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FOCUS AREA: DISEASES OF THE CENTRAL NERVOUS SYSTEM (CNS) AND ORPHAN DISEASES

KEY DATA			SIX: NWRN
MARKET CAPITALIZATION (CHF MN)	212	PRICE ON MAY 02, 2018	11.9
ENTERPRISE VALUE (CHF MN)	140	RISK-ADJUSTED NPV PER SHARE (CHF)	38
CASH (31 DECEMBER 2017) (CHF MN)	72	UPSIDE/DOWNSIDE (%)	217%
MONTHLY OPERATING EXPENSE (CHF MN)	2.5	RISK PROFILE	HIGH RISK
CASH LIFE (YEAR)	UNTIL 2020	SUCCESS PROBABILITY LEAD PIPELINE DRUG	25%
BREAK-EVEN (EXCL. MILESTONES) (YEAR)	2020	EMPLOYEES (GROUP)	24
FOUNDED (YEAR)	1998	LISTED (YEAR)	2006
KEY PRODUCTS:	STATUS	MAJOR SHAREHOLDERS:	(%)
- XADAGO (PARKINSON'S DISEASE)	APPROVED	- DUBA AB (INVESTOR AB)	9.4
- SARIZOTAN (RETT SYNDROME)	PHASE III	- AVIVA	7.8
- EVENAMIDE (SCHIZOPHRENIA)	PHASE III (END 2018)	- ZAMBON GROUP	4.4
		- EXECUTIVE MANAGEMENT	0.5
		- FREE FLOAT	99.5
		- AVERAGE TRADING VOLUME (30-DAYS)	52,517
UPCOMING CATALYSTS:	DATE	ANALYST(S):	BOB POOLER
- XADAGO - START NEW LABEL TRIAL IN PD-LID*	END 2018		BP@VALUATIONLAB.COM
- EVENAMIDE - START PIVOTAL TRIALS SCHIZOPHRENIA	END 2018		+41 79 652 67 68
- SARIZOTAN - TOPLINE RESULTS "STARS"	END 2018		

* PD-LID = PARKINSON'S DISEASE LEVODOPA-INDUCED DYSKINESIA
 ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Three orphans in a row

Rett syndrome, PD-LID and resistant schizophrenia

Newron Pharmaceuticals has a product pipeline that targets diseases of the peripheral & central nervous system (CNS) and rare diseases. The company's key value drivers include: 1) Xadago, a once daily oral add-on therapy for Parkinson's disease with a unique dual mechanism of action, approved in the EU (2015) and US (2017), with a potential new label in PD-LID (Parkinson's disease levodopa-induced dyskinesia, an orphan-like indication; 2) sarizotan for Rett syndrome (orphan disease); and 3) evenamide an add-on therapy for schizophrenia and CTRS (clozapine treatment-resistant schizophrenia, an orphan-like indication). With cash of EUR 60.1 mn (31 December 2017) and increasing Xadago revenues, Newron has a cash runway until 2020, and is adequately funded beyond key value inflection points including phase III development of sarizotan for Rett syndrome, and two potentially pivotal phase III trials with evenamide in schizophrenia and CTRS. We derive a risk-adjusted NPV value of CHF 38 per share with 33% of the value related to Xadago, 31% to sarizotan, 27% to evenamide, and 10% to cash. Newron's risk profile is currently High Risk as the company is loss making and revenues stem solely from Xadago royalties. A re-rating should occur once profitability is reached in the next 2 years.

Key catalysts:

- 1) Start new label trial Xadago in PD-LID (end 2018):** Our risk-adjusted NPV for Xadago in PD-LID will rise to CHF 3/share with a 65% (phase III) success rate from currently CHF 1/share with a 15% (proof-of-concept) success rate.
- 2) Start potentially pivotal program of evenamide in schizophrenia/CTRS (end 2018):** Our risk-adjusted NPV jumps by CHF 39/share with a 50% (potentially pivotal) success rate from currently CHF 11/share with a 15% (proof-of-concept) success rate.
- 3) Topline results sarizotan "STARS" trial (end 2018):** On positive topline results, our risk-adjusted NPV will jump by CHF 22/share with a 65% (phase III) success probability from currently CHF 13/share with a 25% (phase II/III orphan drug) success rate.

Strategy & Cash Position

Italian biopharmaceutical company specialized in CNS and rare diseases

Newron Pharmaceuticals S.p.A. is an Italian biopharmaceutical company specialized in prescription drugs to treat peripheral & central nervous system (CNS) disorders and rare, so-called orphan diseases. The company is based in Bresso, near Milan, Italy and was established in December 1998 as a spin-off from Pharmacia & Upjohn (now part of Pfizer). Newron was listed on the SIX Swiss Stock Index in 2006 with the stock ticker: NWRN. In 2014 Newron opened a US office in Morristown, New Jersey, USA. Currently the group has 24 employees.

Three core products with a focus on two major and three orphan indications:

- 1) **Xadago (safinamide):** Launched in the EU and US as an add-on treatment to levodopa in patients with mid to late stage Parkinson's disease (major indication), Japanese approval expected in 2019 (triggering milestone); label extension in PD-LID (Parkinson's disease levodopa-induced dyskinesia – an orphan indication), potential pivotal trial in PD-LID to start end 2018
- 2) **Evenamide:** proof-of-concept established in 2017 as an add-on to antipsychotics in schizophrenia (major indication) with potential in CTRS (clozapine treatment-resistant schizophrenia – an orphan indication), potential pivotal trials in both indications to start end 2018
- 3) **Sarizotan:** topline results of potentially pivotal “STARS” trial targeting breathing disturbances in patients as young as six years of age with Rett syndrome (orphan indication) expected end 2018; “Burden of Illness” health economic outcome research study in Rett syndrome started to support regulatory approval, pricing and reimbursement; potential for Rare Disease Pediatric Priority Review Voucher on US approval with an average selling price of USD 154 mn

Newron's current therapeutic focus in Parkinson's disease, schizophrenia and Rett syndrome is a result of:

- The company's expertise in ion channel research, an important class of CNS drugs (e.g. Xadago, evenamide)
- A development agreement signed with Merck KGaA in 2011 (sarizotan)

Strategy to develop CNS drugs to optimal value and then out-license and to commercialize orphan drugs

Newron's strategy is to develop drugs originated from earlier discovery capabilities, acquire or in-license CNS disease drugs and develop them to their optimal value, and in case of rare diseases like sarizotan for Rett syndrome and/or potentially CTRS, whenever possible commercialize them. Where necessary or advantageous, the company seeks co-development and commercialization agreements to reduce research and development costs and generate revenue through R&D funding, milestone payments and royalties on future sales.

Product development strategy poised to optimize value and development risk

Newron has a pipeline with multiple catalysts on the horizon. The pipeline consists of a nice mix of major indications such as Xadago, which already generates revenues in Parkinson's

disease and evenamide as an add-on to antipsychotics in schizophrenia, and orphan indications such as sarizotan in Rett syndrome, Xadago in PD-LID and evenamide in CTRS (clozapine treatment-resistant schizophrenia). Currently, the majority of Newron's valuation is based on the (low) sales royalties and milestone payments from Xadago in Parkinson's disease. Substantial value will be unlocked with the approval and launch of sarizotan in Rett syndrome and evenamide in schizophrenia and CTRS. Newron's individual product strategy includes:

- **Xadago – Global rollout and PD-LID label extension to boost sales uptake**
Xadago is Newron's first ever approved drug for treating patients with mid to late stage Parkinson's disease and was launched in the EU in 2015 and in the US in 2017. Newron receives sales royalties and milestone payments from its development and commercialization partners Zambon (worldwide rights excluding Meiji Seika territories) and Meiji Seika (Japan and Asia). To date Newron has received roughly EUR 36 mn milestone and royalty payments from sales of Xadago. Japanese approval is expected in 2019. Newron and Zambon plan to expand Xadago's label to include PD-LID, a lucrative orphan-like indication in the US, to strengthen its label and boost sales. The potentially pivotal trial is expected to start end 2018 and will largely be paid by Zambon.
- **Sarizotan – A game changer that can be sold through an own sales force**
Sarizotan has the potential to be a First-to-Market approved treatment, with a TPP (target product profile) that promises to be a "Life-Modifying Drug" - a game changer for Newron. On positive potentially pivotal "STARS" trial results in treating Rett syndrome patients with breathing disturbances at the end of 2018, the company plans to establish a small specialist sales force (25-30 medical liaison managers) to commercialize sarizotan at least in the US and Europe to maximize the value of sarizotan. Sarizotan has orphan drug designation in the EU and US and is eligible for priority review. Hence, first launches are expected by end 2019/early 2020. Upon US approval Newron is eligible for a Rare Disease Pediatric Priority Review Voucher, which it can sell freely. The average value of recently sold RDPVR Vouchers is USD 154 mn, which could easily fund the buildup of the specialist sales force.
- **Evenamide – New paradigm in schizophrenia, short-term pain for long-term gain**
Evenamide is Newron's pipeline project with the highest peak sales potential targeting a USD 12 bn schizophrenia market and will be transformational for Newron upon approval. In 2017, evenamide established proof-of-concept as an add-on to current antipsychotics in patients with schizophrenia. Discussions with key opinion leaders and regulators highlighted the potential of evenamide as a new treatment paradigm for schizophrenia. A faster development pathway has been recognized by parallel development in clozapine treatment-resistant schizophrenia, an orphan-like indication with high unmet medical need, and in development as an add-on to antipsychotics in patients with schizophrenia. This cuts roughly 2-3 years off the development time initially expected in schizophrenia. Based on these findings Newron raised CHF 27 mn in September 2017 to fund these new development plans instead of out licensing evenamide to a major CNS player. Consequently, evenamide could be earlier on the market at far better licensing terms than initially expected with the potential to market evenamide in CTRS by an own specialist sales force, boosting the long-term potential substantially.

Newron's key priorities in the next 12-18 months, include:

1. The continued rollout of Xadago in Parkinson's disease by its partners in new countries/areas (e.g. Japan in 2019) and the signing on of new commercialization/distribution partners for Xadago outside the EU and US

2. The expansion of Xadago's label to include PD-L1D, a lucrative orphan indication, together with partner Zambon with the initiation of a potentially pivotal efficacy trial in end 2018
3. The conclusion of the final trial design and initiation of two potentially pivotal phase IIb/III trials of evenamide as: 1) an add-on to current antipsychotic therapy in schizophrenia (major indication), and 2) as an add-on to clozapine in patients with CTRS (clozapine treatment-resistant schizophrenia – an orphan indication), at the end of 2018; both trials will be funded by the recent CHF 27 mn private placement in September 2017
4. The conclusion of the international Burden of Disease study in Rett syndrome patients with breathing disorders to support regulatory approval, pricing and reimbursement of sarizotan
5. The announcement of the topline results of the potentially pivotal phase III "STARS" trial of sarizotan in Rett syndrome at the end of 2018
6. The filing and approval of sarizotan in Rett syndrome under priority review in 2019
7. The buildup of a US and European specialist sales organization to commercialize sarizotan in the lucrative US market and signing on commercialization partners elsewhere

Almost EUR 270 mn raised since inception in 1998

Since inception Newron has been quite successful in raising money and has invested significant resources and time mostly in developing Xadago in Parkinson's disease and ralfinamide in neuropathic low back pain, and now sarizotan in Rett syndrome and evenamide in schizophrenia. The company raised EUR 267 mn, of which EUR 114 mn in several private placements, most recently in September 2017, raising CHF 27 mn (EUR ~23mn) with existing and new investors. The recent private placement will be used to fund the two potentially pivotal trials of evenamide in schizophrenia and CTRS, thereby maximizing the long-term potential of this novel compound.

MONEY RAISED		EUR MN
PRE-IPO		62
IPO		74
PRIVATE PLACEMENTS		114
NEURONOVA ACQUISITION		16
TOTAL RAISED		267

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Prior to the IPO in 2006, management raised EUR 62 mn in three financing rounds. Newron was seed funded in 1999 by 3i with the company raising EUR 7 mn, followed with a EUR 25 mn B round (3i, Atlas, Apax) and a EUR 30 mn C round (3i, Atlas, Apax, HBM, TVM). Newron had one of the largest biotech IPO's in 2006 that provided the company with sufficient funds to develop ralfinamide up to phase IIb dose ranging trials in neuropathic low back pain. The NeuroNova acquisition added another EUR 16 mn to the cash position and committed cash-inflows in 2012.

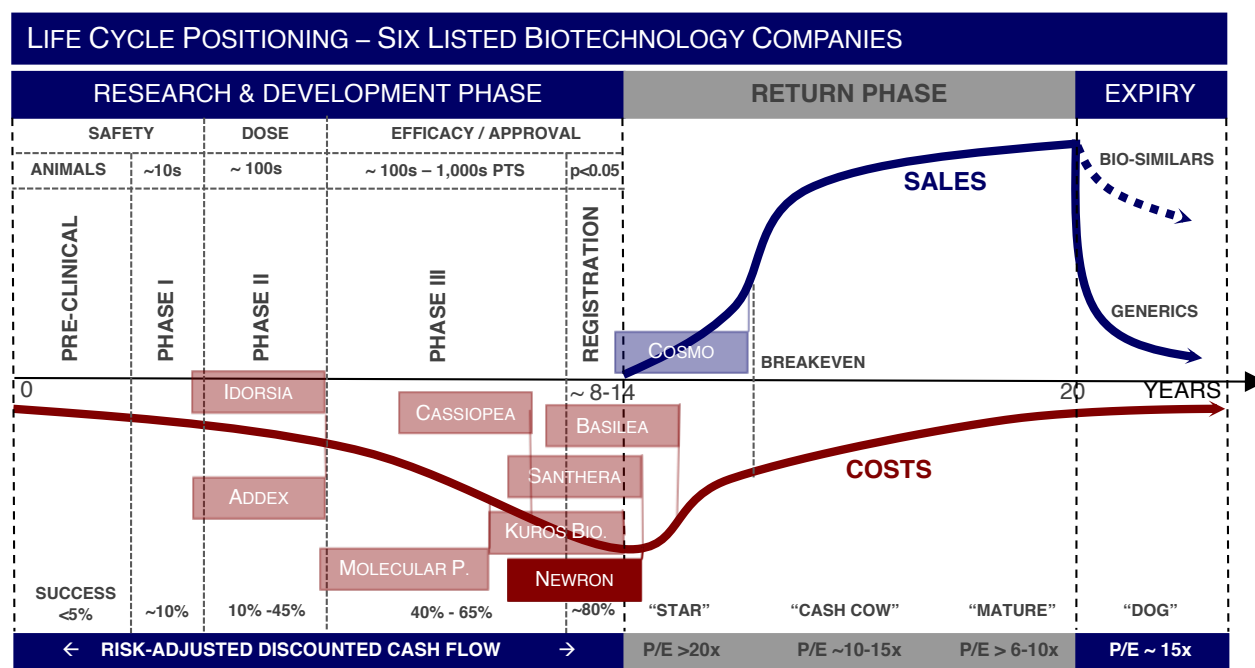
Newron comfortably funded to approach profitability in 2020

Newron had EUR 60.1 mn (CHF ~72 mn) in cash and short-term investments at hand on 31 December 2017. In 2017, the company received a EUR 11.3 mn milestone payment triggered by the US approval of Xadago and CHF 27 mn from the private placement. Together with increasing royalty payments on Xadago sales, Newron should have sufficient funds to develop its key pipeline projects sarizotan and evenamide up to their next value

inflection points. We assume operating expenses of EUR 81 mn for the next two years to fully develop sarizotan in Rett syndrome and build a small global specialist sales force for sarizotan and complete two potentially pivotal trials of evenamide in schizophrenia and CTRS before licensing the compound to a major CNS player for higher upfront, development and sales milestones and royalties on sales. We expect the buildup of a sales force for sarizotan (estimated at EUR 27 mn in 2019) should be offset by the upfront payment for the global rights for evenamide in schizophrenia (estimated at EUR 55 mn) and CTRS (estimated at EUR 18 mn). The cash position may be further boosted when Newron receives a rare disease pediatric priority review (RDPPR) voucher upon US approval of sarizotan in Rett syndrome in 2019 with an average selling price of USD 154 mn. Therefore, we believe Newron is comfortably funded to successfully execute its development plans and reach profitability in 2020.

Life Cycle Positioning – High Risk (from Speculative)

We qualify Newron's risk profile as High Risk as the company is still loss making and revenues are solely dependent on Xadago. On reaching profitability in 2020 and successful development of sarizotan in Rett syndrome and completion of the pivotal development of evenamide in schizophrenia and CTRS, the company should see a re-rating of the risk profile to Medium Risk. (see Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 38 per share

We derive a risk-adjusted NPV of CHF 38 per share, with cash of CHF 4 per share (31 December 2017), overhead of CHF 6 per share, using a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS							
PRODUCT NAME	INDICATION	PEAK SALES (EUR MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE	SUCCESS PROBABILITY	RISK-ADJUSTED	PERCENTAGE OF TOTAL
XADAGO (SAFINAMIDE)	PARKINSON'S DISEASE	401	2015(EU) / 2017(US)	14	100%	14	31%
XADAGO (SAFINAMIDE)	PARKINSON'S DISEASE LEVODOPA-INDUCED DYKINESIA (PD-LID)	236	2020	5	15%	1	2%
SARIZOTAN	RETT SYNDROME	396	2019/2020	53	25%	13	31%
EVENAMIDE	SCHIZOPHRENIA	1,299	2022	69	15%	10	24%
EVENAMIDE	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)	133	2022	8	15%	1	3%
RALFINAMIDE	NEUROPATHIC PAIN	NON CORE		7			
RDPPR VOUCHER * (ON US APPROVAL OF SARIZOTAN)		125		8			
CASH (31 DECEMBER 2017)		60		4		4	10%
TOTAL ASSETS				169		43	100%
OVERHEAD EXPENSES				-6		-6	
NPV/SHARE (CHF)				164		38	
SHARE PRICE ON MAY 02, 2018						11.9	
PERCENTAGE UPSIDE / (DOWNSIDE)						217%	

* RDPPR VOUCHER – RARE DISEASE PEDIATRIC PRIORITY REVIEW VOUCHER PROGRAM
ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

Newron's key value drivers, include:

Xadago (Parkinson's disease) - risk-adjusted NPV of CHF 14 per share

Xadago is Newron's first ever drug to be approved and launched. In 2015 the drug was launched in the EU to treat mid-to-late stage Parkinson's disease and is now available in 14 European countries, with more to come. In July 2017 US WorldMeds launched Xadago in the US. We assume Newron will receive EUR 29 mn in milestone payments from its partners Zambon (and sub-licensors) and Meiji Seika (and partner Eisai), with royalties on sales ranging between 10-15% in EU/ROW, 7.5% in the US, and 2.5% in Japan. We calculate an NPV of CHF 14 per share with peak sales of EUR 400 mn for Xadago in Parkinson's disease.

Xadago (PD-LID) [NEW] – risk-adjusted NPV of CHF 1 per share

To reflect the planned line extension of Xadago in PD-LID we have added detailed forecasts to value this new indication. We assume first launches in 2020, and conservatively assume similar pricing as for Xadago in Parkinson's disease. Based on conservative peak penetration rates ranging between 5-7% we derive peak sales of EUR 236 mn. We calculate a risk-adjusted NPV of CHF 1 per share for Xadago in PD-LID with a conservative 15% (proof-of-concept) success probability.

NOTE: Our success probability will increase to 65% (phase III) on the start of the phase III trial in PD-LID at the end of 2018.

Sarizotan (Rett syndrome) – risk-adjusted NPV of CHF 13 per share

Top line results of the potentially pivotal "STARS" trial evaluating sarizotan in Rett syndrome expected to report at the end of 2018. We forecast peak sales of EUR 400+ mn with a 25% (phase II/III orphan drug) success probability and conservative annual treatment costs ranging between USD 60,000 (US) and EUR 30,000 (EU/ROW) per patient. Sarizotan targets respiratory disturbances in Rett syndrome, a rare neurological disorder affecting primarily girls. All rights were licensed from Merck KGaA. Newron will market sarizotan through an own specialist field force globally. Orphan drug designation and pediatric exclusivity provides substantial exclusivity from approval in the EU (12 years) and US (7 1/2 years).

