VALUATIONLAB
FINANCIAL ANALYSIS

SANTHERA PHARMACEUTICALS

FOCUS AREA: NOVEL THERAPIES IN RARE NEUROMUSCULAR AND PULMONARY (LUNG) DISORDERS

KEY DATA			SIX: SANN
MARKET CAPITALIZATION (CHF MN)	154	**SHARE PRICE ON JUNE 05, 2019**	13.8
ENTERPRISE VALUE (CHF MN)	132	**RISK-ADJUSTED NPV PER SHARE**** (CHF)	64
CASH (31 DECEMBER 2018) (CHF MN)	22	**UPSIDE/DOWNSIDE** (%)	364%
MONTHLY OPERATING EXPENSE (CHF MN)	6.8	**RISK PROFILE**	HIGH
CASH LIFE *	2020	**SUCCESS PROBABILITY LEAD PROJECT**	65%
BREAK-EVEN (YEAR)	2022	**EMPLOYEES**	120
FOUNDED (YEAR)	2004	**LISTED** (YEAR)	2006
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- RAXONE (LHON)	LAUNCHED (EU)	- IDORSIA	11.9
- PULDYSA (DMD - NON-STEROID PATIENTS)	FILING (EU)	- BERTARELLI FAMILY	6.8
- PULDYSA (DMD - STEROID PATIENTS)	PHASE III	- IGLU GROUP	3.8
- VAMOROLONE (DMD - ALL PATIENTS)	PIVOTAL PHASE IIB	- EXECUTIVE MANAGEMENT & BOARD	1.2
- POL6014 (CYSTIC FIBROSIS)	PHASE I	**- FREE FLOAT**	**98.8**
- OMIGAPIL (CMD)	PHASE I	- AVERAGE DAILY VOLUME (30-DAY)	37,677
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- POL6014 (CYSTIC FIBROSIS) PHASE I RESULTS	H2 2019		BP@VALUATIONLAB.COM
- PULDYSA DMD (NON-STEROID) EU APPROVAL	MID 2020		+41 79 652 67 68
- VAMOROLONE (DMD) PIVOTAL TRIAL RESULTS	MID 2020		

* INCLUDING CHIESI PROCEEDS & CHF 7.1 MN PLACEMENT IN 2019; ** BASED ON 16.9 MN FULLY DILUTED SHARES TO RAISE CHF 80 MN TO FULLY DEVELOP ALL KEY R&D PROJECTS UP TO COMMERCIALIZATION

ESTIMATES AS OF 5 JUNE, 2019 SOURCE: VALUATIONLAB ESTIMATES, SANTHERA PHARMACEUTICALS

All-in on DMD

Sufficient funds to reach turning point in 2020

Santhera is focused on the development and commercialization of treatments for rare neuromuscular and lung diseases. Key drivers in neuromuscular diseases includes two late stage drugs for Duchenne Muscular Dystrophy (DMD) namely, Puldysa (idebenone) filed for EU conditional approval, and vamorolone in pivotal development; and two early stage drugs for Congenital Muscular Dystrophy (CMD) including, omigapil and a novel gene therapy. Key driver in lung diseases is POL6014, a first-in-class drug for cystic fibrosis (CF) acquired from Polyphor in February 2018. Puldysa, vamorolone and POL6014 target multibillion-dollar markets with high unmet medical need. The Chiesi license agreement for the global rights (excluding North America) of Raxone (idebenone) in Leber's Hereditary Optic Neuropathy (LHON) marks Santhera's exit in rare neuro-ophthalmological diseases. The agreement worth up to CHF 105 mn will be reinvested in the current pipeline to bridge a funding gap to reach a major turning point in 2020 with the anticipated EU approval of Puldysa in DMD and topline results of the vamorolone pivotal trial in DMD. Idorsia became an anchor investor, when Santhera acquired the option to the global rights (excluding Japan/South Korea) of vamorolone in November 2018. We derive a sum-of-parts risk-adjusted (r)NPV of CHF 64/share, conservatively based on 16.9 mn shares to raise CHF ~80 mn to reach profitability at current share prices. We qualify Santhera as High Risk as it has to timely secure sufficient funding.

Key catalysts in order of importance:

1) **Puldysa EU approval in DMD (mid 2020):** should trigger a significant re-rating of Santhera's stock which is grossly undervalued according to our detailed forecasts.
2) **Vamorolone "VISION-DMD" pivotal trial results (mid 2020):** would increase our rNPV by CHF 17/share and lead to filing for US accelerated approval and EU conditional approval in DMD adding another CHF 8/share.
3) **POL6014 phase I trial results (H2 2019):** results of the multiple ascending dose trial; the start of a proof-of-concept trial would increase or rNPV by CHF 10/share.

Strategy & Cash Position

Swiss specialty pharma focused on rare neuromuscular & pulmonary diseases
Santhera Pharmaceuticals is a Swiss specialty pharmaceutical company focused on the development and commercialization of prescription drugs to treat rare neuromuscular and pulmonary (lung) diseases. With over 200 such diseases, this is an area of high unmet medical need that includes many orphan (rare) and niche indications typically with no effective therapies. These conditions are usually genetic (inherited), are treated by a small number of physicians (implying lower marketing costs), and typically command premium pricing. Development is spurred through special "orphan drug" programs with a more focused development timeframe and prolonged market exclusivity protection.

Santhera Pharmaceuticals was founded in September 2004 through a merger between Germany-based Graffinity Pharmaceuticals AG and Swiss-based Myocontract AG, which were both privately held. In November 2006, Santhera was listed on the SIX Swiss Stock Exchange through a successful IPO (initial public offering). The company is based in Pratteln, Switzerland (near Basel), and currently has ~120 employees globally.

Strategy to create value by becoming a full-fledged rare disease specialty company
Santhera's strategy is to create value by building a comprehensive portfolio of compounds in rare diseases through in-licensing, subsequently developing these compounds up to market approval through their development capabilities and expertise in rare diseases, and ultimately commercialize these compounds through an own small specialist sales force in key markets to retain and maximize value.

Santhera is engaged in the development and commercialization of drugs in rare diseases with a special focus on two therapeutic areas:

1. **Neuromuscular diseases:** treatments for diseases that impair the functioning of the muscles, including the muscles directly, or indirectly affecting the nerves that control muscles or the communication between muscles and nerves; Santhera's key neuromuscular drugs include:
    - **Puldysa (idebenone)** for the treatment of Duchenne muscular dystrophy (DMD) patients with mid- to late-stage disease; filed for conditional approval in the EU (patients not using steroids) May 2019 with expected EU conditional approval mid 2020; top line results phase III "SIDEROS" trial mid 2021 expanding use to all patients irrespective of steroid use, US approval and line extension in EU in 2022; protected by orphan drug exclusivity US (7-years) and EU (10-years); peak sales CHF 800 mn
    - **Vamorolone** for the treatment of DMD patients with early- to mid-stage disease; acquired option to global rights (excl. Japan/South Korea) from Idorsia in 2018; top line results pivotal "VISION-DMD" trial mid 2020; one-time consideration of CHF 30 mn to acquire vamorolone rights from Idorsia; US accelerated approval 2021; EU conditional approval 2022; peak sales CHF 550+ mn in DMD alone; potential for out licensing in major inflammatory diseases such as inflammatory bowel disease (IBD), multiple sclerosis (MS), asthma or chronic obstructive pulmonary disease (COPD)

- **Omigapil** for the treatment of CMD (congenital muscular dystrophy); phase I completed; discussions on pivotal pathway ongoing; peak sales CHF 150 mn
- **LAMA2-MD gene therapy** for the treatment of LAMA2-deficient congenital muscular dystrophy; preclinical research collaboration with the Biozentrum of the University of Basel started in 2019; Innosuisse and Santhera jointly invest CHF 1.2 mn; peak sales to be determined

2. **Pulmonary (lung) diseases:** treatments for diseases that affect the airway, lung tissue or lung circulation leading to difficulty in breathing, infection, inflammation or heart/lung complications; Santhera's key pulmonary drugs include:
    - **POL6014** for the treatment of cystic fibrosis (CF) and other neutrophilic lung diseases; global rights acquired from Polyphor in 2018; results phase Ib multiple ascending dose (MAD) trial in cystic fibrosis H2 2019; peak sales of CHF 1 bn; potential in other rare lung disorders

Chiesi license agreement marks Santhera's exit in neuro-ophthalmological diseases
Santhera has enjoyed commercial success with Raxone (idebenone) in the rare neuro-ophthalmological disease Leber's Hereditary Optic Neuropathy (LHON), an ultra-rare genetic eye disease that leads to sudden blindness, with an incidence of 1 in a million. Since approval in 2015, Raxone has accumulated sales of CHF 80 mn in LHON with another CHF 35-37 mn guided for 2019. Raxone was commercialized largely by Santhera's own specialist sales force in the EU. In May 2019, the company entered into an exclusive license agreement with the Italian private pharmaceutical company Chiesi Group for the global rights (excluding North America) of Raxone in LHON and all other ophthalmological indications. In a second step, following certain reimbursement and post-regulatory commitments on the part of Santhera, Chiesi has the option to change the license to an acquisition of ex-North American rights to Raxone in LHON. The North American rights could be acquired by another company. This marks Santhera's exit from neuro-ophthalmological diseases, the company's first therapeutic area with commercial success.

Funding gap until turning point in 2020; reinvesting in DMD with 26x higher multiple
The Chiesi agreement is worth up to CHF 105 mn, with an upfront payment of CHF 50 mn on closing of the transaction (expected in September 2019) and near- to mid-term sales milestone payments of up to CHF 55 mn. The proceeds will be reinvested in the current pipeline to bridge a funding gap until the turning point in 2020 with the expected EU approval of Puldysa in DMD (80% filing success rate) and topline results of the vamorolone pivotal "VISION-DMD" trial in DMD (35% phase IIb success rate). To put the Chiesi agreement into perspective, Santhera is reinvesting the rights for Raxone in LHON (excluding North America) with estimated peak sales of CHF 52 mn largely into its two late stage DMD drugs Puldysa and vamorolone with combined estimated peak sales of CHF 1.4 bn with a staggering 26-times higher peak sales potential than Raxone in LHON (excluding North America). Given the relatively high success probability of EU conditional approval of Puldysa in DMD in mid 2020, we believe the sale of the Raxone LHON rights to Chiesi should pay out nicely.

LHON specialist force retained for DMD – too important to restructure short-term
Santhera will retain its European specialist sales force infrastructure to continue to grow the sales of Raxone in LHON during the transition period until completion of the Chiesi agreement in September 2019 and to prepare for the anticipated EU conditional approval

of Puldysa in DMD in mid 2020. Actually, the European launch of Puldysa in DMD is not so far from the closing of the Chiesi agreement and is too critical to temporarily restructure ahead of the launch. Moreover, the cost of retaining the European specialist sales force is largely paid by the Raxone LHON revenues booked until completion of the Chiesi transaction and Raxone LHON sales in France, which are expected to be transferred to Chiesi at a later stage.

Santhera specialist field force for key markets to retain and maximize pipeline value
The commercialization of Santhera's rare disease drugs such as Puldysa (DMD), vamorolone (DMD) and POL6014 (cystic fibrosis) requires a relatively small field staff that targets specialists with strong profit margins as a result. To commercialize Raxone in LHON in 2015, Santhera established an own sales infrastructure covering Western European countries. Santhera rapidly expanded its staff to ~120 employees to facilitate the European rollout of Raxone in LHON. In 2017, Santhera also started to build US operations with an initial focus on regulatory and clinical operations support, medical affairs, patient advocacy liaison and commercial strategy. Santhera intends to rapidly build up an own US sales infrastructure on FDA approval of vamorolone (2021) and Puldysa (2022) in DMD, leading to considerable synergies in marketing and sales costs. The company will seek distributors in other countries and regions outside the EU and US.

Pipeline expanded by CHF 1.6 bn reducing reliance on initial cornerstone idebenone
In 2018, Santhera's pipeline, which heavily relied on idebenone (branded Raxone in LHON and Puldysa in DMD), was substantially expanded with two new compounds, POL6014 for rare lung disease including cystic fibrosis; and vamorolone for inflammatory diseases including DMD; with an estimated CHF 1.6 bn in additional peak sales for their two lead indications alone. Both products broaden Santhera's pipeline in neuromuscular and pulmonary diseases, leveraging its development capabilities and specialist sales force infrastructure. In 2019, the company signed a preclinical research collaboration with Biozentrum University of Basel for a novel gene therapy for congenital muscular dystrophy (CMD).

Vamorolone - Excellent strategic fit – DMD pipeline covers all disease stages
In particular, vamorolone is an excellent strategic fit with Puldysa. Vamorolone is targeted at DMD patients with early- to mid-stage disease to preserve muscle function. Puldysa is targeted at DMD patients with mid- to late-stage disease with breathing difficulties to preserve lung function. Both treatments can be used irrespective of the underlying genetic mutation targeting a broad DMD target population. There is also a potential for combination therapy. Santhera could become the undisputed market leader in DMD. Vamorolone is a first-in-class dissociative steroid targeted at replacing mainstay (gluco)steroids in DMD such as prednisone and deflazacort, which have side effects that hamper long-term use. Raxone and vamorolone have a favorable safety and tolerability profile that suits chronic use. Results of the pivotal phase IIb "VISION-DMD" trial are eagerly awaited in mid 2020 allowing for accelerated approval in the US by 2021.
In November 2018, the option to the global rights (excluding Japan/South Korea) of vamorolone in all indications was acquired from Idorsia (ticker: IDIA), which received a cash payment of USD 20 mn and retained a 13.3% stake (1 mn shares) in Santhera, effectively becoming an anchor shareholder with the largest stake in Santhera. The in-licensing agreement is back-loaded with regulatory and sales milestones up to USD 415 mn (DMD & 3 additional indications) and tiered single-

digit to low double-digit percentage royalties on net sales. Santhera may exercise the option at any time but likely will do so upon receipt of data from the pivotal phase IIb "VISION-DMD" trial and following a one-time consideration to Idorsia of USD 30 mn. We conservatively forecast vamorolone peak sales of CHF 550+ mn in DMD alone.

POL6014 - Potential blockbuster leveraging clinical expertise in lung disease
We believe POL6014 nicely complements Santhera's product pipeline targeting rare diseases such as DMD. Santhera has gained significant knowledge in clinical development of investigational drugs for lung disease with the development program of Puldysa in treating respiratory complications in DMD. Cystic fibrosis is a rare genetic and progressive disorder that affects mostly the lungs with approximately 70,000 patients globally with no cure and poor prognosis. We forecast peak sales could amount to approximately CHF 1 bn in cystic fibrosis alone. Due to the early stage of development, the compound is in phase Ib multiple ascending dose escalation trials, we do not include any forecasts for POL6014, yet. POL6014 was acquired from Polyphor (ticker: POLN) in February 2018 for CHF 6.5 mn in Santhera shares and additional back-loaded cash milestone payments up to CHF 121 mn and tiered royalty payments on sales.

LAMA2-MD gene therapy - Preclinical research collaboration with Biozentrum
In May 2019, a preclinical research collaboration was announced with the Biozentrum of the University of Basel to advance gene therapy research for the treatment of LAMA2-deficient CMD (congenital muscular dystrophy). Innosuisse, the public Swiss innovation agency, and Santhera will jointly invest CHF 1.2 mn in the project. The novel gene therapy approach and omigapil could act complementary in CMD. Due to the early development stage of both products, we have not included any forecasts for CMD in our valuation.

Santhera's key priorities for the next 12-18 months include:

- **Completion of Chiesi license agreement Raxone in LHON:** Complete the transfer of the global rights (excluding North America) for the development, commercialization and distribution of Raxone in LHON and any other potential ophthalmological indications. Closing is subject to customary approvals and is expected to occur in Q3 2019 triggering the CHF 50 mn upfront payment.

- **EU approval of Puldysa in DMD:** In May 2019, a CMA (conditional marketing authorization) was filed in the EU for approval of Puldysa in DMD patients not using steroids based on the phase II "DELPHI" trial, the long-term "DELPHI-Extension" trial, the pivotal phase III "DELOS" trial, the open-label long-term "SYROS" trial, a collection of long-term data from patients who completed the "DELOS" trial and continued treatment with Puldysa for up to six years. CHMP opinion is expected by mid-2020 and EU conditional approval anticipated Q3 2020.

- **Top line results vamorolone "VISION-DMD" pivotal trial & file for US approval:** The top line results of the pivotal phase IIb "VISION-DMD" of vamorolone in DMD are expected to report in mid 2020. The trial was developed under FDA and EMA scientific advice and is considered a pivotal trial for US accelerated approval and EU conditional approval, with approvals expected in 2021 and 2022, respectively.

- **Establish and leverage relationship with ReveraGen:** Following the in-licensing of the global rights (excluding Japan/South Korea) from Idorsia, Santhera will establish a relationship with ReveraGen to leverage their shared expertise and network in DMD and rare diseases

- **Expand use of Puldysa in DMD patients treated with steroids:** Santhera plans to expand the use of Puldysa in DMD patients who are treated with steroids, which represents ~60% of patients 8 years and older. The company started a second confirmatory phase III "SIDEROS" trial in this patient population in September 2016. Top line results are anticipated mid 2021

- **Expanded use program for DMD patients:** In February 2018, Santhera launched the US expanded access program "BreatheDMD" for Puldysa in DMD. Eligible DMD patients can now be treated with Puldysa. Furthermore, the EAMS, the UK early access program for Puldysa in DMD was renewed for another year in June 2018. Importantly, real life data from this program can be used to support regulatory filings, while the program can build support among treating physicians, patients and the powerful DMD patient groups.

- **Complete phase Ib MAD trial of POL6014 in cystic fibrosis:** The multiple ascending dose (MAD) trial started in October 2018 with top line results due in H2 2019. On positive results, Santhera will conduct a phase IIa proof-of-concept trial.

- **Discuss clinical pathway of omigapil/gene therapy in CMD:** Discussions will be held with key experts and regulators for a pivotal trial design of omigapil in the rare disease CMD (congenital muscular dystrophy), while Santhera will leverage its expertise in the preclinical collaboration with the Biozentrum of the University of Basel to advance gene therapy research in LAMA2-deficient CMD.

- **Broaden product pipeline offering:**
  - In-license new development projects in rare diseases
  - In-license new products to leverage the current sales force infrastructure

Almost CHF 400 mn raised since founded in 2004

Santhera has been very successful in raising money since it was founded in 2004. The company raised CHF 102 mn during its IPO in November 2006, while an additional CHF 145 mn was raised in eight private placements, one in 2008 (Ares Life Sciences), one in 2013 (YA Global), two in 2014 (IGLU Group, others), two in 2015 (others), one in 2018 to fund the vamorolone option from Idorsia (Idorsia, Bertarelli, others) and one in 2019 (others). In February 2017, Santhera successfully placed a CHF 60 mn Convertible Bond with a 5-year maturity due in 2022 and 5% coupon paid annually.

MONEY RAISED	CHF MN
PRE-IPO	85
IPO (INITIAL PUBLIC OFFERING) INCL. OVER-ALLOTMENT	102
PRIVATE PLACEMENTS / SHARE SALES	145
CONVERTIBLE BONDS	60
TOTAL RAISED	**392**

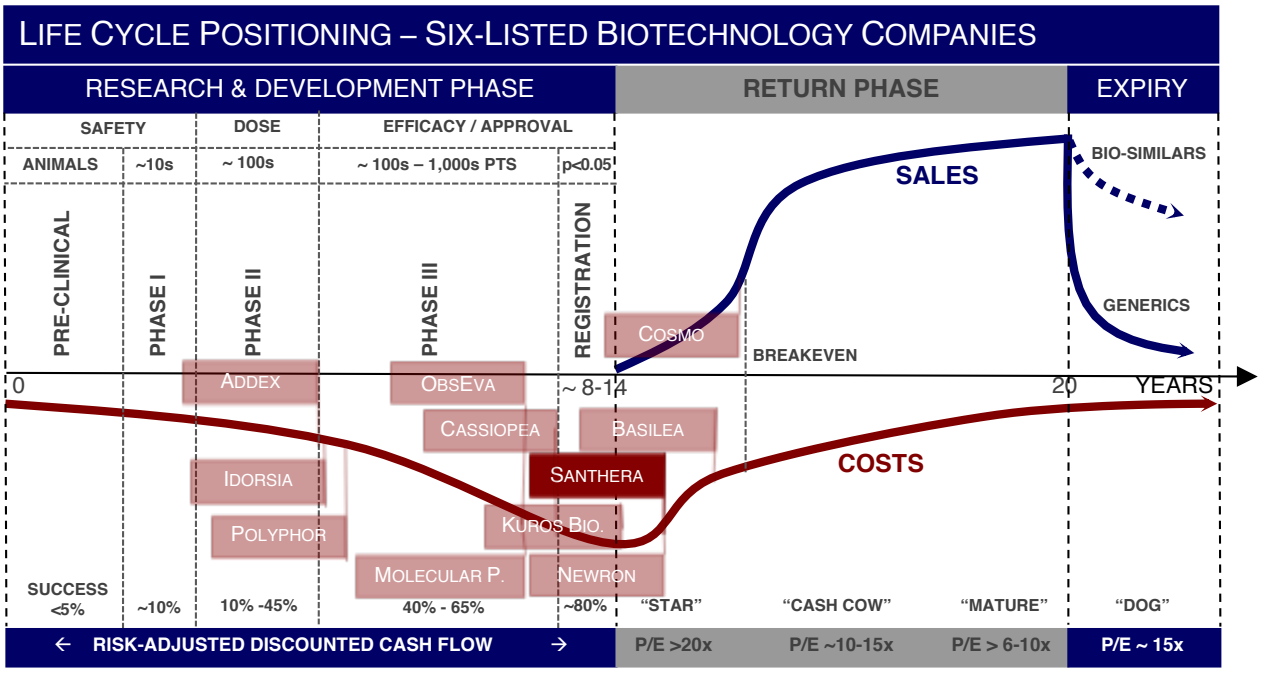
SOURCE: VALUATIONLAB, SANTHERA PHARMACEUTICALS

In April 2019, Santhera secured a CHF 15 mn short-term syndicated loan to bridge a potential funding gap in 2019. This is no longer needed due to the Chiesi licensing agreement worth up to CHF 105 mn with a CHF 50 upfront cash payment in September 2019.

For Santhera to fully develop all its key pipeline projects up to commercialization, we calculate an additional CHF 80 mn will be needed before reaching profitability. Upon reaching the two key inflection points in 2020 - EU approval of Puldysa in DMD or positive top line results of the pivotal "VISION-DMD" trial of vamorolone in DMD - Santhera should easily replenish its cash position, in our view. The company will have far more options to raise cash, including monetizing the North American rights of Raxone in LHON, the rights to Puldysa and vamorolone in geographic regions outside the EU and US, the rights of large vamorolone indications outside DMD such as inflammation, or raise cash in the financial markets at considerably higher share prices than at the current depressed valuation, minimizing share dilution. To account for the funding gap, we conservatively calculate our per share forecasts based on 16.9 mn shares (11.16 mn shares outstanding plus an estimated 5.76 mn new shares to raise CHF 80 mn at the current low share price) to raise the remaining cash needed to reach profitability expected in 2022. This leads to a share dilution of 52% based on the current depressed share price level.

Life Cycle Positioning – High Risk

We qualify Santhera's risk profile as High Risk. The company has secured sufficient funds to reach the key turning point in 2020, thanks to the sale of the global rights (excluding North America) of Raxone in LHON and all ophthalmology indications to Chiesi for up to CHF 105 mn in upfront and commercial milestones. Upon EU approval of Puldysa in DMD (patients not using steroids) with an 80% (filing) success probability or positive pivotal "VISION-DMD" trial result of vamorolone in DMD with a 35% (phase IIb) success probability, Santhera will need to timely replenish its cash position to fund the development of its other pipeline projects. (See Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 64 per share
We derive a sum-of-parts risk-adjusted NPV of CHF 64 per share for Santhera, conservatively based on a share dilution of 52% (16.9 mn shares) based on the current depressed market capitalization to raise CHF 80 mn to fully fund its pipeline up to profitability, with net cash of CHF 1 per share (31 December 2018) and overhead expenses of CHF 15 per share (including the CHF 60 mn convertible bond repayment in 2022), assuming a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT	INDICATION	PEAK SALES (CHF MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE * (CHF)	SUCCESS PROBABILITY	RISK-ADJUSTED NPV/SHARE * (CHF)	PERCENTAGE OF TOTAL
RAXONE (IDEBENONE)	LHON (US & CANADA ONLY)	56	2015 (EU)	9	65%	**6**	8%
PULDYSA (IDEBENONE)	DMD (NON-STEROID PATIENTS)	357	2020	33	72.5%	**24**	30%
PULDYSA (IDEBENONE)	DMD (STEROID PATIENTS)	442	2022	43	65%	**28**	35%
VAMOROLONE	DMD (STEROID REPLACEMENT)	569	2022	56	35%	**20**	25%
POL6014	CYSTIC FIBROSIS	1,030	>2023	66			
OMIGAPIL	CMD	150	>2023	8			
LAMA2-MD GENE THERAPY - **NEW**	CMD	TBD	>2023	TBD			
NET CASH POSITION (31 DECEMBER 2018)		22		1		**1**	2%
TOTAL ASSETS				226		**79**	**75%**
OVERHEAD EXPENSES (INCL. REPAYMENT OF CHF 60 MN CONVERTIBLE BOND DUE 2022)				-15		**-15**	
NPV/SHARE (CHF)				211		**64**	
SHARE PRICE ON JUNE 05, 2019						14	
PERCENTAGE UPSIDE / (DOWNSIDE)						364%	

* NOTE: 16.9 MN SHARES USED FOR CALCULATION NPV/SHARE, ASSUMING CHF 80 MN IN FUND RAISES AND PAY BACK CHF 60 MN CONVERTIBLE BOND IN 2022 (INCLUDED IN OVERHEAD EXPENSES
NOTE: 11.9 MN SHARES OUTSTANDING INCLUDES 694,440 REGISTERED SHARES RESERVED FOR POTENTIAL CONVERSION OF THE CONVERTIBLE BOND
ESTIMATES AS OF 5 JUNE, 2019 SOURCE: VALUATIONLAB ESTIMATES

Santhera's key drivers, include:

Raxone in LHON (North America only) - rNPV of CHF 6 per share
Santhera retained North American rights to Raxone in LHON, which could be sold as part of the strategy to exit neuro-ophthalmology. The value of these rights is calculated assuming US approval for Raxone in LHON to occur in 2023, roughly one year after approval of Puldysa in DMD. We forecast peak sales in North America to amount to CHF 56 mn with an assumed average annual treatment price of USD 90,000 per patient. Furthermore, we include the remaining Raxone LHON revenues until the Chiesi license agreement closes in September 2019, including the CHF 50 mn upfront payment and only CHF 30 mn additional sales milestones (maximum is up to CHF 55 mn). We calculate a rNPV of CHF 6/share for Raxone in LHON with a 65% (phase III) success probability.

