
AAT, NCFB and PCD	POL6014		to be explored				
Chronic Obstructive Pulmonary Disease	POL6014						

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

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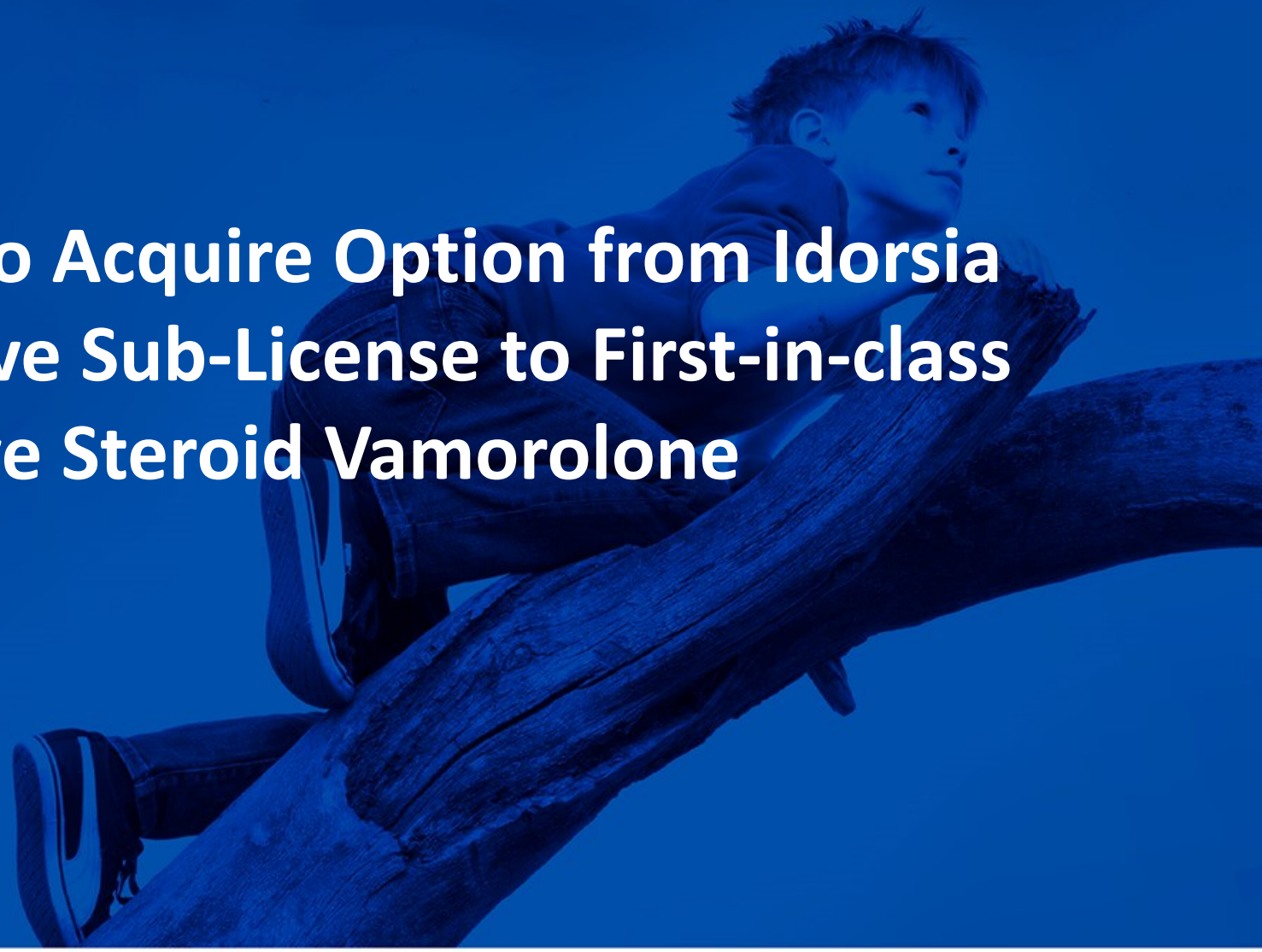

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