NOTE: The clinical effect will drive the pricing of sarizotan, which could lead to a substantially higher price point than we conservatively forecast. Moreover, Newron is eligible for a valuable RDPPR voucher on US approval, currently with an average selling price of USD 154 mn (not in forecasts).

Evenamide (schizophrenia) – risk-adjusted NPV of CHF 10 per share

Evenamide, a proprietary discovery project for treating schizophrenia, targets a global USD 12 bn antipsychotic market opportunity. Newron plans to develop evenamide as an add-on to antipsychotics in schizophrenia (major indication) and in CTRS (clozapine treatment-resistant schizophrenia – an orphan indication) to speed up development timelines by 2-3 years. The company is in final discussions with regulators on the definitive trial design of two potentially pivotal trials, one in schizophrenia and one in CTRS, which are planned to start at the end of 2018 (both 18 months to completion) and funded by the CHF 27 mn private placement in September 2017. On successful development in schizophrenia, Newron plans to license the compound to a strong CNS player in return for substantial upfront, development and sales milestone payments and royalties on sales. We forecast peak sales to amount to EUR 1.3 bn for evenamide in its major indication schizophrenia. We assume first launches in 2022 (two years earlier than our previous forecast!) with annual treatment costs conservatively ranging between EUR 3,650 (EU/ROW) and USD 5,475 per patient with peak penetration rates of ~20%. We calculate a risk-adjusted NPV of CHF 10 per share with a 15% (proof-of-concept) success rate, with Newron receiving EUR 229 mn global upfront and sales milestones and 25% sales royalties (from previously 20%).

NOTE: Our success rate will increase to 50% when the phase III trial starts at the end of 2018. We conservatively use a 50% success rate instead of the usual phase III success rate to reflect the potentially pivotal trial design with two cross-supportive phase III trials, one in schizophrenia and one in CTRS. Additional upside could come from higher pricing (e.g. USD 12-15,000/year in the US) if results of the phase III program point to a new treatment paradigm with evenamide.

Evenamide (CTRS) [NEW] – risk-adjusted NPV of CHF 1 per share

The high unmet medical need for new treatments in CTRS, studies suggesting the involvement of the glutamate system in CTRS, and US orphan disease designation, have triggered Newron's new development plans for evenamide to include this indication next to schizophrenia. CTRS provides a fast to market indication (we expect first launches in 2022) with 7-years orphan disease market exclusivity upon US approval, and the potential for Newron to market evenamide in this indication with an own specialist sales force. We conservatively assume commercialization in CTRS by Newron's partners for schizophrenia in return for EUR 36 mn upfront and sales milestones and 25% sales royalties. We forecast peak sales to amount to EUR 133 mn assuming the same annual treatment cost as for schizophrenia and peak penetrations ranging between 38% (EU/ROW) and 50% (US) to reflect the high unmet medical need and lack of alternatives. Our risk-adjusted NPV amounts to CHF 1 per share with a 15% (proof-of-concept) success rate.

NOTE: Our success rate will increase to 50% when the phase III trial starts at the end of 2018. We conservatively use a 50% success rate instead of the usual phase III success rate to reflect the potentially pivotal trial design with two cross-supportive phase III trials, one in schizophrenia and one in CTRS. Additional upside could come from higher pricing (e.g. USD 12-15,000/year in the US) if results of the phase III program point to a new treatment paradigm with evenamide.

Sensitivities that can influence our valuation

Development risk: With Xadago approved in the major markets (Japan expected in 2019), Newron's major risk is the development risk of its key pipeline projects sarizotan for Rett syndrome and evenamide as an add-on therapy for treating schizophrenia. Sarizotan is in the potentially pivotal phase III "STARS" trial for Rett syndrome with a conservative success rate of 25%, representing an orphan drug in phase II/III development, however, with no data in Rett syndrome patients. Sarizotan has substantial human safety data in Parkinson's disease where it was initially developed but failed phase III development. We have a 15% success rate for evenamide, which represents the historical success rate of a phase IIa proof-of-concept compound. Newron has secured the necessary funds to develop evenamide in schizophrenia and CTRS. Given the early stage the development risk remains high. Successful completion will boost the long-term value of evenamide substantially.

Pricing and reimbursement: Following EMA and FDA approval, Xadago must be priced and reimbursed by local health care providers. In the EU pricing and reimbursement occurs on a country-by-country base, which can lead to different pricing and reimbursement, and potential market launch delays. US pricing is quite straightforward and has been established with the drug being reimbursed by health insurers. However, the impact of Medicare (federal program for the elderly) can complicate the sales uptake in the first 9-12 months post-launch.

Partnering: In 2012 Newron out-licensed Xadago rights to Meiji Seika that gained rights for Japan and Asia, and to Zambon that gained worldwide rights (excluding Meiji Seika territories). Zambon does not have a strong presence in all markets, including the lucrative US, and will need to secure commercialization partners in these regions. Consequently, there is limited visibility on the timing and terms on which these sub-licensors will be contracted. Positively, Zambon signed on US WorldMeds in March 2016 for the critical US market, where Newron received a total of EUR 11.3 mn US approval milestone payments, with further sales milestones and mid to-high single digit royalties on sales.

Commercialization: Newron's revenues and earnings on Xadago will be entirely dependent on its commercialization partners to successfully position and market Xadago against existing Parkinson's treatments, in particular against Teva's Azilect (rasagiline). Newron plans to build up an own global specialist field force for sarizotan and potentially for evenamide in CTRS, which could require additional funding. Newron needs a major CNS partner to successfully commercialize evenamide in schizophrenia.

Patent and market exclusivity: Xadago's composition of matter patent expired in 2010. Patent protection and market exclusivity beyond this period will rely heavily on the combination patent with levodopa that runs until 2024 (EU) and 2026 (US) with extensions up to 5 years. A synthesis patent provides additional protection until 2027. We conservatively assume patent protection for Xadago until 2029 (including extension). Sarizotan will be protected by orphan drug and pediatric market exclusivity that offers 12 years protection in the EU and 7 ½ years in the US from the first day of approval. Sarizotan could potentially receive a Rare Pediatric Disease Designation Voucher in the US with an average selling price of USD 154 mn. Evenamide's patent protection runs until 2028 with extensions up to another 5 years. NCE (new chemical entity) exclusivity amounts to 5 years in the US, orphan disease exclusivity adds 7 years upon US approval, while data protection provides 10 years exclusivity in the EU.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT PER
2018					
1 FEB	XADAGO	PARKINSON'S	PHASE II/III JAPAN	PRIMARY ENDPOINT MET IN PHASE II/III TRIAL IN JAPAN; PARTNER MEIJI SEIKA PLANS TO FILE FOR APPROVAL IN JAPAN IN 2018	
8 FEB			CHANGE IN BOARD	BO JESPER HANSEN TO STEP DOWN AS NON-EXECUTIVE DIRECTOR; NO NEW DIRECTOR APPOINTMENTS AT THIS TIME	
28 FEB			RARE DISEASE DAY	NEWRON SUPPORTS GLOBAL RARE DISEASE DAY; PARTNERING WITH RETT COMMUNITY TO WORK ON FIRST BURDEN OF DISEASE (BOD) STUDY	
1 MAR			FY 2017 RESULTS	CASH: EUR 60.1 MN; FUNDED UNTIL 2020 BEYOND VALUE INFLECTION POINTS; TOTAL REVENUES: EUR 13.4 MN (EUR 6.7 MN IN 2016); XADAGO ROYALTIES: EUR 2.9 MN (+71%) FROM EUR ~29 MN XADAGO SALES; LICENSE INCOME: 10.4 MN (EUR 3.0 MN IN 2016) BOOSTED BY MILESTONE ON US APPROVAL XADAGO	
27 MAR			AGM	ALL MOTIONS ACCEPTED, INCLUDING GRANT TO ISSUE SHARES AND/OR CONVERTIBLE BONDS UP TO EUR 1,426,987.60 AND TO CREATE ADR'S (AMERICAN DEPOSITARY SHARES) FOR E.G. NASDAQ LISTING	
MID	SARIZOTAN	RETT SYNDROME	"STARS" TRIAL	COMPLETION ENROLMENT SINGLE POTENTIALLY PIVOTAL PHASE III "STARS" TRIAL	
MID	SARIZOTAN	RETT SYNDROME	HEOR TRIAL	HEALTH ECONOMIC OUTCOME RESEARCH (HEOR) "INTERNATIONAL BURDEN OF DISEASE IN RETT SYNDROME" STUDY RESULTS REPORT AT SAME TIME AS "STARS" TRIAL	
END	XADAGO	PD-LID *	NEW LABEL TRIAL	START OF NEW LABEL TRIAL IN PD-LID (PARKINSON'S DISEASE LEVODOPA INDUCED DISKINESIA) LARGELY FUNDED BY PARTNER ZAMBON	+ CHF 3
END	XADAGO	PARKINSON'S	FILING JAPAN	MEIJI SEIKA PLANS TO FILE FOR APPROVAL IN JAPAN IN 2018	
END	EVENAMIDE	CTRS **	PHASE III	START OF POTENTIALLY PIVOTAL TRIAL IN CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS (ORPHAN INDICATION)	+ CHF 4
END	EVENAMIDE	SCHIZOPHRENIA	PHASE III	START OF POTENTIALLY PIVOTAL PHASE III TRIAL IN SCHIZOPHRENIA PATIENTS (MAJOR INDICATION)	+ CHF 35
END	SARIZOTAN	RETT SYNDROME	"STARS" TRIAL RESULTS	TOP LINE RESULTS SINGLE POTENTIALLY PIVOTAL PHASE III "STARS" TRIAL AT WEEK 24	+ CHF 22
2019					
H1	SARIZOTAN	RETT'S SYNDROME	FILING US & EU	FILING IN THE EU AND US (6-MONTH PRIORITY REVIEW)	+ CHF 8
	XADAGO	PARKINSON'S	JAPANESE APPROVAL	APPROVAL TRIGGERS MILESTONE PAYMENT FROM MEIJI SEIKA; EISAI WILL BE RESPONSIBLE FOR COMMERCIALIZATION IN JAPAN AND ASIA	
MID	XADAGO	PD-LID *	LABEL EXTENSION TRIAL	RESULTS OF LABEL EXTENSION TRIAL IN PD-LID (PARKINSON'S DISEASE LEVODOPA INDUCED DISKINESIA) LARGELY FUNDED BY PARTNER ZAMBON	
END	SARIZOTAN	RETT'S SYNDROME	APPROVAL & LAUNCH	FIRST LAUNCHES IN US & EU	
END	SARIZOTAN	RETT'S SYNDROME	RARE PDV	ELIGIBLE TO RECEIVE RARE PEDIATRIC DISEASE VOUCHER ON US APPROVAL	+CHF 10
H2	XADAGO	PD-LID *	FILING	US AND EU FILING FOR APPROVAL IN PD-LID; PRIORITY REVIEW IN US	+CHF 1

* PD-LID = PARKINSON'S DISEASE LEVODOPA-INDUCED DYSKINESIA; ** CTRS = CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA
ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Key catalysts:

- 1) Start new label trial Xadago in PD-LID (end 2018):** Our risk-adjusted NPV for Xadago in PD-LID will rise to CHF 3/share with a 65% (phase III) success rate from currently CHF 1/share with a 15% (proof-of-concept) success rate.
- 2) Start potentially pivotal program of evenamide in schizophrenia/CTRS (end 2018):** Our risk-adjusted NPV jumps by CHF 39/share with a 50% (potentially pivotal) success rate from currently CHF 11/share with a 15% (proof-of-concept) success rate.
- 3) Topline results sarizotan "STARS" trial (end 2018):** On positive topline results, our risk-adjusted NPV will jump by CHF 22/share with a 65% (phase III) success probability from currently CHF 13/share with a 25% (phase II/III orphan drug) success rate.

Technology & Pipeline

Search & Development company focused on CNS and orphan diseases

Currently, Newron has two drugs addressing multibillion-dollar markets including Xadago (Parkinson's) and evenamide (schizophrenia), with each drug addressing an orphan indication, PD-LID with Xadago and CTRS with evenamide; and one compound, sarizotan, addressing a rare disease, called Rett syndrome. In October 2015, Newron terminated two of its rare disease drugs from the NeuroNova acquisition, namely, sNN0029 for ALS (amyotrophic lateral sclerosis or Lou Gehrig's disease) and sNN0031 for severe treatment-resistant Parkinson's disease. Both compounds were administered through a critical catheter delivery device from a third party, which faced ongoing regulatory issues. This led to considerable development delays and ultimately the discontinuation of both projects.

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
XADAGO (SAFINAMIDE)	ALPHA-AMINOAMIDE	PARKINSON'S DISEASE (MAJOR INDICATION)	EU: LAUNCHED US: APPROVED	EU: H1 2015 US: JULY 2017	ZAMBON/MEIJI SEIKA/ EISAI/US WORLDMEDS	EUR 400 MN
XADAGO (SAFINAMIDE)	ALPHA-AMINOAMIDE	LEVADOPA-INDUCED DYSKINESIA (ORPHAN INDICATION)	PIVOTAL TRIAL (START END 2018)	2020	ZAMBON/MEIJI SEIKA/ EISAI/US WORLDMEDS	EUR 200+ MN
SARIZOTAN	DOPAMINE RECEPTOR BLOCKER	RETT SYNDROME (ORPHAN INDICATION)	PHASE III PIVOTAL TRIAL	2019	ESTABLISH A SMALL TEAM OF MEDICAL LIAISON MANAGERS	EUR 400 MN
EVENAMIDE	ION CHANNEL BLOCKER	SCHIZOPHRENIA (MAJOR INDICATION)	PIVOTAL TRIAL (START END 2018)	2022	PARTNER AFTER PIVOTAL TRIAL	EUR 1.3 BN
EVENAMIDE	ION CHANNEL BLOCKER	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (ORPHAN INDICATION)	PIVOTAL TRIAL (START END 2018)	2022	PARTNER AFTER PIVOTAL TRIAL	EUR 100+ MN
RALFINAMIDE	ION CHANNEL BLOCKER	NON-RESPONDING SEVERE NEUROPATHIC PAIN (ORPHAN INDICATION)	POC*		PARTNER AHEAD OF TRIALS	NON-CORE

* POC = PROOF-OF-CONCEPT

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Xadago generating product sales in the EU and the US

Parkinson's drug Xadago received EU approval in February 2015. In May 2015, Germany was the first member state to launch Xadago. The European roll out of Xadago is well on its way, and is now available in 14 countries including Switzerland, Austria, Spain, Portugal, Italy, the Benelux, Denmark, Sweden, Norway, Finland, the UK with more European country launches expected. In March 2017 Xadago received US approval, triggering a total of EUR 11.3 mn milestone payments from Zambon. The US specialty pharmaceutical company US WorldMeds launched Xadago in the US in July 2017. With sufficient cash secured, Newron has stepped up its development plans for sarizotan in Rett syndrome and evenamide in schizophrenia and CTRS.

Non-core projects are up for partnering or to be monetized

Ralfinamide (neuropathic pain), a pipeline project stemming from Newron's own ion channel blocker discovery platform, is considered non-core that the company wants to partner or monetize.

CNS and orphan diseases a good mix for a small biopharmaceutical company

With the exception of sarizotan, which was licensed from Merck KGaA, Newron's development programs are primarily focused on new generation ion channel blockers for the treatment of CNS-related diseases and pain. With existing treatments for CNS disorders lacking efficacy, tolerability and long-term safety, demand is set to rise as the population ages. This is an attractive opportunity for a small, specialized biopharmaceutical company. Moreover, many large pharmaceutical companies have withdrawn from this field due to clinical setbacks and the high risks involved.

Strategy to complement CNS portfolio with rare disease opportunities

With the acquisition of the privately held Swedish NeuroNova AB at the end of 2012, Newron expanded its development focus with so-called orphan or rare diseases, such as ALS

Please see important research disclosures at the end of this document

Page 11 of 49

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(sNN0029) and severe treatment-resistant Parkinson's disease (sNN0031), now terminated. Newron had licensed the global rights of sarizotan from Merck KGaA, already in 2011. Sarizotan was originally targeted for Parkinson's disease by Merck KGaA but failed to demonstrate an effect in two pivotal phase III trials. Newron has repositioned the compound for treating breathing difficulties in patients with Rett syndrome, a rare disease that affects girls. Newron plans to seek new orphan drug opportunities, after the termination of both NeuroNova compounds, to replenish its development pipeline.

Orphan diseases are life-threatening or chronically debilitating diseases with an incidence less than 1 per 2,000/5,000 people. Although individually, orphan diseases may be classified as rare, collectively, they affect a large portion of the population and health care 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 less common disorders.

Key advantages for orphan drugs include:

- High unmet medical need for a relatively small patient population
- 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
- Competition is not present or limited
- Faster speed to market, lower development costs, lower regulatory hurdles
- Higher selling prices and profit margins
- Specialists can be addressed by a relatively small sales force

However, there are also considerable hurdles, including:

- Insufficient understanding of the history or mechanism of disease
- A very low number of patients to conduct clinical trials – lack of robust clinical data, slow enrollment, study delays
- A lack of widespread expertise in clinical centers
- 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 – they are considered to have a conflict in interest

Renewed interest in orphan drugs with attractive partnering opportunities

Orphan indications typically carry a high development risk. However, the low development costs and fast development times mitigate the financial impact and therefore are quite suitable for small, specialized biopharmaceutical companies to pursue. Moreover, many patient organizations provide valuable (financial) support. In the past, Big Pharma largely discarded orphan indications. Now there seems to be a renewed interest, with Big Pharma desperately seeking new profitable revenue streams to replenish their product portfolios affected by patent expirations. This provides Newron additional partnering opportunities for its emerging pipeline of orphan drugs, next to mid-sized specialty pharmaceutical companies.

In the following section we provide an in-depth analysis for Newron's key drivers including Xadago for treating Parkinson's disease and PD-LID (NEW), evenamide as an add-on therapy for schizophrenia and CTRS (NEW), and sarizotan for treating breathing disorders in Rett syndrome.

Forecasts & Sensitivity Analysis

Xadago (Parkinson's disease)

Product Analysis

Xadago all indications: Peak sales EUR 600+ mn; Risk-adjusted NPV CHF 15/share

1) Parkinson's peak sales of EUR ~400 mn - Risk-adjusted NPV of CHF 14 per share

We forecast peak sales of EUR 401 mn for Xadago in its major indication Parkinson's disease. Xadago was launched in the EU in 2015 followed by the US in July 2017, with a Japanese launch expected in 2020. We assume global patent protection until 2029 (including 5 years patent term extensions), a daily treatment cost of USD 9 (US), EUR 2.80 (EU/ROW) and EUR 4 (Japan/Asia), and a market penetration peaking at around 7-8%. Our risk-adjusted NPV amounts to CHF 244 mn, or CHF 14 per share, assuming Newron receives a total of EUR 29 mn milestone payments, royalties on sales ranging between 2.5% (Japan), 7.5% (US) and 10-15% (EU/ROW), with a 100% success probability and a WACC of 7% (reflecting the low Swiss interest environment).

2) PD-LID peak sales of EUR 200+ mn – Risk-adjusted NPV of CHF 1 per share

For Xadago's planned line extension in PD-LID (Parkinson's disease levodopa-induced dyskinesia), defined by the FDA as an orphan indication, we forecast peak sales of EUR 236 mn. The potentially pivotal trial is expected to start at the end of 2018 with first approvals expected in 2020. We assume similar dosing and pricing for Xadago in PD-LID as in Parkinson's disease and a market penetration conservatively peaking between 5-7%. Our risk-adjusted NPV amounts to CHF 14 mn or CHF 1 per share with a conservative 15% (proof-of-concept) success probability.