Puldysa in DMD (non-steroid patients) - rNPV of CHF 24 per share
In May 2019, a CMA (conditional marketing authorization) was filed in the EU for approval of Puldysa in DMD patients not using steroids based on the phase II "DELPHI" trial, the long-term "DELPHI-Extension" trial, the pivotal phase III "DELOS" trial, the open-label long-term "SYROS" trial, a collection of long-term data from patients who completed the "DELOS" trial and continued treatment with Puldysa for up to six years. EU conditional approval is anticipated mid 2020. We forecast Puldysa peak sales in DMD (non-steroid patients) to amount to CHF 357 mn based on a yearly treatment price per patient of EUR 62,415 (EU/ROW) and USD 90,000 (US) with peak penetration rates of ~40% (EU/ROW) and ~65% (US) accounting for COGS (10%) and M&S costs. Our forecasts are based on eligible DMD patients (ages 8 years and older) who are not on steroids (~40% of patients).

We calculate a rNPV of CHF 24/share with a 72.5% success rate, the average of EU (80% filing) and US (65% phase III).

Puldysa in DMD (steroid patients) - rNPV of CHF 28 per share

Santhera plans to expand Puldysa's use to eligible DMD patients who are treated with steroids (~60% of treated patients) triggered by CINRG natural history data showing that at a certain stage of disease progression patients on steroids will experience the same rate of lung function loss as patients not using steroids. The phase III "SIDEROS" trial includes DMD patients treated with steroids and started in September 2016 with top line results expected in mid 2021. The US NDA (new drug application) filing will be based on the EU data package for DMD patients not on steroids (see above) and the "SIDEROS" trial. Filing is expected at the end of 2021 with approval and launch to occur in 2022. We forecast peak sales for Puldysa in DMD (steroid patients) of CHF 442 mn. Using a 65% (phase III) success rate, we derive a rNPV of CHF 28/share.

Vamorolone in DMD (all patients) – risk-adjusted NPV of CHF 20/share

Vamorolone is an excellent strategic fit with Puldysa. Vamorolone is targeted at DMD patients with early- to mid- stage disease to preserve muscle function, effectively replacing mainstay steroid therapy, while Puldysa is targeted at patients with mid- to late-stage disease with breathing difficulties to preserve lung function, both irrespective of the underlying genetic mutation. There is a potential for combination therapy. ReveraGen started enrollment of the pivotal phase IIb "VISION-DMD" trial in August 2018 with top line results due in mid 2020. We forecast vamorolone peak sales to amount to CHF 569 mn in DMD alone, with first launches in the US to occur at the end of 2021 (thanks to fast-track designation), followed by EU approval and launch in 2022 with significant marketing & sales synergies using the same sales infrastructure that commercializes Puldysa in DMD. We calculate a rNPV of CHF 20/share applying a conservative 35% (phase IIb) success rate.

Currently no value attributed to early stage pipeline projects

We have conservatively not accounted for Santhera's early stage pipeline projects due to the lack of sufficient proof-of-concept at the moment. Santhera's unadjusted NPV provides a "sneak preview" on what the value could amount to, if all our assumptions were reached.

POL6014 in Cystic Fibrosis (CF) & other breathing disorders– Phase I, launch >2023

In February 2017, Santhera acquired the exclusive global rights for POL6014, a novel, selective human neutrophil elastase (hNE) inhibitor for treating cystic fibrosis and other rare lung disorders from Polyphor for CHF 6.5 mn in Santhera shares in a back-loaded agreement with little impact on Santhera's cash position. Cystic fibrosis is a rare genetic and progressive disorder that affects mostly the lungs, but also the pancreas, liver, kidneys and intestine, and affects approximately 70,000 patients in Europe and the US. In October 2018, Santhera started a phase Ib multiple ascending dose (MAD) trial in cystic fibrosis patients with results due in H2 2019. The trial was already designed by Polyphor and is financially supported by the Cystic Fibrosis Foundation. Upon dose selection, a phase IIa proof-of-concept trial could start in 2020 with a potential read-out 12 months later. Assuming POL6014 captures a conservative 15% of the market with a USD 70,000 to USD 100,000 annual treatment price, peak sales for POL6014 could easily amount to CHF 1 bn for cystic fibrosis alone, with the potential for Santhera to leverage its US and European sales infrastructure to commercialize POL6014.

Omigapil/gene therapy in CMD - Phase I/preclinical, launch >2023

Novartis originally developed omigapil, a deprenyl analog, for Parkinson's disease and ALS (Lou Gehrig's disease) but terminated development in these indications due to lack of efficacy. Santhera obtained an exclusive license to develop the compound in congenital muscular dystrophies (CMD) in 2007. These are a variety of inherited neuromuscular disorders characterized by different forms of progressive loss of muscle tissue. In April 2018, omigapil successfully completed the phase I "CALLISTO" trial in patients with two forms of CMD conducted by the US NIH (National Institutes of Health). The multiple ascending dose cohort trial met its primary objective to establish a favorable pharmacokinetic profile of omigapil and was well tolerated in children and adolescents with CMD. Following further data analysis, Santhera is in discussion with clinical experts such as the TREAT-NMD Advisory Committee for Therapeutics (TACT) and regulators to prepare for a pivotal trial in patients with CMD. Peak sales for omigapil in CMD could reach CHF 150+ mn.

In May 2019, a preclinical research collaboration was announced with the Biozentrum of the University of Basel to advance gene therapy research for the treatment of LAMA2-deficient CMD (congenital muscular dystrophy). Innosuisse, the public Swiss innovation agency, and Santhera will jointly invest CHF 1.2 mn in the project. The novel gene therapy approach and omigapil could act complementary in CMD. Due to the early development stage of both products, we have not included any forecasts in our valuation.

Sensitivities that can influence our valuation

Timely securing sufficient funding: Following the completion of the Chiesi license agreement in September 2019, triggering a CHF 50 mn upfront payment with sales milestones of up to CHF 55 mn, we calculate that Santhera will need funds of around CHF 80 mn to fully develop its expanded key pipeline projects up to commercialization with profitability expected in 2022. We expect Santhera to raise the remaining funds when it reaches key turning point in 2020, including the EU conditional approval of Puldysa in DMD or positive "VISION-DMD" trial results of vamorolone in DMD, at far higher share prices to minimize share dilution. Moreover, Santhera can monetize several pipeline assets, such as out licensing rights to regions such as Japan or Asia to local partners.

Threat of generic idebenone: Puldysa's active ingredient idebenone no longer enjoys robust "composition of matter" patent protection as the compound was discovered in the early eighties and this has long expired. Consequently, orphan drug exclusivities and use patents are Santhera's main line of defense against generic versions of idebenone. Once approved, we believe orphan drug exclusivity should provide sufficient protection against generics for at least 7 years in the US and 10 years in the EU. The FDA and EMA actively enforce orphan drug exclusivity, which in the case of rare diseases is relatively easy, as most patients and distribution channels are known. Furthermore, reimbursement of Puldysa in approved indications will remove the need for patients to seek unapproved idebenone that is not reimbursed. The FDA and EMA are actively closing down illegal online pharmacies in a globally coordinated action, which distribute these unapproved sources. We believe this should provide investors an acceptable level of comfort.

Substitution by CoQ10 or vitamin E and analogs: Although Puldysa's molecule idebenone shares similarities with related molecules, such as the naturally occurring CoQ10, these molecules are chemically different. Idebenone is a synthetic short-chain benzoquinone, while CoQ10 is a long-chain molecule, which is practically insoluble in water and body fluids. These molecules have distinct pharmacological activities leading to major differences in efficacy and cannot be substituted. CoQ10 is not hydrophilic, is not a substrate for the enzyme NAD(P)H:quinone oxidoreductase (NQO1) and does not have the ability to shuttle in and out of mitochondria to restore cellular energy in defective mitochondria cells and protect from oxidative stress. No clinical evidence shows efficacy of vitamin E and its analogs or CoQ10 in LHON or DMD, as is the case with Raxone/Puldysa.

Pricing and reimbursement: Following approval in the EU, Santhera has to negotiate pricing and reimbursement with each individual member state. In the US, pricing is more straightforward. Pricing could be lower, and negotiations could take longer than forecast. Orphan drugs such as Puldysa or vamorolone typically command a high price. Santhera plans to price its drugs "attractively" compared to competitors thanks to lower COGS, thereby enhancing reimbursement and market penetration.

New sales infrastructure: Santhera established an own sales organization in regional clusters in Western Europe and with distribution partners in Eastern Europe and Greece to launch its drugs. Santhera is also building up US operations with initial focus on regulatory and clinical operations. Delays could occur in the buildup and rollout. Santhera is dependent on the sales efforts of distributors in the remaining countries & regions, where delays can occur, and actual distributor transfer prices could differ from our estimates.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	WHAT	COMMENT	IMPACT
2019					
25 FEB	PULDYSA (IDEBENONE)	DMD (NSP*)	"SYROS" TRIAL RESULTS	"SYROS" OPEN LABEL STUDY SHOWS LONG-TERM EFFICACY WITH PULDYSA IN SLOWING RESPIRATORY FUNCTION LOSS IN DMD	
12 MAR	RAXONE (IDEBENONE)	LHON**	"LEROS" TRIAL ENROLLMENT	COMPLETION OF PATIENT ENROLLMENT IN "LEROS" PHASE IV (POST-MARKETING) LONG-TERM TRIAL IN LHON PATIENTS; TOP LINE RESULTS DUE BY Q2 2021	
28 MAR	PULDYSA (IDEBENONE)	DMD (NSP*)	EU FILING UPDATE	INTENTION TO FILE A CMA (CONDITIONAL MARKETING AUTHORIZATION) FOR PULDYSA (IDEBENONE) FOR TREATMENT OF RESPIRATORY DYSFUNCTION IN DMD WITH THE EMA IN Q2 2019 FOLLOWING SCIENTIFIC ADVICE FROM EU REGULATORY AUTHORITIES	
4 APR			UP TO CHF 22.1 MN RAISED	A SYNDICATED CREDIT LINE OF UP TO CHF 15 MN OVER A PERIOD OF 9 MONTHS WAS TAKEN OUT; SANTHERA ISSUED THE REMAINING 500,000 REGISTERED SHARES AT CHF 14.25/SHARE FOR GROSS PROCEEDS OF CHF 7.1 MN; THE COMPANY IS CONSIDERING MONETIZING CERTAIN ASSETS	
15 APR	PULDYSA (IDEBENONE)	DMD (NSP*)	"SYROS" TRIAL PRESENTED AT MDA	POSITIVE RESULTS OPEN LABEL LONG-TERM "SYROS" TRIAL CONSISTENT WITH "DELOS". SWITCHING AND MAINTAINING LONG-TERM TREATMENT REDUCED THE RATE OF LUNG FUNCTION LOSS BY 50%; TREATMENT EFFECT WAS CONSISTENTLY MAINTAINED YEAR-ON-YEAR FOR UP TO 6 YEARS	
29 APR			FY 2018 RESULTS	RAXONE SALES UP 38% TO CHF 31.7 MN (2017: CHF 22.9 MN); NET RESULT OF CHF -54.2 MN (2017: CHF -51.5 MN) AFFECTED BY IN-LICENSING POL6014; GUIDANCE 2019: RAXONE SALES TO REACH CHF 35-37 MN	
21 MAY	LAMA2 MD/MDC1A	CMD***	COLLABORATION WITH BIOZENTRUM UNIVERSITY OF BASEL	COLLABORATION WITH THE BIOZENTRUM OF THE UNIVERSITY OF BASEL TO ADVANCE GENE THERAPY RESEARCH FOR THE TREATMENT OF LAMA2-DEFICIENT CONGENITAL MUSCULAR DYSTROPHY (LAMA2 MD OR MDC1A); SANTHERA AND INNOSUISSE WILL JOINTLY INVEST CHF 1.2 MN IN PRECLINICAL RESEARCH	
23 MAY	RAXONE (IDEBENONE)	LHON**	CHIESI AGREEMENT	CHIESI ACQUIRES GLOBAL RIGHTS (EX> NORTH AMERICA) TO RAXONE IN LHON AND ALL OTHER OPHTHALMOLOGICAL INDICATIONS FOR AN UPFRONT PAYMENT OF CHF 50 MN (EUR 44 MN) AND NEAR- TO MID-TERM SALES MILESTONES OF UP TO CHF 55 MN (EUR 49 MN); CLOSING OF TRANSACTION EXPECTED IN SEPTEMBER 2019	
27 MAY	PULDYSA (IDEBENONE)	DMD (NSP*)	EU CMA FILING	FILING FOR EU CONDITIONAL MARKETING AUTHORIZATION BASED ON PHASE III "DELOS" TRIAL PLUS NEW DATA PACKAGE INCL. "SYROS" LONG-TERM TRIAL AND NATURAL HISTORY DATA	
Q2	RAXONE (IDEBENONE)	LHON**	APPROVAL SOUTH KOREA	APPROVAL IN SOUTH KOREA, AN IMPORTANT ASIAN MARKET, WHERE ORPHAN DRUG DESIGNATION WAS GRANTED PROVIDING UP TO 10 YEARS MARKET EXCLUSIVITY FROM APPROVAL DATE	
SEP	RAXONE (IDEBENONE)	LHON**	CHIESI AGREEMENT	CLOSING OF CHIESI TRANSACTION FOR GLOBAL RIGHTS (EX. NORTH AMERICA) TO RAXONE IN LHON AND ALL OTHER OPHTHAMOLOGICAL INDICATIONS, SUBJECT TO CUSTOMARY APPROVALS; TRIGGERS CHF 50 MN UPFRONT PAYMENT	
H2	PULDYSA (IDEBENONE)	DMD (SP****)	"SIDEROS" PHASE III	PHASE III "SIDEROS" DMD TRIAL IN STEROID PATIENTS FULLY ENROLLED	
H2	POL6014	CYSTIC FIBROSIS	PHASE IB	TOP LINE RESULTS OF THE MULTIPLE ASCENDING DOSE (MAD) TRIAL	
2020					
MID	PULDYSA (IDEBENONE)	DMD (NSP*)	EU APPROVAL	EU APPROVAL FOR DMD PATIENTS NOT TREATED WITH STEROIDS; EXPECTED TO TRIGGER A RE-RATING OF SANTHERA STOCK	+CHF 3
MID	VAMOROLONE	DMD (ALL)	"VISION-DMD" PIVOTAL PHASE IIB TRIAL	TOP LINE RESULTS OF THE PIVOTAL PHASE IIB DOSE RANGING "VISION-DMD" TRIAL IN DMD PATIENTS AGED 4 TO <7 YEARS	+CHF 17
Q3	VAMOROLONE	DMD (ALL)	EXERCISE OPTION	EXERCISE OPTION TO ACQUIRE GLOBAL RIGHTS (EX. JAPAN/SOUTH KOREA) OF VAMOROLONE IN ALL INDICATIONS FROM IDORSIA FOR A ONE-TIME CONSIDERATION OF USD 30 MN	
Q3	PULDYSA (IDEBENONE)	DMD (NSP*)	EU LAUNCH	EU LAUNCH FOR DMD PATIENTS NOT TREATED WITH STEROIDS USING THE EXISTING EU SPECIALIST SALES FORCE THAT SOLD RAXONE IN LHON	
Q4	VAMOROLONE	DMD (ALL)	US NDA FILING (ACCELERATED APPROVAL)	US NEW DRUG APPLICATION SUBMISSION FOR ACCELERATED APPROVAL BASED ON SINGLE "VBP15-004" PIVOTAL TRIAL	+CHF 4
	POL6014	CYSTIC FIBROSIS	PHASE IIA TRIAL	START PHASE IIA PROOF-OF-CONCEPT TRIAL	+CHF 10
	OMIGAPIL	CMD***	PHASE II POC	START OF PHASE IIA PROOF-OF-CONCEPT TRIAL	+CHF 1

*NSP = NON-STEROID PATIENT; **LHON = LEBER'S HEREDITARY OPTIC NEUROPATHY; ***CMD = CONGENITAL MUSCULAR DYSTROPHY; ****SP = STEROID PATIENT;

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

Technology & Pipeline

Aim to successfully develop re-profiled compounds in rare diseases
Santhera does not have an own discovery or research platform but has vast experience in clinical development in rare diseases. Moreover, the company was one of the first specialty pharmaceutical companies to see substantial value in developing and repositioning existing compounds neglected by "Big Pharma" in rare (orphan) diseases. Consequently, all compounds have been licensed in, acquired, or no longer enjoy patent protection from their originators.

Orphan disease programs provides attractive incentives for Raxone:
Although individually, orphan diseases may be classified as uncommon, collectively, they affect a large portion of the population and healthcare expenditure. The US and EU orphan disease programs have been developed to provide pharmaceutical companies a strong incentive to pursue and develop orphan prescription drugs for these rare disorders providing additional years of market exclusivity. Idebenone (branded Raxone for LHON and Puldysa for DMD), vamorolone, POL6014, and omigapil all enjoy these market exclusivities.

Key advantages to develop drugs in orphan indications include:

- Strong orphan disease market exclusivity of 7 years (US) or 10 years (EU) starting from first day of launch – this provides sufficient time for an attractive return
- Two years additional market exclusivity in pediatric indications
- There are often no approved drugs for these indications or only few
- Effective treatments can command a relatively high price resulting in high margins
- Competition is not present (LHON) or limited (DMD, cystic fibrosis)
- Specialists can be addressed by a relatively small field force
- Conditional (EU)/Accelerated (US) early approval can be granted in the absence of robust trial data

However, there are also considerable hurdles, including:

- A very low number of patients to conduct clinical trials – lack of robust clinical data, slow enrollment, trial delays
- A lack of widespread expertise in clinical centers
- Insufficient understanding of the history or mechanism of the disease
- Absence of a clear regulatory pathway on how to set up the pivotal clinical trial, including what the right endpoints should be
- The small number of experts who conduct the trials are often banned from advisory panels

Specialized in rare neuromuscular & pulmonary diseases.
Santhera's special focus on rare neuro-ophthalmology (now to be exited following the Chiesi global license agreement) and neuromuscular diseases is a result of the high unmet medical need and lead compound idebenone is believed to address this area. Neuromuscular disease is a broad term that covers many disorders that undermine the correct functioning of the muscles. This can be, either directly, caused by defects of the muscle, or indirectly, caused by defects in the nerves that control the muscle. Mitochondrial defects in cells can also lead to loss of signal transduction, as is the case for

the optic nerve in LHON and other optic disorders such as dominant optic atrophy.

Idebenone was originally developed by Takeda Pharmaceuticals and was launched in Japan for the treatment of cognitive disorders in 1986; the approved dose was 10x lower than Santhera's development program. It was later pulled from the market due to lack of efficacy in later trials. Takeda had European licensing rights for idebenone in Friedreich's Ataxia (a genetic movement disorder) and DMD. After the failure of the compound in Friedreich's Ataxia, development was discontinued in this disease. Santhera regained European rights from Takeda in 2013, in return for a low and capped royalty on income from the DMD program (up to CHF 11mn). While idebenone is no longer protected by robust composition of matter patents, use patents and orphan drug designations (ODD) have been granted, which should provide exclusivity for many years. Santhera obtained full rights to idebenone in all indications and regions, including the important US market. In May 2019, Chiesi licensed the global rights (excluding North America) of Raxone in LHON and all other ophthalmological diseases.

Idebenone (branded "Raxone" in LHON and "Puldysa" in DMD) is thought to work by:

1) Restoring the energy production in affected cells, and;
2) Decreasing oxidative stress created by radical oxygen molecules, which can be toxic and destroy cells.

Most of these neuromuscular and mitochondrial diseases are inherited and typically affect only a relatively small group of patients. Many times, there are no effective treatments, limited companies developing new treatments, and few physicians conducting research in these areas. Research in recent years demonstrates mitochondrial involvement in an increasing number of diseases. Santhera is well positioned to become a leader in this expanding disease area.

Pipeline noticeably expanded in 2018 through in-licensing

With the option to in-license vamorolone and the in-licensing of POL6014 in 2018, Santhera noticeably expanded its pipeline by an estimated CHF 1.6 bn in additional peak sales for both drugs in their lead indications in DMD and cystic fibrosis, respectively. This considerably reduced the heavy reliance of the company on cornerstone therapy idebenone (branded Raxone for LHON and Puldysa for DMD). The in-licensing agreements underline Santhera's expertise in successfully developing and marketing drugs in rare diseases.

Vamorolone, where Santhera acquired the option to the global rights (excluding Japan/South Korea) from Idorsia in November 2018, is an excellent strategic fit with Puldysa in DMD, with the potential of combination therapy, and substantial marketing & sales cost synergies benefiting from the same US and European sales infrastructure. Vamorolone is targeted at DMD patients with early- to mid-stage of disease to preserve muscle function. Puldysa is targeted at DMD patients with mid- to late-stage disease with breathing difficulties to preserve lung function, irrespective of the underlying genetic mutation.

POL6014, in-licensed from Polyphor in February 2018, targets cystic fibrosis where current therapies are not adequate. A phase Ib multiple ascending dose (MAD) trial in cystic

fibrosis (already set up by Polyphor and financially supported by the Cystic Fibrosis Foundation) started in October with results due in H2 2019.

Pipeline expansion with POL6014 and vamorolone – exit LHON & ophthalmology

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	GLOBAL PEAK SALES
NEUROMUSCULAR DISEASES						
PULDYSA (IDEBENONE)	SHORT-CHAIN BENZOQUINONE	DUCHENNE MUSCULAR DYSTROPHY (NON-STEROID PATIENTS)	CMA FILED (EU)	2020 (EU) 2022 (US)	DISTRIBUTORS OUTSIDE SANTHERA TERRITORIES	CHF ~350 MN
PULDYSA (IDEBENONE)	SHORT-CHAIN BENZOQUINONE	DUCHENNE MUSCULAR DYSTROPHY (STEROID PATIENTS)	PHASE III	2022 (EU) 2022 (US)	DISTRIBUTORS OUTSIDE SANTHERA TERRITORIES	CHF ~450 MN
VAMOROLONE	DISSOCIATIVE STEROID	DUCHENNE MUSCULAR DYSTROPHY (ALL PATIENTS)	PHASE IIB PIVOTAL	2021 (US) 2022 (EU)	DISTRIBUTORS OUTSIDE SANTHERA TERRITORIES	CHF 550+ MN
OMIGAPIL	DEPRENYL ANALOG	CONGENITAL MUSCULAR DYSTROPHY	PHASE I COMPLETED	>2023	TBD	CHF 150+ MN
LAMA2-MD GENE THERAPY	GENE THERAPY	CONGENITAL MUSCULAR DYSTROPHY	PRECLINICAL	>2023	TBD	TBD
PULMONARY DISEASES						
POL6014	HUMAN NEUTROPHIL ELASTASE INHIBITOR	CYSTIC FIBROSIS	PHASE I	>2023	DISTRIBUTORS OUTSIDE SANTHERA TERRITORIES	CHF 1 BN
NEURO-OPHTHALMOLOGICAL DISEASES (NON-CORE)						
RAXONE (IDEBENONE)	SHORT-CHAIN BENZOQUINONE	LEBER'S HEREDITARY OPTIC NEUROPATHY	APPROVED (EU)	Q4 2015 (EU) 2023 (US)	CHIESI (EXCLUDING US & CANADA FROM Q4 2019)	CHF ~50 MN (US & CAN)

ESTIMATES AS OF 5 JUNE, 2019 SOURCE: VALUATIONLAB ESTIMATES

Santhera's key pipeline projects include:

Puldysa (idebenone) – only DMD drug with positive phase III trial results

Duchenne muscular dystrophy is a fatal genetic muscle wasting disease that affects males in early childhood, confining patients generally to a wheelchair by the age of 12 and death at the age of ~30, with few effective treatments. In May 2019, Santhera filed for conditional approval of Puldysa in DMD (non-steroid patients, ~40% of patients) in the EU based on the positive phase III "DELOS" trial, other supportive trials, and natural history data. Santhera intends to expand use to patients treated with steroids (~60% of patients) with the second phase III "SIDEROS" trial to report in mid 2021 with US and EU launches expected in 2022. We forecast worldwide peak sales of approximately CHF 800 mn in DMD patients, irrespective of steroid use.

Rationale for Puldysa in DMD

DMD is characterized by the complete loss of the protein dystrophin, a protein responsible for the mechanical stability of muscle cells. This leads to cell damage and impaired Calcium homeostasis followed by oxidative damage and reduced energy production in muscle cells. Puldysa is capable of restoring cellular energy by stimulating the mitochondrial electron transport chain and reduces the level of oxidative stress.

Vamorolone (NEW) – Novel steroid replacement in DMD without typical side effects

Vamorolone is an excellent strategic fit to Santhera's DMD portfolio and complements Raxone in treating DMD patients irrespective of their underlying genetic mutation. Potentially both drugs could be used in combination. Vamorolone is targeted to replace current glucocorticoid treatment used to preserve muscle strength, however, without the typical steroid safety issues. We forecast peak sales to amount to CHF 550+ mn.