PD-LID – new orphan indication label to boost sales

Xadago available in the EU & US – First NCE launched for Parkinson's in a decade

Xadago is Newron's first ever launched product stemming from its own ion channel research and was launched in the EU in 2015 and in the US in 2017 for treating mid to late stage Parkinson's patients experiencing "off" episodes in combination with mainstay levodopa or other Parkinson medications (~80% of treated patients). Xadago is the first NCE (new chemical entity) approved and launched in Europe or the US in a decade for treating Parkinson's disease. In 2012, Xadago was licensed to Meiji Seika (Japan & Asian markets) and Zambon (worldwide excluding Meiji Seika markets). Xadago is commercialized by these partners and their sublicensees (e.g. US WorldMeds in the US, Medison Parma for Israel), while Newron receives milestone and (low) royalty payments from sales of Xadago, totaling EUR 36 mn to date. Xadago has now been launched in fourteen European countries, including Switzerland, Austria, Portugal, Spain, Italy, the Benelux, Denmark, Sweden, Norway, Finland and the UK with more countries to follow. In 2017, partner Zambon entered into a partnership with Seqirus for commercialization of Xadago in Australia and New Zealand and with Valeo for Canada, while Eisai acquired exclusive rights of Xadago for Japan and Asia from Newron's Japanese development partner Meiji Seika. Japanese approval is expected in 2019. Dossiers for marketing authorization are currently under review in Australia, Brazil, Canada and Columbia.

PD-LID label extension to enhance sales uptake and underline unique offering

Xadago product sales have recently trailed expectations due to a slower uptake, in particular in the US, by US WorldMeds. To strengthen and expand Xadago's label, Newron and Zambon, have decided to develop Xadago in Parkinson's disease patients with levodopa-induced dyskinesia (PD-LID), a debilitating side effect of long-term use with mainstay Parkinson's treatment levodopa. PD-LID is now considered an orphan disease with less than 200,000 patients in the US, with only a single treatment specifically approved for this indication: Adamas' Gocovri, a sustained-release formulation of generic amantadine, with an annual treatment price of USD 26,000. In Xadago's pivotal phase III trials, which led to approval in Parkinson's disease, it showed a long-lasting (2-years) effect on reducing dyskinesia in the double-blind placebo-controlled extension trial "Study 016/018" in patients experiencing dyskinesia at baseline by about 37%. A pivotal trial in PD-LID with participating centers in the US, Europe and ROW is expected to start in mid 2018 with topline results due in 2019 and approval in PD-LID expected in 2020.

Xadago can piggyback on the commercial success of Azilect without competition

Xadago is a so-called MAO-B inhibitor and belongs to the same class as Teva's Azilect (rasagiline). We believe Xadago has the potential to piggyback on the commercial success of Azilect, with a similar positioning in patients with mid to late stage disease. Importantly, Xadago has several advantages, in particular with regards to safety and tolerability and long-term efficacy. The positioning of Xadago by US WorldMeds will be critical. Azilect no longer enjoys patent protection in the US since February 2017, with cheap generics now replacing the branded product. Global sales of Azilect peaked at USD 700 mn in 2014, the year before it lost patent protection in several EU countries, with the bulk of sales stemming from patients with mid to late stage disease.

US WorldMeds with its marketing muscle in Parkinson's disease has a major advantage to position Xadago as the new cornerstone therapy next to levodopa for patients with mid to late stage disease. Moreover, Xadago is the first new chemical entity approved for Parkinson's disease for over a decade with many physicians eager to find out how the drug can help treat patients who no longer adequately respond to mainstay levodopa treatment or are affected by treatment side effects. These side effects typically develop after 4–10 years of levodopa therapy and affect approximately 50-75% of all patients. The "wearing-off" effect is the most common type, and "delayed-on," "no-on," and "on-off" fluctuations, as well as dyskinesia and cognitive worsening, may also develop as the disease progresses.

Treatment goal is to limit or delay the onset of levodopa-related complications

Collectively, motor fluctuations represent a significant source of disability in advanced Parkinson's patients, and reducing these is a major goal of patient management. Adjunctive medications, including dopamine agonists, anticholinergics, MAO-B inhibitors, and COMT inhibitors, each may reduce the frequency or duration of "off" periods, but none does so completely, and each contributes its own side effects which may limit optimal dosing. These problems have led to the development of strategies, which aim to limit or delay the onset of levodopa-related complications and have become the key drivers for the Parkinson's disease market. We believe Xadago with its unique dual mechanism of action and excellent tolerability profile is well positioned.

Xadago is a MAO-B inhibitor with unique and attractive qualities

Although Azilect and Xadago both belong to the MAO-B inhibitor class, we believe Xadago has distinct properties, which can position the compound as the new cornerstone therapy in treating patients with mid to late stage Parkinson's disease.

Xadago is believed to be a unique compound with a novel **dual mechanism** of action based on:

- 1) **The enhancement of the dopaminergic function** (through potent reversible inhibition of MAO-B and of dopamine uptake)
- 2) **Ion channel blockade** that leads to inhibition of stimulated release of glutamate (which may be the mechanism underlying potential neuro-protecting and anti-dyskinetic properties).

There are no head-to-head clinical studies of Azilect and Xadago, making comparisons difficult. However, certain observations can be made.

- Xadago is a reversible MAO-B inhibitor, whereas Azilect is an irreversible MAO-B inhibitor given its long half-life. This can be an important safety aspect in case of serious side effects caused by e.g. drug interactions; Xadago is cleared faster out of the body. Xadago appears to have a superior side effect profile in patients with mid to late stage Parkinson's disease who are treated with levodopa and other medications.
- Xadago has unparalleled 18/24 months clinical data backing long-term efficacy and safety
- Xadago improves "on-time" without troublesome dyskinesia – this is the quality time patients are seeking; reducing "off-time", Azilect's primary endpoint, does not translate directly in improving "on-time" without troublesome dyskinesia
- Xadago has a fast onset of action, which lasts up to 2 years (backed by double-blinded clinical trials)
- Xadago has the potential to reduce (levodopa-induced) dyskinesia due to its unique ability to reduce glutamatergic activity (needs to be further investigated)
- Xadago has the potential to reduce depression due to its unique ability to reduce glutamatergic activity (needs to be further investigated)

Superior safety and tolerability when compared to Azilect

The difference in safety and tolerability is apparent when we compare Xadago and Azilect based on the US prescribing information or so-called label provided by the FDA. The label is the key marketing message a company may actively promote to physicians.

ADVERSE EVENTS COMPARISON

ADVERSE EVENTS > 2%	AZILECT			XADAGO		
	"STUDY 3" (+ L-DOPA); 26 WEEKS			"STUDIES 1 & 2" (+ L-DOPA); 24 WEEKS		
	1 MG/DAY (N=149)	0.5 MG/DAY (N=164)	PLACEBO (N=159)	50 MG/DAY (N=223)	100 MG/DAY (N=498)	PLACEBO (N=497)
	(%)	(%)	(%)	(%)	(%)	(%)
DYSKINESIA (UNCONTROLLABLE MOVEMENT)	18	18	10	21	17	9
FALL	11	12	8	4	6	4
NAUSEA (DISCOMFORT UPPER STOMACH)	12	10	8	3	6	4
INSOMNIA (SLEEPLESSNESS)				1	4	2
ORTHOSTATIC HYPOTENSION (FALL IN BLOOD PRESSURE)	9	6	3	2	2	1
ANXIETY				2	2	1
COUGH				2	2	1
DYSPEPSIA (INDIGESTION)	5	4	4	0	2	1
ACCIDENTAL INJURY	12	8	5			
VOMITING	7	4	1			
CONSTIPATION	9	6	4			
ARTHRALGIA (JOINT PAIN)	8	6	4			
ABDOMINAL PAIN	5	2	1			
ANOREXIA (EATING DISORDER)	5	2	1			
HEADACHE	11	8	10			
WEIGHT LOSS	9	2	8			
ECCHYMOSIS (BRUISING)	5	2	3			
PARESTHESIA (PINS AND NEEDLES)	5	2	3			
SOMNOLENCE (SLEEPINESS)	6	4	4			
DRY MOUTH	6	2	3			
RASH	6	3	3			
DIARRHEA	5	7	4			
ABNORMAL DREAMS	4	1	1			
HALLUCINATIONS	4	5	3			
ATAXIA (UNCOORDINATED MUSCLE MOVEMENT)	3	6	1			
DYSPNEA (SHORTNESS OF BREATH)	3	5	2			
INFECTION	3	2	2			
SWEATING	3	2	1			
TENOSYNOVITIS (INFLAMMATION OF TENDON)	3	1	0			
DYSTONIA (MUSCLE CONTRACTIONS)	3	2	1			
GINGIVITIS (INFLAMMATION OF GUM TISSUE)	2	1	1			
HEMORRHAGE (BLEEDING)	2	1	1			
HERNIA	2	1	1			
MYASTHENIA (MUSCLE WEAKNESS)	2	2	1			

SOURCE: VALUATIONLAB, FDA PRESCRIBING INFORMATION

In the table above, we compared the adverse events, which occurred in more than 2% of treated patients for Azilect and Xadago in similar patient populations, namely in Parkinson's patients with mid to late stage disease patients treated with mainstay levodopa and other treatments such as dopamine agonists. As can be seen above, it is clear that Xadago has far less adverse events that occur in more than 2% of patients compared to Azilect. The most frequent adverse event that occurs with Xadago is dyskinesia, which occurs in a similar rate as with Azilect and is mostly transient in nature when therapy is started. With regards to all other frequent adverse events that occur with Azilect, the occurrence with Xadago is far less (e.g. fall, nausea, orthostatic hypotension) or less than 2% (e.g. accidental injury, vomiting, constipation, joint pain, abdominal pain, anorexia). Moreover, the incidence of hallucinations, dystonia (painful muscle contractions) and abnormal dreams, a main reason for patients to stop Azilect treatment, is below the 2% threshold with Xadago.

Xadago has the potential to reduce PD-LID over a long treatment period

Therefore, we believe Xadago has the potential to surpass Azilect as the leading MAO-B inhibitor in treating Parkinson's patients with mid to late stage disease thanks to its superior safety and tolerability profile and proven long-term efficacy up to 2 years of treatment. Moreover, Xadago has the potential to reduce dyskinesia in Parkinson's patients with moderate dyskinesia (DRS>4) as seen in "Study 016/018. Currently there are no drugs on the market that have shown reducing dyskinesia over such a period.

"Study 016/018" shows benefits maintained for at least 2 years

This double blind, placebo-controlled extension study, which was presented in 2011, shows the benefit of adding 50 or 100 mg/day of Xadago (safinamide) to levodopa in mid to late stage Parkinson's patients are maintained for at least 2 years. Several patient and physician-rated outcomes reached statistical significance including, total ON time, OFF time, PDQ total, UPDRS II, III & IV total.

"STUDY 016/018"	PLACEBO (N=69)	SAFINAMIDE 50 MG/DAY (N=78)	SAFINAMIDE 100 MG/DAY (N=74)
DYSKINESIA RATING SCALE			
- VALUE AT MONTH 24	7.0 +/- 3.53	6.6 +/- 3.54	6.4 +/- 4.45
- LS DIFFERENCE VS. PLACEBO	0.0	-0.7	-1.22
- P-VALUE VS. PLACEBO	N/A	0.1999	0.0317

SOURCE: NEWRON PHARMACEUTICALS

Importantly, in Parkinson's patients with moderate dyskinesia (DRS>4) at baseline "Study 016/018" showed under double-blind, placebo-controlled conditions that Xadago (safinamide) 100 mg/day reduces dyskinesia.

Global PD-LID trial design almost finalized and expected to start at end of 2018

Based on the above findings, Newron and its partner Zambon, together with academic and regulatory experts, are in the process of designing a potentially pivotal efficacy study to evaluate the effects of Xadago in patients with levodopa-induced dyskinesia (PD-LID). The trial design and pre-clinical data for PD-LID, is being discussed with regulators in the European Union and the US and is expected to be finalized by Q3 2018. A potentially pivotal efficacy trial with participating centers in the US, Europe and ROW enrolling more than 200 patients with a 2-years treatment duration is expected to start at the end of 2018.

Xadago has global peak sales potential of EUR 600+ mn

To correctly reflect and value Newron's plans to expand Xadago's label, we have made separate forecasts for PD-LID next to our current Parkinson's disease forecasts for Xadago (which we have conservatively lowered on the disappointing uptake in the US). Based on current pricing, we forecast global peak sales for Xadago of EUR 200+ mn in PD-LID next to EUR 400 mn global peak sales in mid to late stage Parkinson's disease. Xadago would provide a unique offering with a proven long-lasting effect on treating mid to late stage Parkinson's disease as an add-on to existing mainstay levodopa, while also reducing dyskinesia, the debilitating side effect of long-term levodopa use, at a far more attractive price than Gocovri.

1) Parkinson's disease (major indication) peak sales of EUR 400 mn

We have used the same base for our forecasts for Xadago in mid to late stage Parkinson's disease as previously. However, we have excluded patients with PD-LID as these are now captured in our new forecasts for Xadago in PD-LID. In our detailed Xadago forecasts we have accounted for Newron's three major commercialization regions, namely:

- 1) **Europe/ROW (Zambon & partners):** we forecast peak sales to amount to EUR 188 mn assuming a daily treatment price of EUR 2.80 and a lower peak penetration rate of ~7% (previously ~9%). We assume a tiered royalty rate from 10% to 15%.
- 2) **US (US WorldMeds):** peak sales could amount to around EUR 213 mn with a daily treatment price of USD 9 and a peak penetration of ~8% (previously ~10%). US approval in 2017 triggered a total of EUR 11.3 mn milestone payments from Zambon.

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Page 17 of 49

We assume further sales milestones of up to EUR 26 mn and royalties of 7-8% in the US. We assume a royalty rate of 7.5%.

- 3) **Japan/Asia (Meiji Seika & Eisai):** we forecast a launch in 2019 with peak sales amounting to EUR 17 mn. We assume a EUR 5 mn milestone payment on Japanese approval and royalties on sales to amount to 2.5%.

We derive a risk-adjusted NPV of CHF 14 per share for Xadago in mid to late stage Parkinson's disease using a 100% success probability and a WACC of 7% (reflecting the low Swiss interest environment).

2) PD-LID (orphan indication) peak sales of EUR 200+ mn

We have based our Xadago forecasts for PD-LID on the number of patients with mid to late stage Parkinson's disease treated with levodopa that develop PD-LID after long-term use of this cornerstone treatment. We assume the same pricing for Xadago in PD-LID as for Parkinson's disease, which may prove to be conservative once the label is extended to treat PD-LID providing a unique treatment offering. Our peak sales forecast in Newron's three major commercialization regions amount to:

- 1) **Europe/ROW (Zambon & partners):** we forecast first launches to occur in 2020 with peak sales to amount to EUR 94 mn assuming a daily treatment price of EUR 2.80 and a peak penetration rate of ~5%. We assume a tiered royalty rate from 10% to 15% with no additional milestone payments.
- 2) **US (US WorldMeds):** we forecast a 2020 launch and peak sales to amount to around EUR 127 mn with a daily treatment price of USD 9 and a conservative peak penetration of ~7%. We assume a 7.5% royalty rate on sales with no additional milestone payments.
- 3) **Japan/Asia (Meiji Seika & Eisai):** we forecast a launch in 2021 with peak sales amounting to EUR 15 mn. We assume royalties on sales to amount to 2.5% with no further milestone payments.

We calculate a risk-adjusted NPV of CHF 1 per share for Xadago in PD-LID, currently using a conservative 15% (proof-of-concept) success rate and the same 7% WACC. Our risk-adjusted NPV will jump by CHF 2 per share once the pivotal trial in PD-LID starts at the end of 2018 due to a higher 65% (phase III) success rate.

Our detailed forecasts and sensitivity analysis for Parkinson's disease and PD-LID can be seen on the following two pages.

Forecasts & Sensitivity Analysis

XADAGO (SAFINAMIDE) - FINANCIAL FORECASTS FOR PARKINSON'S DISEASE

INDICATION	ADD ON THERAPY TO LEVODOPA/CARBIDOPA OR IN COMBINATION WITH OTHER PARKINSON'S DISEASE (PD) DRUGS IN MID-TO-LATE STAGE PATIENTS
DOSAGE	50 OR 100 MG / DAY
PRICE	EUROPE/ROW: EUR 2.80 PER DAY; US: USD 10 PER DAY; JAPAN: EUR 4 PER DAY
STANDARD OF CARE	DOPAMINE AGONISTS (EARLY STAGE PD), LEVODOPA +/- CARBIDOPA (MID-TO-LATE STAGE PD)

UNIQUE SELLING POINT ONCE DAILY ADD-ON THERAPY FOR MID-TO-LATE STAGE PARKINSON'S DISEASE WITH A UNIQUE DUAL MECHANISM OF ACTION WITH POTENTIAL ANTI-DYSKINETIC PROPERTIES

7Ps ANALYSIS

PATENT	PROTECTION IN EU (2029) AND US (2031): LEVODOPA COMBINATION PATENT 2026 (US) / 2024 (EU) + UP TO 5 YEAR EXTENSION I SYNTHESIS PATENT: 2027
PHASE	EU: APPROVED FEB 2015; US: APPROVED MAR 2017 (LAUNCH JULY 2017); JAPAN: POSITIVE PHASE II/III CONFIRMATORY TRIAL JAN 2018, APPROVAL 2019
PATHWAY	1) AT LEAST ONE POSITIVE PHASE III TRIAL (6 MONTHS TREATMENT), 2) AT LEAST 100 PATIENTS TREATED FOR 1 YEAR, 3) A TOTAL OF AT LEAST 1,500 TREATED PATIENTS
PATIENT	IMPROVING QUALITY OF LIFE IN EARLY DISEASE AND DELAYING IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PHYSICIAN	HELPS DELAY USE OF MAINSTAY LEVODOPA TREATMENT THAT LEADS TO IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA AND "WEARING OFF"
PAYER	DELAYS SIGNIFICANT COSTS RELATED TO DYSKINESIA AND "WEARING OFF" WHERE PATIENTS NEED EXTENSIVE CARE OR HAVE TO BE INSTITUTIONALIZED
PARTNER	ZAMBON (WORLDWIDE EXCL. JAPAN & KEY ASIAN MARKETS), MEIJI SEIKA (JAPAN & KEY ASIAN MARKETS) - NEWRON SHARES IN MILESTONE & ROYALTY PAYMENTS

REVENUE MODEL

EUROPE / REST OF WORLD (ZAMBON & PARTNERS)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	3.6	3.6	3.7	3.8	3.9	3.9	4.0	4.1	4.2	4.3	4.3
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS ON MEDICATION (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS TREATED	2,492,648	2,542,501	2,593,351	2,645,218	2,698,122	2,752,085	2,807,126	2,863,269	2,920,534	2,978,945	3,038,524
-/- PATIENTS WITH PD-LID	478,588	488,160	497,923	507,882	518,039	528,400	538,968	549,748	560,743	571,957	583,397
PATIENTS TREATED WITHOUT PD-LID	2,014,060	2,054,341	2,095,428	2,137,336	2,180,083	2,223,684	2,268,158	2,313,521	2,359,792	2,406,988	2,455,127
PENETRATION (%)	1%	3%	4%	5%	5%	6%	6%	7%	7%	7%	7%
NUMBER OF PATIENTS	26,483	51,665	73,652	96,499	109,329	122,634	136,427	150,724	159,638	167,644	175,907
COST OF THERAPY PER YEAR (EUR)	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022
SALES (EUR MN)	27	53	75	99	112	125	139	154	163	171	180
CHANGE (%)	33%	95%	43%	31%	13%	12%	11%	10%	6%	5%	5%
ROYALTY (%)	10%	12%	14%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	3	6	11	15	17	19	21	23	24	26	27
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	3	6	11	15	17	19	21	23	24	26	27
TAXES (EUR MN)	0	0	-1	-3	-3	-6	-7	-7	-8	-8	-8
PROFIT (EUR MN)	3	6	10	12	14	13	14	16	17	18	18