Rationale for vamorolone in DMD

Vamorolone is a novel first-in-class dissociative steroidal anti-inflammatory compound and is a close analog to prednisone, a standard glucocorticoid, however,

without the typical steroid side effects such growth stunting, facial puffiness, weight increase, cough and unwanted hair growth. Vamorolone binds to the glucocorticoid receptor (GR) and activates the anti-inflammatory (NFkB) “non-genomic” pathway as vamorolone/GR monomer (anti-inflammatory response), but does not activate gene transcription, the “genomic” pathway and therefore does not form vamorolone/GR dimers (side effects). The differential activation of GR-mediated pathways results in therapeutic (anti-inflammatory) activity but does not activate the pathway associated with glucocorticoid-class side effects (GR dimers). Moreover, vamorolone is an antagonist for mineralocorticoid receptor adding to the favorable safety profile compared to glucocorticoids.

POL6014 (NEW) – Blockbuster potential in cystic fibrosis & rare lung disease

Cystic fibrosis is a rare, genetic progressive and life-threatening disease affecting approximately 70,000 patients in the US and Europe. There is no cure for cystic fibrosis. The disease is characterized by persistent lung infection and chronic inflammation. Long-term issues include difficulty breathing and coughing up thick and sticky mucus as a result of frequent lung infections. The average life expectancy is between 42 and 50 years, where lung problems account for death in ~80% of cystic fibrosis patients. We believe POL6014 could achieve peak sales of CHF 1 bn in cystic fibrosis alone. We have not included forecasts for POL6014 in cystic fibrosis due to the early development stage

Rationale for POL6014 in cystic fibrosis

POL6014 is a novel, highly potent, selective and reversible inhibitor of human neutrophil elastase (hNE), one of the major lung-tissue degrading enzymes under pathological conditions and leading to respiratory decline and exacerbations in cystic fibrosis patients. Chronic inflammation is thought to be caused by neutrophil elastase from neutrophils present in the lung due to the buildup of thick mucus. High levels of hNE have been detected in cystic fibrosis sputa and these high levels of hNE correlate with disease severity and measured by functional lung parameters such as FEV1 reduction and are therefore important surrogate markers of disease.

In the following sections we will provide an in-depth analysis and forecasts for Santhera's key drivers, including:

- **Puldysa in DMD**
- **Vamorolone in DMD**
- **Raxone in LHON (non-core)**
- **Early stage pipeline projects** (POL6014 (NEW), omigapil, LAMA2-MD gene therapy (NEW); not included in our forecasts, yet)

Forecasts & Sensitivity Analysis

Puldysa (Duchenne Muscular Dystrophy)

Product Analysis

Puldysa total DMD peak sales of CHF 800 mn - rNPV of CHF 52 per share

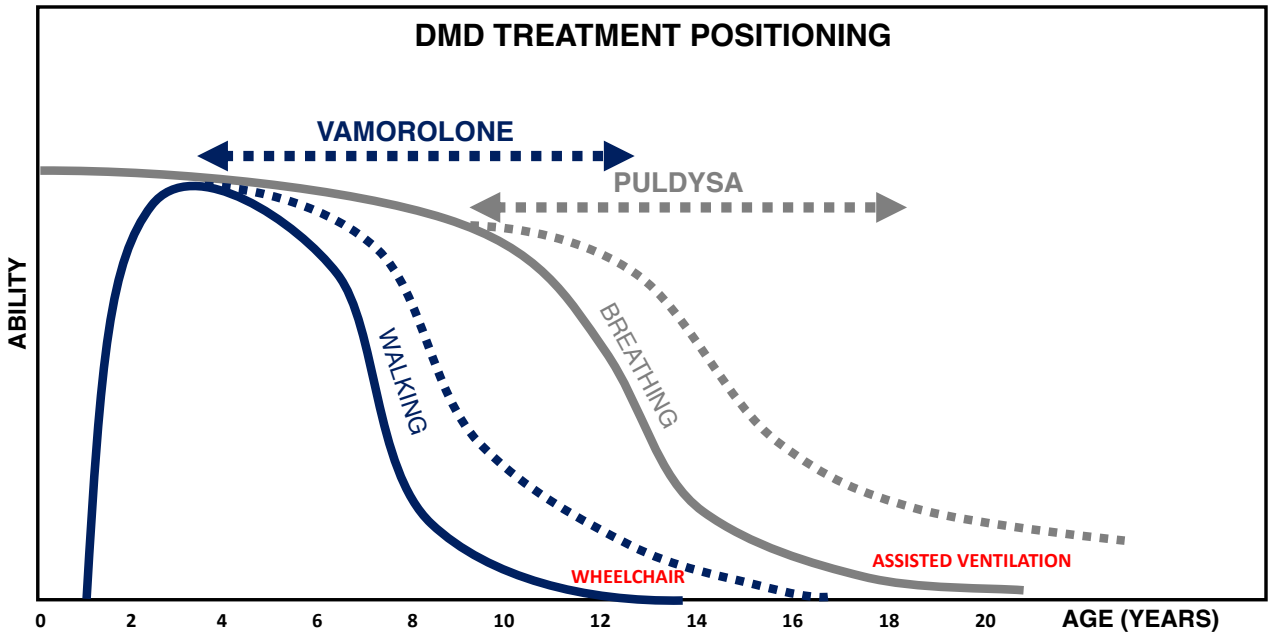
DMD (non-steroid patients), CHF 350 mn peak sales; rNPV of CHF 24/share:
We forecast peak sales of CHF 357 mn for Puldysa in DMD patients not treated with steroids (~40% of eligible patients) assuming EU conditional approval and launch in 2020, US approval and launch in 2022 and orphan drug market exclusivity until Q3 2025 (EU/ROW) and 2029 (US). We assume an annual treatment cost between EUR 62,415 (EU/ROW) and USD 90,000 (US), and a market penetration up to ~60% in eligible DMD patients not treated with steroids. Our rNPV amounts to CHF 364 mn, or CHF 24 per share, accounting for COGS (10%), M&S costs, a distributor transfer price (60-70% of wholesale price) outside its own sales territories in Europe and the US, with a 72.5% success rate, the average of EU (80% filing) and US (65% phase III), and a WACC of 7% (for details see page 30).

DMD (steroid patients), CHF 400+ mn peak sales; rNPV of CHF 28/share:
We forecast peak sales of CHF 442 mn for Puldysa in DMD patients treated with steroids (~60% of eligible patients) assuming US and EU launch in 2022 and a market penetration up to 40%. Using similar pricing assumptions as for Puldysa in DMD patients not treated with steroids, "SIDEROS" development costs of approximately CHF 30 mn, significantly lower M&S costs as much of the sales infrastructure has been established with the rollout of Puldysa in DMD non-steroid patients and vamorolone in DMD, and a 65% (phase III) success rate, our rNPV amounts to CHF 472 mn, or CHF 28 per share (for details see page 31)

Towards market leadership in DMD with Puldysa & vamorolone

With the purchase of the option to in-license the global rights (excluding Japan/South Korea) for vamorolone in all indications from Idorsia in November 2018, Santhera could become the undisputed market leader in DMD with two treatments, Puldysa and vamorolone targeting the vast majority of patients at all disease stages. Vamorolone is a first-in-class dissociative steroid targeted at replacing mainstay glucosteroids in DMD such as prednisone and deflazacort, which have side effects that hamper long-term use. Vamorolone is an excellent strategic fit with Puldysa. Vamorolone can be given to DMD patients with early- to mid-stage disease to preserve muscle function, while Puldysa can be given patients with mid- to late stage disease with breathing difficulty to preserve respiratory function. Both drugs can be given to DMD patients irrespective of the underlying genetic mutation with the potential of combination therapy (including PTC Therapeutics' Translarna and Sarepta's EXONDYS 51). Moreover, vamorolone and Puldysa have been developed for chronic treatment in DMD, both with an excellent safety and tolerability profile.

We conservatively forecast combined peak sales of Puldysa and vamorolone to reach CHF 1.4 bn.



SOURCE: VALUATIONLAB

2020 a critical turning point with EU approval of Puldysa and vamorolone results
Santhera's aim is to have both DMD drugs on the market as soon as possible according to the following development strategy and schedule:

Puldysa (DMD patients with mid- to late-stage disease):

EU: seek conditional approval for DMD patients not treated with steroids based on single "DELOS" phase III trial supported by positive long term data from the "SYROS" trial; EU CMA filed May 2019; conditional approval mid 2020; EU launch Q3 2020; regular approval (including DMD patients treated with steroids) will be sought after "SIDEROS" results become available, launch Q4 2022

US: seek regular approval for all DMD patients based on two phase III trials, the "DELOS" & "SIDEROS" trial; "SIDEROS" top line results mid 2021; filing Q4 2021, approval Q3 2022, launch Q4 2022

Vamorolone (DMD patients with early- to mid-stage disease):

US: seek accelerated approval based on the single "VISION-DMD" phase IIb trial deemed pivotal; "VISION-DMD" top line results mid 2020; NDA filing (fast-track review) Q4 2020, accelerated approval Q3 2021, launch Q4 2021

EU: seek conditional approval based on single "VISION-DMD" phase IIb trial deemed pivotal; "VISION-DMD" top line results mid 2020; CMA filing Q1 2021, conditional approval Q1 2022; launch Q2 2022

As stated, 2020 will be a critical turning point for Santhera with the anticipated EU conditional approval of Puldysa in DMD patients not treated with steroids and the top line results of the "VISION-DMD" pivotal trial of vamorolone, which is the basis for accelerated approval in the US and conditional approval in the EU.

Puldysa most advanced and undervalued late stage DMD drug

Puldysa is currently the most advanced DMD drug in development that has shown efficacy, safety and good tolerability in a well-controlled phase III trial. DMD is an inherited and fatal muscle wasting disease that affects boys at an early age and worsens quickly with a life expectancy of around 30 years. Santhera has developed a rigorous phase III

development program for approval of Puldysa in all DMD patients that experience breathing difficulty, irrespective of concomitant steroid treatment.

Puldysa's late stage clinical development program consists of two phase III trials:

1. **"DELOS"** in 64 DMD patients aged 10-18 years not treated with mainstay steroids, >90% could not walk; primary endpoint met in delaying the loss of expiratory respiratory function (peak expiratory flow percentage predicted, PEF%p) after 12 months treatment with Puldysa compared to placebo (for details see page 22)
2. **"SIDEROS"** second confirmatory phase III trial enrolling approximately 266 DMD patients aged 10 years and older with treatment extended to patients on mainstay steroids; primary endpoint of delaying the loss of respiratory function (forced vital capacity percent predicted, FVC%p) after 78 weeks treatment of Puldysa compared to placebo; top line results anticipated mid 2021 (for details see page 26)

Puldysa is the only DMD drug that has shown positive phase III results in the "DELOS" trial to date. In the "DELOS" trial patients were not on concomitant steroid treatment. Raxone significantly delayed the rate of lung function loss in DMD patients after one-year treatment compared to placebo and therefore showed efficacy in a clinically relevant endpoint. Lung function loss is the main cause of premature morbidity and mortality in DMD patients.

EU conditional approval expected mid 2020 based on strengthened data package
In May 2019, a CMA (conditional marketing authorization) was filed in the EU for approval of Puldysa in DMD patients not treated with steroids based on the phase II "DELPHI" trial, the long-term "DELPHI-Extension" trial, the pivotal phase III "DELOS" trial, the open-label long-term "SYROS" trial, a collection of long-term data from patients who completed the "DELOS" trial and continued treatment with Puldysa for up to six years.

The strengthened data package follows the advice of the CHMP (Committee for Medicinal Products for Human Use) that issued a negative opinion in September 2017, which was maintained in an appeal in January 2018. The CHMP concluded that approval for Puldysa in DMD, applied as a Type II variation of the existing marketing authorization in LHON, which did not allow for a conditional regulatory pathway at the time, could not be granted based on the data presented then. Although the positive outcome of the phase III "DELOS" trial was acknowledged, the CHMP invited Santhera to present additional data to further link the observed treatment effects on respiratory function outcomes to patient benefit. Importantly, the CHMP also supported the intended indication for Puldysa to slow the decline of respiratory function in patients with DMD who are currently not taking glucocorticoids. Santhera has now strengthened the clinical data package through the open label long term "SYROS" trial, further analyses and natural history studies linking the treatment effects of Puldysa on respiratory outcomes to patient benefit. No additional clinical trials were needed. Additional data from the US Expanded Access Program also contributed to the data package.

EU conditional approval in DMD patients not treated with steroids is now expected in mid 2020. Santhera will launch and market Puldysa in the key EU markets with the same dedicated specialist sales force that it built up to commercialize Raxone in LHON.

Regular approval route in the US opposed to typical accelerated approval in DMD

In the US, Santhera aims to file for regular approval of Puldysa. Regular approval is based on two positive phase III trials, opposed to the accelerated approval route based on a single pivotal phase III trial, which is generally available for treatments of high unmet medical need such as DMD. This follows the unexpected FDA advice in July 2016 that Santhera should not file Puldysa for accelerated approval for treating DMD patients who are not on steroids (approximately 40% of eligible patients) based solely on the positive phase III "DELOS" trial. The company was advised to wait for the outcome of the second confirmatory phase III "SIDEROS" trial in DMD patients treated with steroids (approximately 60% of eligible patients), which had already started, before filing in the US. "SIDEROS" is expected to report top line results mid 2021. US filing of Puldysa in DMD patients, irrespective of steroid use, is now expected in Q4 2021 with approval and launch in 2022.

DMD landscape affected by new DMD drugs based on negative or questionable data

In recent years, the DMD landscape has changed dramatically, from no specific treatment for DMD, except for the off-label use of steroids such as prednisone or deflazacort (not generically available in the US), to several new specific treatments for DMD. Currently, there is one approved DMD treatment in the EU, PTC Therapeutics' Translarna (ataluren), a stop codon read through therapy; and two in the US, Sarepta's EXONDYS 51, an exon-51 skipping therapy, and PTC Therapeutics' Emflaza, a branded version of the steroid deflazacort.

Important to note, the conditional approval of Translarna in the EU in 2014 and the accelerated approval of EXONDYS 51 in 2016 in the US were based on a negative single phase III trial and a questionable single phase II trial, respectively. Emflaza received accelerated approval in the US based on a positive *and* a negative phase III trial.

LATE STAGE DUCHENNE MUSCULAR DYSTROPHY LANDSCAPE

BRAND GENERIC NAME COMPANY (COUNTRY) 2018 SALES MARKET CAPITALIZATION (20.11.2018)	**RAXONE** IDEBENONE SANTHERA (SWITZERLAND) EU LAUNCH 2020 CHF 155 MN	**TRANSLARNA** ATALUREN PTC THERAPEUTICS (US) USD 171 MN USD 1.6 BN	**EXONDYS 51** ETEPLIRSEN SAREPTA THERAPEUTICS (US) USD 301 MN USD 8.4 BN	**EMFLAZA** DEFLAZACORT PTC THERAPEUTICS (US) USD 92 MN USD 1.6 BN	**VAMOROLONE** VAMOROLONE SANTHERA/REVERAGEN US LAUNCH 2021 CHF 155 MN
CLASS	SHORT-CHAIN BENZOQUINONE	STOP CODON READTHROUGH THERAPY	EXON 51 SKIPPING	GLUCOCORTICOSTEROID	DISSOCIATIVE GLUCOSTEROID
ADMINISTRATION	ORAL (3X DAILY)	ORAL (3X DAILY)	1-HOUR INFUSION (1X WEEKLY)	ORAL (1X DAILY)	ORAL (1X DAILY)
ELIGIBLE DMD PATIENTS (%)	UP TO ~100%	~13% (NON-SENSE MUTATION)	~13% (EXON-51)	UP TO ~100%	UP TO ~100%
STATUS (UNITED STATES)	**FILING Q4 2021**	**COMPLETE RESPONSE LETTER**	**ACCELERATED APPROVAL**	**ACCELERATED APPROVAL**	**PHASE IIB PIVOTAL TRIAL**
STATUS (EUROPEAN UNION)	**CMA FILED MAY 2019**	**CONDITIONAL APPROVAL**	**NEGATIVE CHMP RE-EXAMINATION**	**GENERICALLY AVAILABLE**	**PHASE IIB PIVOTAL TRIAL**
PIVOTAL TRIAL	**"DELOS" PHASE III TRIAL**	**"ACT DMD" PHASE III TRIAL**	**"STUDY 201/202" PHASE II TRIAL**	**PHASE III TRIAL**	**"VISION-DMD" PHASE IIB TRIAL**
NUMBER OF PATIENTS	64	228	12	196	120
ABILITY TO WALK (%)	8%	100%	100%	100%	100%
AGE (YEARS)	10-18	7-16	7-13	5-15	5-<7
TREATMENT TIME (WEEKS)	52	48	24 (STUDY 201); 180 (STUDY 202)	52 (STUDY 1); 104 (STUDY 2)	24 (PERIOD #1); 20 (PERIOD #2)
PRIMARY ENDPOINT	PEAK EXPIRATORY FLOW (CLINICAL ENDPOINT)	6-MINUTE WALK TEST (CLINICAL ENDPOINT)	CHANGE IN NUMBER OF DYSTROPHIN POSITIVE FIBERS (SURROGATE ENDPOINT)	CHANGE IN AVERAGE MUSCLE STRENGTH SCORE (18 MUSCLE GROUPS)	MUSCLE FUNCTION BY TIME TO STAND; BODY WEIGHT BY BMI
RESULT	**POSITIVE**	**NEGATIVE**	**DISPUTED BY FDA REVIEWERS**	**POSITIVE STUDY 1 ; NEG. STUDY 2**	**RESULTS DUE MID 2020**
DIFFERENCE VS. PLACEBO	6.27 (71% REDUCTION IN LOSS OF PEF%P)	15 M VS. PLACEBO	SRPT: +23% (WK24); +52% (WK 48) FDA: +13% (WK 24); + ~4% (WK 180)	STUDY 1: 0.15 EMFLAZA 0.9 MG/KG/DAY VS. -0.10 PLACEBO	DIFFERENCE VS. PREDNISON & PLACEBO
P-VALUE	0.03	0.213	N.A. FOR FDA RE-ANALYZED DATA	0.017 (ONLY STUDY 1)	TBD
SIDE EFFECTS	WELL TOLERATED, SIDE EFFECTS SIMILAR OR LESS THAN PLACEBO	HEADACHE, NAUSEA, INCREASES IN CHOLESTEROL & CREATININE	SAMPLE SIZE TOO SMALL TO DETERMINE SIDE EFFECTS	MOON FACE, WEIGHT GAIN, INFECTIONS, FACIAL HAIR GROWTH	AIM LESS STEROID SIDE EFFECTS E.G. MOON FACE, WEIGHT GAIN
FDA REQUIREMENTS FOR FILING FOR ACCELERATED APPROVAL (REGULATORY PATHWAY TO SPEED AVAILABILITY OF DRUGS FOR SERIOUS UNMET NEED)					
TRIAL PROVIDES MEANINGFUL ADVANTAGE OVER CURRENT THERAPY	✓	✗	✗	✓	TBD
USED CLINICAL ENDPOINT THAT DIRECTLY MEASURES A THERAPEUTIC EFFECT	✓	✓	✓	✓	✓
USED SURROGATE ENDPOINT REASONABLY LIKELY TO PREDICT CLINICAL BENEFIT			?		
PROVIDED RIGOROUS BLINDING AND CONTROL PROCEDURES	✓	✓	✗	✓	✓
CONDUCT NATURAL HISTORY TRIALS BEFORE CLINICAL TRIALS BEGIN	✓		✗	✗	✗
CONFIRMATORY TRIAL SHOULD BE STARTED BEFORE ACCELERATED APPROVAL IS GRANTED	✓	✗	✗	✗	✗

* CRL = COMPLETE RESPONSE LETTER; **MAA = MARKETING AUTHORIZATION APPLICATION

SOURCE: VALUATIONLAB, FDA, EMA, COMPANY DATA

We believe the questionable approvals in the recent past have led to a more rigorous stance for new DMD drug applications by the regulatory authorities in both the US and EU.

Translarna conditional approval still upheld in the EU – turned down in the US
After Translarna's second confirmatory phase III proved negative, PTC Therapeutics now has to request each year for an annual review and renewal of EU marketing authorization with a specific obligation to conduct a confirmatory phase III trial, dubbed "Study 041", to be submitted to the EMA by the end of Q3 2021. In February 2019, together with authorization renewal request to the EMA, the company filed for an extension of this term by a year due to slow enrolment. Translarna generated USD 171 mn sales in 2018.

In the US, PTC Therapeutics has not been successful in convincing the FDA to approve Translarna. In October 2017, PTC Therapeutics received a Complete Response Letter from the FDA for its new application of Translarna for the treatment of nonsense mutation DMD. The FDA stated that it was unable to approve the application in its current form and that evidence of the effectiveness from an additional adequate and well-controlled clinical trial(s) will be necessary at a minimum to provide substantial evidence of effectiveness. PTC Therapeutics filed a formal dispute resolution request challenging the FDA decision.

EXONDYS 51 approved on personal title of the CDER Director overruling own staff
In a surprise move, the FDA'S Director of the CDER, Janet Woodcock, granted accelerated approval for Sarepta Therapeutics' eteplirsen (branded EXONDYS 51) in September 2016. She overruled her own scientific review staff's advice, as well as an external Advisory Committee of experts that voted against approval, leading to a fallout of key staff at the FDA and questioning the high scientific standard to receive accelerated approval for a rare disease in the US.

EXONDYS 51 received a harsh review by the FDA staff concluding, "The data overall did not provide statistical evidence to support the efficacy in subjects who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping". The FDA questioned the methodology used to measure dystrophin positive fibers, and therefore the results presented by Sarepta, as well as the small patient sample size. In April 2016, the Advisory Committee of independent experts voted 3-7, with three abstentions, against "finding substantial evidence based on the clinical results of the single historically controlled study (Study "201/202") that EXONDYS 51 is effective for treatment of DMD."

Although a clinical benefit has not yet been established, Sarepta was allowed to sell EXONDYS 51 in the US for the treatment of DMD in patients who have a confirmed mutation in the DMD gene that is amendable to exon 51 skipping. Continued approval is contingent upon verification of a clinical benefit in confirmatory trials. We believe this will be difficult to perform now EXONDYS 51 has been approved. The annual treatment cost is priced at approximately USD 300,000 for a patient weighing 25 kilograms.

Nevertheless, 2018 sales for EXONDYS 51 amounted to a staggering USD 301 mn, despite that the drug faces reimbursement issues in the US, where several major insurers refuse to reimburse the USD ~300,000 annual treatment cost per patient and qualify the drug as a "scientific elegant placebo" questioning the efficacy and safety.

Emflaza acquired by PTC Therapeutics – US launch was far from smooth
Marathon Pharmaceutical's Emflaza (deflazacort) became the first steroid that the FDA approved to treat all forms of DMD in patients of 5 years and older in February 2017. In the US, physicians typically prescribe the steroid prednisone off-label for treating young DMD patients to prevent muscle deterioration. Deflazacort was never approved in the US

despite being widely generically available in the EU and large parts of the world. Emflaza has the typical steroid side effects, including facial puffiness (30% of patients), weight increase (20%), increased appetite (14%), upper respiratory tract infections (12%), cough (12%), frequent daytime urination (12%), and unwanted hair growth (10%), among others.

Emflaza's US launch was far from smooth. PTC Therapeutics bought the rights from Marathon in April 2017 in the midst of controversy over its price, for an upfront of USD 140 mn and low- to mid-20's percentage of net sales, with the option to receive a single USD 50 mn sales-based milestone. PTC Therapeutics cut Marathon's initial USD 89,000 annual treatment cost per patient to around USD 35,000. However, the USD 35,000 annual estimate applies to boys who weigh up to 25 kg and increases significantly for older boys that weigh far more. Emflaza pricing continues to cause controversy, because its active ingredient is generically available as deflazacort outside the US at a considerably lower annual treatment cost per patient of around USD 1,200. FY 2018 sales for Emflaza amounted to USD 92 mn.

Puldysa better positioned – potentially for all eligible DMD patients and as a combo

We believe that Puldysa is better positioned than genetically based approaches as Puldysa can be given to all DMD patients irrespective of their genetic mutation and disease status (ambulatory/non-ambulatory). No expensive genetic testing is required. Translarna's use is limited to those patients with nonsense mutation DMD, which affects roughly 13% of the DMD population. A genetic test is needed to diagnose nonsense mutation patients before start of therapy. This is also the case with Sarepta's EXONDYS 51 that targets a limited population of roughly 13% of DMD patients who are amendable to exon-51 skipping. In the "DELOS" trial Puldysa was assessed in patients irrespective of the underlying dystrophin gene mutation who did not use concomitant steroids. The patient's steroid status could become irrelevant if "SIDEROS" results are positive in this DMD population. Due to its different mechanism of action and benign side effect profile, Puldysa is complementary to these genetic drugs and has the potential to be given in combination. Puldysa could also be used in combination with PTC's Emflaza or newly developed steroids with a better safety profile such as vamorolone, a first-in-class dissociative steroid, which Santhera acquired the option to the global rights (excluding Japan/South Korea) from Idorsia in November 2018.

Other DMD drugs lack proof of efficacy in wheelchair patients due to endpoint

Translarna, and the other DMD drugs, used the 6-minute walk test (6-MWT) as their primary endpoint, to monitor the delay in exercise tolerability. As a result, later stage DMD patients, who are wheelchair bound, have not been tested for efficacy. Puldysa was predominantly tested in later stage patients, the majority of whom were non-ambulatory. A lung function test (PEF – peak expiratory flow) was used as primary endpoint and other lung function tests as supportive secondary endpoints. These endpoints can be applied to all patients, while they also address the main cause of premature morbidity and mortality in DMD - the progressive loss in lung function.

Clinical data "DELOS" first-ever positive phase III trial in DMD

Santhera's "DELOS" trial is the first-ever positive pivotal phase III trial in DMD. The "DELOS" study (DuchEnne Muscular Dystrophy Long-term IdebenOne Study) was a 52-week, multi-center (US and Europe), double-blind, and randomized, placebo-controlled trial in DMD. There were 64 DMD patients aged 10 to 18 years at baseline enrolled and

treated with Puldysa or placebo. There was no selection for mutational status and patients had to be off chronic steroids. The overwhelming majority of patients (92%) could not walk at enrolment (non-ambulatory) and were confined to a wheelchair. Puldysa (idebenone) was dosed at 900 mg/day (two 150 mg oral tablets given three times daily).

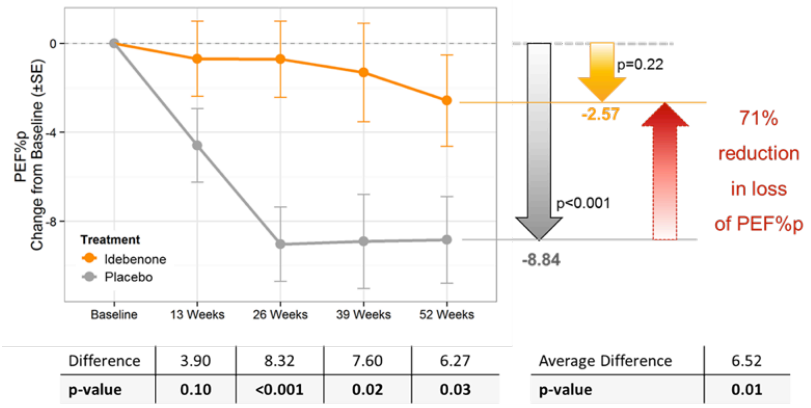
Respiratory function endpoints address the main cause of premature death

The objective of the trial was to delay the loss of lung function in Puldysa treated patients compared to placebo. DMD causes progressive weakness in the muscles of the lungs, which leads to a restrictive pulmonary syndrome, and ultimately premature death. The change in respiratory function measured by Peak Expiratory Flow percent predicted (PEF%p), from baseline to week 52, was chosen as the primary endpoint. Secondary endpoints included other respiratory parameters, muscle strength and motor function, as well as quality of life. The selection of respiratory function primary and secondary endpoints differs from the 6-minute walk test others used in their DMD trials with a younger population who are still capable of walking.

Primary endpoint met – clinically meaningful delay in lung function loss

For all randomized and treated patients, the change in PEF%p measured between baseline and week 52 showed a statistically significant decline by 8.8% in the placebo arm (N=33). On the other hand, no statistically significant worsening was observed in the Puldysa treated group (N=31). The decline was reduced by ~70% resulting in a change of only of 2.6% from baseline.

Peak Expiratory Flow percent predicted



Difference	3.90	8.32	7.60	6.27	Average Difference	6.52
p-value	**0.10**	**<0.001**	**0.02**	**0.03**	**p-value**	**0.01**

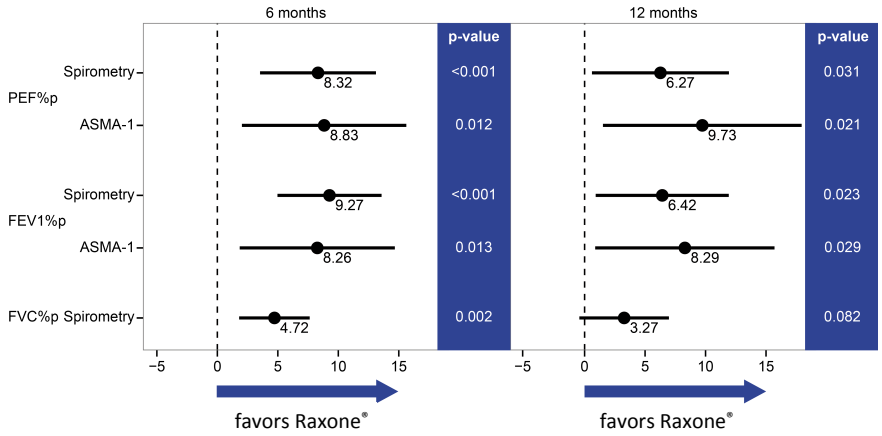
Source: Santhera Pharmaceuticals

The difference between treatment groups at week 52 was 6.3% (p=0.03). As can be seen in the graph above, the change in PEF%p from baseline was already statistically significant at week 26 (p<0.001). The average difference over the entire treatment period was clinically meaningful at 6.5% with a p-value of 0.01.

Secondary endpoints consistent with primary endpoint across all parameters

Similar positive effects were seen in other key endpoints tracking lung function. Multiple lung function tests favor the use of Puldysa (previously branded Raxone), demonstrating a consistent effect as can be seen in the chart below. For instance, the change in Forced Vital Capacity as percent predicted (FVC%p), a clinically relevant secondary endpoint, showed a difference between treatment groups of 4.72% (p=0.002) at week 26 and of 3.27% (p=0.08) at week 52. The change in Forced Expiratory Volume 1 percent predicted

(FEV1%p) led to a difference between treatment groups of 8.26% (p=0.01) at week 26 and 8.29% (p=0.03) at week 52. The consistent results of these supportive lung function endpoints bode well for EU and US approval, in our view.



Source: Santhera Pharmaceuticals

Additional data analyses completed in Q4 2015 in support of regulatory filings

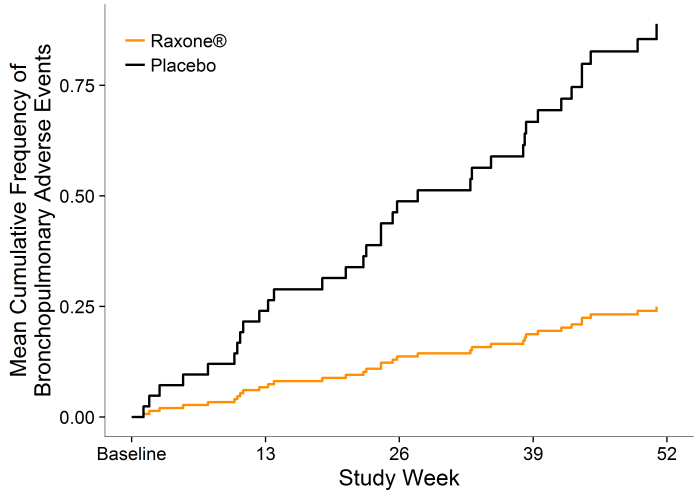
Following early discussions with the FDA in 2015, Santhera completed the following analyses and reports:

- Significant correlations between Peak Expiratory Flow (PEF), the primary endpoint of the "DELOS" trial, and Forced Vital Capacity (FVC), a well-validated marker of irreversible morbidity and mortality in DMD, and incidence of severe respiratory events, confirming the relevance of PEF as an intermediate clinical endpoint.
- Comprehensive demonstration of the robustness of the positive outcome of the "DELOS" trial by excluding the effect of potential imbalances in baseline demographics, previous steroid use and dropouts on the overall outcome.
- Additional analyses of the "DELOS" trial outcome demonstrating effect of Puldysa on bronchopulmonary events (including airway infections). The resulting hazard ratio for the number of patients reporting at least one bronchopulmonary event was 0.332 (95% CI: 0.131, 0.843; p = 0.020) and 0.271 (95% CI: 0.118, 0.623; p = 0.002) for the total cumulative number of events in favor of Puldysa treatment. Similar analysis of systemic antibiotic use showed that patients treated with Puldysa clearly used less antibiotics compared to patients receiving placebo.

BRONCHOPULMONARY ADVERSE EVENTS	PULDYSA (N=31) EVENT COUNT [PATIENT COUNT]	PLACEBO (N=31) EVENT COUNT [PATIENT COUNT]	FISHER'S EXACT TEST
TOTAL BRONCHOPULMONARY ADVERSE EVENTS	**7 [6]**	**28 [17]**	**P = 0.0096**
UPPER RESPIRATORY TRACT INFECTION	2 [2]	10 [6]	
BRONCHITIS	5 [4]	5 [5]	
PNEUMONIA		3 [2]	
COUGH		2 [2]	
INFLUENZA		2 [2]	
VIRAL INFECTION		2 [2]	
ACUTE RESPIRATORY FAILURE		1	
DYSPNEA		1	
LARYNGITIS		1	
RESPIRATORY FAILURE		1	

SOURCE: VALUATIONLAB, SANTHERA PHARMACEUTICALS

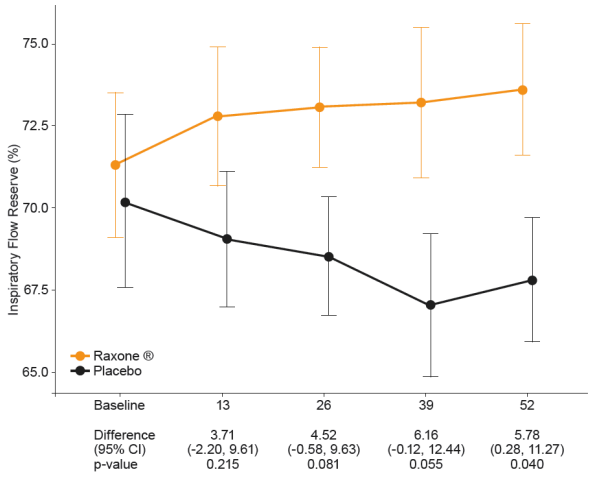
Mean Cumulative Frequency of Bronchopulmonary AE's



Source: Santhera Pharmaceuticals

- While previous published results from the DELOS trial focused on expiratory muscle function in patients with DMD, new data demonstrate also positive effect of Puldysa on inspiratory muscle function. Specifically, Puldysa compared to placebo stabilized the maximum inspiratory flow based on the measurement of inspiratory flow reserve and inspiratory forced vital capacity over the 52-week study period.

Impact on Inspiratory Flow Reserve (%)



Source: Santhera Pharmaceuticals

- The first successful comparison of the outcomes for a clinical trial population ("DELOS") with the outcomes for a natural history population (CINRG) matched patient-by-patient to the "DELOS" population. For this external validation of the "DELOS" study findings, CINRG compared the annual rate of change in PEF%p in its natural history population with that seen in "DELOS". CINRG identified a matched patient for each "DELOS" patient by considering the baseline PEF%p value, previous use of steroids and the age of the patient. The matching and comparison were based on a prospective analysis plan prepared by CINRG in collaboration with Santhera and resulted in comparable baseline characteristics of the CINRG patients and the "DELOS" patients. The analysis of the longitudinal data met the pre-specified criterion of showing that the annual decline among the untreated CINRG natural history patients in PEF%p was at -6.3% (95% CI: -10.6%

to -2.0%) closer to the decline of the placebo-treated "DELOS" patients at -8.5% (95% CI: -12.8% to -4.2%) than the change in those treated with Puldysa -2.4% (95% CI: -6.5% to 1.7%).

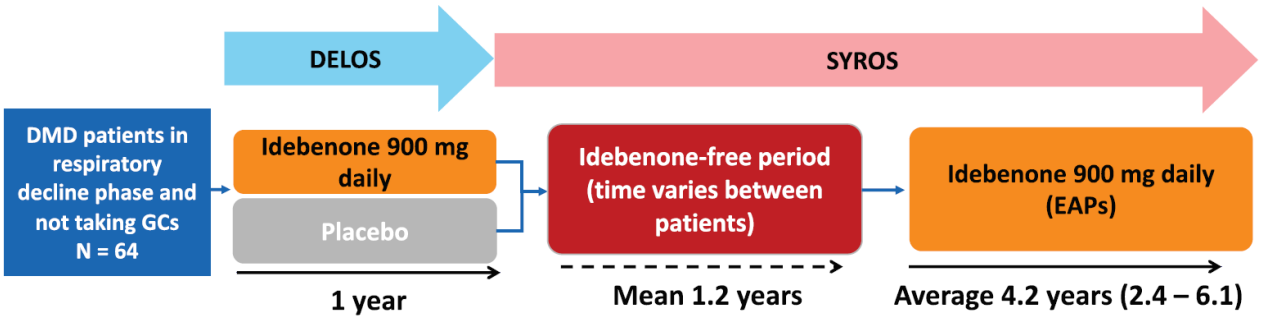
New data further supports clinical relevance of PEF & links Puldysa with outcomes

New data further supports the clinical relevance of PEF (peak expiratory flow) - a primary endpoint in the positive phase III "DELOS" trial - and provides a link between the treatment of Puldysa observed in "DELOS" and measures of disease progression. The new data shows that:

- PEF%p (peak expiratory flow as percent predicted) is a sensitive and early marker of respiratory function decline in DMD applicable over a wide range
- PEF and FVC (forced vital capacity) are predictors of time to clinically relevant events including time to hospitalization due to respiratory causes, time to initiation of assisted ventilation and death
- Comparative analysis of the outcome of "DELOS" and data from natural history studies allows the extrapolation of the observed treatment benefit of Puldysa in PEF%p. The treatment effect with Puldysa in "DELOS" can be linked to a delay in the initiation of assisted ventilation by 3 years, which is of high clinical relevance

"SYROS" shows Puldysa reduces decline in lung function loss for up to 6 years

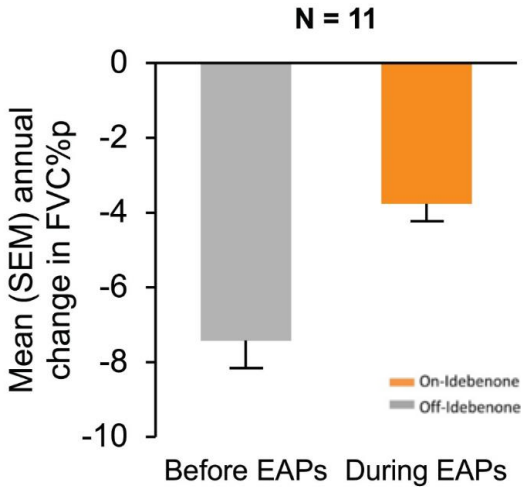
In February 2019, Santhera announced positive results of the "SYROS" trial. The "SYROS" trial was a prospectively planned collection of long-term, retrospective real-world data from patients who completed the positive phase III "DELOS" trial (18 out of 64) and were subsequently treated with Puldysa (idebenone) 900 mg/day for on average 4.2 years (range 2.4-6.1 years) under Expanded Access Programs (EAPs). The primary objective of the trial was to evaluate the long-term progression of respiratory function in patients who maintained treatment with Puldysa for up to 6 years compared to their preceding off-Puldysa period.



Source: Santhera Pharmaceuticals

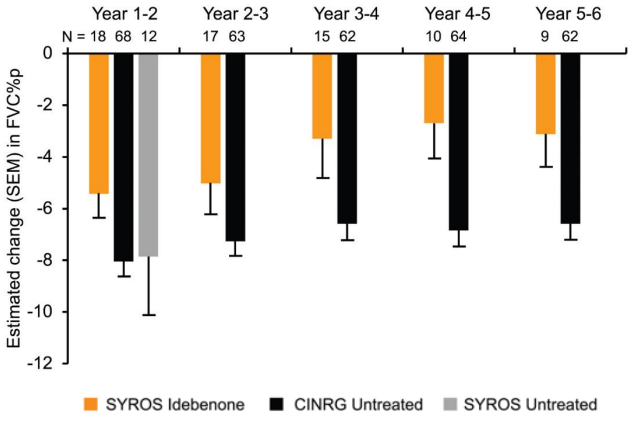
The result of the "SYROS" trial, which is consistent with outcomes from the pivotal "DELOS" trial, demonstrated that:

- Switching to and maintaining long-term treatment with Puldysa reduced the annual rate of decline in forced vital capacity percent of predicted (FVC%p) by 50%.



Source: Santhera Pharmaceuticals

- The treatment effect was consistently maintained year-on-year for up to 6 years: the annual decline in FVC%p in patients on Puldysa was consistently smaller than in untreated patients from a matched external control group (from CINRG Duchenne natural history study)



Source: Santhera Pharmaceuticals

These findings are further supported by consistent reductions in the rate of both inspiratory and expiratory respiratory function loss over the same period. Prolonged treatment with Puldysa also reduced the risk of important patient-relevant outcomes, including bronchopulmonary adverse events and hospitalizations due to respiratory causes.

Extensive data supports EU conditional approval of Puldysa in DMD (non-steroids)

We believe the extensive data package for Puldysa as discussed above, including the phase II "DELPHI" trial, the long-term "DELPHI-Extension" trial, the pivotal phase III "DELOS" trial, the open-label long-term "SYROS" trial, a collection of long-term data from patients who completed the "DELOS" trial and continued treatment with Puldysa for up to six years, supports conditional approval of Puldysa for the treatment of respiratory dysfunction in DMD patients who are not using steroids in the EU. This is anticipated mid

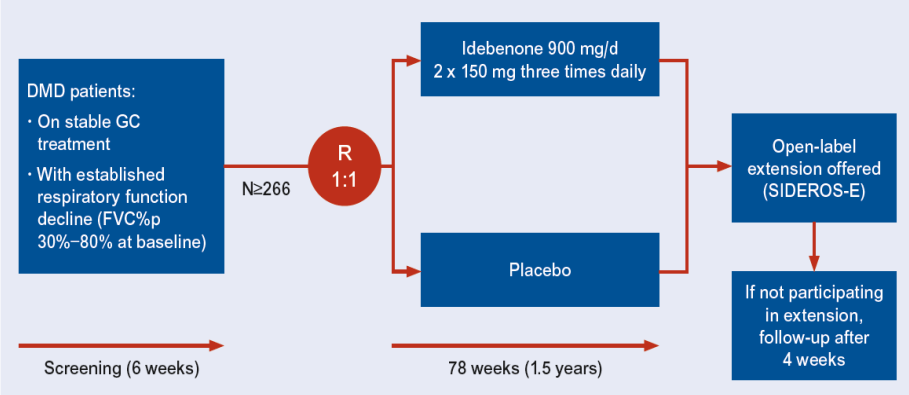
2020. This extended data package will be integrated for use in the US regulatory filing and extended with the findings of the second confirmatory pivotal phase III "SIDEROS" trial.

"SIDEROS" DMD trial planned to expand Puldysa use beyond non-steroid patients

In September 2016, Santhera started the phase III "SIDEROS" clinical trial to investigate whether Puldysa treatment could also slow respiratory function loss in DMD patients treated with steroids, a population previously not included in the successful "DELOS" trial. The "SIDEROS" trial was planned based on CINRG natural history data demonstrating that at a certain stage of disease progression patients on glucocorticoid steroids will experience the same rate of respiratory function loss as patients not using steroids, presenting an urgent medical need for treatment.

Patients who will be eligible to enroll will have already started to decline on respiratory function whilst on stable steroid treatment. Trial participants will receive either Puldysa (idebenone) 900 mg/day or placebo for the duration of 78 weeks (18 months). The trial targets to enroll approximately 266 DMD patients. To date, the trial has enrolled 214 patients at approximately 60 clinical trial sites in Europe, the US and Israel, with patient recruitment expected to complete in Q4 2019. Eligible patients who complete "SIDEROS" are offered to enroll in the open-label "SIDEROS-Extension" trial. Topline results of "SIDEROS" are expected in mid 2021.

"SIDEROS" Clinical Trial Design



SOURCE: SANTHERA PHARMACEUTICALS

Competitive pricing of Raxone should lead to broad acceptance and rapid uptake

In our view, Puldysa will be priced very competitively for an orphan drug. We assume an average annual DMD treatment price in Europe of EUR 62,415 and USD 90,000 in the US, similar to the pricing for Raxone in LHON. Santhera's "acceptable" pricing strategy should lead to broad acceptance of the drug across the globe; enhance pricing negotiations, reimbursement and ultimately uptake. In comparison, PTC Therapeutics' Translarna and Sarepta's EXONDYS 51 have an annual treatment cost of USD ~300,000 per patient (excluding genetic diagnostic testing).

Using LHON sales infrastructure and building US presence to enhance profits

Santhera plans to sell Puldysa in DMD through the same sales infrastructure set up to market Raxone in LHON (i.e. 4 selected regional clusters in Europe), and to build an own sales organization in the US upon accelerated approval of vamorolone in the US in 2021. Santhera will seek distributors in other territories, who will sell the drugs at a discounted distributor transfer price. We assume discounts to range between 40% of the wholesale

price (a transfer price of 60%) in the launch period, declining to 30% as sales rise. The distributor makes a profit off the price difference between the wholesale price and transfer price. Santhera benefits from no other costs outside COGS and taxes on profits in these regions, while still capturing a large share of the profits.

CHF ~350 mn peak sales in DMD (non-steroid patients) with first launches in 2020

For DMD (non-steroid patients), we expect conditional EU approval in mid 2020 with EU launch in Q3 2020 commercialized by Santhera's specialist sales force that sold Raxone in LHON. We assume a penetration rate of up to ~40% in treatment eligible DMD patients aged 7-22 years, and up to ~20% in patients aged 23 and above, with none of the patients treated with steroids, resulting in EU/ROW peak sales of CHF ~200 mn. US launch is expected in 2022 boosting peak sales to CHF ~350 mn. We also account for the heavy upfront investment in M&S costs to successfully establish Puldysa as a leading DMD treatment. We calculate a rNPV of CHF 24 per share for Puldysa in DMD (non-steroid patients) with a 72.5% success rate, the average of EU (80% filing) and US (65% phase III), with a 7% WACC (for details see page 30).

DMD (steroid patients) adds CHF ~450 mn peak sales – expands use to all patients

The successful development of Puldysa in DMD patients treated with steroids, assessed in the second confirmatory phase III "SIDEROS" trial, would expand the availability of Puldysa to the remaining 60% of eligible DMD patients. We forecast peak sales of CHF 442 mn, assuming a penetration rate of up to ~40% in treatment eligible DMD patients aged 7-22 years and up to ~25% in patients aged 23 and above. We conservatively assume a 65% (phase III) success rate for the ongoing phase III "SIDEROS" trial based on the early evidence seen in the phase II "DELPHI" trial that Puldysa can potentially delay lung function loss in this patient population, too. We assume lower M&S costs in this treatment group as we have included the heavy upfront investment in the earlier launch in DMD non-steroid patients, leading to higher profit margins thereby boosting the rNPV. We calculate a higher rNPV of CHF 28 per share for Puldysa in DMD (steroid patients) despite a lower success rate compared to DMD (non-steroid patients) thanks to substantial M&S cost synergies for both indications. Our profit margins could prove too conservative, as Santhera will be able to leverage the M&S costs for vamorolone as well, targeting the same physicians as with Puldysa (for details see page 31.