UNITED STATES (ZAMBON PARTNER US WORLDMEDS)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.4	1.4
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS ON MEDICATION (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS TREATED (MN)	918,949	937,328	956,074	975,196	994,699	1,014,593	1,034,885	1,055,583	1,076,695	1,098,229	1,120,193
-/- PATIENTS WITH PD-LID	176,438	179,967	183,566	187,238	190,982	194,802	198,698	202,672	206,725	210,860	215,077
PATIENTS TREATED WITHOUT PD-LID	742,510	757,361	772,508	787,958	803,717	819,791	836,187	852,911	869,969	887,369	905,116
PENETRATION (%)	0%	2%	4%	5%	6%	6%	7%	7%	7%	8%	8%
NUMBER OF PATIENTS	743	15,905	27,810	36,246	45,008	51,647	57,697	60,557	63,508	66,553	69,694
COST OF THERAPY PER YEAR (USD)	3,285	3,285	3,285	3,285	3,285	3,285	3,285	3,285	3,285	3,285	3,285
COST OF THERAPY PER YEAR (EUR)	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671
SALES (EUR MN)	2	42	74	97	120	138	154	162	170	178	186
CHANGE (%)		2042%	75%	30%	24%	15%	12%	5%	5%	5%	5%
ROYALTY (%)	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
ROYALTIES (EUR MN)	0	3	6	7	9	10	12	12	13	13	14
UPFRONT & MILESTONE PAYMENTS (EUR MN)	10			8				16			
PROFIT BEFORE TAX (EUR MN)	11	3	6	15	9	10	12	28	13	13	14
TAXES (EUR MN)	0	0	0	-3	-1	-3	-4	-9	-4	-4	-4
PROFIT (EUR MN)	11	3	5	12	8	7	8	19	9	9	10

PEAK PENETRATION RATE	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS	282,301	287,947	293,706	299,580	305,572	311,683	317,917	324,275	330,761	337,376	344,123
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
PATIENTS DIAGNOSED (MN)	282,301	287,947	293,706	299,580	305,572	311,683	317,917	324,275	330,761	337,376	344,123
PATIENTS ON MEDICATION (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS TREATED (MN)	225,841	230,358	234,965	239,684	244,457	249,346	254,333	259,420	264,608	269,901	275,299
-/- PATIENTS WITH PD-LID	43,361	44,229	45,113	46,015	46,938	47,875	48,832	49,809	50,805	51,821	52,857
PATIENTS TREATED WITHOUT PD-LID	182,479	186,129	189,852	193,649	197,522	201,472	205,501	209,611	213,804	218,080	222,441
PENETRATION (%)	0%	0%	1%	2%	3%	4%	5%	5%	6%	5%	5%
NUMBER OF PATIENTS	0	0	949	3,873	5,926	8,059	9,248	10,481	11,759	11,776	11,789
COST OF THERAPY PER YEAR (EUR)	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460
SALES (EUR MN)	0	0	1	6	9	12	14	15	17	17	17
CHANGE (%)				308%	53%	36%	15%	13%	12%	0%	0%
ROYALTY (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
ROYALTIES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (EUR MN)			5								
PROFIT BEFORE TAX (EUR MN)	0	0	5	0	0	0	0	0	0	0	0
TAXES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	0	0	5	0	0	0	0	0	0	0	0

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
GLOBAL SALES (EUR MN)	29	95	151	201	241	275	307	331	350	366	383
CHANGE (%)	43%	228%	58%	33%	20%	14%	12%	8%	6%	5%	5%
GLOBAL PROFIT (EUR MN)	13	10	20	25	22	20	23	36	26	27	28
CHANGE (%)	180%	-28%	111%	23%	-11%	-8%	11%	58%	-27%	5%	5%
WACC (%)	7.0%										
NPV TOTAL PROFIT (CHF MN)	242										
NUMBER OF SHARES (MN)	17.8										
RISK ADJUSTED NPV PER SHARE (CHF)	14										

SENSITIVITY ANALYSIS

		WACC (%)							
		CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
PEAK SALES	550	21	20	19	19	18	18	17	17
	500	19	18	18	17	17	16	16	16
	450	17	16	16	15	15	15	14	14
	400	15	15	14	14	13	13	13	13
	350	13	13	12	12	12	11	11	11
	300	11	11	11	10	10	10	9	9
	250	9	9	9	9	8	8	8	8

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

XADAGO (SAFINAMIDE) - FINANCIAL FORECASTS FOR PD-LID (LEVODOPA-INDUCED DYSKINESIA)

INDICATION	ADD ON THERAPY TO LEVODOPA/CARBIDOPA OR IN COMBINATION WITH OTHER PARKINSON'S DISEASE (PD) DRUGS IN MID-TO-LATE STAGE PATIENTS TO TREAT DYSKINESIA
DOSAGE	50 OR 100 MG / DAY
PRICE	EUROPE/ROW: EUR 2.80 PER DAY; US: USD 10 PER DAY; JAPAN: EUR 4 PER DAY
STANDARD OF CARE	ADAMAS' GOCOVRI (AMANTADINE ER) FIRST TREATMENT SPECIFICALLY APPROVED FOR PD-LID BUT HAMPERED WITH SAFETY AND TOLERABILITY ISSUES

UNIQUE SELLING POINT ONCE DAILY ADD-ON THERAPY FOR PATIENTS WITH PD-LID WITH SUPERIOR SAFETY AND TOLERABILITY PROFILE

7Ps ANALYSIS

PATENT	PROTECTION IN EU (2029) AND US (2031); LEVODOPA COMBINATION PATENT 2026 (US) / 2024 (EU) + UP TO 5 YEAR EXTENSION SYNTHESIS PATENT: 2027
PHASE	POTENTIALLY SINGLE PIVOTAL TRIAL IN PD-LID DESIGN IN DISCUSSION WITH US, EU, ROW REGULATORS; TRIAL START END 2018, 1 YEAR TRIAL DURATION
PATHWAY	PD-LID IS A RECOGNIZED ORPHAN DRUG INDICATION IN THE US ELIGIBLE FOR 7 YEARS ORPHAN DRUG EXCLUSIVITY, FAST TRACK DESIGNATION WITH PRIORITY REVIEW
PATIENT	IMPROVING QUALITY OF LIFE BY REDUCING DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PHYSICIAN	WELL TOLERATED AND SAFE TREATMENT THAT EFFECTIVELY REDUCES DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
PAYER	DELAYS SIGNIFICANT COSTS RELATED TO DYSKINESIA AND "WEARING OFF" WHERE PATIENTS NEED EXTENSIVE CARE OR HAVE TO BE INSTITUTIONALIZED
PARTNER	ZAMBON (WORLDWIDE EXCL. JAPAN & KEY ASIAN MARKETS), MEIJI SEIKA (JAPAN & KEY ASIAN MARKETS) - NEWRON SHARES IN MILESTONE & ROYALTY PAYMENTS

REVENUE MODEL

EUROPE / REST OF WORLD (ZAMBON & PARTNERS)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	3.6	3.6	3.7	3.8	3.9	3.9	4.0	4.1	4.2	4.3	4.3
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS DIAGNOSED (MN)	2.5	2.5	2.6	2.6	2.7	2.8	2.8	2.9	2.9	3.0	3.0
PATIENTS TREATED WITH LEVODOPA (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
PATIENTS TREATED WITH LEVODOPA	1,495,589	1,525,501	1,556,011	1,587,131	1,618,873	1,651,251	1,684,276	1,717,961	1,752,321	1,787,367	1,823,114
MID TO LATE STAGE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MID TO LATE STAGE PATIENTS	1,196,471	1,220,400	1,244,808	1,269,705	1,295,099	1,321,001	1,347,421	1,374,369	1,401,856	1,429,894	1,458,491
MID TO LATE STAGE PATIENTS WITH PD-LID (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
PATIENTS WITH PD-LID	478,588	488,160	497,923	507,882	518,039	528,400	538,968	549,748	560,743	571,957	583,397
PENETRATION (%)	0%	0%	0%	1%	2%	3%	3%	4%	4%	4%	4%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	15871.3	32377.5	41281.3	50528.3	60128.6	70092.8	75963.1	81128.6
COST OF THERAPY PER YEAR (EUR)	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022
SALES (EUR MN)	0	0	0	16	33	42	52	61	72	78	83
CHANGE (%)	-100%				104%	28%	22%	19%	17%	8%	7%
ROYALTY (%)	12%	14%	15%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	0	0	0	2	5	6	8	9	11	12	12
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	0	0	0	2	5	6	8	9	11	12	12
TAXES (EUR MN)	0	0	0	0	-1	-2	-2	-3	-3	-4	-4
PROFIT (EUR MN)	0	0	0	2	4	4	5	6	7	8	9

UNITED STATES (ZAMBON PARTNER US WORLDMEDS)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	1.4	1.4
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PATIENTS DIAGNOSED (MN)	0.9	0.9	1.0	1.0	1.0	1.0	1.0	1.1	1.1	1.1	1.1
PATIENTS TREATED WITH LEVODOPA (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
PATIENTS TREATED WITH LEVODOPA	551,369	562,397	573,644	585,117	596,820	608,756	620,931	633,350	646,017	658,937	672,116
MID TO LATE STAGE PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MID TO LATE STAGE PATIENTS	441,095	449,917	458,916	468,094	477,456	487,005	496,745	506,680	516,813	527,150	537,693
MID TO LATE STAGE PATIENTS WITH PD-LID (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
PATIENTS WITH PD-LID	176,438	179,967	183,566	187,238	190,982	194,802	198,698	202,672	206,725	210,860	215,077
PENETRATION (%)	0.0%	0.0%	0%	2%	4%	5%	5%	6%	6%	6%	6%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	11702.3	20888.7	27394.0	31046.6	34834.2	38761.0	40854.1	43015.4
COST OF THERAPY PER YEAR (EUR)	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671	2,671
SALES (EUR MN)	0	0	0	31	56	73	83	93	104	109	115
CHANGE (%)					79%	31%	13%	12%	11%	5%	5%
ROYALTY (%)	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
ROYALTIES (EUR MN)	0	0	0	2	4	5	6	7	8	8	9
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	0	0	0	2	4	5	6	7	8	8	9
TAXES (EUR MN)	0	0	0	0	-1	-2	-2	-2	-2	-3	-3
PROFIT (EUR MN)	0	0	0	2	4	4	4	5	5	6	6

JAPAN & ASIA PACIFIC (MEIJI SEIKA PARTNER EISAI)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS	282,301	287,947	293,706	299,580	305,572	311,683	317,917	324,275	330,761	337,376	344,123
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH PD-LID	43,361	44,229	45,113	46,015	46,936	47,875	48,832	49,809	50,805	51,821	52,857
PENETRATION (%)	0%	0%	0%	0%	2%	4%	5%	5%	6%	6%	6%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	29933.5	5236.3	6867.0	7782.6	8732.1	9716.4	10241.1
COST OF THERAPY PER YEAR (EUR)	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460	1,460
SALES (EUR MN)	0	0	0	0	4	8	10	11	13	14	15
CHANGE (%)						78%	31%	13%	12%	11%	5%
ROYALTY (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
ROYALTIES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
UPFRONT & MILESTONE PAYMENTS (EUR MN)											
PROFIT BEFORE TAX (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
TAXES (EUR MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (EUR MN)	0	0	0	0	0	0	0	0	0	0	0

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
GLOBAL SALES (EUR MN)	0	0	0	47	93	123	145	166	188	201	213
CHANGE (%)	-100%				96%	32%	18%	15%	13%	7%	6%
GLOBAL PROFIT (EUR MN)	0	0	0	4	8	8	10	11	13	14	15
CHANGE (%)	-100%				101%	6%	18%	16%	14%	7%	6%

WACC (%) 7.0%

NPV TOTAL PROFIT (CHF MN) 89

NUMBER OF SHARES (MN) 17.8

NPV PER SHARE (CHF) 5

SUCCESS PROBABILITY 15%

RISK ADJUSTED NPV PER SHARE (CHF) 1

SENSITIVITY ANALYSIS

		WACC (%)							
		CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	65%	4	3	3	3	3	3	3	3
	55%	3	3	3	3	3	3	3	2
	45%	3	2	2	2	2	2	2	2
	35%	2	2	2	2	2	2	2	2
	25%	1	1	1	1	1	1	1	1
	15%	1	1	1	1	1	1	1	1
	5%	0	0	0	0	0	0	0	0

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

Once daily oral add-on therapy given together with levodopa in Parkinson's patients with mid to late stage disease, with a unique dual mechanism of action. Xadago reduces levodopa dose and increases "on-time" without troublesome dyskinesia with proven safety and efficacy over a 2-years treatment period. The potential to reduce dyskinesia owing to Xadago's unique dual mechanism will be addressed in the upcoming PD-LID trial.

7P's Analysis

Patent: Granted combination patents protect Xadago until 2024 in the EU and 2026 in the US with a likely 5-year patent extension. A synthesis patent protects until 2027. We assume patent protection in both regions up to 2029. As the first product launch occurred in 2015, the drug has an effective patent life of approximately 14 years.

Phase: Launched in the EU in early 2015 and in the lucrative US market in 2017. Japanese approval is expected in 2019 after Meiji Seika successfully concluded registrational trials. A new, global trial in PD-Lid is expected to start in mid 2018 with first approvals in this orphan indication expected in 2020.

Pathway: To receive US approval, Xadago needed at least one positive phase III trial for each Parkinson's indication (early and mid-to-late stage disease), at least 1,500 patients treated with Xadago of which several hundred treated for six months and at least 100 treated for one year. With two positive phase III trials for each Parkinson's indication and more than 1,500 patients treated with Xadago, including over 1,000 patients treated for at least one year and several hundred treated for four years, Newron comfortably fulfilled these requirements and received US approval in March 2017.

Patient: The major benefit for patients is that they can shift back the use of mainstay levodopa that causes irreversible side effects related to long-term use of this drug. In early disease, Xadago in combination with dopamine agonists helps improve motor fluctuations. Furthermore, in late stage patients, improvement is seen of multiple domains without any increase in troublesome dyskinesia.

Physician: Xadago adds a new treatment option for Parkinson's disease that fits nicely in current levodopa-sparing treatment strategies with the aim to reduce the burden of the long-term side effects from this effective drug. Potential anti-dyskinetic effects of Xadago would add to the use of the drug (will be addressed in potentially pivotal PD-LID trial).

Payer: The largest share of direct costs in Parkinson's comes from inpatient care and nursing homes, while the share from medication is substantially lower. Any delay in the progression of the disease or reduced debilitating side effects, in particular dyskinesia, has a substantial impact on total treatment costs.

Partner: Zambon acquired the global rights (excluding Japan & Asian territories owned by Meiji Seika) for Xadago in May 2012. Zambon has a strong presence in Southern Europe, France and Latin America, where it will market the drug. US WorldMeds will commercialize Xadago in the US. US approval in March 2017 triggered a total of EUR 11.3 mn milestone payments. Newron shares in future milestone and royalty payments. Meiji Seika has Japanese & Asian rights, which were sublicensed to Eisai for certain Asian territories in 2017.

Parkinson's Disease Market

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. Nevertheless, the Parkinson's disease market is relatively small in terms of sales at around USD 4 bn, reflecting the lack of new efficacious treatment introductions, with most drugs no longer patent protected. Major players included Novartis, Bristol-Myers Squibb and GlaxoSmithKline. Several smaller players have developed new formulations (extended/controlled-release, patches, orally disintegrating tablets) extending the patent life of some existing branded drugs. The combined direct (medication, inpatient care) and indirect cost (inability to work) of Parkinson's disease is estimated to be nearly USD 25 bn per year in the US alone.

PARKINSON'S DISEASE - KEY FACTS

MARKET SIZE	USD 4 BN
PREVALENCE	7-10 MN GLOBALLY, 1 MN IN US, > 1 MN IN EU
INCIDENCE	300,000 GLOBALLY, 100,000 IN US, >100,000 IN EU; 0.3% OF POPULATION
UNDERLYING CAUSE	- LOSS AND DEGENERATION OF DOPAMINERGIC NEURONS IN STRIATA NIGRA - LOSS OF STRIATAL NEUROTRANSMITTER DOPAMINE
SYMPTOMS	- TREMOR (SHAKING OF HANDS, ARMS, LEGS, JAW, FACE) - RIGIDITY (LIMBS, TRUNK) - BRADYKINESIA (SLOWNESS OF MOVEMENT) - POSTURAL INSTABILITY (POOR BALANCE AND COORDINATION)
DRUG CLASS (KEY BRANDS)	- LEVODOPA/CARBIDOPA (MADOPAR, SINEMET CR, PARCOPA, STALEVO, DUODOPA) - DOPAMINE AGONIST (MIRAPEX, REQUIP, APOKYN, PARLODEL, NEUPRO PATCH) - MAO-B INHIBITORS (AZILECT, ELDEPRYL, ZELAPAR ODT, XADAGO) - COMT INHIBITORS (COMTAN, TASMAR) - ANTICHOLINERGICS (COGENTIN, ARTANE) - OTHER (SYMMETREL FOR DYSKINESIA, EXELON FOR DEMENTIA)
MAJOR PLAYERS (KEY BRANDS)	- NOVARTIS (STALEVO, PARLODEL, COMTAN) - BRISTOL MYERS SQUIBB (SINEMET CR) - GLAXOSMITHKLINE (REQUIP) - TEVA (AZILECT) - UCB (NEUPRO PATCH) - BOEHRINGER INGELHEIM (MIRAPEX ER) - US WORLDMEDS (APOKYN, XADAGO) - VALEANT (ZELAPAR ODT, TASMAR) - ABBVIE (DUODOPA) - ENDO PHARMACEUTICALS (SYMMETREL) - ZAMBON/MEIJI SEIKA (XADAGO)

SOURCE: VALUATIONLAB, NIH, WHO, PARKINSONS.ORG, PDF.ORG, COMPANY REPORTS

Parkinson's disease affects an estimated 7-10 million people globally with about 1 million patients in the US and a similar amount in the EU, with significant prevalence growth expected due to an aging population. The disease is a slowly progressive degenerative disorder of the central nervous system that initially affects movement, and later cognition and behavior. Dementia commonly occurs in the advanced stage of disease. The mean age of onset is typically around 60 years (rare in people under the age of 40 years). In people taking medication (levodopa), the progression time of symptoms to a stage of high dependency from caregivers may range from 8 to 15 years.

Three stages of severity are usually distinguished;

- 1) **Early stage**, in which the patient has developed some disability and where drug treatment may be required (dopamine agonists, anticholinergics, MAO-B inhibitors)
- 2) **Mid stage**, where the symptoms can be rather severe and include the inability to walk straight or stand, with a noticeable slowing of movements (bradykinesia).
- 3) **Late or advanced stage**, in which an individual develops severe motor complications (dyskinesia) related to levodopa use. Most patients are unable to complete day-to-day tasks and usually cannot live on their own.

Early in the disease the most obvious symptoms are movement-related. These include tremor, rigidity, slowness of movement, and difficulty with walking and gait. The motor symptoms of the disease result from the death of dopamine-generating cells in the

substantia nigra, a small tract of neurons in the brain containing dopamine, which control voluntary movements. The cause of this cell death is still unknown.

The severity and progression of Parkinson's disease is measured using several rating scales such as the Hoehn and Yahr (focus on movement symptoms) or **UPDRS** (United Parkinson's Disease Rating Scale - more comprehensive than Hoehn and Yahr, taking into account cognitive difficulties, daily activities and treatment complications).

Current drug treatment aims to delay symptoms and use of levodopa

Because there is no cure for Parkinson's disease, the primary aim of treatment is to relieve symptoms and keep the patient functional as long as possible. Current treatments are effective at managing the early motor symptoms, mainly through the use of (generic) levodopa and dopamine agonists. Mainstay treatment is levodopa, an oral precursor of the neurotransmitter dopamine. It is well established as the most effective treatment for Parkinson's disease for over 30 years, with most patients noticing an immediate improvement. However, as the disease progresses and dopamine generating cells continue to be lost, these drugs eventually become ineffective at treating the symptoms and at the same time produce **dyskinesia**, a complication marked by involuntary jerking and twisting movements. Other treatment related complications include end-of-dose deterioration, unpredictable "on/off" motor fluctuations, hypotension, nausea, anorexia and psychiatric effects. These problems have led to the development of strategies that aim to limit or delay the onset of levodopa-related complications and have become the key drivers for the Parkinson's disease market with the introduction of dopamine agonists, MOA-B and COMT inhibitors. Dopamine agonists and MAO-B inhibitors are primarily used as mono-therapy in the early stages of the disease to delay the use of levodopa. **Dopamine agonists** work by directly stimulating the dopamine receptors to bypass degenerating brain cells. **MOA-B inhibitors** block a key enzyme that is responsible for the breakdown of dopamine. **COMT-inhibitors** block an enzyme responsible for the breakdown of levodopa in the body, thereby increasing the amount of levodopa available to reach the brain. Consequently, COMT inhibitors are prescribed together with levodopa. When drug treatment is no longer sufficient to control symptoms, lesional surgery or deep brain stimulation (DBS), through implantation of a so-called brain pacemaker can be of use. In the final stages of disease, palliative care is provided to enhance quality of life.

New market entrants expected to spark growth

The introduction of new drugs, improved formulations of existing drugs, and the ageing of the population (higher prevalence) should drive growth in the Parkinson's disease market.

Improved formulations of existing drugs, including: Abbvie's **Duodopa**, a carbidopa/levodopa intestinal gel (approved), Impax's **Rytary**, an extended-release capsule formulation of carbidopa/levodopa (approved), and NeuroDerm's **ND0612L/H**, a carbidopa/levodopa subcutaneous patch pump (phase II), Mylan's/US WorldMeds' **Apokyn**, a non-ergoline dopamine agonist for the treatment of acute hypomobility, and Adamas' **Gocovri** (sustained-release formulation of amantadine) for treating PD-LID.

New molecules and novel approaches, including: Newron/Zambon's **Xadago** (approved in EU & US) a dual mechanism of action drug that provides both MAO-B and glutamate inhibition, adenosine 2a (A2a) agonists such as Kyowa-Kirin's **istradefylline** (global phase III did not meet primary endpoint, Japan approved as Nourias) and Addex's **dipraglurant** (phase II), which targets metabotropic glutamate receptor 5 (mGluR5).

Evenamide (schizophrenia)

Product Analysis

Evenamide all indications: peak sales EUR 1.4+ bn, risk-adjusted NPV CHF 11/share

1) Schizophrenia peak sales of EUR 1.3 bn - Risk-adjusted NPV of CHF 10 per share

We forecast peak sales of EUR 1.3 bn for evenamide in its major indication as an add-on to existing schizophrenia therapies, assuming Newron starts two cross-supportive potentially pivotal trials, one in schizophrenia and one in the orphan indication CTRS (clozapine treatment-resistant schizophrenia), at the end of 2018. These new development plans could lead to topline results in 2020, shaving off 2-3 years development time than originally expected. On positive headline results, we assume Newron to sign on a major CNS player to fully develop and commercialize evenamide in schizophrenia and potentially other CNS disorders such as mania or depression. We expect first launches to occur in late 2022 and global patent protection until 2033 (including patent term extensions), 10-years data exclusivity on approval in the EU (2034), a conservative daily treatment cost of between USD 15 (US) and EUR 10 (EU/ROW), and a target market penetration peaking at 20%. Our risk-adjusted NPV amounts to CHF 185 mn, or CHF 10 per share, assuming Newron receives a total of EUR 229 mn of upfront and milestone payments, royalties on sales of 25% from its partner(s) with a success probability of 15% (proof-of-concept completed) and a WACC of 7% (reflecting the low Swiss interest environment).

2) CTRS peak sales of EUR 100+ mn – Risk-adjusted NPV of CHF 1 per share

The orphan-like indication CTRS (clozapine treatment-resistant schizophrenia) triggered the new development plans for evenamide. Although, CTRS is a niche market, its high unmet medical need makes evenamide eligible for orphan and fast track designation, where a single potentially pivotal trial is required for approval, which can be combined with a single potentially pivotal trial in schizophrenia. We expect the potentially pivotal trial to start at the end of 2018 with topline results due in 2020 and launch in early 2022 due to priority review. We conservatively forecast peak sales to amount to EUR 133 mn assuming the same pricing as for schizophrenia. We calculate a risk-adjusted NPV of CHF 1 per share assuming Newron partners CTRS to the same partners as for schizophrenia with the same 25% royalty rate and EUR 36 mn milestone payments with a 15% (proof-of-concept) success rate.

CTRS orphan indication prompts new trial design cutting 2-3 years

Newron has come up with a new development plan for evenamide that could potentially cut 2-3 years off the time to market than originally planned, thanks to the positive proof-of-concept data for evenamide in schizophrenia announced at the beginning of 2017, new insights into the orphan indication CTRS (clozapine treatment-related schizophrenia), and securing funding through a successful CHF 27 mn capital increase in September 2017. After active consultations with key opinion leaders and regulators, the company is now completing discussions with the EMA's CHMP and FDA to start parallel development of evenamide in its major indication schizophrenia and the orphan indication CTRS with a single potentially pivotal phase III trial for each indication that will be cross-supportive for approval. CTRS provides a fast to market opportunity being an orphan indication with the potential for shorter development timelines, lower development costs and an expedited review. The phase III program is expected to start at the end of 2018. Each trial is expected to complete in 18

months with topline data expected in 2020. Next to these two trials, Newron plans to start a compassionate use program in CTRS to gather sufficient safety data required for expedited approval.

Targeting a USD 12 bn antipsychotic market with a major and orphan indication

Evenamide stems from Newron's own ion channel discovery efforts and has shown benefit in a range of models of positive symptoms, aggression, cognition (in schizophrenia), mania, depression and obsessive behavior. This novel, small molecule, oral drug has a rapid onset of action and has a high availability in the brain. Evenamide targets a large antipsychotic market worth approximately USD 12 bn currently affected by several branded drugs losing patent protection. The drug can be added to current antipsychotic therapy for patients who no longer respond (roughly 65% of patients). In 2017, Newron successfully completed a phase IIa proof-of-concept (POC) trial of evenamide in schizophrenia. Evenamide enjoys an extensive patent life running until at least 2033 (including 5 years patent term extension), thanks to the US Patent and Trade Organization that granted a solid composition of matter patent in 2013. Assuming evenamide receives orphan drug designation for CTRS, the compound is eligible for 7 and 10-years orphan drug market exclusivity upon approval in the US and EU, respectively.

Evenamide targets a USD 6 bn schizophrenia market in need of new treatments

Evenamide is being developed as an add-on therapy to current antipsychotic medication for schizophrenia patients who respond poorly, including CTRS patients that is considered an orphan indication. The schizophrenia market is currently worth approximately USD 6 bn, despite low patient compliance and many patients responding poorly to current antipsychotic therapy. Evenamide would become a first-in-class voltage gated, selective sodium channel blocker specifically developed as an add-on to existing treatments for schizophrenia and CTRS. Therefore, the drug has the potential to be developed in fixed-dose combinations with existing treatments extending their patent life substantially.

Positive POC results demonstrate unique profile as schizophrenia add-on therapy

In January 2017 Newron reported positive headline results of the phase IIa POC trial of evenamide in schizophrenia. Detailed results of the POC trial were presented at the International Congress on Schizophrenia Research (ICSR) annual meeting at the end of March. Evenamide met the trial objectives of good tolerability, safety and showed preliminary evidence of efficacy.

Rigorous POC trial protocol finalized with FDA input and guidance

The 4-week, double blind, placebo-controlled, randomized, multinational POC trial was designed to assess the safety, tolerability and early evidence of efficacy of evenamide as an add-on treatment in 89 patients with a diagnosis of schizophrenia. The trial protocol, including doses and trial design, was finalized with FDA input and guidance, and was approved by the Indian regulator DCGI (Drug Controller General of India). Patients included in the trial were mostly male (86%) between 19 and 60 years of age, with a mean baseline PANSS (Positive And Negative Syndrome Scale) total score of 62.9 ± 7.4 , and were experiencing breakthrough psychotic symptoms while on stable and adequate doses of mainstay schizophrenia treatments such as JNJ's Risperdal (risperidone) (mean dose: 4.2 ± 2.0 mg/day; n=70) or Lundbeck's Abilify (aripiprazole) (mean dose: 19.7 ± 7.0 mg/day; n=19), the atypical antipsychotics to which they had responded previously. The trial was conducted in two US (61 patients) and three Indian (28 patients) centers, which enrolled patients with schizophrenia with a mean duration of illness of approximately 18 years and

an average of three hospitalizations. Patients were randomized to receive evenamide twice daily (15-25 mg) or placebo on top of their current antipsychotics.

Well tolerated on top of mainstay schizophrenia treatments

Evenamide, given 15-25 mg twice daily, was generally well tolerated in the POC trial, with no meaningful differences between groups in changes from baseline in vital signs, laboratory test results or ECG findings.

As can be seen in the table below, 5 (10%) patients had at least one serious adverse event (SAE) vs. 1 (2.6%) in the placebo group. Two adverse events (atrial fibrillation and seizure) were reported as a SAE. In the patient with atrial fibrillation, the highest concentration of evenamide was ~11-18 fold less than that producing cardiac events in animals. In the patient experiencing a seizure, the highest plasma concentration was ~16-40 fold less than that associated with seizures in animals. Treatment of evenamide in these two patients (3%) was discontinued.

ADVERSE EVENTS (>5% OF PATIENTS)	EVENAMIDE (N=50) N (%)	PLACEBO (N=39) N (%)	TOTAL (N=89) N (%)
AT LEAST ONE SAE (SERIOUS ADVERSE EVENT)	5 (10.0%)	1 (2.6%)	6 (6.7%)
AT LEAST ONE TEAE (TREATMENT EMERGENT ADVERSE EVENT)	23 (46.0%)	12 (30.8%)	35 (39.3%)
SOMNOLENCE (STRONG DESIRE TO SLEEP)	8 (16.0%)	5 (12.8%)	13 (14.6%)
INSOMNIA (TROUBLE SLEEPING)	5 (10.0%) *	1 (2.6%)	6 (6.7%)
HEADACHE	3 (6.0%) **	0	3 (3.4%)
OVERDOSE	3 (6.0%)	1 (2.6%)	4 (4.5%)
DRY MOUTH	3 (6.0%)	2 (5.1%)	5 (5.6%)
DIARRHEA	0	2 (5.1%)	2 (2.2%)
PAIN IN EXTREMITY	0	3 (7.7%)	3 (3.4%)
ADVERSE EVENTS (ALL)	EVENAMIDE	PLACEBO	TOTAL
ADVERSE EVENTS (SERIOUS SEVERITY)	2 OF 69 (3%)	0 OF 34 (3%)	2 OF 103 (2%)
ADVERSE EVENTS (MILD SEVERITY)	58 OF 69 (84%)	30 OF 34 (88%)	88 OF 103 (85%)
ADVERSE EVENTS (MODERATE SEVERITY)	9 OF 69 (13%)	4 OF 34 (12%)	13 OF 103 (13%)

* 1 PATIENT QUALIFIED AS MODERATE SEVERITY; ** 2 PATIENTS QUALIFIED AS MODERATE SEVERITY

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Most adverse events were of mild severity for evenamide (84%) and placebo (88%), while 13% of adverse events in the evenamide group were qualified as moderate compared to 12% on placebo. The evenamide group had a higher incidence of somnolence (strong desire to sleep), insomnia (trouble sleeping), headache, overdose and dry mouth than placebo. Placebo had a higher incidence in diarrhea and pain in extremities compared to the evenamide group.

The proportions of patients with clinically notable abnormalities in vital signs or laboratory values were very low and were similar in the evenamide and placebo groups. The proportion of patients with clinically significant ECG abnormalities was low and similar between groups, and there was no evidence of effects on QTc prolongation (a risk factor for sudden death). Assessment of extrapyramidal symptoms (EPS) using the Extrapyramidal Symptoms Rating Scale did not reveal any treatment-emergent EPS with evenamide treatment.

Promising early efficacy in improving the symptoms of schizophrenia

The results of the POC trial showed a benefit on all measures assessed. Patients treated with evenamide showed improvement on the symptoms of schizophrenia assessed by the Positive and Negative Syndrome Scale (PANSS). The PANSS is a widely used medical scale for measuring symptom severity of patients with schizophrenia, including positive symptoms, which refer to an excess or distortion of normal functions (e.g. hallucinations and delusions) and negative symptoms, which represent a diminution or loss of normal functions (e.g. emotional or social withdrawal).

BASELINE VALUE AND MEAN CHANGE FROM BASELINE AT DAY 28 (MITT POPULATION)

SCALE	BASELINE VALUE				CHANGE FROM BASELINE TO DAY 28			
	EVENAMIDE (N=44)		PLACEBO (N=39)		EVENAMIDE (N=44)		PLACEBO (N=39)	
	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)
PANSS TOTAL (SYMPTOM SEVERITY)	47	57.8 (9.66)	39	59.3 (10.81)	47	-5.1 (9.67)	39	-3.7 (9.65)
LOF TOTAL (PATIENTS' FUNCTIONING)	48	22.04 (3.608)	39	20.64 (4.533)	48	0.72 (3.321)	39	0.31 (3.130)
CGI-S (SEVERITY OF ILLNESS)	47	3.1 (0.68)	39	3.2 (0.77)	47	-0.3 (0.60)	39	-0.2 (0.74)

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

As can be seen in the table above, the mean change from baseline at day 28 for the **PANSS Total score** in the mITT (modified intent to treat) population was greater for evenamide at -5.1 than for placebo at -3.7 (a reduction in score represents an improvement). Numerically greater improvement with evenamide was also observed for patients' functioning with the Strauss-Carpenter **Level of Functioning (LOF) Total scale** (an increase in score represents an improvement); and severity of illness with the Clinical **Global Impression of Severity (CGI-S) score** (a reduction in score represents an improvement), compared to the standard antipsychotic alone.

As can be seen in the following table, for the PANSS Positive Symptoms sub-scale, a statistically significant/near significant improvement from baseline (mean baseline score: 14.8 ± 2.8) to day 28 for evenamide, compared to placebo [LS mean difference (SE)], was noted in the: **1) MMRM** (Mixed-Effect Model Repeated Measure) model [-1.19 (0.643), $p=0.0678$]; **2) ANCOVA-LOCF** (Analysis of Covariance - Last Observation Carried Forward) [-1.28 (0.632), $p=0.0459$]; and **3) ANCOVA-OC** (Analysis of Covariance – Observed Cases) [-1.48 (0.641), $p=0.0237$] analyses.

PANSS POSITIVE SCALE TOTAL SCORE: MEAN CHANGE FROM BASELINE (MITT POPULATION)

DAY 28	CHANGE FROM BASELINE				DIFFERENCE EVENAMIDE VS. PLACEBO		
	EVENAMIDE (N=44)		PLACEBO (N=39)				
	N	LS MEAN (SE)	N	LS MEAN (SE)	LS MEAN (SE)	(95% CI)	P-VALUE
MMRM	47	-2.06 (0.439)	39	-0.87 (0.643)	-1.19 (0.643)	(-2.47, 0.09)	0.0678
ANCOVA (LOCF)	48	-2.31 (0.445)	39	-1.03 (0.477)	-1.28 (0.632)	(-2.54, -0.02)	0.0459
ANCOVA (OC)	43	-2.51 (0.454)	39	-1.03 (0.475)	-1.48 (0.641)	(-2.76, -0.20)	0.0237

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

In addition, a global assessment of change from baseline in the patient's overall condition **Clinical Global Impression of Change (CGI-C)**, performed by a clinician, showed a greater proportion ($p=0.084$; Fisher's exact chi-square test) of evenamide-treated patients rated as improved (54.2%), compared to placebo (35.9%). An improvement was qualified as a rating of 1 (very much improved), 2 (much improved) or 3 (minimally improved).

PROPORTION OF RESPONDERS AT DAY 28

SCALE	RESPONDER CRITERIA	N	EVENAMIDE	N	PLACEBO
PANSS POSITIVE (SYMPTOM IMPROVEMENT)	CHANGE FROM BASELINE LESS THAN 0 (REDUCTION IN SCORE = IMPROVEMENT)	50	35 OF 47 (74.5%) *	39	17 OF 39 (43.6%)
CGI-C (PATIENT'S OVERALL)	RATING OF 1 (VERY MUCH IMPROVED), 2 (MUCH IMPROVED) OR 3 (MINIMALLY IMPROVED)	50	26 OF 47 (55.3%) **	39	14 OF 39 (35.9%)

* P-VALUE < 0.05 VS. PLACEBO, FISCHER'S EXACT CHI-SQUARE TEST; ** P < 0.1 VS. PLACEBO

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

An additional analysis demonstrated that the proportion of patients who showed improvement on the **PANSS Positive sub-scale** at day 28 was significantly greater ($p=0.0043$; Fisher's exact chi-square test) for the evenamide group (74.5%) compared to the placebo group (43.6%). An improvement was qualified in the PANSS Positive score as a change from baseline less than zero (note: a reduction in score is an improvement).

Finally, results indicate that patients who were younger (less than 32 years of age) and earlier in the course of their disease (less than 10 years) experienced greater improvement.

The results from the small POC trial are consistent with the hypothesis that evenamide as an add-on to current antipsychotic treatment will improve symptoms of psychosis in patients who no longer respond adequately to standard antipsychotic treatment. The POC trial would suggest that evenamide could be added to the treatment regimen to enhance response, instead of switching the treatment regimen with another, which leads to discontinuation effects, anti-dopaminergic, metabolic and sexual side effects or the need to hospitalize patients.

CTRS provides faster time to market, orphan drug exclusivity, own sales effort

CTRS affects approximately 21,000 patients in the US and an estimated 45,000 patients in the EU/ROW and is therefore considered an orphan indication. Although CTRS represents only a small niche opportunity for evenamide (conservatively assuming similar pricing as for schizophrenia), it provides major benefits, including:

- Fast time to market (orphan indication with shorter development time, lower development costs, expedited review)
- Potential for parallel development of evenamide in schizophrenia (cutting 2-3 years development time)
- 7-years (US) and 10-years (EU) orphan drug exclusivity upon approval
- Potential for Newron to market evenamide in CTRS through an own small specialist sales force (most patients institutionalized)

Up to 30% of people with schizophrenia do not respond to two (or more) treatments of second generation dopaminergic antipsychotics and are said to have treatment-resistant schizophrenia, which typically develops after 3-5 years of treatment. 10-20% of patients already show symptoms of resistance in the first period of treatment. These patients continue to be psychotic with unresolved symptoms such as delusions, hallucinations, social withdrawal, hostility, grandiosity, and cognitive impairment. Treatment-resistant schizophrenia has a high morbidity (e.g. hospitalization) and mortality rate (e.g. suicide) with some of the highest rates of hospitalization and costs to society with an estimated USD 34 bn in direct healthcare costs in the US alone.

30% of treatment-resistant schizophrenia patients fail clozapine treatment

Clozapine, a dopamine and serotonin antagonist (5HT_{2A}) that was first introduced in the 1960's with a few unique differences compared to other second generation dopaminergic antipsychotics, is still the only effective treatment for treatment-resistant schizophrenia. It is the only drug with an FDA indication for treatment-resistant schizophrenia and reducing suicidal behavior. No drug other than clozapine has shown efficacy in these patients or a reduction of suicide attempt. Unfortunately, 30% of treatment-resistant schizophrenia patients on clozapine do not respond adequately or develop resistance to its effects and are

defined as clozapine treatment-resistant schizophrenia (CTRS) patients. These patients have no other treatment options, with an estimated 80% of patients in the US institutionalized in selected Veteran Affairs, state, city hospitals and prison system. A similar prevalence is estimated for the EU, Japan and Canada.