Forecasts & Sensitivity Analysis

PULDYSA - FINANCIAL FORECASTS FOR DUCHENNE MUSCULAR DYSTROPHY (NON-STEROID PATIENTS)

INDICATION	PRESERVATION OF LUNG FUNCTION IN DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS WHO ARE NOT ON CORTICOSTEROID TREATMENT
DOSAGE	900 MG/DAY (TWO 150 MG TABLETS 3X DAILY)
PRICE	EU/ROW: EUR 62,415 ANNUAL TREATMENT COST; US: USD 90,000 ANNUAL TREATMENT COST
STANDARD OF CARE	NO FULLY APPROVED TREATMENTS - STEROIDS (OFF-LABEL); EXONDYS 51 ACCELERATED APPROVAL (US ONLY); TRANSLARNA CONDITIONAL APPROVAL (EU ONLY)
UNIQUE SELLING POINT	POTENTIALLY FIRST-EVER APPROVED TREATMENT THAT REDUCES THE DECLINE IN LUNG FUNCTION, THE MAIN CAUSE OF DEATH IN DUCHENNE MUSCULAR DYSTROPHY

7PS ANALYSIS

PATENT	COMPOUND PATENT EXPIRED. EXCLUSIVITY EU: ORPHAN EXCLUSIVITY (SEP 2025); US: ORPHAN EXCLUSIVITY (2027E); USE PATENT (+ PEDIATRIC EXTENSION) UP TO 2027
PHASE	EU: FILING CONDITIONAL APPROVAL Q2 2019, LAUNCH Q3 2020; US: FILING Q4 2021, APPROVAL Q3 2022, LAUNCH Q4 2022
PATHWAY	ODD IN EU & US; EU: FILED Q2 2016 VARIATION TO LHON (NEGATIVE CHMP JAN 2018), FILING CONDITIONAL APPROVAL MAY 2019; US: FILING NDA (ALL DMD PATIENTS) 2021
PATIENT	REDUCTION IN PROGRESSIVE DECLINE IN LUNG FUNCTION MEANS IMPROVED QUALITY OF LIFE FOR PATIENT WITH LESS COMPLICATIONS
PHYSICIAN	FIRST EFFECTIVE TREATMENT WITH GOOD TOLERABILITY THAT REDUCES THE DECLINE IN LUNG FUNCTION, WHICH IS THE LEADING CAUSE OF DEATH IN DMD PATIENTS
PAYER	SUBSTANTIAL SAVINGS DUE TO LESS HOSPITALIZATIONS, LESS COMPLICATIONS AND LOWER SUPPORTIVE CARE COSTS
PARTNER	OWN SALES FORCE FOR 4 EUROPEAN REGIONAL CLUSTERS & NORTH AMERICA - SEEKING DISTRIBUTORS FOR REMAINING COUNTRIES/REGIONS

REVENUE MODEL

EUROPE 4 CLUSTERS (SANTHERA SALES FORCE)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
POPULATION 4 CLUSTERS											
PREVALENCE (40-50 PER MN)											
NUMBER OF PATIENTS	18,610	18,982	19,361	19,749	20,144	20,546	20,957	21,376	21,804	22,240	22,685
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS AGE 8-22 YEARS (~47%)	8,746	8,921	9,100	9,282	9,467	9,657	9,850	10,047	10,248	10,453	10,662
PERCENTAGE NON-STEROIDS (~40%)	3,499	3,569	3,640	3,713	3,787	3,863	3,940	4,019	4,099	4,181	4,265
PENETRATION (%)	0%	0%	6%	12%	24%	34%	41%	38%	8%	2%	0%
NUMBER OF PATIENTS (AGE 8-22, NON-STEROIDS)	0	0	218	446	909	1,313	1,615	1,524	311	63	13
PATIENTS AGE 23+ YEARS (~24%)	4,466	4,556	4,647	4,740	4,834	4,931	5,030	5,130	5,233	5,338	5,444
PERCENTAGE NON-STEROIDS (~40%)	1,787	1,822	1,859	1,896	1,934	1,972	2,012	2,052	2,093	2,135	2,178
PENETRATION (%)	0%	0%	3%	6%	14%	20%	21%	19%	4%	1%	0%
NUMBER OF PATIENTS (AGE 23+, NON-STEROIDS)	0	0	56	114	271	394	412	389	79	16	3
TOTAL PATIENTS ON TREATMENT (AGE 8+, NON-STEROIDS)	**0**	**0**	**274**	**559**	**1,180**	**1,708**	**2,028**	**1,913**	**390**	**80**	**16**
COST OF THERAPY PER YEAR (CHF)	71,460	71,094	71,147	71,147	71,147	71,147	71,147	71,147	71,147	71,147	71,147
SALES (CHF MN)	**0**	**0**	**20**	**40**	**84**	**122**	**144**	**136**	**28**	**6**	**1**
CHANGE (%)				104%	111%	45%	19%	-6%	-80%	-80%	-80%
COGS (10%) (CHF MN)	0	0	-2	-4	-8	-12	-14	-14	-3	-1	0
ROYALTY PAYMENTS TO TAKEDA (CHF MN)	0	-3									
ROYALTY PAYMENTS TO UNIVERSITY OF LEUVEN (CHF MN)	0	0	-1	-2	-4	-6	-7	-7	-1	0	0
R&D COSTS (CHF MN)	-3	-3	-3	0	0	0	0	0	0	0	0
M&S COSTS (CHF MN)	-2	-5	-16	-17	-18	-26	-31	-29	-6	-1	0
PROFIT BEFORE TAX (CHF MN)	**-5**	**-11**	**-2**	**17**	**53**	**77**	**92**	**87**	**18**	**4**	**1**
TAXES (CHF MN)	0	0	0	-3	-11	-15	-18	-17	-4	-1	0
PROFIT (CHF MN)	**-5**	**-11**	**-2**	**13**	**43**	**62**	**73**	**69**	**14**	**3**	**1**

CEE / REST OF WORLD (DISTRIBUTORS)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NUMBER OF PATIENTS	10,782	10,998	11,218	11,442	11,671	11,904	12,142	12,385	12,633	12,886	13,143
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
TOTAL PATIENTS ON TREATMENT (AGE 8+, NON-STEROIDS)	**0**	**0**	**53**	**108**	**419**	**720**	**964**	**909**	**115**	**23**	**5**
DISTRIBUTOR TRANSFER PRICE (% OF WHOLESALE)	60%	60%	65%	65%	65%	70%	70%	70%	70%	70%	70%
DISTRIBUTOR PRICE OF THERAPY PER YEAR (CHF)	42,876	42,656	46,245	46,245	46,245	49,803	49,803	49,803	49,803	49,803	49,803
SALES (CHF MN)	**0**	**0**	**2**	**5**	**19**	**36**	**48**	**45**	**6**	**1**	**0**
CHANGE (%)				104%	288%	85%	34%	-6%	-87%	-80%	-80%
COGS (10%) (CHF MN)	0	0	0	0	-2	-4	-5	-5	-1	0	0
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**2**	**4**	**17**	**32**	**43**	**41**	**5**	**1**	**0**
TAXES (CHF MN)	0	0	0	-1	-3	-6	-9	-8	-1	0	0
PROFIT (CHF MN)	**0**	**0**	**2**	**4**	**14**	**26**	**35**	**33**	**4**	**1**	**0**

UNITED STATES / CANADA (SANTHERA SALES FORCE)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NUMBER OF PATIENTS	15,608	15,920	16,239	16,564	16,895	17,233	17,577	17,929	18,287	18,653	19,026
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
TOTAL PATIENTS ON TREATMENT (AGE 8+, NON-STEROIDS)	**0**	**0**	**0**	**0**	**80**	**862**	**1,476**	**1,911**	**2,277**	**2,569**	**2,773**
COST OF THERAPY PER YEAR (CHF)	88,980	91,424	91,620	91,620	91,620	91,620	91,620	91,620	91,620	91,620	91,620
SALES (CHF MN)	**0**	**0**	**0**	**0**	**7**	**79**	**135**	**175**	**209**	**235**	**254**
CHANGE (%)						981%	71%	30%	19%	13%	8%
COGS (10%) (CHF MN)	0	0	0	0	-1	-8	-14	-18	-21	-24	-25
R&D COSTS (CHF MN)	0	-1	0	0	0	0	0	0	0	0	0
M&S COSTS (CHF MN)	-5	-5	-5	-5	-25	-67	-61	-61	-63	-71	-76
PROFIT BEFORE TAX (CHF MN)	**-5**	**-6**	**-5**	**-5**	**-18**	**4**	**61**	**96**	**125**	**141**	**152**
TAXES (CHF MN)	0	0	0	1	4	-1	-12	-19	-25	-28	-30
PROFIT (CHF MN)	**-5**	**-6**	**-5**	**-4**	**-15**	**3**	**49**	**77**	**100**	**113**	**122**

	2018E	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
GLOBAL SALES (CHF MN)	**0**	**0**	**22**	**45**	**111**	**236**	**327**	**357**	**242**	**242**	**255**
CHANGE (%)				104%	147%	114%	39%	9%	-32%	0%	5%
GLOBAL PROFIT (CHF MN)	**-10**	**-17**	**-5**	**13**	**42**	**91**	**157**	**179**	**118**	**117**	**123**
CHANGE (%)	-38%	70%	-69%	-350%	221%	117%	73%	14%	-34%	-1%	5%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**560**	
NUMBER OF SHARES (MN)	17.0	
NPV PER SHARE (CHF)	**33**	
SUCCESS PROBABILITY	72.5%	= AVERAGE OF EU (80% FILED) AND US (65% PHASE III)
RISK ADJUSTED NPV PER SHARE (CHF)	**24**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	37	35	34	33	32	31	30
	95%	35	34	33	31	30	29	28
	90%	33	32	31	30	29	28	27
SUCCESS PROBABILITY	85%	31	30	29	28	27	26	25
	80%	29	28	27	26	26	25	24
	72.5%	27	26	25	**24**	23	22	22
	70%	26	25	24	23	22	22	21

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

PULDYSA - FINANCIAL FORECASTS FOR DUCHENNE MUSCULAR DYSTROPHY (STEROID PATIENTS)

INDICATION	PRESERVATION OF LUNG FUNCTION IN DUCHENNE MUSCULAR DYSTROPHY (DMD) PATIENTS WHO ARE ON CORTICOSTEROID TREATMENT
DOSAGE	900 MG/DAY (TWO 150 MG TABLETS 3X DAILY)
PRICE	EU/ROW: EUR 62,415 ANNUAL TREATMENT COST; US: USD 90,000 ANNUAL TREATMENT COST
STANDARD OF CARE	NO FULLY APPROVED TREATMENTS - STEROIDS (OFF-LABEL); EXONDYS 51 ACCELERATED APPROVAL (US ONLY); TRANSLARNA CONDITIONAL APPROVAL (EU ONLY)
UNIQUE SELLING POINT	POTENTIALLY FIRST-EVER APPROVED TREATMENT THAT REDUCES THE DECLINE IN LUNG FUNCTION, THE MAIN CAUSE OF DEATH IN DUCHENNE MUSCULAR DYSTROPHY

7PS ANALYSIS

PATENT	COMPOUND PATENT EXPIRED. EXCLUSIVITY EU: ORPHAN EXCLUSIVITY (SEP 2025); US: ORPHAN EXCLUSIVITY (2027E); USE PATENT (+ PEDIATRIC EXTENSION) UP TO 2027
PHASE	PHASE III "SIDEROS" TRIAL IN DMD PATIENTS TREATED WITH STERIOIDS STARTED SEP 2016, TOP-LINE RESULTS MID 2021; US & EU LAUNCH 2022
PATHWAY	ORPHAN DRUG DESIGNATION IN EU AND US - FILING EXPECTED IN EU AND US IN Q3 2021 - EXPEDITED REVIEW IN US (6 MONTHS)
PATIENT	REDUCTION IN PROGRESSIVE DECLINE IN LUNG FUNCTION MEANS IMPROVED QUALITY OF LIFE FOR PATIENT WITH LESS COMPLICATIONS
PHYSICIAN	FIRST EFFECTIVE TREATMENT WITH GOOD TOLERABILITY THAT REDUCES THE DECLINE IN LUNG FUNCTION, WHICH IS THE LEADING CAUSE OF DEATH IN DMD PATIENTS
PAYER	SUBSTANTIAL SAVINGS DUE TO LESS HOSPITALIZATIONS, LESS COMPLICATIONS AND LOWER SUPPORTIVE CARE COSTS
PARTNER	OWN SALES FORCE FOR 4 EUROPEAN REGIONAL CLUSTERS & NORTH AMERICA - SEEKING DISTRIBUTORS FOR REMAINING COUNTRIES/REGIONS

REVENUE MODEL

EUROPE 4 CLUSTERS (SANTHERA SALES FORCE)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NUMBER OF PATIENTS	18,610	18,982	19,361	19,749	20,144	20,546	20,957	21,376	21,804	22,240	22,685
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS AGE 8-22 YEARS (~47%)	8,746	8,921	9,100	9,282	9,467	9,657	9,850	10,047	10,248	10,453	10,662
PERCENTAGE ON STEROIDS (~60%)	5,248	5,353	5,460	5,569	5,680	5,794	5,910	6,028	6,149	6,272	6,397
PENETRATION (%)	0%	0%	0%	0%	2%	14%	24%	32%	10%	3%	1%
NUMBER OF PATIENTS (AGE 8-22, ON STEROIDS)	0	0	0	0	114	811	1,418	1,929	590	181	55
PATIENTS AGE 23+ YEARS (~24%)	4,466	4,556	4,647	4,740	4,834	4,931	5,030	5,130	5,233	5,338	5,444
PERCENTAGE ON STEROIDS (~60%)	2,680	2,733	2,788	2,844	2,901	2,959	3,018	3,078	3,140	3,203	3,267
PENETRATION (%)	0%	0%	0%	0%	2%	10%	15%	18%	5%	2%	0%
NUMBER OF PATIENTS (AGE 23+, ON STEROIDS)	0	0	0	0	58	296	453	554	170	52	16
TOTAL PATIENTS ON TREATMENT (AGE 8+, ON STEROIDS)	**0**	**0**	**0**	**0**	**172**	**1,107**	**1,871**	**2,483**	**760**	**233**	**71**
COST OF THERAPY PER YEAR (CHF)	0	0	0	0	71,147	71,147	71,147	71,147	71,147	71,147	71,147
SALES (CHF MN)	**0**	**0**	**0**	**0**	**12**	**79**	**133**	**177**	**54**	**17**	**5**
CHANGE (%)						545%	69%	33%	-69%	-69%	-69%
COGS (10%) (CHF MN)	0	0	0	0	-1	-8	-13	-18	-5	-2	-1
ROYALTY PAYMENTS TO UNIVERSITY OF LEUVEN (CHF MN)	0	0	0	0	-1	-4	-7	-9	-3	-1	0
R&D COSTS (CHF MN)	-8	-8	-3	-4	-2	0	0	0	0	0	0
M&S COSTS (CHF MN)	0	0	0	0	-2	-16	-27	-35	-11	-3	-1
PROFIT BEFORE TAX (CHF MN)	**-8**	**-8**	**-3**	**-4**	**6**	**51**	**87**	**115**	**35**	**11**	**3**
TAXES (CHF MN)	0	0	0	1	-1	-10	-17	-23	-7	-2	-1
PROFIT (CHF MN)	**-8**	**-8**	**-3**	**-3**	**5**	**41**	**69**	**92**	**28**	**9**	**3**

CEE / REST OF WORLD (DISTRIBUTORS)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NUMBER OF PATIENTS	10,782	10,998	11,218	11,442	11,671	11,904	12,142	12,385	12,633	12,886	13,143
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
TOTAL PATIENTS ON TREATMENT (AGE 8+, ON STEROIDS)	**0**	**0**	**0**	**0**	**165**	**641**	**1,084**	**1,023**	**313**	**96**	**29**
DISTRIBUTOR TRANSFER PRICE (% OF WHOLESALE)					65%	70%	70%	70%	70%	70%	70%
DISTRIBUTOR PRICE OF THERAPY PER YEAR (CHF)	0	0	0	0	46,245	49,803	49,803	49,803	49,803	49,803	49,803
SALES (CHF MN)	**0**	**0**	**0**	**0**	**8**	**32**	**54**	**51**	**16**	**5**	**1**
CHANGE (%)						318%	69%	-6%	-69%	-69%	-69%
COGS (10%) (CHF MN)	0	0	0	0	-1	-3	-5	-5	-2	0	0
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**7**	**29**	**49**	**46**	**14**	**4**	**1**
TAXES (CHF MN)	0	0	0	0	-1	-6	-10	-9	-3	-1	0
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**6**	**23**	**39**	**37**	**11**	**3**	**1**

UNITED STATES / CANADA (SANTHERA SALES FORCE)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NUMBER OF PATIENTS	15,608	15,920	16,239	16,564	16,895	17,233	17,577	17,929	18,287	18,653	19,026
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
TOTAL PATIENTS ON TREATMENT (AGE 8+, ON STEROIDS)	**0**	**0**	**0**	**0**	**239**	**1,221**	**1,918**	**2,338**	**2,617**	**2,749**	**2,885**
COST OF THERAPY PER YEAR (CHF)	0	0	0	0	91,620	91,620	91,620	91,620	91,620	91,620	91,620
SALES (CHF MN)	**0**	**0**	**0**	**0**	**22**	**112**	**176**	**214**	**240**	**252**	**264**
CHANGE (%)						410%	57%	22%	12%	5%	5%
COGS (10%) (CHF MN)	0	0	0	0	-2	-11	-18	-21	-24	-25	-26
R&D COSTS (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
M&S (%)	0%	0%	0%	0%	23%	20%	20%	20%	20%	20%	20%
M&S COSTS (USD MN)	0	0	0	0	-5	-22	-35	-42	-47	-49	-52
M&S COSTS (CHF MN)	0	0	0	0	-5	-22	-35	-43	-48	-50	-53
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**15**	**78**	**123**	**150**	**168**	**176**	**185**
TAXES (CHF MN)	0	0	0	0	-3	-16	-25	-30	-34	-35	-37
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**12**	**63**	**98**	**120**	**134**	**141**	**148**

	2018E	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**42**	**223**	**363**	**442**	**309**	**273**	**271**
CHANGE (%)						433%	63%	22%	-30%	-12%	-1%
GLOBAL PROFIT (CHF MN)	**-8**	**-8**	**-3**	**-3**	**22**	**127**	**207**	**248**	**174**	**153**	**152**
CHANGE (%)	-27%	0%	-63%	7%	-789%	475%	63%	20%	-30%	-12%	-1%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**726**	
NUMBER OF SHARES (MN)	17.0	
NPV PER SHARE (CHF)	**43**	
SUCCESS PROBABILITY	65%	= PHASE III DEVELOPMENT ("SIDEROS" TRIAL)
RISK ADJUSTED NPV PER SHARE (CHF)	**28**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	95%	45	44	42	41	39	38	37
	90%	43	41	40	39	37	36	35
	85%	40	39	38	36	35	34	33
	80%	38	37	36	34	33	32	31
	75%	36	34	33	32	31	30	29
	70%	33	32	31	30	29	28	27
	65%	31	30	29	**28**	27	26	25

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

First-ever therapy that significantly delays the loss in lung function after one-year treatment, in eligible DMD patients not treated with steroids, and potentially in patients treated with steroids (pending positive "SIDEROS" results). The worsening of lung function is the main cause of early morbidity and death in DMD. Puldysa was well tolerated with side effects comparable to placebo.

7P's Analysis

Patent: The composition of matter patent has expired. A use patent provides protection until 2027 (with an extension in the US). We believe the overriding protection will come from the granted orphan drug market exclusivity of 10 years in the EU (Q3 2025) and 7 years in the US (2029).

Phase: The pivotal "DELOS" showed a statistically significant impact in delaying the loss of lung function compared to placebo after one-year treatment, in Duchenne patients not treated with steroids aged 10-18. Santhera filed for conditional approval for these patients in May 2019 with approval expected mid 2020. First launches in DMD (non-steroid patients) are expected to occur globally in 2022 on positive results of the second confirmatory phase III "SIDEROS" trial in DMD (steroid patients) that started in September 2016 with results anticipated mid 2021.

Pathway: Puldysa enjoys in both the EU and US orphan drug designation; an incentive to develop drugs for rare disease. Furthermore, Puldysa received FDA "fast track designation", potentially speeding up the US review time to only 6 months. At times with life-threatening diseases, such as in the case of DMD, patients can get early access through compassionate use programs or accelerated/conditional approval.

Patient: Slowing down of progressive lung function leads to fewer complications for the patient, improved quality of life, and potentially prolonged life expectancy.

Physician: For the first-time physicians have a well-tolerated treatment for DMD that slows the progressive loss in lung function, the main cause of premature death in this fatal disease. Puldysa is particularly positioned to substitute steroids in older non-ambulatory patients in whom use of steroids is counter-indicated due to side effects (e.g. excessive weight gain). Moreover, Puldysa has the potential to be combined with other DMD drugs.

Payer: A treatment that slows down progressive lung function loss in DMD patients should save costs that are related to lung function loss, such as assisted ventilation, rescue medication, supportive care and hospitalization.

Partner: Santhera will sell Puldysa through its own field force in 4 regional clusters in Europe: 1) France & Benelux; 2) Germany, Austria & Switzerland; 3) UK & Nordic Europe; and 4) Southern Europe. The company will seek distributors for other countries and regions (e.g. Ewopharma for Central Eastern Europe and the Baltics). We assume Santhera supplies Puldysa to its distributors at a transfer price (30-40% discount to wholesale price). The distributor retains the price difference, while Santhera benefits with no other costs than COGS and taxes.

Vamorolone (Duchenne Muscular Dystrophy)

Product Analysis

DMD peak sales of CHF 550+ mn - rNPV of CHF 20 per share

We forecast peak sales of CHF 569 mn for vamorolone in DMD assuming first launches in the US in Q4 2021 and EU in 2022, method of use patent protection until 2030, and orphan drug market exclusivity until 2028 (US) and 2032 (EU), respectively. We conservatively assume an annual weight-based treatment cost in the US similar to PTC Therapeutics' Emflaza (deflazacort) of USD 46,900 for patients weighing ~34 kg (aged 4-11 years) up to USD 87,500 for patients weighing ~63 kg (aged 11-22 years). In the EU and ROW, we apply a 30% and 50% discount to the US pricing. In patients aged 4-11 years we assume peak penetration rates of up to 48% (US) and half the amount (24%) in patients aged 11-22 as disease progresses. We account for COGS of 10%, M&S cost synergies with the commercialization of Puldysa in DMD in the US and EU, a distributor transfer price (60-70% of wholesale price) outside the US and EU sales territories, regulatory and commercialization milestones payments up to USD 210 mn and tiered single to low double-digit percentage sales royalty payments. Our rNPV amounts to CHF 336 mn or CHF 20 per share, conservatively applying a 35% (phase IIb) success probability and a WACC of 7% (for details see page 38)

Santhera's DMD pipeline is on steroids with vamorolone

With the option to in-license the global rights (excluding Japan/South Korea) of vamorolone in all indications, in particular DMD, from Idorsia in November 2018, Santhera now has the potential to become the undisputed market leader in DMD with Puldysa and vamorolone both in pivotal development. The agreement underlines Santhera's first-rate development capabilities in rare diseases and is an excellent strategic fit, strengthening the company's pipeline further. Vamorolone complements Santhera's current DMD program with Puldysa, resulting in significant synergies such as marketing and sales costs, boosting margins considerably. Idorsia also became an anchor shareholder with the largest stake (13.3%) in Santhera. Vamorolone is a first-in-class dissociative steroid in pivotal phase IIb development for DMD, where we conservatively forecast peak sales to amount to CHF 550+ mn in DMD alone.

Vamorolone rights originally acquired by Actelion from ReveraGen in 2016

Originally, Actelion acquired the exclusive option for the global rights from the private US biopharmaceutical company ReveraGen in November 2016. Idorsia (ticker: IDIA), the SIX-listed spin-off of Actelion, which was acquired by Johnson & Johnson in 2017 for USD 30 bn, retained the exclusive option for the global rights of vamorolone. Many of Idorsia's executives were responsible for the exceptional success of Actelion, including co-founders and CEO Jean-Paul Clozel and CSO Martine Clozel. In November 2018, Idorsia renegotiated the vamorolone rights with ReveraGen and paid the company USD 15 mn following the receipt of the clinical study report for the phase IIa proof-of-concept trial with vamorolone in DMD. Under the new structure, milestone payments will be more dependent on commercial success and more back-end loaded than the original agreement. The Idorsia agreement with Santhera largely reflects the recent new deal terms.

The vamorolone in-licensing deal terms with Idorsia include:

- **Upfront payment:** USD 20 mn paid in cash
- **Strategic shareholding:** Idorsia received 1 mn Santhera shares (locked up until US approval of vamorolone) equaling an 13.3% equity stake with Idorsia effectively becoming Santhera's largest shareholder (unconditional and not redeemable)
- **Regulatory & sales milestones:** up to USD 80 mn in the DMD indication
- **Sales milestones:** four one-time payments of up to USD 130 mn in aggregate
- **Royalties on net sales:** tiered single digit to low double-digit percentage of sales
- **Regulatory milestones:** for three additional indications up to USD 205 mn in aggregate

Santhera may exercise the option at any time but likely will do so upon receipt of data from the phase IIb "VISION-DMD" trial and following a one-time consideration to Idorsia of USD 30 mn (booked in Santhera R&D costs).

Perfect strategic fit covering all DMD patients irrespective of genetic mutation

Vamorolone is targeted at replacing glucocorticoids (steroids) such as prednisone or deflazacort, the current standard of care in DMD patients with early- and mid-stage disease to prevent muscle deterioration. Chronic use of glucosteroids is often hampered by side effects such as growth stunting, facial puffiness, weight increase and obesity, upper respiratory infection and cough, or unwanted hair growth. Vamorolone appears to have a superior safety and tolerability profile largely lacking these typical steroid side effects. Puldysa is targeted at DMD patients in mid- to late-stage disease with breathing difficulty to prevent lung function decline. Both drugs can be given to DMD patients irrespective of the underlying genetic mutation with the potential of combination therapy (including PTC Therapeutics' Translarna and Sarepta's EXONDYS 51). Moreover, vamorolone and Puldysa have been developed for chronic treatment in DMD, both with an excellent safety and tolerability profile.

Unique anti-inflammatory activity of a steroid without the typical steroid side effects

Vamorolone was developed by the US-based private biopharmaceutical company ReveraGen as a "dissociative" steroid – chemically separating the aspects of efficacy (clinical benefit) from safety concerns (side effects) and is first-in-class. Vamorolone is a close analog to prednisone, a standard glucocorticoid (steroid), however, without the typical steroid side effects. Toxicity, pharmacokinetics, pharmacodynamics, and ADME (absorption, distribution, metabolism and excretion) studies have been conducted. Results demonstrated that most short-term (acute) properties of vamorolone were similar to traditional steroids. In animal models for DMD (mdx mouse model of DMD), vamorolone consistently showed improvements in muscle function that were similar or superior to prednisone and showed a dose-dependent reduction in muscle inflammation and improved muscle strength. Vamorolone showed loss of side effects typically seen with prednisone, including loss of growth stunting, heart fibrosis and immunosuppressive side effects.

Clinical development program in DMD to seek parallel approval in the US and EU

ReveraGen is seeking parallel regulatory approval in the US and EU. Vamorolone was granted orphan drug designation in the EU and US (including fast-track designation) with the potential of accelerated approval in the US and conditional approval in the EU, based on a single pivotal trial. In the US, pre-IND (investigational new drug) meetings were held with the FDA in October 2013, and the IND was filed in December 2014. Phase I clinical

trials were completed in late 2015 in adult volunteers with SAD (single ascending dose) and MAD (multiple ascending dose) trials, which have been funded through venture philanthropy contracts by the Muscular Dystrophy Association (US), Joining Jack (UK), Duchenne Research Fund (UK) and Duchenne Children's Trust (UK). The DMD clinical program is being developed and run by a collaboration between the CINRG (Cooperative International Neuromuscular Research Group) and Newcastle University.

Phase IIa POC trials completed triggering a USD 15 mn payment from Idorsia
The phase IIa proof-of-concept (POC) trials were recently completed, triggering a USD 15 mn payment by Idorsia to maintain the agreement in November 2018. Idorsia agreed to support R&D activities for an additional year with up to a maximum amount of USD 1 mn until mid-2020.

The phase IIa POC development consisted of two trials: **1) Study VBP15-002:** a 2-week open label, 4-dose trial in 48 steroid-naïve (not have taken prednisone or deflazacort) DMD patients aged 4 to 7 years; and **2) Study VBP15-003:** a 6-months, open label, multiple dose extension trial where all 48 patients from Study '002 were enrolled, with 46 completed. All patients in Study '003 are now being enrolled in **Study VBP15-LTE** a long term, open label extension trial with top line results expected in 2020.

Study VBP-15-002 showed that vamorolone was safe and well tolerated up to 6 mg/kg/day (approximately ten times the standard steroid dose), with improved safety compared to steroids by reduction of insulin resistance, beneficial changes in bone turnover, and reduction in adrenal suppression. **Study VBP15-003** extension trial used timed function tests (e.g. time to stand, time to run/walk, 6-minute walk test) in comparison to standard steroids and natural history data. Vamorolone showed dose-dependent efficacy in timed function tests comparable to standard steroids with improved safety signals in biomarkers of insulin resistance, bone formation, and adrenal suppression.