Glutamate system appears to be involved with treatment-resistant schizophrenia

Studies suggest treatment-resistant schizophrenia may be differentiated by abnormalities in brain glutamate concentrations not seen in treatment-responsive schizophrenia patients. This suggests a categorical difference rather than one of severity, indicating treatment-resistant schizophrenia is a different kind of illness than treatment-responsive schizophrenia. Interestingly, case studies, small placebo-controlled trials and meta-analyses suggest a benefit of the anticonvulsant drug lamotrigine (branded Lamictal by GlaxoSmithKline) as add-on treatment in CTRS, albeit with considerable variability among trials. Lamotrigine is a member of the sodium channel blocking class of antiepileptic drugs, which suppress the release of glutamate and aspartate, two of the dominant excitatory neurotransmitters in the central nervous system. The benefits of lamotrigine are most likely due to the suppression of glutamate release.

Evenamide antagonizes (in vivo): 1) the effect of ketamine (a glutamate antagonist) on PPI, and 2) effects of MK-801 and PCP (glutamate releasers). In animal models of schizophrenia, evenamide mimics effects of clozapine. However, clozapine does not reduce glutamate while evenamide does, making it an attractive add-on treatment for CTRS patients.

Next steps: start two cross-supportive pivotal trials in schizophrenia and CTRS

Based on the positive findings of the POC trial, and new insights into the potential of evenamide in CTRS, Newron is completing meetings with regulatory authorities on finalizing trial designs for future development of evenamide in:

- 1) **Major indication schizophrenia:** a placebo-controlled potentially pivotal phase III trial to demonstrate efficacy, safety and tolerability of three fixed doses of evenamide as an add-on to antipsychotics in patients experiencing worsening of symptoms of schizophrenia with 18 months to completion; estimated cost of EUR ~18 mn
- 2) **Orphan indication CTRS:** a placebo-controlled potentially pivotal phase III trial as an add-on therapy to treatment-resistant schizophrenia patients not responding to clozapine with 18 months to completion and expedited review; estimated costs of EUR ~7 mn

Both potentially pivotal phase III trials are expected to start at the end of 2018 and intended to be cross-supportive for approval of evenamide in both indications. This would cut 2-3 years in development time originally thought for schizophrenia. Newron expects to start expanded access and compassionate use programs in treatment-resistant schizophrenia patients to add to the safety database required for approval. On positive results Newron should achieve far higher milestone payments and royalties on sales than partnering on the positive POC trials. Moreover, Newron could potentially optimize the value of evenamide in CTRS by commercializing the drug with an own small specialist sales force (we conservatively assume Newron partners rights to CTRS to the same commercialization partners as for schizophrenia).

Evenamide has global peak sales potential of EUR 1.4+ bn

To correctly reflect and value Newron's plans to develop evenamide in two indications, a major indication schizophrenia and an orphan indication CTRS, we have made separate

forecasts for each indication. Although CTRS is a niche orphan indication with estimated peak sales of EUR 100+ mn (assuming similar pricing as for schizophrenia and not expensive “orphan drug” pricing), it considerably cuts the development time by 2-3 years initially planned for schizophrenia with estimated peak sales potential of EUR 1.3+ bn.

1) Schizophrenia (major indication) peak sales potential of EUR 1.3 bn

Worldwide there are more than 21 mn people suffering from schizophrenia, of which more than 2 mn are in the US, and around 5 mn in the EU, Japan and Australia. These are the major markets for evenamide. Roughly 70% of schizophrenia patients experience positive symptoms and are treated with typical and atypical antipsychotics, of which only 25% of patients is on treatment due to poor patient compliance. This is the main target population where evenamide will be used as an add-on for standard schizophrenia treatment. Evenamide could potentially lead to higher patient compliance and less switching of antipsychotic therapy due to patients responding longer to the combination therapy, providing substantial upside to our forecasts in schizophrenia.

In our forecasts we assume Newron will out license evenamide on positive pivotal trial results in 2020 to a strong CNS player in return for substantial upfront, development and sales milestone payments and 25% royalties on sales. First launches in schizophrenia are expected in late 2022.

In our detailed evenamide forecasts we have accounted for two major regions, namely:

- 1) **Europe/ROW:** we forecast peak sales to amount to EUR 787 mn assuming a conservative daily treatment price of EUR 10, 10 years data exclusivity until 2032, and a peak penetration rate amounting to 20%. We assume total milestone payments to amount to EUR 140 mn.
- 2) **US:** peak sales could amount to around EUR 523 mn assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including 5 years patent term extension), and a peak penetration rate amounting to 22%. We assume total milestone payments of EUR 89 mn.

2) CTRS (orphan indication) peak sales potential of EUR 100+ mn

Of the treatment-resistant schizophrenia patients approximately 12% are treated with clozapine, which is the target population for evenamide where it will be used as an add-on to clozapine. We expect high peak market penetration rates due to the severity of the illness and lack of alternative medications. We conservatively assume similar pricing in CTRS as for schizophrenia. Higher “orphan drug” pricing could lead to considerable upside to our forecasts. First launches are expected in early 2020. We expect Newron to out license CTRS rights to the same commercialization partners as for schizophrenia with 25% sales royalties and upfront and commercialization milestone payments. Further upside to our forecasts could come if Newron decides to commercialize evenamide in CTRS through an own small specialist sales force.

- 1) **Europe/ROW:** we forecast peak sales to amount to EUR 76 mn assuming a conservative daily treatment price of EUR 10, 10 years orphan drug exclusivity until 2032, and a peak penetration rate amounting to 38%. We assume total milestone payments to amount to EUR 130 mn and 20% royalties on sales.
- 2) **US:** peak sales could amount to around EUR 502 mn assuming a conservative daily treatment price of USD 15, patent protection until 2033 (including 5 years patent term extension).

extension), and a peak penetration rate amounting to 50%. We assume total milestone payments of EUR 16 mn

Our detailed forecasts and sensitivity analysis for schizophrenia and CTRS can be seen on the following two pages.

NOTE: Evenamide's potential could be substantially larger than our forecasts given the size of the market, additional indications such as depression or mania.

Forecasts & Sensitivity Analysis

Schizophrenia (major indication)

EVENAMIDE - FINANCIAL FORECASTS FOR SCHIZOPHRENIA

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYMPTOMS AND PSYCHOTIC WORSENING IN PATIENTS WITH SCHIZOPHRENIA
DOSAGE	15-25 MG TWICE DAILY (TBD)
PRICE	USA: USD 15/DAY, EU/ROW: EUR 10/DAY
STANDARD OF CARE	ATYPICAL (2ND GENERATION) ANTIPSYCHOTICS SUCH AS ZYPREXA, SEROQUEL, RISPERDAL, GEODON, ABILIFY
UNIQUE SELLING POINT	POTENTIALLY FIRST ADD-ON THERAPY TO ANTIPSYCHOTICS IN PATIENTS WITH SCHIZOPHRENIA, SCHIZO-AFFECTIVE AND BIPOLAR DISORDERS

7Ps ANALYSIS

PATENT	US COMPOSITION OF MATTER PATENT GRANTED UNTIL 2028 + 5 YEARS EXTENSION; EU: 10-YEARS DATA EXCLUSIVITY
PHASE	POSITIVE POC RESULTS AS ADD-ON THERAPY TO ANTIPSYCHOTICS (PRELIMINARY EVIDENCE OF EFFICACY); FIRST PHASE IIB/III TRIAL TO START H1 2018, RESULTS 2019
PATHWAY	1) TWO POSITIVE PHASE III TRIALS (6 MONTHS TREATMENT); 2) AT LEAST 1,500 TREATED (INCL. SEVERAL HUNDRED FOR 6 MONTHS); 3) AT LEAST 100 TREATED FOR 1 YEAR
PATIENT	POORLY RESPONDING PATIENTS CAN POTENTIALLY REGAIN A NORMAL SOCIAL AND PRODUCTIVE LIFE WITH A HIGHER LIFE EXPECTANCY
PHYSICIAN	POTENTIAL TO ADDRESS POORLY RESPONDING PATIENTS OR PATIENTS WITH BREAKTHROUGH SYMPTOMS ON CURRENT ANTIPSYCHOTIC TREATMENT
PAYER	SUBSTANTIAL REDUCTION OF ASSOCIATED COSTS SUCH AS UNEMPLOYMENT, LONG-TERM CARE, HOSPITALIZATION, SUICIDE RISK
PARTNER	PHASE IIA POC COMPLETED; NEXT STEPS: RAISE FUNDS TO START PHASE IIB OR PARTNER; RESULTS PHASE IIB 2019E

REVENUE MODEL

EUROPE / REST OF WORLD	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	5.2	5.3	5.4	5.5	5.6	5.6	5.7	5.8	5.9	6.0	6.1
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	3.7	3.7	3.8	3.8	3.9	3.9	4.0	4.1	4.1	4.2	4.3
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	916,390	930,136	944,088	958,249	972,623	987,212	1,002,020	1,017,051	1,032,306	1,047,791	1,063,508
-/- PATIENTS WITH CTRS	45,038	45,713	46,399	47,095	47,801	48,518	49,246	49,985	50,735	51,496	52,268
PATIENTS TREATED WITHOUT CTRS	871,352	884,422	897,689	911,154	924,821	938,694	952,774	967,066	981,572	996,295	1,011,240
PENETRATION (%)	0%	0%	0%	0%	0%	2%	5%	9%	13%	16%	18%
NUMBER OF PATIENTS	0	0	0	0	0	18,774	47,639	87,036	127,604	159,407	182,023
COST OF THERAPY PER YEAR (EUR)	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650
SALES (EUR MN)	0	0	0	0	0	69	174	318	466	582	664
CHANGE (%)							154%	83%	47%	25%	14%
ROYALTY (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
ROYALTIES (EUR MN)	0	0	0	0	0	17	43	79	116	145	166
UPFRONT & MILESTONE PAYMENTS (EUR MN)				30		10			50		50
R&D COSTS	-2	-4	-9	-8	-2	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	-2	-4	-9	22	-2	27	43	79	166	145	216
TAXES (EUR MN)	0	0	0	-4	0	-9	-14	-25	-52	-46	-68
PROFIT (EUR MN)	-2	-4	-9	18	-2	19	30	54	114	100	148

UNITED STATES	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	2.4	2.5	2.5	2.6	2.6	2.6	2.7	2.7	2.8	2.8	2.8
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	1.7	1.7	1.8	1.8	1.8	1.8	1.9	1.9	1.9	2.0	2.0
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED	427,290	433,700	440,205	446,808	453,510	460,313	467,218	474,226	481,339	488,559	495,888
-/- PATIENTS WITH CTRS	21,000	21,315	21,635	21,959	22,289	22,623	22,962	23,307	23,656	24,011	24,371
PATIENTS TREATED WITHOUT CTRS	406,290	412,385	418,570	424,849	431,222	437,690	444,255	450,919	457,683	464,548	471,516
PENETRATION (%)	0%	0%	0%	0%	0%	3%	7%	11%	14%	16%	17%
NUMBER OF PATIENTS (MN)	0	0	0	0	0	13,809	32,705	52,165	67,388	78,170	84,301
COST OF THERAPY PER YEAR (EUR)	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452
SALES (EUR MN)	0	0	0	0	0	61	146	232	300	348	375
CHANGE (%)							137%	60%	29%	16%	8%
ROYALTY (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
ROYALTIES (EUR MN)	0	0	0	0	0	15	36	58	75	87	94
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	24	0	8	0	0	24	0	33
PROFIT BEFORE TAX (USD MN)	0	0	0	30	0	29	45	71	122	107	155
TAXES (EUR MN)	0	0	0	-5	0	-7	-11	-18	-31	-27	-40
PROFIT (EUR MN)	0	0	0	20	0	16	25	40	68	60	87

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
GLOBAL SALES (EUR MN)	0	0	0	0	0	130	319	550	766	930	1,040
CHANGE (%)							146%	72%	39%	21%	12%
GLOBAL PROFIT (EUR MN)	-2	-4	-9	38	-2	35	55	94	182	159	235
CHANGE (%)	-67%	100%	114%	-540%	-104%	-2160%	58%	72%	93%	-13%	47%

WACC (%)	7.0%
NPV TOTAL PROFIT (CHF MN)	1,236
NUMBER OF SHARES (MN)	17.8
NPV PER SHARE (CHF)	69
SUCCESS PROBABILITY	15% = PROOF-OF-CONCEPT COMPLETED
RISK ADJUSTED NPV PER SHARE (CHF)	10

SENSITIVITY ANALYSIS

		WACC (%)							
		CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	65%		52	50	47	45	43	41	39
	55%		44	42	40	38	36	35	33
	45%		36	34	33	31	30	28	27
	35%		28	27	25	24	23	22	21
	25%		20	19	18	17	16	16	15
	15%		12	11	11	10	10	9	9
	5%		4	4	4	3	3	3	3

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

Clozapine treatment-resistant schizophrenia (orphan indication)

EVENAMIDE - FINANCIAL FORECASTS FOR CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYMPTOMS & PSYCHOTIC WORSENING IN CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (CTRS)
DOSAGE	15-25 MG TWICE DAILY (TBD)
PRICE	USA: USD 20,000 PER YEAR; EU/ROW: EUR 15,000 PER YEAR
STANDARD OF CARE	CLOZAPINE AND OTHER ATYPICAL (2ND GENERATION) ANTIPSYCHOTICS SUCH AS ZYPREXA (OLANZAPINE), SEROQUEL (QUETIAPINE), RISPERDAL (RISPERIDONE)
UNIQUE SELLING POINT	POTENTIALLY FIRST ADD-ON THERAPY TO ANTIPSYCHOTICS IN PATIENTS WITH CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA (ORPHAN INDICATION)

7Ps ANALYSIS

PATENT	US COMPOSITION OF MATTER PATENT GRANTED UNTIL 2028 + 5 YEARS EXTENSION; EU: 10-YEARS DATA EXCLUSIVITY; ORPHAN EXCLUSIVITY: 7 YEARS (US) & 10 YEARS (EU)
PHASE	FILINGS RELATING TO ORPHAN/PRIME/FAST TRACT DESIGNATION; START PIVOTAL PHASE III TRIAL IN CTRSTOWARDS END 2018
PATHWAY	1) PHASE III TRIAL FOR ORPHAN INDICATION (CTRS); 2) PHASE III TRIAL FOR MAJOR INDICATION (SCHIZOPHRENIA); 18 MONTHS TO COMPLETION FOR BOTH TRIALS
PATIENT	CLOZAPINE TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS CAN POTENTIALLY REGAIN A NORMAL SOCIAL AND PRODUCTIVE LIFE WITH A HIGHER LIFE EXPECTANCY
PHYSICIAN	POTENTIAL TO ADDRESS TREATMENT-RESISTANT PATIENTS WHERE CLOZAPINE NO LONGER WORKS OR OTHER ATYPICAL ANTIPSYCHOTICS
PAYER	TREATMENT-RESISTANT SCHIZOPHRENIA IS ASSOCIATED WITH SOME OF THE HIGHEST HOSPITALIZATION COSTS, COSTS TO SOCIETY AND RISK OF SUICIDE
PARTNER	PHASE IIA POC COMPLETED IN SCHIZOPHRENIA; FUNDS RAISED TO COMPLETE BOTH PHASE III TRIALS, POTENTIAL PARTNERING ON COMPLETION OF PHASE III

REVENUE MODEL

EUROPE / REST OF WORLD	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	5.2	5.3	5.4	5.5	5.6	5.6	5.7	5.8	5.9	6.0	6.1
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	3.7	3.7	3.8	3.8	3.9	3.9	4.0	4.1	4.1	4.2	4.3
TREATMENT-RESISTANT SCHIZOPHRENIA (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
TREATMENT-RESISTANT SCHIZOPHRENIA PATIENTS ON CLOZAPINE (%)	1,282,946	1,302,190	1,321,723	1,341,549	1,361,672	1,382,097	1,402,828	1,423,871	1,445,229	1,466,907	1,488,911
PATIENTS ON CLOZAPINE	150,126	152,378	154,663	156,983	159,338	161,728	164,154	166,616	169,116	171,652	174,227
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPHRENIA PATIENTS	45,038	45,713	46,399	47,095	47,801	48,518	49,246	49,985	50,735	51,496	52,268
PENETRATION (%)	0%	0%	0%	0%	0%	0%	15%	23%	29%	33%	35%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	2425.9	7386.9	11496.5	14713.1	16993.6	18293.8
COST OF THERAPY PER YEAR (EUR)	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650	3,650
SALES (EUR MN)	0	0	0	0	0	9	27	42	54	62	67
CHANGE (%)							205%	56%	28%	16%	8%
ROYALTY (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
ROYALTIES (EUR MN)	0	0	0	0	0	2	7	10	13	16	17
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	10	5	5	0	0	0	0	0
R&D COSTS	0	-1	-5	-2	-1	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	0	-1	-5	8	-1	7	7	10	18	16	17
TAXES (EUR MN)	0	0	0	-1	0	-2	-2	-3	-6	-5	-5
PROFIT (EUR MN)	0	-1	-4	6	-1	5	5	7	13	11	11

UNITED STATES	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS (MN)	2.4	2.5	2.5	2.6	2.6	2.6	2.7	2.7	2.8	2.8	2.8
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PERCENTAGE WITH POSITIVE SYMPTOMS (%)	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
PATIENTS WITH POSITIVE SYMPTOMS (MN)	1.7	1.7	1.8	1.8	1.8	1.8	1.9	1.9	1.9	2.0	2.0
TREATMENT-RESISTANT (%)	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
TREATMENT-RESISTANT SCHIZOPHRENIA	598,206	607,180	616,287	625,532	634,914	644,438	654,105	663,916	673,875	683,983	694,243
PATIENTS ON CLOZAPINE (%)	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
PATIENTS ON CLOZAPINE	70,000	71,050	72,116	73,197	74,295	75,410	76,541	77,689	78,854	80,037	81,238
CLOZAPINE-RESISTANT SCHIZOPHRENIA (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CLOZAPINE-RESISTANT SCHIZOPHRENIA PATIENTS	21,000	21,315	21,635	21,959	22,288	22,623	22,962	23,307	23,656	24,011	24,371
PENETRATION (%)	0%	0%	0%	0%	0%	8%	22%	32%	40%	45%	47%
NUMBER OF TREATED PATIENTS	0	0	0	0	0	1,810	5,052	7,458	9,463	10,805	11,455
COST OF THERAPY PER YEAR (EUR)	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452	4,452
SALES (EUR MN)	0	0	0	0	0	8	22	33	42	48	51
CHANGE (%)							179%	48%	27%	14%	6%
ROYALTY (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
ROYALTIES (EUR MN)	0	0	0	0	0	2	6	8	11	12	13
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	8	0	4	0	0	0	0	4
PROFIT BEFORE TAX (USD MN)	0	0	0	10	0	7	7	10	13	15	21
TAXES (EUR MN)	0	0	0	-2	0	-2	-2	-3	-3	-4	-5
PROFIT (EUR MN)	0	0	0	7	0	4	4	6	7	8	12

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
GLOBAL SALES (EUR MN)	0	0	0	0	0	17	49	75	96	110	118
CHANGE (%)							192%	52%	27%	15%	7%
GLOBAL PROFIT (EUR MN)	0	-1	-4	13	-1	9	8	13	20	19	23
CHANGE (%)	-100%		787%	-389%	-107%	-1182%	-7%	52%	54%	-5%	22%

WACC (%)	7.0%
NPV TOTAL PROFIT (CHF MN)	135
NUMBER OF SHARES (MN)	17.8
NPV PER SHARE (CHF)	8
SUCCESS PROBABILITY	15% = PROOF-OF-CONCEPT COMPLETED
RISK ADJUSTED NPV PER SHARE (CHF)	1

SENSITIVITY ANALYSIS

	CHF/SHARE	WACC (%)						
		5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	65%	6	5	5	5	5	5	4
	55%	5	5	4	4	4	4	4
	45%	4	4	4	3	3	3	3
	35%	3	3	3	3	3	2	2
	25%	2	2	2	2	2	2	2
	15%	1	1	1	1	1	1	1
	5%	0	0	0	0	0	0	0

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

Evenamide will be uniquely developed as an add-on to mainstay antipsychotic therapy for schizophrenia patients who no longer adequately respond to their current therapy, including patients with clozapine treatment-resistant schizophrenia. Evenamide has the potential to prolong response rates of current antipsychotics, improve poor patient compliance and reduce the frequent switching of therapy in schizophrenia.