Pivotal phase IIb "VISION-DMD" trial started with top line results in H2 2020
The phase IIb trial "VISION-DMD" (VBP15-004) trial was developed under FDA and EMA scientific advice and is considered a pivotal trial for US accelerated approval and EU conditional approval.

"VISION-DMD" is a phase IIb randomized, double-blind, parallel group, placebo- and active-controlled trial with a double-blind extension. The trial will be conducted in 30 sites in the US (recruiting), EU, Canada, Australia and Israel and will enroll 120 ambulant boys from 4 to <7 years of age, who have not taken steroids (prednisone or deflazacort) to be randomized in 4 treatment groups: 1) low dose vamorolone 2 mg/kg/day, 2) high vamorolone 6 mg/kg/day, 3) prednisone 0.75 mg/kg/day, or 4) placebo. Treatment consists of a 24-week Treatment Period #1 (weeks 1-24), a 4-week transition period (weeks 25-28) where the prednisone and placebo groups will cross-over to low or high dose vamorolone, a 20-week Treatment Period #2 (weeks 28-48) and a 4-week dose-tapering period (weeks 49-52); with one visit per month.

The primary endpoint consists of muscle function measured by time to stand (velocity) and body size as measured by BMI (body mass index) z-score. Secondary endpoints include 33 secondary outcomes such as safety, cardiac function, efficacy (e.g. 6-minute walk test, time to run/walk test).

The EMA (European Medicines Agency) requested a prednisone arm to demonstrate superior efficacy compared to standard of care (e.g. prednisone or deflazacort). First patient enrolment started in August 2018 with top line results expected to report in mid 2020.

In the US, NDA (new drug application) filing is anticipated by the end of 2020 with approval in 2021 and launch in late 2021. In the EU, MAA (marketing authorization application) filing is anticipated in early 2021 with approval approximately a year later with first launches in 2022.

Peak sales of CHF 550+ mn for vamorolone in DMD alone

We have based our vamorolone forecasts on detailed bottom up analysis based on the number of DMD patients in three distinct regions, including the US and the Europe 4 clusters, where Santhera plans to market vamorolone (and Puldysa) by an own small specialist sales force, and CEE and ROW (excluding Japan/South Korea) where we expect distributors to commercialize vamorolone (and Puldysa).

We provide a breakdown of DMD patients in three groups from age 4-11 years (~32% of patients), age 12-22 years (~44% of patients), and age 23+ years (~24% of patients). As vamorolone is expected to be given in early stages of disease, we exclude the latter patient group. We expect the annual cost of treatment per patient will be weight dependent. We assume an average weight of ~34 kg for patients of age 4-11 years and ~63 kg for patients of age 12-22 years.

We conservatively assume similar pricing in the US as PTC Therapeutics' Emflaza (deflazacort), which amounts to an annual treatment cost per patient of age 4-11 years (average weight of ~ 34 kg) of approximately USD 46,900 and USD 87,500 for patients of age 12-22 years (average weight of ~63 kg). Note that Emflaza still has the typical steroid side effects, including facial puffiness (33% of patients), weight increase (20%), increased appetite (14%), cough (12%), frequent daytime urination (12%), upper respiratory tract infection (12%), central obesity (10%) and unwanted hair growth (10%). Vamorolone's superior safety and tolerability profile could justify premium pricing over Emflaza. In the EU we conservatively assume a 30% price discount, and in the CEE/ROW a 50% discount to the US pricing, to reflect the generic availability of prednisone and deflazacort in these regions.

We assume that steroids are used in ~60% of DMD patients in these age groups. Vamorolone is targeted at replacing current steroids in DMD with an efficacious but safer and more tolerable dissociative steroid. In the US, we assume vamorolone will penetrate 80% of DMD patients of age 4-11 years treated with steroids leading to a 48% peak market penetration. In the higher age 12-22 years patient group, we assume a lower peak penetration of 24% (half the penetration rate as in the younger 4-11 years patient group). In the EU, we assume a lower peak penetration rate of 36% in the younger patient group and 18% in the older patient group, and in CEE/ROW we assume peak penetration rates of 30% and 15% in the respective age groups. Note that we do not account for a higher steroid use in DMD patients, which could be the case with vamorolone due to its superior safety and tolerability profile compared to mainstay steroid (prednisone or deflazacort) therapy.

Our conservative bottom up approach (pricing, penetration, steroid use) results in vamorolone peak of CHF 569 mn in DMD alone. Vamorolone could potentially be developed in other diseases where steroids are involved such as asthma, inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, cystic fibrosis, among others.

Accounting for 10% COGS, regulatory and sales milestone payments of up to USD 210 mn payable to ReveraGen and Idorsia, sales royalty payments in tiered single to double digits if product sales USD >1 bn, and marketing and sales cost synergies with the commercialization of Puldysa in DMD, we calculate a rNPV of CHF 336 mn or CHF 20 per share, applying a conservative 35% (phase IIb) success rate and a WACC of 7%.

Forecasts & Sensitivity Analysis

VAMOROLONE - FINANCIAL FORECASTS FOR DUCHENNE MUSCULAR DYSTROPHY

INDICATION	PRESERVATION OF MUSCLE FUNCTION IN DMD WITH IMPROVED SAFETY AND TOLERABILITY PROFILE THAN EXISTING STEROIDS
DOSAGE	TO BE DETERMINED (2 MG UP TO 6 MG/KG/DAY)
PRICE	ANNUAL COST PER KG WEIGHT: US: USD ~1,400 (SIMILAR TO EMFLAZA AT USD ~35,000/YEAR); EU: EUR ~870; ROW: EUR ~622; ALL VERY CONSERVATIVE PRICING
STANDARD OF CARE	STEROIDS (OFF-LABEL); PTC'S STEROID EMFLAZA (DEFLAZACORT); EXONDYS 51 ACCELERATED APPROVAL (US ONLY); TRANSLARNA CONDITIONAL APPROVAL (EU ONLY)
UNIQUE SELLING POINT	REPLACEMENT OF EXISTING STANDARD OF CARE STEROIDS, WHICH REDUCES THE DECLINE IN MUSCLE FUNCTION WITHOUT THE TYPICAL STEROID SIDE EFFECTS

7Ps ANALYSIS

PATENT	METHOD OF USE PATENT EXPIRY 2028-2030; ORPHAN DRUG EXCLUSIVITY POST-APPROVAL: US 7 YEARS; EU: 10 YEARS
PHASE	PHASE IIA COMPLETED (LONG-TERM EXTENSION TRIAL ONGOING WITH RESULTS H2 2020); PHASE IIB "VISION-DMD" PIVOTAL TRIAL STARTED AUG 2018, RESULTS MID 2020
PATHWAY	ORPHAN DRUG DESIGNATION IN EU & US (FAST TRACK) - US: FILING Q4 2020, APPROVAL Q3 2021, LAUNCH Q4 2021; EU: FILING Q1 2021, APPROVAL Q1 2022, LAUNCH Q2 2022
PATIENT	REDUCTION IN PROGRESSIVE DECLINE IN MUSCLE FUNCTION MEANS IMPROVED QUALITY OF LIFE FOR PATIENT WITH LESS COMPLICATIONS
PHYSICIAN	EFFECTIVE TREATMENT WITH GOOD TOLERABILITY THAT REDUCES THE DECLINE IN MUSCLE FUNCTION, WHICH LEADS TO LOSS OF MOBILITY AND PREMATURE DEATH
PAYER	SUBSTANTIAL SAVINGS DUE TO LESS HOSPITALIZATIONS, LESS COMPLICATIONS AND LOWER SUPPORTIVE CARE COSTS
PARTNER	RIGHTS ACQUIRED FROM IDORSIA IN 2018; UP TO USD 250 MN REGULATORY & SALES MILESTONES IN DMD; INCREASING TIERED SINGLE- TO DOUBLE-DIGIT ROYALTIES

REVENUE MODEL

EUROPE 4 CLUSTERS (SANTHERA SALES FORCE)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
NUMBER OF PATIENTS	18,610	18,982	19,361	19,749	20,144	20,546	20,957	21,376	21,804	22,240	22,685
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS AGE 4-11 YEARS (~32%)	5,955	6,074	6,196	6,320	6,446	6,575	6,706	6,840	6,977	7,117	7,259
PENETRATION (%)	0%	0%	0%	0%	4%	16%	24%	30%	32%	34%	36%
TREATED PATIENTS (AGE 4-11 YEARS)	0	0	0	0	258	1,052	1,610	2,052	2,233	2,420	2,613
ANNUAL COST OF THERAPY (AVE. ~34 KG) (CHF)					34,197	34,197	34,197	34,197	34,197	34,197	34,197
SALES PATIENTS AGE 4-11 YEARS (CHF MN)					**9**	**36**	**55**	**70**	**76**	**83**	**89**
PATIENTS AGE 12-22 YEARS (~44%)	8,188	8,352	8,519	8,689	8,863	9,040	9,221	9,406	9,594	9,786	9,981
PENETRATION (%)	0%	0%	0%	0%	0%	0%	8%	12%	15%	16%	17%
TREATED PATIENTS (AGE 12-22 YEARS)	0	0	0	0	0	0	738	1,129	1,439	1,566	1,697
ANNUAL COST OF THERAPY (AVE. 63 KG) (CHF)					62,695	62,695	62,695	62,695	62,695	62,695	62,695
SALES PATIENTS AGE 12-22 YEARS (CHF MN)					**0**	**0**	**46**	**71**	**90**	**98**	**106**
SALES (CHF MN)	**0**	**0**	**0**	**0**	**9**	**36**	**101**	**141**	**167**	**181**	**196**
COGS (10%) (CHF MN)	0	0	0	0	-1	-4	-10	-14	-17	-18	-20
TIERED ROYALTY PAYMENTS (CHF MN)	0	0	0	0	0	-2	-5	-7	-8	-9	-10
MILESTONE PAYMENTS (CHF MN)	0	0	0	0	-15	0	-5	-10	0	0	-20
R&D COSTS (INCL. IDORSIA OPTION PAYMENTS) (CHF MN)	-21	-5	-34	-4	0	0	0	0	0	0	0
M&S COSTS (CHF MN)	0	0	0	-5	-9	-11	-20	-21	-25	-27	-29
PROFIT BEFORE TAX (CHF MN)	**-21**	**-5**	**-34**	**-9**	**-17**	**20**	**61**	**88**	**117**	**127**	**117**
TAXES (CHF MN)	0	0	0	0	0	0	-12	-18	-23	-25	-23
PROFIT (CHF MN)	**-21**	**-5**	**-34**	**-9**	**-17**	**20**	**49**	**71**	**93**	**101**	**93**

CEE / REST OF WORLD (EX. JAPAN) (DISTRIBUTORS)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
NUMBER OF PATIENTS	5,169	5,272	5,378	5,485	5,595	5,707	5,821	5,937	6,056	6,177	6,301
TREATED PATIENTS (AGE 4-11 YEARS)	0	0	0	0	0	37	186	304	426	514	565
ANNUAL COST OF THERAPY (AVE. ~34 KG) (CHF)						23,938	23,938	23,938	23,938	23,938	23,938
SALES PATIENTS AGE 4-11 YEARS (CHF MN)						**1**	**4**	**7**	**10**	**12**	**14**
TREATED PATIENTS (AGE 12-22 YEARS)	0	0	0	0	0	0	27	140	228	319	385
ANNUAL COST OF THERAPY (AVE. ~63 KG) (CHF)						35,091	35,091	35,091	35,091	35,091	35,091
SALES PATIENTS AGE 12-22 YEARS (CHF MN)						**0**	**1**	**5**	**8**	**11**	**14**
PRODUCT SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**1**	**5**	**12**	**18**	**24**	**27**
DISTRIBUTOR TRANSFER PRICE (% OF WHOLESALE)						60%	60%	60%	65%	65%	65%
SALES DISTRIBUTORS (CHF MN) - BOOKED BY SANTHERA	**0**	**0**	**0**	**0**	**0**	**1**	**3**	**7**	**12**	**15**	**18**
TIERED ROYALTY PAYMENTS (CHF MN)	0	0	0	0	0	0	0	-1	-1	-1	-2
COGS (10%) (CHF MN)	0	0	0	0	0	0	-1	-1	-2	-2	-3
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**5**	**9**	**12**	**13**
TAXES (CHF MN)	0	0	0	0	0	0	0	-1	-2	-2	-3
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**4**	**7**	**9**	**10**

UNITED STATES / CANADA (SANTHERA SALES FORCE)	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
NUMBER OF PATIENTS	15,608	15,920	16,239	16,564	16,895	17,233	17,577	17,929	18,287	18,653	19,026
PATIENTS AGE 4-11 YEARS (~32%)	4,995	5,095	5,196	5,300	5,406	5,514	5,625	5,737	5,852	5,969	6,088
PENETRATION (%)	0%	0%	0%	2%	22%	32%	40%	44%	46%	47%	48%
TREATED PATIENTS (AGE 4-11 YEARS)	0	0	0	106	1,189	1,765	2,250	2,524	2,692	2,805	2,922
ANNUAL COST OF THERAPY (AVE. ~34 KG) (CHF)					47,744	47,744	47,744	47,744	47,744	47,744	47,744
SALES PATIENTS AGE 4-11 YEARS (CHF MN)				**0**	**57**	**84**	**107**	**121**	**129**	**134**	**140**
PATIENTS AGE 12-22 YEARS (~44%)	7,336	7,483	7,632	7,785	7,941	8,099	8,261	8,427	8,595	8,767	8,942
PENETRATION (%)	0%	0%	0%	0%	0%	0%	11%	16%	20%	22%	23%
TREATED PATIENTS (AGE 12-22 YEARS)	0	0	0	0	0	0	909	1,348	1,719	1,929	2,057
ANNUAL COST OF THERAPY (AVE. ~63 KG) (CHF)					89,075	89,075	89,075	89,075	89,075	89,075	89,075
SALES PATIENTS AGE 12-22 YEARS (CHF MN)				**0**	**0**	**0**	**81**	**120**	**153**	**172**	**183**
SALES (CHF MN)	**0**	**0**	**0**	**0**	**57**	**84**	**188**	**241**	**282**	**306**	**323**
TIERED ROYALTY PAYMENTS (CHF MN)	0	0	0	0	-3	-4	-9	-12	-14	-15	-21
MILESTONE PAYMENTS (CHF MN)	0	0	0	-61	0	0	-15	-31	0	0	-41
COGS (10%) (CHF MN)	0	0	0	0	-6	-8	-19	-24	-28	-31	-32
M&S COSTS (CHF MN)	0	0	0	-10	-17	-21	-38	-36	-42	-46	-48
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**-71**	**31**	**51**	**107**	**138**	**197**	**214**	**180**
TAXES (CHF MN)	0	0	0	0	0	0	-21	-28	-39	-43	-36
PROFIT (CHF MN)	**0**	**0**	**0**	**-71**	**31**	**51**	**86**	**110**	**158**	**171**	**144**

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
GLOBAL PRODUCT SALES (CHF MN)	**0**	**0**	**0**	**0**	**66**	**121**	**295**	**394**	**466**	**510**	**546**
CHANGE (%)						85%	144%	33%	18%	9%	7%
GLOBAL PROFIT (CHF MN)	**-21**	**-5**	**-34**	**-80**	**15**	**71**	**136**	**185**	**258**	**282**	**248**
CHANGE (%)		-76%	589%	133%	-118%	383%	93%	36%	39%	9%	-12%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**959**	
NUMBER OF SHARES (MN)	17.0	
NPV PER SHARE (CHF)	**56**	
SUCCESS PROBABILITY	35%	= PHASE IIB PIVOTAL TRIAL (EU CONDITIONAL/US ACCELERATED APPROVAL)
RISK ADJUSTED NPV PER SHARE (CHF)	**20**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	65%	42	40	39	37	35	34	32
	60%	39	37	36	34	33	31	30
	55%	36	34	33	31	30	29	27
SUCCESS PROBABILITY	50%	32	31	30	28	27	26	25
	45%	29	28	27	26	24	23	22
	40%	26	25	24	23	22	21	20
	35%	23	22	21	**20**	19	18	17

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

First-in-class dissociative steroid with the potential to replace current DMD standard of care steroid therapy (prednisone, deflazacort) due a superior safety and tolerability profile with similar efficacy. Vamorolone can be given to DMD patients irrespective of the underlying genetic mutation and potentially in combination with other DMD treatments

7P's Analysis

Patent: Method of use patents expire in 2028-2030. Orphan drug exclusivity should provide protection in the EU until 2032 (10 years) and in the US until 2028 (7 years) from the date of approval.

Phase: Phase I is completed and phase IIa proof-of-concept has been established successfully. In August 2018, ReveraGen started patient enrolment of the pivotal phase IIb "VISION-DMD" trial in ~120 ambulant steroid naïve DMD boys of age 4 to <7 years. Top line results are due in mid 2020. This trial was developed under FDA and EMA scientific advice and is considered a pivotal trial for US accelerated and EU conditional approval.

Pathway: Vamorolone enjoys in both the EU and US orphan drug designation; an incentive to develop drugs for rare disease. Vamorolone has also received FDA "fast track designation", potentially speeding up the US review time to only 6 months.

Patient: Slowing down of progressive muscle function leads to longer patient mobility. The superior safety and tolerability profile lead to better patient compliance with less complications for the patient, improved quality of life, and potentially prolonged life expectancy.

Physician: Vamorolone has the potential to replace standard of care steroid therapy (prednisone or deflazacort) with an effective steroid with a superior safety and tolerability profile, enhancing patient compliance and hence long-term outcomes. Vamorolone slows the progressive loss in muscle function and the of loss of mobility. Vamorolone has the potential to be combined with other DMD drugs such as Santhera's Puldysa (filed in EU, phase III in US), PTC Therapeutics' Translarna (approved only in the EU) or Sarepta's EXONDYS 51 (approved only in the US).

Payer: A treatment that slows down progressive muscle function loss in DMD patients may save costs related to loss of mobility (e.g. wheel chair, special bed), rescue medication, supportive care and hospitalization. The superior safety and tolerability profile compared to mainstay steroids should lead to less secondary complications and increased patient compliance and long-term treatment outcomes.

Partner: Santhera will sell vamorolone through its own field force in 4 regional clusters in Europe: 1) France & Benelux; 2) Germany, Austria & Switzerland; 3) UK & Nordic Europe; and 4) Southern Europe. Santhera will use the same sales force to sell its other drugs such as Puldysa in DMD. The company will seek distributors for other countries and regions (e.g. Ewopharma for Central Eastern Europe and the Baltics). We assume Santhera supplies vamorolone to its distributors at a transfer price (30-40% discount to wholesale price). The distributor retains the price difference, while Santhera benefits with no other costs than COGS and taxes.

Duchenne Muscular Dystrophy Market

The Duchenne Muscular Dystrophy market has started to take off. PTC Therapeutics' Translarna was granted conditional approval in the EU in 2014, while its recently acquired steroid Emflaza (deflazacort) was approved in the US in February 2017. Sarepta Therapeutics' EXONDYS 51 was granted accelerated approval in the US in 2016. Santhera's Puldysa was filed for EU conditional approval in May 2019, while pivotal results of vamorolone, recently in-licensed by Santhera from Idorsia, are expected in 2020. At present systemic steroids are used off-label and have become the mainstay treatment for DMD. Due to their severe side effects the use of steroids is generally limited to certain disease stages. Excessive weight gain is particularly problematic in older non-ambulatory patients. In the next few years the DMD market is set to increase substantially with the introduction of new treatments that have an impact on lung function and mobility, potentially delaying the progression of this fatal muscle wasting disease that starts in early childhood. We expect widespread combination therapy and possibly reduction in the use of steroids. With annual treatment costs ranging from USD 35,000 up to USD 500,000, the DMD market could rapidly grow to USD 4 bn.

DUCHENNE MUSCULAR DYSTROPHY - KEY FACTS	
MARKET SIZE	USD ~ 400 MN (EXCL. OFF-LABEL STEROIDS) - POTENTIAL UP TO USD 4 BN (vL ESTIMATE)
PREVALENCE	4-5 PER 100,000; APPR. 14,500 IN THE US/CAN; APPR. 22,000 IN THE EU; APPR. 5,000 IN JAPAN
INCIDENCE	1 OUT OF 3,500 MALE INFANTS
UNDERLYING CAUSE	DUCHENNE MUSCULAR DYSTROPHY (DMD) IS CAUSED BY A DEFECTIVE GENE ENCODING FOR DYSTROPHIN (A PROTEIN RESPONSIBLE FOR THE MECHANICAL STABILITY OF MUSCLE CELLS). BECAUSE OF THE WAY IT IS INHERITED ONLY BOYS ARE AFFECTED. WOMEN CAN BE CARRIERS OF THE DEFECTIVE GENE BUT DEVELOP NO SYMPTOMS. SONS OF THESE WOMEN HAVE A 50% CHANCE OF HAVING THE DISEASE. UNFORTUNATELY, THE FAMILY HISTORY IS OFTEN UNKNOWN UNTIL THE DISEASE APPEARS.
SYMPTOMS	SYMPTOMS USUALLY APPEAR BEFORE AGE 6 AND AS EARLY AS INFANCY, INCLUDING: - MUSCLE WEAKNESS (STARTS IN LEGS AND PELVIS FOLLOWED BY WEAKNESS IN ARMS, NECK) - DELAYED MOTOR SKILLS (RUNNING, HOPPING, JUMPING, FREQUENT FALLS) - PROGRESSIVE DIFFICULTY WITH WALKING (ABILITY TYPICALLY LOST DURING EARLY TEENAGE YEARS THEN CONFINED TO WHEELCHAIR) - PROGRESSIVE RESPIRATORY INSUFFICIENCY REQUIRING ASSISTED VENTILATION - CARDIAC COMPLICATIONS - FATIGUE - LEARNING DIFFICULTIES (IQ CAN BE BELOW 75) DMD LEADS TO QUICKLY WORSENING DISABILITY. DEATH USUALLY OCCURS AROUND AGE 30 PREDOMINANTLY FROM RESPIRATORY FAILURE
DRUG CLASS (KEY BRANDS)	CURRENT STANDARD OF CARE: - STEROIDS - NOTE: OFF-LABEL USE, EMFLAZA (DEFLAZACORT) APPROVED IN US ONLY EMERGING THERAPIES: - SHORT-CHAIN BENZOQUINONE (PULDYSA) - DYSTROPHIN READ-THROUGH THERAPY (TRANSLARNA) - EXON-SKIPPING THERAPIES (EXONDYS 51) - DISSOCIATIVE STEROIDS (VAMOROLONE, EDASALONEXENT)
MAJOR PLAYERS (KEY BRANDS)	- PTC THERAPEUTICS (TRANSLARNA, EMFLAZA) - SAREPTA THERAPEUTICS (EXONDYS 51) - SANTHERA (PULDYSA, VAMOROLONE) - CATABASIS (EDASALONEXENT)

SOURCE: VALUATIONLAB, NIH, WHO, ORPHA.NET, COMPANY DATA

Duchenne muscular dystrophy is an inherited and fatal muscle wasting disease that worsens quickly. The disease is caused by a defective dystrophin gene, the largest gene located on the human X chromosome, which codes for the protein dystrophin. This protein is an important component within muscle tissue that provides structural stability during cycles of muscle contraction and relaxation. Lack of dystrophin protein leads to muscle cell damage and ultimately loss. DMD often occurs in people without a known family history of the condition. Because of the way DMD is inherited, only boys are affected, not girls. Genetic tests performed can detect DMD with approximately 95% accuracy. DMD occurs in 1 out of ~3,500 male infants. There are roughly 40,000 DMD patients in the EU, North America and Japan. Symptoms appear at early age, as early as infancy, and worsen

rapidly. Generally, muscle weakness starts in the legs and pelvis, but also occurs less severely in the arms, neck and other areas of the body. These boys fall frequently and have difficulties running, hopping, jumping, climbing stairs or getting up from a lying position. Furthermore, the ability to walk deteriorates quickly and may be lost during early teenage years, with the child confined to a wheelchair. Slowly the lungs and heart are affected resulting in breathing difficulties and heart disease. Death occurs around the age of 30, typically from respiratory failure.

Current treatment limited to steroids, unproven remedies and supportive care

To date, no cure has been found for DMD. Systemic steroids use, such as prednisone or deflazacort (branded Emflaza in the US), is given as first line treatment. Such steroids can slow the loss of muscle strength and prolong the patient's ambulatory status and delay loss of respiratory function. However, chronic use of steroids impacts normal growth and weakens bones, which is particularly problematic in young patients. In older patients, excessive weight gain and the risk of diabetes are additional complications typically limiting the use of steroids to a window stating around 5-7 years of age and ending by the time patients become non-ambulatory. Supplements with no proven efficacy include, amino acids, creatine or nutritional supplements such as fish oil, carnitine, coenzyme Q10, vitamin E, or green tea extracts. Further treatment is focused on encouraging activity to maintain muscle strength and function, such as physiotherapy. Orthopedic appliances such as braces and wheelchairs are used to improve mobility. Assisted ventilation is used during day or night to help breathing.

DMD market on the verge of rapid growth by the introduction of new treatments

The introduction of new therapies is driving growth in the currently small DMD market. PTC Therapeutics' **Translarna** (ataluren), a dystrophin nonsense mutation read-through therapy aiming at ~13% of a DMD cases, received conditional approval in the EU in May 2014, based on a failed phase IIb trial. This was extended in November 2016 with the request to conduct a new phase III trial. Translarna became the first novel DMD therapy to reach the market for a selective patient subgroup. In the US Translarna received a Complete Response Letter (CRL) in October 2017. PTC's appeal of the CRL was rejected by the FDA in February 2018. Sarepta Therapeutics' **EXONDYS 51** (eteplirsen) received accelerated approval to treat nonsense mutation DMD, aiming at ~13% of DMD cases, in September 2016. Despite a high annual price tag of USD ~300,000, reimbursement issues due to the questionable efficacy, EXONDYS 51 FY 2017 sales reached USD 155 mn. PTC Therapeutics recently acquired Marathon's steroid **Emflaza** (deflazacort), which was approved in the US in February 2017. The net price of USD ~35,000 per year per patient fails to ease the concerns of some federal lawmakers who had criticized Marathon's initial USD 89,000 list price (~70 times higher than the drug's UK price). Deflazacort is a decades-old generic steroid that is available outside the US. Santhera's synthetic short-chain benzoquinone **Puldysa** (idebenone) is the only novel compound with a positive phase III trial in DMD. Raxone significantly delayed the loss in lung function compared to placebo after one-year treatment, in DMD patients aged between 10-18 years, who were not treated with steroids. Novel steroids without the dreadful side effects are also being developed, including Santhera/ReveraGen's dissociated steroid **vamorolone** (pivotal phase IIb) and Catabasis' **edasalonexent** (phase III). Early stage projects that are still years away from market introduction, include Tivorsan Pharma's **biglycan/TVN-102** (pre-clinical), and stem cell and gene therapies. For example, US-based Asklepios BioPharmaceutical is conducting the first biostrophin gene therapy trial for DMD in the US.

Raxone (Leber's Hereditary Optic Neuropathy)

Product Analysis

LHON: Peak sales (North America only) of CHF 50 mn; rNPV of CHF 6 per share
We forecast peak sales for North America of CHF 56 mn for Raxone in LHON, based on a US launch in 2023 (roughly one year after the US approval of Puldysa in DMD), a yearly treatment cost per patient of USD 90,000, 2 years treatment, and a market penetration peaking at around 65% in newly diagnosed patients with orphan drug market exclusivity until end 2029. Our rNPV amounts to CHF 103 mn, or CHF 6 per share, accounting for COGS of 10% and M&S costs in the single-digit CHF millions, a 65% (phase III) success rate and a WACC of 7%.

NOTE: Following the completion of the license agreement with Chiesi Farmaceutici for the global rights (excluding North America) to Raxone in LHON and all other ophthalmological indications, expected in September 2019, neuro-ophthalmological disorders will no longer be core for Santhera. In a second step, Chiesi has the option to change the license to an acquisition of ex-North America rights of Raxone in LHON.

Chiesi deal funds the gap for drugs with far higher peak sales

Chiesi license agreement marks Santhera's exit in neuro-ophthalmological diseases
Santhera has enjoyed commercial success with Raxone (idebenone) in the rare neuro-ophthalmological disease Leber's Hereditary Optic Neuropathy (LHON), an ultra-rare genetic eye disease that leads to sudden blindness, with an incidence of 1 in a million. Since approval in 2015, Raxone has accumulated sales of CHF 80 mn in LHON with another CHF 35-37 mn guided for 2019. Raxone was commercialized largely by Santhera's own specialist sales force in the EU. In May 2019, the company entered into an exclusive license agreement with the Italian private pharmaceutical company Chiesi Group for the global rights (excluding North America) of Raxone in LHON and all other ophthalmological indications. In a second step, following certain reimbursement and post-regulatory commitments on the part of Santhera, Chiesi has the option to change the license to an acquisition of ex - North American rights to Raxone in LHON. This marks Santhera's exit from neuro-ophthalmological diseases, the company's first therapeutic area with commercial success.

Funding gap until turning point in 2020; reinvesting in DMD with 26x higher multiple
The Chiesi agreement is worth up to CHF 105 mn, with an upfront payment of CHF 50 mn on closing of the transaction (expected in September 2019) and near- to mid-term sales milestone payments of up to CHF 55 mn. The proceeds will be reinvested in the current pipeline to bridge a funding gap until the turning point in 2020 with the expected EU approval of Puldysa in DMD (80% filing success rate) and topline results of the vamorolone pivotal "VISION-DMD" trial in DMD (35% phase IIb success rate). To put the Chiesi agreement into perspective, Santhera is reinvesting the rights for Raxone in LHON (excluding North America) with estimated peak sales of CHF 52 mn largely into its two late stage DMD drugs Puldysa and vamorolone with combined estimated peak sales of CHF 1.4 bn with a staggering 26-times higher peak sales potential than Raxone in LHON (excluding North America). Given the relatively high success probability of EU conditional

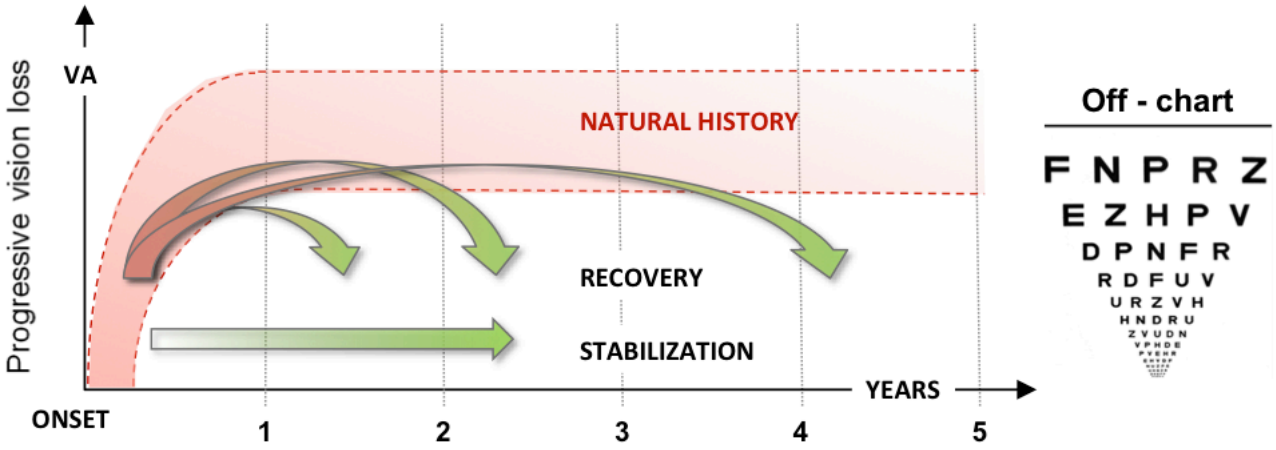
approval of Puldysa in DMD in mid 2020, we believe the sale of the Raxone LHON rights to Chiesi should pay out nicely.

First drug ever approved for LHON or a mitochondrial disease

Raxone is the first drug ever approved for LHON, for a mitochondrial disorder, as well as for a neuro-ophthalmological disease. The "exceptional circumstances" marketing authorization was granted on 9 September 2015 and is applicable to all 28 member states of the European Union as well as Iceland, Liechtenstein and Norway. Raxone has orphan designation, which provides 10 years of market exclusivity from the date of the European Commission's approval. Germany was the first EU member state to launch Raxone in LHON in October 2015 and Raxone is now sold in more than 20 European countries and Israel and reached profitability in 2018. The anticipated peak sales potential for EU/ROW is about CHF 50 mn.

LHON - a catastrophic disease leading to sudden blindness finally gets a treatment

LHON affects predominantly young people around the age of 20-30 years and has a devastating impact on the quality and productivity of life. Hallmark of this genetic disorder is the rapid loss of central vision. More than 90% of LHON patients become legally blind within the first year of symptom onset. Typically, patients can only read the top line of an eye chart or less ("Natural History" in graph below depicts LHON progression)



Source: Santhera Pharmaceuticals

The incidence of LHON is very low affecting approximately 1 in a million people every year. The prevalence, or amount of people affected by LHON, is estimated to be 1 in 30,000 to 50,000 people.

Raxone is the first treatment in LHON patients that has demonstrated:

1) **Prevention of further vision loss in acutely affected patients** (57%* of patients were prevented from becoming legally blind)
2) **Recovery of vision** (49%* of patients saw clinically meaningful improvement in vision)

* Based on latest update (mid 2015) of the "Expanded Access Program" (93 patients treated vs. 48 in 2014)

Broad label and limited post-approval commitments that help build the market

Positively, the label has no restriction on mutation, disease status or time of onset of disease. This means that a large pool of LHON patients where first symptoms have

occurred several years ago can also apply for Raxone treatment, next to newly diagnosed patients.

Santhera has agreed to several post-approval commitments, including:

1) **"LEROS" open label study:** this will be run primarily in countries where early launch might not be possible, thereby providing LHON patients access to Raxone. In addition, natural history data will be collected to serve as a comparator group
2) **A patient registry:** monitor patients in a real life setting and collecting long-term treatment data.

The estimated timeline for completion of these post-approval commitments is around 2021. We have included the costs of these post-approval commitments in our forecasts, which will be conducted and paid by Santhera (we assume low single-digit million Swiss francs over several years).

LHON specialist sales force retained for DMD – too important to restructure

Santhera will retain its European specialist sales force infrastructure to continue to grow the sales of Raxone in LHON during the transition period until completion of the Chiesi agreement expected in September 2019 and to prepare for the upcoming EU conditional approval of Puldysa in DMD expected in mid 2020. Therefore, as the European launch of Puldysa for DMD is anticipated for mid next year, the company will build on its commercial structure to prepare for this milestone event. Moreover, the cost of retaining the Western European specialist sales force is largely paid by the Raxone revenues booked until completion of the Chiesi transaction and continued Raxone LHON sales in France, which are expected to be transferred to Chiesi at a later stage. In those countries not covered by the Santhera sales organization, the company intends to have Puldysa distributed by partners.

Our rNPV values North America rights for Raxone in LHON at CHF 103 mn

Santhera guides Raxone sales for LHON to range between CHF 35-37 mn in 2019. Assuming a closing of the Chiesi license agreement in September 2019, we assume in 2019 that Santhera books ¾ of Raxone revenues (and costs) with Chiesi booking the remainder. From 2020 onwards, Chiesi books all Raxone LHON revenues, excluding North America, where Santhera maintains the rights. Santhera still owns the North America rights for Raxone in LHON, where our rNPV points to a value of CHF 103 mn or CHF 6 per share, assuming a 65% (phase III) success probability. We forecast North America peak sales for Raxone in LHON to amount to CHF 56 mn with first launches in 2023, approximately one year after launch of Puldysa in DMD, based on a yearly treatment price per patient of 90,000, two years treatment, and a peak penetration rate reaching 65%, accounting for COGS and M&S costs.

Forecasts & Sensitivity Analysis

RAXONE - FINANCIAL FORECASTS FOR LEBER'S HEREDITARY OPTIC NEUROPATHY

INDICATION	THE TREATMENT OF VISUAL IMPAIRMENT IN ADOLESCENT AND ADULT PATIENTS WITH LEBER'S HEREDITARY OPTIC NEUROPATHY (LHON)
DOSAGE	900 MG/DAY (TWO 150 MG TABLETS 3X DAILY)
PRICE	EU/ROW: EUR 62,415 ANNUAL TREATMENT COST; US: USD 90,000 ANNUAL TREATMENT COST - WE ASSUME 2 YEARS TREATMENT DURATION (BASED ON EAP)
STANDARD OF CARE	NO TREATMENT AVAILABLE
UNIQUE SELLING POINT	FIRST-EVER TREATMENT APPROVED FOR TREATING LHON THAT IMPROVES VISION AND PROTECTS FROM FURTHER VISION LOSS

7Ps ANALYSIS

PATENT	COMPOSITION OF MATTER (COM) PATENT PROTECTION EXPIRED - EU: ORPHAN PROTECTION 10 YEARS (SEP 2025); US: ORPHAN PROTECTION 7 YEARS (2026)
PHASE	EU: APPROVED SEP 2015; US: LHON FILING 2022 (AFTER DMD APPROVAL), US LAUNCH 2023
PATHWAY	ORPHAN DRUG DESIGNATION IN EU AND US - WE CONSERVATIVELY EXPECT NORMAL (10-12 MONTHS) REVIEW TIME IN US
PATIENT	ONLY OPTION TO REGAIN VISION AFTER BECOMING LEGALLY BLIND SHORTLY AFTER ONSET OF DISEASE OR PROTECT FROM FURTHER VISION LOSS
PHYSICIAN	FIRST-APPROVED TREATMENT THAT HAS THE POTENTIAL FOR PATIENTS TO PREVENT VISION LOSS OR REGAIN VISION PARTIALLY OR FULLY
PAYER	MANY PATIENTS SHOULD REGAIN SUFFICIENT VISION THAT THEY ARE NO LONGER LEGALLY BLIND AND NEED EXPENSIVE SUPPORT
PARTNER	CHIESI ACQUIRED GLOBAL RIGHTS (EXCL. NORTH AMERICA) IN 2019 FOR UP TO CHF 105 MN UPFRONT & SALES MILESTONES; SANTHERA RETAINS NORTH AMERICA RIGHTS

REVENUE MODEL

EUROPE 4 CLUSTERS (ACQUIRED BY CHIESI IN 2019)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NEWLY DIAGNOSED PATIENTS (= INCIDENCE 1/1,000,000)	465	475	484	494	504	514	524	534	545	556	567
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PENETRATION (%)	46.3%	50%	52%	54%	55%	55%	56%	52%	15%	2%	0%
PATIENTS (1ST TREATMENT YEAR)	215	239	253	268	276	284	292	276	84	9	1
PATIENTS (2ND TREATMENT YEAR)	192	215	239	253	268	276	284	292	276	84	9
TOTAL NEWLY DIAGNOSED PATIENTS TREATED (2-YEARS)	408	454	492	521	544	560	576	568	360	93	9
COST OF THERAPY PER YEAR (CHF)	71,460	71,094	71,147	71,147	71,147	71,147	71,147	71,147	71,147	71,147	71,147
SALES (CHF MN) - BOOKED BY CHIESI FROM Q4 2019	**29**	**8**	**23**	**37**	**39**	**40**	**41**	**40**	**26**	**7**	**1**
SALES (CHF MN) - BOOKED BY SANTHERA UNTIL Q4 2019		**24**	**12**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
COGS (10%) (CHF MN)	-3	-1	-1	0	0	0	0	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (CHF MN)		50		15			15				
R&D COSTS (CHF MN)	-2	-2	-2	0	0	0	0	0	0	0	0
M&S COSTS (CHF MN)	-16	-11	-2	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	**8**	**60**	**7**	**15**	**0**	**0**	**15**	**0**	**0**	**0**	**0**
TAXES (CHF MN)	0	0	0	-3	0	0	-3	0	0	0	0
PROFIT (CHF MN) - BOOKED BY CHIESI FROM Q4 2019	**8**	**60**	**7**	**12**	**0**	**0**	**12**	**0**	**0**	**0**	**0**

CEE / REST OF WORLD (ACQUIRED BY CHIESI IN 2019)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NEWLY DIAGNOSED PATIENTS (= INCIDENCE 1/1,000,000)	270	275	280	286	292	298	304	310	316	322	329
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PENETRATION (%)	14.0%	24%	31%	34%	36%	37%	38%	35%	10%	1%	0%
PATIENTS (1ST YEAR TREATMENT)	38	66	87	97	105	110	114	107	33	3	0
PATIENTS (2ND YEAR TREATMENT)	21	38	66	87	97	105	110	114	107	33	3
TOTAL NEWLY DIAGNOSED PATIENTS TREATED (2-YEARS)	59	104	153	184	202	215	224	221	140	36	4
DISTRIBUTOR TRANSFER PRICE (% OF WHOLESALE)	60%	65%	65%	65%	70%	70%	70%	70%	70%	70%	70%
DISTRIBUTOR PRICE OF THERAPY PER YEAR (CHF)	42,876	46,211	46,245	46,245	49,803	49,803	49,803	49,803	49,803	49,803	49,803
SALES (CHF MN) - BOOKED BY CHIESI FROM Q4 2019	**3**	**1**	**7**	**9**	**10**	**11**	**11**	**11**	**7**	**2**	**0**
SALES (CHF MN) - BOOKED BY SANTHERA UNTIL Q4 2019		**4**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
COGS (10%) (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	**2**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
TAXES (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (CHF MN) - BOOKED BY CHIESI FROM Q4 2019	**2**	**3**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

UNITED STATES / CANADA (SANTHERA SALES FORCE)	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
NEWLY DIAGNOSED PATIENTS (= INCIDENCE 1/1,000,000)	390	398	406	414	422	431	439	448	457	466	476
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PENETRATION (%)	0%	0%	0%	0%	0%	10%	35%	50%	60%	65%	65%
PATIENTS (1ST TREATMENT YEAR)	0	0	0	0	0	43	154	224	274	303	309
PATIENTS (2ND TREATMENT YEAR)	0	0	0	0	0	0	43	154	224	274	303
TOTAL NEWLY DIAGNOSED PATIENTS TREATED (2-YEARS)	0	0	0	0	0	43	197	378	498	577	612
COST OF THERAPY PER YEAR (CHF)	0	0	0	0	0	91,620	91,620	91,620	91,620	91,620	91,620
SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**4**	**18**	**35**	**46**	**53**	**56**
CHANGE (%)							357%	92%	32%	16%	6%
COGS (10%) (CHF MN)	0	0	0	0	0	0	-2	-3	-5	-5	-6
M&S COSTS (CHF MN)	0	0	-5	-5	-5	-5	-5	-5	-7	-8	-8
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**-5**	**-5**	**-5**	**-2**	**11**	**26**	**34**	**40**	**42**
TAXES (CHF MN)	0	0	0	0	0	0	-2	-5	-7	-8	-8
PROFIT (CHF MN)	**0**	**0**	**-5**	**-5**	**-5**	**-1**	**9**	**21**	**28**	**32**	**34**

	2018E	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
GLOBAL SALES (CHF MN)	**32**	**37**	**42**	**46**	**49**	**55**	**70**	**86**	**78**	**61**	**57**
CHANGE (%)	38%	17%	13%	8%	7%	12%	29%	23%	-9%	-22%	-7%
GLOBAL PROFIT (CHF MN)	**10**	**64**	**2**	**7**	**-5**	**-1**	**21**	**21**	**28**	**32**	**34**
CHANGE (%)	-876%	507%	-97%	304%	-174%	-76%	-1800%	0%	32%	16%	6%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**158**
NUMBER OF SHARES (MN)	17.0
NPV PER SHARE (CHF)	**9**
SUCCESS PROBABILITY	65% = US PHASE III
RISK ADJUSTED NPV PER SHARE (CHF)	**6**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	95%	10	9	9	9	9	8	8
	90%	9	9	9	8	8	8	8
	85%	9	8	8	8	8	8	7
	80%	8	8	8	7	7	7	7
	75%	8	7	7	7	7	7	7
	70%	7	7	7	7	6	6	6
	65%	7	6	6	**6**	6	6	6

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

First-ever therapy approved for treating Leber's Hereditary Optic Neuropathy that otherwise leads to rapid blindness in most patients at an early stage of life, with no apparent competition on the horizon. Raxone is a well-tolerated drug and has shown clinical benefit both in prevention of vision loss and recovery from vision loss.

7P's Analysis

Patent: The composition of matter patent has expired. Protection is safeguarded through orphan drug exclusivity of 10 years in the EU (Q3 2025) and 7 years in the US (2029). The FDA and EMA actively enforce orphan drug market exclusivity and this should be sufficient to block unapproved idebenone with questionable quality. Moreover, patients will receive reimbursement for Raxone. The active ingredient idebenone is chemically and pharmacologically distinct from vitamin E and CoQ10 and therefore cannot be substituted.

Phase: On September 9th, 2015 the EU approved Raxone for treating visual impairment in adolescents and adult patients with LHON. Regulatory filings included roughly 3x more patient data than in the original EU filing, including the open-label Expanded Access Program and Case Study Program. The company will approach the FDA to discuss the regulatory pathway to US approval. We assume a launch approximately one year after DMD approval of Puldysa in the US.

Pathway: Raxone enjoys in both the EU and US orphan drug designation; an incentive to develop drugs for rare disease. Safety and effectiveness of an orphan drug must be established through adequate and well-controlled studies. At times with life-ruining diseases, such as in the case of LHON, patients can get early access through compassionate use programs.

Patient: The improvement in quality of life is huge for those patients that regain vision. They can pick up normal daily activities that they could no longer do when they were legally blind. Even for those patients where the vision loss no longer progresses there is a benefit, as they may not need as much supportive care if they were to turn blind.

Physician: For the first-time ever, physicians will have a convenient and well-tolerated treatment that in a large portion of LHON patients either halts the progression of central vision loss or even improves eyesight in a clinically meaningful way. Raxone will become the standard of care for LHON patients.

Payer: An improvement of central vision or mere stopping vision loss, leads to substantial cost savings in supportive care. Furthermore, Raxone treatment is not a chronic treatment and payers are not confronted with life-long treatment costs as with many other orphan treatments.

Partner: Santhera will sell Raxone through its own field force in the EU until completion of the transfer of the global rights (excluding North America) to Chiesi expected in September 2019. Santhera may seek a partner to the North America rights. On US approval of Puldysa in DMD, we assume Santhera will exit neuro-ophthalmology, at latest.

Leber's Hereditary Optic Neuropathy Market

Previously, the LHON market was non-existent and limited to use of Santhera's Raxone in named patient programs and the temporary approval in France in 2014. The market developed with the launch of Santhera's Raxone in the EU. Germany was the first EU member state to launch Raxone in LHON in October 2015 and is now approved in 20 European countries and Israel. Raxone is the first-ever treatment approved for LHON, and therefore the first for a mitochondrial disease and a neuro-ophthalmological disease. We believe the global LHON market, only consisting of Raxone, could reach peak sales of CHF 100 mn split evenly between Europe and the US. In May 2019, Chiesi licensed the global rights (ex. North America) for Raxone in LHON.

LEBER'S HEREDITARY OPTIC NEUROPATHY - KEY FACTS	
MARKET SIZE	POTENTIAL UP TO USD 100 MN (vL ESTIMATE)
PREVALENCE	APPR. 1/30,000-50,000 PEOPLE; 9,000 IN US/CANADA; 12,000 IN THE EU; 3,000 IN JAPAN
INCIDENCE	APPR. 1/1,000,000 PEOPLE
UNDERLYING CAUSE	GENETIC DISEASE THAT AFFECTS RETINAL GANGLION CELLS OF THE EYE. THREE PRIMARY MITOCHRONDIAL DNA MUTATIONS ACCOUNT FOR APPROXIMATELY >90% OF CASES: 1) G11778A (50-70% OF PATIENTS); 2) T14484C (10-15%); AND 3) G3460A (8-25%). PREDOMINANTLY YOUNG AND OTHERWISE HEALTHY MALES IN ALL ETHNIC GROUPS ARE AFFECTED. MALES ARE MORE AFFECTED THAN FEMALES.
SYMPTOMS	FIRST SYMPTOMS TYPICALLY APPEAR BETWEEN 20-30 YEARS OF AGE (95% OF VISION LOSS OCCURS BEFORE THE AGE OF 50): - BLURRED VISION TYPICALLY STARTS IN ONE EYE - RAPID LOSS OF CENTRAL VISION (WITHIN WEEKS OF FIRST SYMPTOMS) - SECOND EYE AFFECTED AROUND A FEW WEEKS LATER - PATIENTS ARE LEGALLY BLIND WITHIN 1 YEAR OF SYMPTOM START - IMPAIRMENT OF COLOR CONTRAST VISION - NO PAIN ON EYE MOVEMENT VISUAL LOSS IN MOST CASES VERY SEVERE AND PATIENTS REMAIN BLIND THE REST OF THEIR LIVES. FEW INDIVIDUALS RECOVER VISION SPONTANEOUSLY.
DRUG CLASS (KEY BRANDS)	- SHORT-CHAIN BENZOQUINONE (RAXONE) - APPROVED IN EU IN 2015 EMERGING THERAPIES: - GENE THERAPY (GS010)
MAJOR PLAYERS (KEY BRANDS)	- CHIESI (RAXONE) - APPROVED IN EU IN 2015 EMERGING PLAYERS: - GENSIGHT BIOLOGICS (GS010) - PHASE III, NOT INCLUDED IN MARKET SIZE ESTIMATE

SOURCE: VALUATIONLAB, NIH, WHO, LHON.ORG, ORPHA.NET, COMPANY DATA

Leber's Hereditary Optic Neuropathy (LHON) is an inherited form of vision loss and is the most common of the primary mitochondrial DNA (mtDNA) disorders. The disease causes unexplained sudden, severe loss of central vision and color desaturation that is often irreversible. The German eye doctor Theodor Leber first described the disease in 1871.

LHON is a rare (orphan) disease, which has a prevalence of approximately 1: 30,000 to 1: 50,000 people and can be found in all ethnic groups. There are approximately 20-30,000 people living with LHON in North America, EU and Japan. The incidence, or the number of new cases per year, amounts to approximately 1 per 1,000,000. Actual prevalence and incidence numbers could be higher due to under- and misdiagnosis, which often occurs with orphan diseases.

The disease is related to changes in mitochondrial DNA (mtDNA), which leads to a defect in the complex I subunit of the mitochondrial electron transport chain. This defect leads to decreased ATP (adenosine triphosphate) synthesis resulting in lower cellular energy. This is accompanied by increased production of oxygen free radicals resulting in oxidative stress/damage, which is believed to affect the retinal ganglion cells which become dysfunctional and are ultimately lost to programmed cell death. Retinal ganglion cells are a

type of nerve cells in the eye that collectively transmit visual information to the brain through long axons (nerve fibers). Together these axons form the optic nerve.
Three mtDNA mutations account for over 90% of cases: 1) the G11778A mutation (50-70% of cases); 2) the T14484C mutation (10-15%); and 3) the G3460A mutation (8-25%).

LHON is transmitted through the mother as it is primarily due to mutations in the mitochondrial genome, and only the egg contributes mitochondria to the embryo. Men cannot pass on the disease to their children.

It remains unclear what triggers these genetic mutations to cause retinal ganglion cells to become dysfunctional resulting in the specific pathology of LHON. Additional factors such as smoking and alcohol may be involved, although there are conflicting studies. Expression of the gene varies with the mitochondrial mutation and the family, but in general the chances of the eyes of female carriers remaining healthy are over 85% and of males over 50%. While LHON occurs 80% of the time in young men in their twenties, it can occur in men and women, of all ages. LHON may also occur in someone who has no family history of LHON or blindness. Without a known family history, diagnosis usually requires a neuro-ophthalmological evaluation and a genetic blood test.