7P's Analysis

Patent: Evenamide has a granted solid composition of matter patent with protection running until at least 2028. With 5 years patent extension terms the drug is protected until 2033. In the EU evenamide will enjoy at least 10 years data protection from approval. With first launches expected to occur in 2022, evenamide should have an effective patent life of 10 years in the EU and 9 years in the US. Fixed-dose combinations with current antipsychotics could substantially extend evenamide's effective patent life.

Phase: Newron has successfully completed a phase IIa POC trial in schizophrenia, which justifies a 15% success probability. The start of the two potentially pivotal trials in schizophrenia and CTRS at the end of 2018 justifies a 50% (phase III cross-supportive trial) success rate adding a staggering CHF 39 to our risk-adjusted NPV per share.

Pathway: To gain approval in the US and EU, Newron will have to submit two pivotal phase III trials as an add-on to other antipsychotics; grant of a breakthrough designation for CTRS may reduce this to one cross-supportive trial for each indication. Usually, at least 1,500 patients treated with evenamide, including several hundred treated 6 months, and at least 100 treated 1 year are required.

Patient: Adding evenamide to a patient's current therapy once the patient no longer adequately responds provides a more stable treatment regimen than e.g. switching to another antipsychotic with a different dosing regime, effect and side effects. Evenamide has the potential to prolong the patient's response to effective antipsychotics and restore normal social and economic life.

Physician: The physician can maintain patients on antipsychotic therapy where they initially responded but where the effect wanes over time. By simply adding evenamide therapy response is restored and prolonged without the need to switch a patient to another antipsychotic treatment with a different risk benefit profile.

Payer: Prolonging the effect of mainstay antipsychotic treatment avoids the cost of switching to other treatments with the potential to reduce other costs such as inpatient and outpatient and long-term care, and costs that arise from the productivity loss suffered by individuals with schizophrenia.

Partner: In 2020 topline results in schizophrenia and CTRS are expected. We assume Newron will then sign on a major CNS commercialization partner for both indications. We assume upfront, development and sales milestones of up to EUR 265 mn with 25% royalties on sales. More upside to our forecasts could be added if Newron decides to commercialize evenamide in CTRS itself through an own small specialist sales force

Schizophrenia Disease Market

The market for antipsychotics was valued at USD 12 bn in 2015, of which approximately half were for treating schizophrenia, according to Grand View Research. Over the last few years the market has been shrinking due to patent expirations of key brands such as Eli Lilly's Zyprexa, AstraZeneca's Seroquel, Pfizer's Geodon and Otsuka/Bristol-Myer Squibb's Abilify. The market is expected to bounce back thanks to new (long-acting) formulations of existing drugs that command higher prices and new drugs that can be priced at a premium. For instance, JNJ's Invega Trinza, a long-acting injectable version of Risperdal, generated sales of USD 641 mn in 2016. New formulation sales are expected amount to USD 3 bn 2021 with the total schizophrenia market amounting to almost USD 8 mn. Population growth will also help push up the number of patients who need treatment.

SCHIZOPHRENIA - KEY FACTS

MARKET SIZE	USD ~6 BN
PREVALENCE	>21 MN GLOBALLY, ~2.4 MN IN US, ~5.2 MN IN EU/ROW (JAP/AUS/CAN)
INCIDENCE	~1.5 MN GLOBALLY; ~100,000 IN US, ~220,000 IN EU/ROW (JAP/AUS/CAN)
UNDERLYING CAUSE	LARGELY UNKNOWN, COMPLEX INTERPLAY OF GENETICS, BRAIN CHEMISTRY AND STRUCTURE (NEUROTRANSMITTERS), PROBLEMS DURING PREGNANCY, AND ENVIRONMENT; USUALLY STARTS IN LATE ADOLESCENCE OR EARLY ADULTHOOD AND IS A LIFELONG CONDITION
SYMPTOMS	<ul style="list-style-type: none"> - "POSITIVE" SYMPTOMS, INCLUDING: <ul style="list-style-type: none"> - DELUSIONS (OF REFERENCE, PARANOID, SOMATIC, GRANDEUR) - HALLUCINATIONS (VISUAL, AUDITORY, TACTILE, OLFACTORY, GUSTATORY) - DISORGANIZED SPEECH - GROSSLY DISORGANIZED OR CATATONIC BEHAVIOUR - "NEGATIVE SYMPTOMS" INCLUDING: <ul style="list-style-type: none"> - LACK OF EMOTION/INTEREST - LOW ENERGY - AFFECTIVE FLATTENING - SOCIAL ISOLATION
DRUG CLASS (KEY BRANDS)	<ul style="list-style-type: none"> - TRADITIONAL, 1ST GEN. ANTIPSYCHOTICS: (HALDOL, THORAZINE, STELAZINE) - ATYPICAL, 2ND GEN. ANTIPSYCHOTICS: (CLOZARIL, GEODON, SEROQUEL, RISPERDAL, ZYPREXA, SYMBYAX, ABILIFY, INVEGA, SAPHIRIS)
MAJOR PLAYERS (KEY BRANDS)	<ul style="list-style-type: none"> - ELI LILLY (ZYPREXA, SYMBYAX) - JOHNSON & JOHNSON (RISPERDAL, INVEGA) - ASTRAZENECA (SEROQUEL) - PFIZER (GEODON) - BRISTOL-MYERS SQUIBB (ABILIFY) - NOVARTIS (CLOZARIL) - MERCK & CO (SAPHIRIS) - DAINIPPON SUMITOMO PHARMA (LONASEN)

ESTIMATES AS OF APRIL 19, 2017

SOURCE: VALUATIONLAB, NIH, WHO, COMPANY REPORTS

According to the WHO, there are more than 21 mn people suffering from either schizophrenia or similar symptoms. Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. People with schizophrenia may seem like they have lost touch with reality. The underlying cause is unknown but is believed to be a complex interplay of genetics, brain structure and chemistry (e.g. imbalance of neurotransmitters such as dopamine and glutamate that brain cells use to communicate with each other), developmental (e.g. hypoxia or infection during fetal development) and environmental factors, such as excessive substance use. Although schizophrenia is not as common as other mental disorders, the symptoms can be very disabling.

Symptoms of schizophrenia usually start between ages 16 and 30. The symptoms of schizophrenia fall into three categories:

1. **Positive symptoms:** these symptoms are psychotic behaviors not generally seen in healthy people. People with positive symptoms may lose touch with some aspects of reality, and include: hallucinations, delusions, thought disorders (unusual or dysfunctional ways of thinking), movement disorders (agitated body movements)
2. **Negative symptoms:** these symptoms are associated with disruptions to normal

emotions and behaviors. Symptoms include: flat affect (reduced expression of emotions via facial expression or voice tone), reduced feelings of pleasure in everyday life, difficulty beginning and sustaining activities, reduced speaking

3. **Cognitive symptoms:** for some patients, the cognitive symptoms of schizophrenia are subtle, but for others, they are more severe, and patients may notice changes in their memory or other aspects of thinking. Symptoms include: poor executive functioning (the ability to understand information and use it to make decisions), trouble focusing or paying attention, problems with working memory (the ability to use information immediately after learning it)

Current drug treatment falls short in treating symptoms with low patient compliance

Because the causes of schizophrenia are still unknown, treatments focus on eliminating the symptoms of the disease. Antipsychotic medications are the cornerstone for the treatment of schizophrenia, often in combination with psychological and social supports. Antipsychotic drugs help to normalize the biochemical balances that cause schizophrenia.

There are two major types of antipsychotics:

1. **First-generation (typical) antipsychotics:** such as Haldol (haloperidol), Thorazine (chlorpromazine), Stelazine (trifluoperazine), primarily block dopamine receptors and were the first drugs approved for treating schizophrenia more than 50 years ago. Although they were effective in treating positive symptoms, they were associated with a high occurrence of extrapyramidal side effects (EPS). This led to the development of second-generation (atypical) antipsychotics, which did not carry the risk of EPS and demonstrated a greater clinical benefit in patients.
2. **Second-generation (atypical) antipsychotics:** such as Novartis' Clozaril (clozapine), JNJ's Risperdal (risperidone), Eli Lilly's Zyprexa (olanzapine), AstraZeneca's Seroquel (quetiapine), Pfizer's Geodon (ziprasidone hydrochloride), Lundbeck's Abilify (aripiprazole), and JNJ's Invega (paliperidone) work on both the serotonin and dopamine receptors and have been available since the 1990's. These drugs appear to be more effective in treating a broader range of symptoms of schizophrenia, however, are associated with considerable weight gain, diabetes and risk of metabolic syndrome, most pronounced with Zyprexa.

Current approved medications for schizophrenia address positive symptoms but fall short in treating negative and cognitive symptoms. It is estimated that 75% of all patients stop taking their medications, regardless of which generation, because they did not make the better or had intolerable side effects. Discontinuation rates remain high even when patients are switched to a new drug, which is often the case

New market entrants

New market entrants include new formulations of existing drugs or combinations of drugs that enhance patient compliance (e.g. controlled release, depot formulations). New approaches to treat schizophrenia - some potentially addressing negative and cognitive symptoms - include, PDE10 inhibitors (**ITI-214**, **OMS824**, **TAK-063**), AMPA receptor modulators (**PF-04958242**), sodium channel blockers (**evenamide**), 5-HT_{2A} receptor antagonists (**lumateperone**, **MIN-101**), 5-HT₆ receptor antagonists (**Lu AF35700**, **avisetron**), and alpha₇ nicotinic acetylcholine receptor modulators (**AVL-3288**), among others.

Sarizotan (Rett syndrome)

Product Analysis

Rett syndrome peak sales of EUR ~400 mn - Risk-adjusted NPV of CHF 13 per share

We forecast peak sales of EUR 396 mn for sarizotan, assuming first market launches in late 2019/early 2020, orphan drug market and pediatric exclusivity until 2031 (EU: 12 years) and 2026 (US: 7 1/2 years), a treatment cost per patient of between USD 60,000 (US) and EUR 35,000 (EU/ROW), and a market penetration peaking at 65% of diagnosed patients with disordered breathing. Accounting for M&S costs (starting from EUR ~30 mn) and COGS (conservatively ranging between 10-14%), our risk-adjusted NPV amounts to CHF 284 mn or CHF 16 per share with a conservative success probability of 25% (phase II/III orphan drug), and a WACC of 7% (reflecting the low Swiss interest environment).

Sarizotan (Rett syndrome) – A bright future written in the STARS

Sarizotan is targeted for the treatment of breathing disturbances in girls with Rett syndrome, a rare disease, where there is a high premature mortality rate and no specific cure. In July 2016 Newron started the single, potentially pivotal phase II/III “STARS” (Sarizotan Treatment of Apnea in Rett Syndrome) trial in the US. In parallel, Newron has started an international Burden of Disease health economic outcome research study in Rett syndrome to provide more information on the economic impact/burden of Rett syndrome to facilitate filing, pricing and reimbursement negotiations of sarizotan, and increases physician awareness. Although sarizotan targets a smaller rare disease market opportunity, the value of sarizotan should be substantially higher than Xadago due to better economics. Newron plans to maximize the value of sarizotan by the buildup an own specialist field force, while Xadago had to be out-licensed at a difficult time for the company at lesser terms. Successful “STARS” results could lead to approval of sarizotan in late 2019/early 2020 and transform the company into a high margin CNS specialty biopharmaceutical company.

Newron has full rights, orphan disease protection, and potential voucher upside

Sarizotan was in-licensed from Merck KGaA in March 2011 and Newron now has the global rights to the compound. Merck KGaA originally developed sarizotan for Parkinson’s disease, but it was discontinued following the failure of two pivotal trials in 2006. Positively, there is a large safety database available for sarizotan in (Parkinson’s disease) patients, making it easier to start clinical trials in Rett patients. Composition of matter patent protection for sarizotan has already expired. Nevertheless, orphan drug designation and pediatric exclusivity should provide 12 years market exclusivity in the EU and 7 ½ years in the US, from the day of approval. Sarizotan is eligible to receive a Rare Disease Pediatric Priority Review Voucher on US approval. Recently, Congress extended this program that provides drug companies an additional incentive to develop drugs for children with rare diseases until mid 2020. These vouchers can be sold freely and are quite valuable with prices ranging between USD 68 and USD 350 mn with an average value of USD 167 mn. We currently exclude any value from a potential voucher sale in our forecasts.

Rett syndrome – a severe neuro-development disorder affecting young girls

Rett syndrome is a rare but severe neuro-development disorder primarily affecting females with approximately 15,000 patients in the US and 20,000 in the EU, with an incidence of 1 out of 10,000 to 15,000 live female births. This is a genetic disease that is caused by abnormalities in the MeCP2 (methyl CpG-binding protein 2) gene, which has important

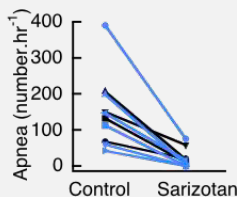
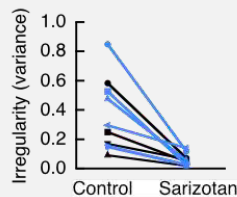
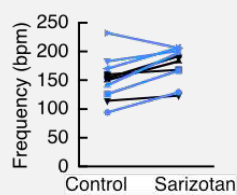
information for the normal functioning of nerve cells. This gene is in the X chromosome, one of the two sex chromosomes (X and Y) that determine the gender. Rett syndrome almost exclusively affects girls (XX). Boys (XY) have only one X chromosome and if affected they usually do not survive until birth. Although the disease is genetic, most girls affected (over 95%) do not inherit it from their parents. Patients develop normally until 6-18 months of life when there is a slowing down or stagnation of skill that includes loss of fine motor skills and speech, stereotypic hand movements, severe digestive problems, irregular heartbeat, seizures, and disordered breathing such as sudden and frequent breath holds. It is estimated that 20-26% of deaths in girls with Rett syndrome are attributed to sudden and severe cardiorespiratory dysregulation (disordered breathing that leads to irregular and often fatal heart beats and sudden death). There is no specific cure for Rett syndrome. Current treatment is limited to the management of symptoms. In 2009 the generic antidepressant desipramine chlorhydrate was granted EU orphan drug designation based on experimental models.

Potential to restore disordered breathing in girls with Rett syndrome

Sarizotan is a new chemical entity from the group of aminomethyl chromanes and is a full agonist at 5HT_{1A} receptors and partial agonist/antagonist at (dopamine) D₂ receptors. These are important receptors implicated in many neurological processes in the body including the regulation of blood pressure and heart beat (5HT_{1A} receptors); and mood, cognition, memory and fine movement (D₂ receptors). Hyper-excited expiratory neurons in the brain stem are believed to be involved in the breathing disturbance in Rett syndrome.

Compelling early evidence in preclinical Rett syndrome animal models

EFFECTS OF SINGLE ADMINISTRATION OF SARIZOTAN (5 MG/KG IP) IN RETT FEMALE MICE (MECP2^{JAE/+} + MECP2^{BIRD/+})

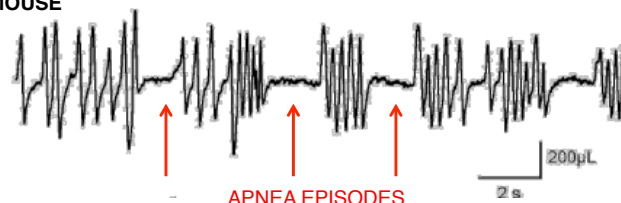
OUTCOMES DEFINITION AND UNITS	MEAN BASELINE DATA IN VEHICLE TREATED RETT MICE	MEAN DATA IN SARIZOTAN TREATED RETT MICE	DATA FROM INDIVIDUAL MICE	CHANGE VS. BASELINE
APNEA INCIDENCE (NUMBER OF APNEAS PER HOUR)	143 +/- 31	20 +/- 8		REDUCED BY 86% (P=0.001)
IRREGULARITY SCORE (VARIANCE)	0.34 +/- 0.07	0.06 +/- 0.01		REDUCED BY 82% (P=0.0001)
RESPIRATORY FREQUENCY (BREATHS PER MINUTE)	153 +/- 12	177 +/- 10		INCREASED BY 16% (P=0.012)

SOURCE: NEWRON PHARMACEUTICALS

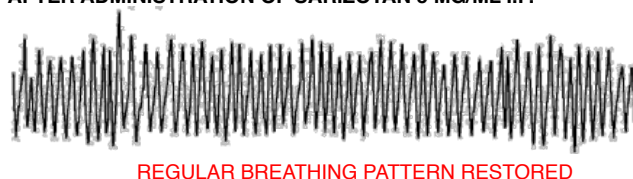
Sarizotan has demonstrated a dramatic effect in a genetic knockout model (a null mutant MeCP2 mouse model of Rett syndrome), and there is a strong rationale for restoring the regular respiratory rhythms through the modulation of the medullary respiratory network with

the drug. In the preclinical Rett syndrome mouse model, sarizotan was able to reduce apnea (breath holds) and correct irregular breathing after administering a single dose to these female mice.

PLETHYSMOGRAPH IN A VEHICLE TREATED MECP^{JAE/+} FEMALE MOUSE



PLETHYSMOGRAPH IN THE SAME MECP^{JAE/+} FEMALE MOUSE AFTER ADMINISTRATION OF SARIZOTAN 5 MG/ML I.P.



SOURCE: NEWRON PHARMACEUTICALS

The incidence of apnea and irregularity were significantly reduced by sarizotan at 20 minutes compared to vehicle.

No loss of efficacy on respiratory function seen over time with sarizotan

EFFECTS OF 14-DAY TREATMENT WITH SARIZOTAN IN RETT FEMALE MICE (MECP2^{R168X/+})

OUTCOMES DEFINITION AND UNITS	RESULTS	CHANGE VS. CONTROL (VEHICLE TREATED) GROUP
APNEA INCIDENCE (NUMBER OF APNEAS PER HOUR)	<p>Day 4 Day 7 Day 10 Day 14</p>	REDUCED BY 73.9% ON DAY 7 ($P < 0.05$) REDUCED BY 75.0% ON DAY 10 ($P < 0.01$) REDUCED BY 75.6% ON DAY 14 ($P < 0.01$)
IRREGULARITY SCORE (VARIANCE)		SIGNIFICANT DECREASE ($P < 0.05$)
RESPIRATORY FREQUENCY (BREATHS PER MINUTE)		NON-SIGNIFICANT

SOURCE: NEWRON PHARMACEUTICALS

Another preclinical trial spanning over 14 days in female Rett mice showed a prolonged effect of sarizotan. A crossover design was used so that half of the MeCP2^{R168X/+} female

mice (n=4) received vehicle (1.25% DMSO + 0.1% saccharin) in their drinking water, and half (n=4) received sarizotan (0.0625 mg/ml). At the end of 14 days, the treatment was reversed. As can be seen in the table above, sarizotan was effective in improving respiration in MeCP2^{R168X/+} female mice. Thirty minutes monitoring of respiratory pattern with plethysmography was performed on the 4th, 7th, 10th, and 14th day that resulted in statistically significant results in the reduction of the number of apneas per hour (p<0.01 to p<0.05) and a significant decrease in the irregularity score. Sarizotan had a non-significant effect on respiratory frequency.

Due to its mechanism of action affecting important neurotransmitters, sarizotan could have other potential benefits for Rett syndrome patients impacting behavior, cognition and neurological deficits.