Two phases of LHON distinguished:

1) **The acute phase** where patients initially experience a painless loss of color vision accompanied by a painless loss in central vision, a blurry or blind spot that increases in size over time. The disease usually starts in one eye, while the second eye usually follows a similar course in a matter of weeks or few months. Most patients progress to a vision loss in both eyes of 20/200 (a threshold of legal blindness in Snellen notation) or worse within 1 year of disease onset.
2) **The chronic phase**, where the central vision loss stabilizes in both eyes with no further improvement, and typically remains life-long. Over the course of several years the retinal nerve fiber progressively degenerates. Although most patients still perceive light, the blurred or blind spot is life ruining and most patients become legally blind. Daily activities such as reading, watching TV, walking, driving, working is no longer possible.

Generally, recovery in vision loss of LHON patients over time is rare, but depending on the disease-causing mtDNA mutation, differences have been described. Patients with the G11778A mutation clearly have the worst prognosis with a reported spontaneous recovery rate of 4-23%, followed by patients with the G3460A mutation (15-25%) and patients with the T14484C mutation (37-71%) having the highest probability of spontaneous improvement in vision.

Current drug treatment – no treatment options, patients remain blind
Currently there are no effective medicines approved for treatment of LHON except for Raxone in the EU.

New market entrants – novel gene therapies still years away from market
We believe Chiesi/Santhera's **Raxone** (idebenone) will dominate the market in the near and medium term for the treatment of LHON. Most novel gene therapies are in early stages of development, with a relatively low success probability and years away from market introduction. GenSight's **GS010** (phase III completed), a single intravitreal injection in the eye, is the most advanced gene therapy lacking clear evidence of efficacy.

Pipeline – Another blockbuster in the early stages

We have conservatively not accounted for Santhera's early stage pipeline projects due to the lack of sufficient clinical proof-of-concept at this moment. These projects could provide substantial upside when developed successfully.

Santhera's early stage clinical projects include:

1. **POL6014** for treating cystic fibrosis and other rare lung disorders
2. **Omigapil / gene therapy** for treating CMD (congenital muscular dystrophy)

1) POL6014 (cystic fibrosis) – Peak sales potential of CHF 1 bn

In February 2018, Santhera expanded its product pipeline in lung diseases where Raxone is being developed to reduce respiratory decline in DMD patients, one of the leading causes of hospitalization and death in this patient group. The company acquired exclusive global rights to POL6014 from the Swiss biopharmaceutical company Polyphor (ticker: POLN). POL6014 is a clinical stage selective human neutrophil elastase (hNE) inhibitor for treating cystic fibrosis and other neutrophilic lung diseases such as non-cystic fibrosis bronchiectasis (NCFB), alpha-1 antitrypsin deficiency (AATD) and primary ciliary dyskinesia (PCD). These are all rare lung diseases, which allow for 10 years orphan drug market exclusivity in the EU and 7 years in the US. POL6014 enjoys composition of matter patent protection until 2025 with potential market protection (patent extensions) until 2030. In addition, method of use and formulation patents have been filed or are in preparation. We believe POL6014 nicely complements Santhera's product pipeline targeting rare diseases such as DMD. Santhera has gained significant knowledge in clinical development of investigational drugs for lung disease with the development program of Puldysa in treating respiratory complications in DMD.

Agreement paid in shares with back-loaded cash milestone payments

Polyphor received an initial payment of CHF 6.5 mn, payable in Santhera shares at an agreed valuation of CHF 27.2053 and is eligible to additional cash milestone payments of up to CHF 121 mn in development, regulatory and particularly sales milestones (indicating back-loaded cash milestone payments) and tiered royalty payments on net sales. Santhera issued 238,924 shares (3.8% of issued shares in February 2018) required for the initial payment to Polyphor out of its existing authorized share capital. Consequently, the transaction provided Santhera with a promising new product candidate for rare lung disorders with little upfront development costs to reach proof-of-concept in cystic fibrosis.

Cystic fibrosis affects 70,000 patients globally with no cure and poor prognosis

Cystic fibrosis is a rare genetic and progressive disorder that affects mostly the lungs, but also the pancreas, liver, kidneys and intestine, and affects approximately 70,000 patients in Europe and the US. It is caused by the presence of mutations in both copies of the gene for cystic fibrosis transmembrane conductance regulator (CFTR) protein. The disease is characterized by persistent lung infection and chronic inflammation. Long-term issues include difficulty breathing and coughing up thick and sticky mucus as a result of frequent lung infections. The average life expectancy is between 42 and 50 years, where lung problems account for death in ~80% of cystic fibrosis patients. Cystic fibrosis is most common among people of Northern European ancestry and affects about one of every 3,000 newborns. The disease is considered an orphan drug disease, which allows for 10

years market exclusivity in the EU and 7 years in the US. There is no known cure for cystic fibrosis.

POL6014 could become a blockbuster in a USD 10 bn cystic fibrosis market…
The global cystic fibrosis market is expected to exceed USD 10 bn over the next ten years. Treatment typically consists of combination therapies, including mucolytics (e.g. Pulmozyme), inhaled antibiotics such as Novartis' Tobi (tobramycin), pancreatic enzyme products such as AbbVie's Creon and CFTR modulators such as Vertex' Kalydeco (ivacaftor) or Orkambi (ivacaftor/lumacaftor combo). However, these treatments do not significantly reduce the chronic lung inflammation. POL6014 is a first-in-class hNE inhibitor that targets chronic inflammation, caused by neutrophil elastase from neutrophils present in the lung due to the buildup of thick mucus. High levels of hNE have been detected in cystic fibrosis sputa and these high levels of hNE correlate with disease severity as measured by lung parameters such as FEV1 reduction and are therefore an important surrogate marker of disease. POL6014 could be potentially used in combination with existing treatments.

…being administered by the Pari eFlow nebulizer…
Previous hNE inhibitors have mostly been given as an oral tablet, which did not deliver adequate concentrations of drug to the lung and safety issues due to systemic exposure leading to their discontinuation. POL6014 will be administered by inhalation using Pari eFlow, a well-accepted rapid nebulizer system used in cystic fibrosis, leading to high concentrations in the lung (1,000 times greater in the lung sputum versus plasma) and favoring local activity in the lung with low systemic exposure, thereby reducing the risk of systemic side effects. Chiesi Farmaceutici is developing CHF6333, a dry-powder inhaler formulation of hNE, which has successfully completed a phase I trial in 72 patients with cystic fibrosis and non-cystic fibrosis bronchiectasis (NCFB).

…by capturing 15% market share and leveraging the existing sales infrastructure
Assuming POL6014 captures a conservative 15% of the market with a USD 70,000 to USD 100,000 annual treatment price, peak sales for POL6014 could amount to CHF 1 bn for cystic fibrosis alone. Santhera can leverage its own EU and US specialist sales infrastructure that it is building up for Puldysa, to commercialize POL6014 in these key regions and maximize profitability. Many of the same pulmonologists who manage the pulmonary aspects of neuromuscular disease such as DMD, also manage rare lung disorders such as cystic fibrosis. Outside these regions, Santhera could sign on distributors or commercialization partners in return for upfront and commercialization milestones and royalties on net sales.

Next development steps with POL6014 in cystic fibrosis
POL6014 has been shown to be effective in various non-clinical and biomarker trials, including human sputum and bronchiolar lavage (BAL) samples for patients with cystic fibrosis and findings from two completed phase I trials: one in a first-in-man trial in 48 healthy volunteers and one in a single ascending dose (SAD) safety and tolerability trial in cystic fibrosis patients. No serious adverse events were observed, and the single-dose was well-tolerated.

Santhera started a phase Ib multiple ascending dose (MAD) trial in cystic fibrosis patients in October 2018, a trial that was already designed by Polyphor and is financially supported by the Cystic Fibrosis Foundation. The trial is conducted in sites in Germany and Poland.

The MAD trial will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of orally inhaled multiple doses of POL6014 in up to 40 cystic fibrosis patients. Patients will be treated for 15 days with one of three ascending doses of POL6014 given once or twice daily or placebo. Top line results are expected in H2 2019.

Proof-of-concept trial in cystic fibrosis could be started in 2020
Upon dose selection, a phase II proof-of-concept trial could be started in 2020 with a potential read-out 12 months later. The company will seek further EU and US regulatory guidance before starting phase II development. In parallel, Santhera will also collaborate with experts to explore not only cystic fibrosis, but potentially other rare lung disorders for which POL6014 offers a treatment option such as non-cystic fibrosis bronchiectasis (NCFB), alpha-1 antitrypsin deficiency (AATD) or primary ciliary dyskinesia (PCD).

Orphan Drug Designation provides 10 years marketing exclusivity from approval
In October 2018, the COMP (Committee for Orphan Medicinal Products) of the EMA (European Medicines Agency) issued a positive opinion on ODD (Orphan Drug Designation) for POL6014 for the treatment of cystic fibrosis, a rare lung disorder that affects around 35,000 people in the EU. An ODD grant typically follows within 30 days (mid-November). ODD is an incentive for pharmaceutical companies to develop treatments for rare diseases and provides up to 10 years marketing exclusivity from the date of approval.

2) Omigapil / gene therapy (CMD) – Peak sales potential of CHF 150+ mn

Novartis originally developed omigapil, a deprenyl analog with anti-apoptotic (anti-cell death) properties, for Parkinson's disease and ALS (Lou Gehrig's disease) but terminated development in these indications due to lack of efficacy. Santhera obtained an exclusive license to develop the compound in congenital muscular dystrophies (CMD) in 2007. These are a variety of inherited neuromuscular disorders with different forms of progressive loss of muscle tissue characterized by early-onset weakness and hypotonia (low muscle tone or strength) alongside associated dystrophic findings in muscle biopsy. Progressive muscle weakness, joint contractures and respiratory insufficiency characterize most CMDs. Pre-clinical studies in a disease-relevant model showed that omigapil inhibits cell death and reduces body weight loss and skeletal deformation, while increasing locomotive activity and protecting from early mortality.

Positive phase I "CALLISTO" trial results of omigapil in CMD reported in April 2018
A phase I study called "CALLISTO" started in July 2015 with CHF 1.3 mn funding provided by EndoStem, an EU 7th Framework program, and from two patient organizations Cure CMD and the Swiss Foundation for Research on Muscle Diseases. In April 2018, omigapil successfully completed the phase I "CALLISTO" trial in patients with two forms of CMD (congenital muscular dystrophy) conducted by the US NIH (National Institutes of Health). The ascending multiple dose cohort trial met its primary objective to establish a favorable pharmacokinetic profile of omigapil and was safe and well tolerated in children and adolescents with CMD. A total of 20 patients aged 5-16 years with either of two of the most common forms of CMD were enrolled in the trial. Following further data analysis, Santhera is in discussion with clinical experts such as the TREAT-NMD Advisory Committee for Therapeutics (TACT) and regulators to prepare for a pivotal trial in patients with CMD. Peak sales could reach CHF 150 mn.

Preclinical research collaboration with Biozentrum Basel in CMD gene therapy

In May 2019, a preclinical research collaboration was announced with the Biozentrum of the University of Basel to advance gene therapy research for the treatment of LAMA2-deficient CMD (congenital muscular dystrophy). Innosuisse, the public Swiss innovation agency, and Santhera will jointly invest CHF 1.2 mn in the project. This novel gene therapy approach and omigapil could act complementary in CMD. Previous work has demonstrated that omigapil provides benefit to LAMA2-deficient mice and has additive effects to gene therapy using linker proteins.

Laminins are proteins of the extracellular matrix that help maintain muscle fiber stability by binding to other proteins. LAMA2-related muscular dystrophy (LAMA2 MD, also called MDC1A), is one of the most common forms of CMD. It is caused by mutations in the LAMA2 gene encoding the alpha2 subunit of laminin-211. Most LAMA2 MD patients show complete absence of laminin-alpha 2, are hypotonic (floppy) at birth, fail to walk, and die to respiratory complications.
It has been demonstrated that two linker proteins, engineered with domains derived of the extracellular matrix proteins agrin, laminin and nidogen, could compensate for the lack of laminin-alpha2 and restore the muscle basement membrane. Through simultaneous expression of artificial linkers (“SEAL”), this gene therapy approach aims to overcome the genetic defect by substituting laminin-alpha2 deficiency with small linker proteins containing necessary binding domains to re-establish muscle fiber integrity. In a transgenic mouse model, the linker expression increased the lifespan of LAMA2-deficient mice fivefold to a median of 81 weeks compared to 15.5 weeks in the disease model without the therapeutic linker expression. Recently, it was demonstrated that such linker constructs could be applied by standard adeno-associated virus (AAV) vectors.

Due to the early development stage of this novel gene therapy approach to treat LAMA2-deficient CMD, we have not included any forecasts in our valuation.

Income Statement

SANTHERA PHARMACEUTICALS									SHARE PRICE (CHF) 13.76		
INCOME STATEMENT (CHF MN)	**2018**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**
PRODUCT SALES (INCL. PARTNER SALES)	**32**	**37**	**64**	**90**	**267**	**634**	**1,056**	**1,358**	**1,300**	**1,410**	**1,598**
CHANGE (%)	38%	17%	73%	41%	195%	138%	66%	29%	-4%	8%	13%
REPORTED SALES (SANTHERA TERRITORIES)	**32**	**28**	**34**	**45**	**218**	**584**	**1,001**	**1,302**	**1,261**	**1,394**	**1,587**
CHANGE (%)	38%	-12%	22%	32%	387%	168%	72%	30%	-3%	11%	14%
ROYALTIES (FROM PARTNER SALES)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
UPFRONT & MILESTONES	**0**	**50**	**0**	**15**	**0**	**0**	**15**	**0**	**0**	**0**	**0**
OTHER REVENUES	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
REVENUES (EXCL. PARTNER SALES)	**32**	**78**	**34**	**60**	**218**	**584**	**1,016**	**1,302**	**1,261**	**1,394**	**1,587**
CHANGE (%)	38%	146%	-56%	76%	265%	168%	74%	28%	-3%	11%	14%
COGS (INCL. PAYMENTS TO POLYPHOR / IDORSIA)	**-5**	**-6**	**-6**	**-12**	**-28**	**-80**	**-132**	**-195**	**-161**	**-173**	**-209**
GROSS PROFIT	**27**	**71**	**28**	**48**	**190**	**504**	**885**	**1,107**	**1,100**	**1,221**	**1,379**
CHANGE (%)	43%	165%	-61%	70%	297%	165%	76%	25%	-1%	11%	13%
MARGIN (%)	85.1%	91.7%	82.6%	79.9%	87.1%	86.3%	87.0%	85.0%	87.2%	87.6%	86.9%
R&D (INCL. IDORSIA OPTION PAYMENTS)	**-38**	**-43**	**-52**	**-29**	**-24**	**-23**	**-13**	**-10**	**-11**	**-12**	**-13**
CHANGE (%)	44%	11%	22%	-45%	-17%	-4%	-44%	-24%	10%	9%	9%
GENERAL & ADMINISTRATIVE	**-15**	**-16**	**-17**	**-18**	**-19**	**-20**	**-21**	**-22**	**-23**	**-24**	**-25**
CHANGE (%)	7%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
MARKETING & SALES	**-25**	**-23**	**-30**	**-44**	**-83**	**-170**	**-223**	**-303**	**-284**	**-308**	**-340**
CHANGE (%)	-13%	-7%	30%	47%	89%	104%	31%	36%	-6%	8%	11%
OTHER OPERATING INCOME/(EXPENSE)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
EBIT	**-51**	**-10**	**-71**	**-43**	**64**	**291**	**628**	**772**	**783**	**878**	**1,001**
CHANGE (%)	2%	-80%	580%	-40%	-251%	352%	116%	23%	1%	12%	14%
MARGIN (%)	-162.4%	-13.4%	-208.6%	-71.3%	29.5%	49.9%	61.8%	59.3%	62.1%	63.0%	63.1%
EBITDA	**-48**	**-6**	**-67**	**-38**	**69**	**296**	**633**	**778**	**789**	**884**	**1,007**
CHANGE (%)	1%	-86%	928%	-43%	-280%	329%	114%	23%	1%	12%	14%
MARGIN (%)	-150.6%	-8.3%	-196.5%	-64.1%	31.6%	50.7%	62.3%	59.7%	62.6%	63.4%	63.4%
D&A	**4**	**4**	**4**	**4**	**5**	**5**	**5**	**5**	**6**	**6**	**6**
NET FINANCIAL INCOME/(EXPENSES)	**-2**	**1**	**2**	**2**	**5**	**5**	**6**	**6**	**6**	**7**	**7**
PROFIT/(LOSS) BEFORE TAXES	**-54**	**-9**	**-69**	**-41**	**69**	**297**	**634**	**779**	**790**	**885**	**1,008**
CHANGE (%)	5%	-83%	674%	-41%	-270%	329%	114%	23%	1%	12%	14%
MARGIN (%)	-170%	-11%	-204%	-68%	32%	51%	62%	60%	63%	63%	63%
TAXES (EXCL. TAX LOSS CARRYFORWARDS)	**0**	**0**	**0**	**-5**	**-16**	**-56**	**-137**	**-168**	**-155**	**-158**	**-147**
TAX RATE (%)	-0.6%	0.0%	0.0%	-13.4%	23.1%	19.0%	21.6%	21.5%	19.7%	17.8%	14.5%
NET PROFIT/LOSS	**-54**	**-9**	**-69**	**-46**	**53**	**240**	**497**	**611**	**634**	**727**	**861**
CHANGE (%)	5%	-84%	674%	-33%	-215%	352%	107%	23%	4%	15%	19%
MARGIN (%)	-171%	-11%	-204%	-77%	24%	41%	49%	47%	50%	52%	54%
NET PROFIT/LOSS (EXCL. MILESTONES)	**-54**	**-59**	**-69**	**-61**	**53**	**240**	**482**	**611**	**634**	**727**	**861**
CHANGE (%)	5%	9%	17%	-12%	-187%	352%	101%	27%	4%	15%	19%
EPS (CHF)	**-7.86**	**-0.80**	**-6.19**	**-4.13**	**4.77**	**21.53**	**44.54**	**54.73**	**56.82**	**65.09**	**77.15**

ESTIMATES AS OF 5 JUNE, 2019 SOURCE: VALUATIONLAB ESTIMATES

NOTE:
Santhera guides Raxone sales for LHON to range between CHF 35-37 mn in 2019. Assuming a closing of the Chiesi license agreement in September 2019, we assume Santhera books ¾ of Raxone revenues (and costs) with Chiesi booking the remainder in 2019. From 2020 onwards, Chiesi books all Raxone LHON revenues, excluding North America, where Santhera maintains the rights.

On 31 December 2018, Santhera had a total of CHF 155.6 mn unrecorded tax loss carryforwards. Due to the uncertainties as to whether Santhera can use these, we have excluded them from our forecasts.

Ratios I Balance Sheet I Cash Flow Statement

SANTHERA PHARMACEUTICALS

SHARE PRICE (CHF) 13.76

RATIOS	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
P/E		-17.2x	-2.2x	-3.3x	2.9x	0.6x	0.3x	0.3x	0.2x	0.2x	0.2x
P/S		2.0x	4.5x	2.6x	0.7x	0.3x	0.2x	0.1x	0.1x	0.1x	0.1x
P/NAV		5.9x	4.2x	-16.6x	-9.6x	0.7x	0.2x	0.1x	0.1x	0.1x	0.0x
EV/EBITDA		-20.3x	-2.0x	-3.4x	1.9x	0.4x	0.2x	0.2x	0.2x	0.1x	0.1x

PER SHARE DATA (CHF)	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
EARNINGS	**-7.86**	**-0.80**	**-6.19**	**-4.13**	**4.77**	**21.53**	**44.54**	**54.73**	**56.82**	**65.09**	**77.15**
CHANGE (%)	-4%	-90%	674%	-33%	-215%	352%	107%	23%	4%	15%	19%
CASH	**3.19**	**2.16**	**3.50**	**0.24**	**1.48**	**28.49**	**85.71**	**155.92**	**227.15**	**306.91**	**397.73**
CHANGE (%)	-56%	-32%	62%	-93%	507%	1830%	201%	82%	46%	35%	30%
DIVIDENDS	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	**4.04**	**2.33**	**3.30**	**-0.83**	**-1.44**	**20.10**	**64.63**	**119.36**	**176.18**	**241.27**	**318.42**
CHANGE (%)	-22%	-42%	42%	-125%	73%	-1499%	222%	85%	48%	37%	32%

BALANCE SHEET (CHF MN)	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
NET LIQUID FUNDS	**22**	**24**	**39**	**3**	**16**	**318**	**957**	**1,741**	**2,536**	**3,426**	**4,440**
TOTAL ASSETS	**110**	**112**	**127**	**91**	**105**	**406**	**1,045**	**1,829**	**2,624**	**3,515**	**4,529**
TOTAL SHAREHOLDERS' EQUITY	**28**	**26**	**37**	**-9**	**-16**	**224**	**722**	**1,333**	**1,967**	**2,694**	**3,555**
CHANGE (%)											
RETURN ON EQUITY (%)	-195%	-34%	-187%	498%	-332%	107%	69%	46%	32%	27%	24%
FINANCIAL DEBT	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
EMPLOYEES	119	113	113	113	113	113	113	113	113	113	113
- CHANGE IN %	*6%*	*-5%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*

CASH FLOW STATEMENT (CHF MN)	2018	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E
PROFIT / (LOSS) BEFORE TAXES	**-54**	**-9**	**-69**	**-41**	**69**	**297**	**634**	**779**	**790**	**885**	**1,008**
DEPRECIATION & AMORTIZATION	4	4	4	4	5	5	5	5	6	6	6
OTHER NON-CASH ITEMS	12										
CASH FLOW FROM OPERATING ACTIVITIES	**-38**	**-5**	**-65**	**-36**	**74**	**302**	**639**	**784**	**795**	**890**	**1,014**
CASH FLOW FROM INVESTING ACTIVITIES	-6										
FREE CASH FLOW	**-44**	**-5**	**-65**	**-36**	**74**	**302**	**639**	**784**	**795**	**890**	**1,014**
CASH FROM FINANCING ACTIVITIES	21	7	80	0	-60	0	0	0	0	0	0
EFFECTS OF EXCHANGE RATE CHANGES ON CASH	0										
CHANGE IN LIQUID FUNDS	**-23**	**2**	**15**	**-36**	**14**	**302**	**639**	**784**	**795**	**890**	**1,014**

ESTIMATES AS OF 5 JUNE, 2019

SOURCE: VALUATIONLAB ESTIMATES

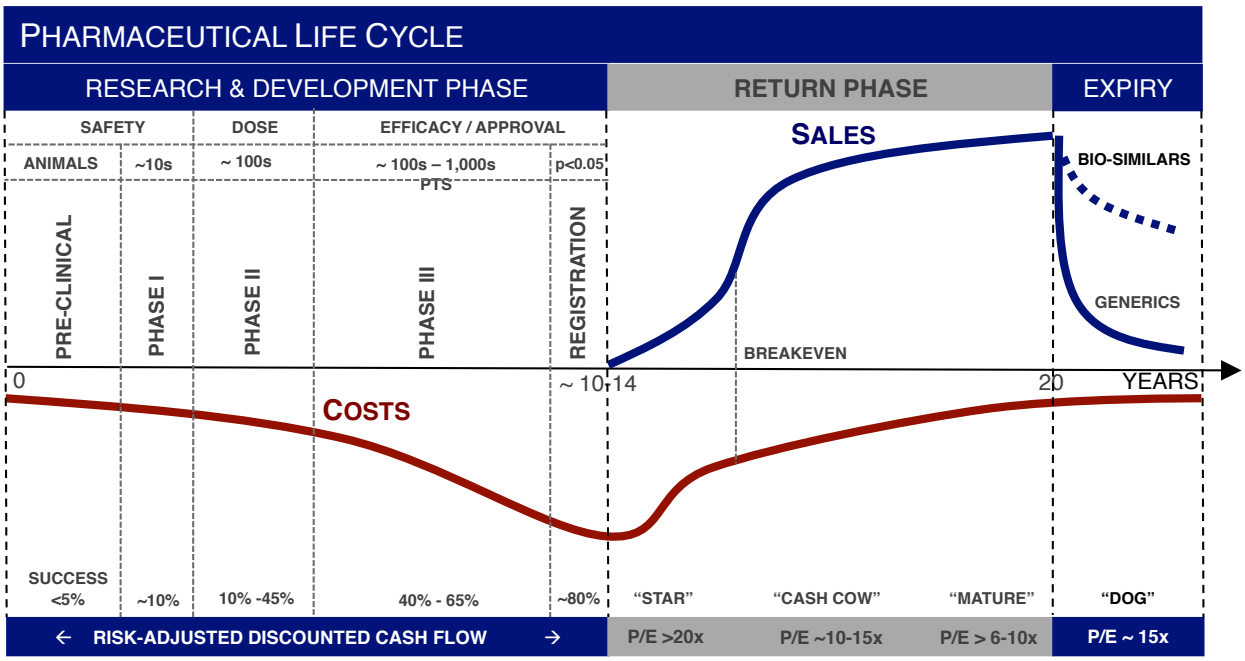
NOTE:

We calculate that Santhera will need a total cash injection of around CHF 80 mn to fully develop its key pipeline projects up to commercialization and profitability expected in 2022. We expect Santhera to raise these additional funds when it reaches key value inflection points including the EU approval of Puldysa in DMD patients (not treated with steroids) and the top line results of the pivotal "VISION-DMD" trial of vamorolone in DMD, at far higher share prices to minimize share dilution or monetize pipeline assets such as geographic product rights to Japan or Asia, or large indications such as inflammation for vamorolone.

APPENDIX

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. Additional protection is provided by orphan drug status (10 years in EU, 7 years in US). The average Research & Development Phase takes 8-14 years, leading to an effective Return Phase of 6-12 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II) and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success Probabilities & Royalties

In our risk-adjusted NPV calculations, we use standardized success probabilities based on historical clinical success rates. The success rate increases as the project progresses through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-20		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

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Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

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Risk Qualification

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

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