“STARS” – A potentially pivotal, phase II/III trial in Rett syndrome patients

In December 2016, Newron started the US enrolment of the international phase II/III single potentially pivotal study, called “STARS” (**S**arizotan **T**reatment of **A**pneas in **R**ett **S**yndrome) in up to 129 Rett syndrome patients with disordered breathing. The “STARS” trial protocol was designed based on extensive discussions with regulatory authorities in Europe (Germany, Spain, and the UK), the US (FDA) and Canada (TPD), a leading advocacy group at Rettsyndrome.com and an international group of physicians specialized in Rett syndrome. The trial will be a double blind, randomized, placebo controlled multi-center trial in up to 129 Rett syndrome patients as young as six years of age (the inclusion age was expanded in May 2017 from originally patients of 13 years or older) with breathing disturbances. The 24-week study is designed to evaluate two fixed-dose groups (5 mg twice daily and 10 mg twice daily) against placebo for efficacy (respiratory functioning), safety and pharmacokinetics. Respiratory function will be measured using the BioRadio system, a lightweight and fully configurable wireless system for recording and analyzing physiological data, making at-home monitoring possible. This should enhance enrolment of these young patients, considerably. The primary endpoint is a reduction in the number of apnea episodes from baseline. After 24 weeks, all study patients will be placed on sarizotan and continue in an extension study for up to 48 weeks with at least 30 patients per dose group. Completion of trial enrolment is expected in mid 2018 with top line results due by end 2018. Assuming priority review (6-months), first country launches of sarizotan are expected to occur in late 2019/early 2020.

“Burden of Disease” study in Rett to support filing, pricing and reimbursement

In 2016 Newron has started an international Burden of Disease in Rett syndrome health economic outcome research study with results due mid 2018 around the same time “STARS” reports top line results. The study aims to deliver data and analytics to quantify the physical, emotional and financial challenges of Rett syndrome. The goals are to identify the unmet need for improving disease management, align economic and clinical outcomes, create awareness to breathing abnormality burden, and to build a leadership position in Rett syndrome. The Burden of Disease study meets Health Technology Assessment (HTA) requirements, including European Network of countries requiring information for treatments access. Moreover, the study fosters partnership and collaboration with Rett advocacy, thought leaders and governing payers. As a result, the study should facilitate global filing of sarizotan, pricing and reimbursement negotiations, and increase physician and public awareness of Rett syndrome to enhance patient uptake.

Peak sales of EUR 455 mn in Rett syndrome – buildup of own sales force pays off

Peak sales for sarizotan in Rett syndrome are estimated to amount to EUR 396 mn assuming a conservative annual treatment price of EUR 35,000 in the EU and USD 60,000 in the US. Annual treatment prices could be substantially higher depending on the efficacy outcomes of the “STARS” trial. Moreover, most orphan disease drugs command far higher treatment prices in the several hundred thousand dollars range. We estimate there are roughly 15,000 Rett syndrome patients in the US and 20,000 in Europe, with the population growing 2% annually, of which roughly 50% have breathing disturbances that sarizotan addresses. We have conservatively excluded other regions due to the lack of clinical diagnosis and affordability of relatively expensive orphan drug treatments.

It is estimated that around 15-20% of patients in the US are currently diagnosed. An educational effort to increase awareness of Rett syndrome among physicians and parents will be crucial to achieve our sales forecasts. Newron has already stepped up its efforts to increase awareness and understanding of disease progression. The company recently joined the global movement to raise awareness for rare diseases, such as Rett syndrome. The initiation of the Global Caregiver Outreach Program, in partnership with Rett foundations, collects and distributes data on the impact of respiratory abnormalities to better understand the natural history of the disease. The company is also helping to establish Step Guidelines for Rett syndrome together with Rett experts and has started discussions with US pharmacy benefit managers and pricing and reimbursement representatives in the EU. Therefore, we have accounted for increased diagnosis in our forecasts with diagnosis rising to and peaking at around 70%. We also assume a 65% peak penetration rate in diagnosed patients, given the impact of disordered breathing on the quality of life for patients (and parents) and premature death due to severe cardiopulmonary dysregulation. Based on these assumptions we forecast peak sales to amount to EUR 396 mn in 2026.

We conservatively assume COGS of 14% of sales at the start of launch gradually declining to 10%. We have also accounted for the buildup of an own specialist sales force in both major regions and substantial marketing/educational spend to increase disease awareness. Nevertheless, EBIT margins should gradually grow to ~65% (EU) and ~75% (US), justifying the decision to build up an own field force.

We conservatively assume a 25% success rate, for the potentially single pivotal “STARS” trial. Typically, a 50-65% success rate would apply for a phase III trial. However, sarizotan has only been tested in the failed Parkinson’s disease trials conducted by Merck KGaA, and not yet in patients with Rett syndrome. It is therefore difficult to assess efficacy in these patients. Hence, our conservative 25% success probability. We calculate a risk-adjusted NPV for sarizotan of CHF 237 mn or CHF 13 per share.

Our detailed forecasts and sensitivity analysis can be seen on the following page.

Forecasts & Sensitivity Analysis

Rett syndrome (orphan indication)

SARIZOTAN - FINANCIAL FORECASTS FOR RETT SYNDROME

INDICATION	TREATMENT OF BREATHING DIFFICULTIES IN PATIENTS WITH RETT SYNDROME
DOSAGE	5 OR 10 MG TWICE DAILY
PRICE	US: USD 60,000 PER YEAR, EU/ROW: EUR 35,000
STANDARD OF CARE	NO EFFECTIVE TREATMENT AVAILABLE; TOPIRAMATE (ANTI-EPILEPTIC) OR NALTREXONE (OPIATE ANTAGONIST) GIVEN OFF-LABEL BUT OFTEN INEFFECTIVE
UNIQUE SELLING POINT	FIRST EFFECTIVE TREATMENT TO ADDRESS DISORDERED BREATHING, A MAJOR CAUSE OF DEATH IN RETT SYNDROME PATIENTS

7Ps ANALYSIS

PATENT	COMPOSITION OF MATTER PATENT (EXPIRED) - ORPHAN DRUG EXCLUSIVITY INCLUDING PEDIATRIC: EU (12 YEARS) AND US (7 1/2 YEARS) FROM APPROVAL
PHASE	SINGLE POTENTIALLY PIVOTAL "STARS" TRIAL IN ~129 RETT SYNDROME PATIENTS WITH BREATHING DISORDERS; TOPLINE RESULTS END 2018, LAUNCH LATE 2019/EARLY 2020
PATHWAY	ORPHAN DRUG INDICATION - SINGLE PIVOTAL "STARS" TRIAL PROBABLY SUFFICIENT FOR APPROVAL
PATIENT	DISORDERED BREATHING HAS A MAJOR IMPACT ON QUALITY OF LIFE FOR PATIENTS, A GREAT CONCERN FOR PARENTS AND A MAJOR CAUSE OF DEATH
PHYSICIAN	FIRST TREATMENT TO ADDRESS BREATHING DIFFICULTIES THAT OCCURS IN ROUGHLY 50% OF PATIENTS AND IS A MAJOR CAUSE OF DEATH
PAYER	CONSIDERABLE REDUCTION OF COSTS CAUSED BY HOSPITALIZATION, COMPLICATIONS AND RESCUE MEDICATION
PARTNER	WORLDWIDE RIGHTS ACQUIRED FROM MERCK KGAA IN 2011 - NEWRON PLANS TO MARKET SARIZOTAN THROUGH AN OWN SPECIALIZED FIELD FORCE

REVENUE MODEL

EUROPE	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS	20,808	21,224	21,649	22,082	22,523	22,974	23,433	23,902	24,380	24,867	25,365
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH BREATHING DISORDERS (50%)	10,404	10,612	10,824	11,041	11,262	11,487	11,717	11,951	12,190	12,434	12,682
PERCENTAGE DIAGNOSED (%)	20%	20%	25%	35%	50%	60%	65%	67%	68%	69%	69%
PATIENTS DIAGNOSED	2,081	2,122	2,706	3,864	5,631	6,892	7,616	8,007	8,289	8,517	8,751
PENETRATION (%)	0%	0%	5%	30%	45%	55%	60%	62%	64%	65%	65%
NUMBER OF PATIENTS	0	0	135	1159	2534	3791	4569	4964	5305	5536	5688
COST OF THERAPY PER YEAR (EUR)	35,000	35,000	35,000	35,000	35,000	35,000	35,000	35,000	35,000	35,000	35,000
SALES (EUR MN)	0	0	5	41	89	133	160	174	186	194	199
CHANGE (%)				757%	119%	50%	21%	9%	7%	4%	3%
COGS (%)	0%	0%	14%	14%	12%	10%	10%	10%	10%	10%	10%
COGS (EUR MN)	0	0	-1	-6	-11	-13	-16	-17	-19	-19	-20
R&D COSTS (EUR MN)	-6	-10	-2	0	0	0	0	0	0	0	0
M&S (%)			62%	37%	35%	33%	31%	29%	27%	25%	25%
M&S COSTS (EUR MN)	0	0	-15	-15	-31	-44	-50	-50	-50	-48	-50
PROFIT BEFORE TAX (EUR MN)	-6	-10	-13	20	47	76	94	106	117	126	129
TAXES (EUR MN)	0	0	1	-4	-7	-24	-30	-33	-37	-40	-41
PROFIT (EUR MN)	-6	-10	-12	16	40	52	65	73	80	86	89

UNITED STATES	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NUMBER OF PATIENTS	15,606	15,918	16,236	16,561	16,892	17,230	17,575	17,926	18,285	18,651	19,024
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH BREATHING DISORDERS (50%)	7,803	7,959	8,118	8,281	8,446	8,615	8,787	8,963	9,142	9,325	9,512
PERCENTAGE DIAGNOSED (%)	20%	20%	25%	35%	50%	60%	65%	67%	68%	69%	69%
PATIENTS DIAGNOSED	1,561	1,592	2,030	2,898	4,223	5,169	5,712	6,005	6,217	6,388	6,563
PENETRATION (%)	0%	0%	10%	35%	50%	60%	65%	65%	65%	65%	7%
NUMBER OF PATIENTS (MN)	0.0	0.0	203.0	1014.4	2111.6	3101.5	3712.7	3903.5	4041.0	4152.1	426.6
COST OF THERAPY PER YEAR (EUR)	48,790	48,793	48,790	48,790	48,790	48,790	48,790	48,790	48,790	48,790	48,790
SALES (EUR MN)	0	0	10	49	103	151	181	190	197	203	21
CHANGE (%)				400%	108%	47%	20%	5%	4%	3%	-90%
COGS (%)	0%	0%	14%	14%	12%	10%	10%	10%	10%	10%	10%
COGS (EUR MN)	0	0	-1	-7	-12	-15	-18	-19	-20	-20	-2
M&S (%)			35%	33%	31%	29%	27%	25%	20%	20%	20%
M&S COSTS (EUR MN)	0	0	-12	-16	-32	-44	-49	-48	-39	-41	-4
PROFIT BEFORE TAX (USD MN)	0	0	-5	32	72	114	140	152	170	174	18
TAXES (EUR MN)	0	0	0	-5	-9	-29	-36	-39	-43	-45	-5
PROFIT (EUR MN)	0	0	-3	21	50	63	78	85	95	97	10

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
GLOBAL SALES (EUR MN)	0	0	15	90	192	284	341	364	383	396	220
CHANGE (%)				515%	113%	48%	20%	7%	5%	4%	-45%
GLOBAL PROFIT (EUR MN)	-6	-10	-16	37	89	115	143	158	175	184	99
CHANGE (%)	-6%	67%	58%	-337%	138%	29%	24%	10%	11%	5%	-46%

WACC (%)	7.0%
NPV TOTAL PROFIT (CHF MN)	948
NUMBER OF SHARES (MN)	17.8
NPV PER SHARE (CHF)	53
SUCCESS PROBABILITY	25% = PHASE II/III ORPHAN DRUG
RISK ADJUSTED NPV PER SHARE (CHF)	13

SENSITIVITY ANALYSIS

		WACC (%)							
		CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	70%		42	40	39	37	36	35	33
	65%		39	37	36	35	33	32	31
	55%		33	31	30	29	28	27	26
	45%		27	26	25	24	23	22	21
	35%		21	20	19	19	18	17	17
	25%		15	14	14	13	13	12	12
	15%		9	9	8	8	8	7	7

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

Unique Selling Point

First effective treatment to address disordered breathing, a major cause of death in Rett syndrome patients.

7P's Analysis

Patent: Composition of matter patent for sarizotan has expired. In the US sarizotan will enjoy at least 7 years orphan drug market exclusivity with an additional 6 months pediatric exclusivity from the date of regulatory approval. In the EU, sarizotan will enjoy at least 12 years orphan drug and pediatric market exclusivity upon approval.

Phase: In July 2016 Newron started the single, potentially pivotal phase II/III “STARS” trial in up to 129 Rett syndrome patients with disordered breathing in the US and Europe. The trial protocol was designed following extensive discussions with regulatory authorities in the US, Europe and Canada. Typically, a new compound has to start first with phase I safety trials. However, Merck KGaA has largely established the safety of sarizotan in two large phase III Parkinson’s disease trials. Moreover, there are no effective treatments for Rett syndrome patients with breathing disorders, a rare disease where enrolment of large patient numbers would be difficult. Topline results are expected by the end of 2018.

Pathway: Sarizotan has received orphan drug designation (ODD) in the US and EU in 2015 due to the small number of Rett syndrome patients, and the lack of an effective treatment to address disordered breathing that affects roughly half of patients. As a result, a single, potentially pivotal trial with relatively low patient numbers is most likely sufficient for approval. Sarizotan is entitled shorter, expedited review by the regulatory authorities. Moreover, on US approval Newron may receive a transferable Rare Pediatric Disease Priority Review Voucher, which can be sold freely to a third party.

Patient: Reduction of breathing abnormalities such as apnea (breath stops), hyperventilation, and forced exhalation of air or saliva during awake time will have a significant impact on the quality of life for the patient, as well as reduce the parents’ concerns. Onset is as early as 3 years of age and may persist for 10-15 years.

Physician: First specific treatment to treat breathing irregularities, which occurs in roughly 50% of patients and is a main cause of death in Rett syndrome. These apneic episodes may occur as frequently as 10-60 times an hour during awake time. It is estimated that approximately 25% of sudden deaths in Rett syndrome patients is caused by cardiorespiratory abnormalities.

Payer: An effective treatment for breathing disorders will lead to substantial savings such as emergency hospital visits or outpatient care.

Partner: Given the relatively small size of the market and target specialists, Newron plans to build up an own global specialist field force to commercialize sarizotan and maximize long-term profitability with EBIT margins rising up to 65-75%. The company can potentially finance its own sales infrastructure through the royalty and milestone payments it receives for Xadago, potential upfront payments from a licensing agreement for evenamide in 2020, or alternatively a potential financing round.

Rett Syndrome Market

Currently, the Rett syndrome market is virtually non-existent, with no cure available, and is estimated to be less than USD 50 mn, largely consisting of off-label use of drugs, such as seizure medications, to control the symptoms of the disorder. The market is set to grow once new treatments become available to treat symptoms or the underlying cause of the disease, a mutation of the MeCP2 gene. An effective treatment to address breathing disorders in Rett syndrome, which occurs in roughly 50% of patients points to a USD 875 mn market potential in the US and EU alone, assuming an average annual treatment cost of USD 50,000.

RETT SYNDROME - KEY FACTS

MARKET SIZE	<USD 50 MN
PREVALENCE	~100,000 GLOBALLY, ~15,000 US; ~20,000 EU; ~60,000 ROW
INCIDENCE	1 OUT OF EVERY 10,000-15,000 LIVE FEMALE BIRTHS
UNDERLYING CAUSE	A PROGRESSIVE DEVELOPMENTAL DISORDER FIRST RECOGNIZED IN INFANCY SEEN ALMOST EXCLUSIVELY IN GIRLS, RARELY IN BOYS, AND IS CAUSED BY MUTATIONS ON THE X CHROMOSOME ON A GENE CALLED MECP2. LESS THAN 1% OF PATIENTS HAVE A HISTORY OF RETT SYNDROME IN THE FAMILY.
SYMPTOMS	SYMPTOMS APPEAR AFTER AN EARLY PERIOD OF NORMAL OR NEAR NORMAL DEVELOPMENT UNTIL 6-18 MONTHS OF LIFE WHEN THERE IS A SLOWING DOWN OR STAGNATION OF SKILLS, AND INCLUDE: - LOSS OF SPEECH AND MOTOR CONTROL - COLD HANDS AND FEET, COLOR RANGES FROM PINK TO BLUE - FUNCTIONAL HAND USE REPLACED BY COMPULSIVE HAND MOVEMENTS - DISORDERED BREATHING: APNEA (BREATH-HOLDING), HYPERVENTILATION, FORCEFUL EXHALATION OF AIR OR SALIVA - SEVERE DIGESTIVE PROBLEMS - ORTHOPEDIC ABNORMALITIES INCL. SCOLIOSIS, FRAGILE BONES - DISRUPTED SLEEP PATTERNS - EXTREME ANXIETY, SEIZURES, TREMOR, IMPAIRED CARDIAC AND CIRCULATORY FUNCTION
DRUG THERAPY (KEY BRANDS)	NO CURE OR SPECIFIC TREATMENTS AVAILABLE - ANTI-EPILEPTIC (TOPIRAMATE) - GIVEN OFF-LABEL BUT OFTEN INEFFECTIVE - OPIATE ANTAGONIST (NALTREXONE) - GIVEN OFF-LABEL BUT OFTEN INEFFECTIVE - SELECTIVE 5-HT _{1A} RECEPTOR AGONIST & D ₂ RECEPTOR ANTAGONIST (SARIZOTAN) - IGF-1 ANALOG (TROFINETIDE) - INSULIN-LIKE GROWTH FACTOR 1 (IGF-1)
MAJOR PLAYERS (KEY BRANDS)	NO CURE OR SPECIFIC TREATMENTS AVAILABLE - GENERIC (TOPIRAMATE) - GENERIC (NALTREXONE) - NEWRON (SARIZOTAN) - SINGLE PIVOTAL PHASE II/III "STARS" TRIAL STARTED IN 2016 - NEUREN PHARMA (TROFINETIDE) - PHASE II TRIAL WITH HIGHER DOSE STARTED IN 2016

SOURCE: VALUATIONLAB, NIH, WHO, IRSF, RSRT, COMPANY REPORTS

Rett syndrome is a neurodevelopmental disorder that occurs almost exclusively in girls. It is characterized by normal early growth and development followed by a slowing of development, loss of purposeful use of the hands, distinctive hand movements, slowed brain and head growth, problems with walking, disordered breathing, seizures, and intellectual disability. Dr. Andreas Rett, an Austrian physician, identified the disorder in 1966. Rett syndrome is estimated to affect one in every 10,000 to 15,000 live female births and in all racial and ethnic groups worldwide. Despite the difficulties with symptoms, many individuals with Rett syndrome continue to live well into middle age and beyond. Because the disorder is rare, very little is known about long-term prognosis and life expectancy.

The course of Rett syndrome, including the age of onset and the severity of symptoms, varies from child to child, and is generally classified in four stages:

1. **Stage I (early onset):** typically begins between 6-18 months of age and lasts for a few months up to more than a year. Often overlooked because symptoms (e.g. less eye contact, reduced interest in toys, hand-wringing, decreasing head growth) may be vague, and the subtle slowing of development may not be noticed.
2. **Stage II (rapid destructive stage):** usually begins between ages 1-4 and may last for weeks or months. Onset may be rapid or gradual as the child loses purposeful hand skills and spoken language. Characteristic hand movements such as wringing, washing, clapping, or tapping, as well as repeatedly moving the hands to the mouth often begin during this stage. The movements continue while the child is awake but

disappear during sleep. Breathing irregularities such as episodes of apnea (breath holds) and hyperventilation may occur, although breathing usually improves during sleep. Some girls also display autistic-like symptoms such as loss of social interaction and communication. Slowed head growth is usually noticed.

3. **Stage III (plateau or pseudo-stationary stage):** usually begins between ages 2-10 and can last for years. Movement problems, and seizures are prominent. An improvement in behavior, with less irritability, crying, and autistic-like features may occur. Patients may show more interest in their surroundings and alertness, attention span, and communication skills may improve, with most remaining in this stage most of their lives.
4. **Stage IV (late motor deterioration stage):** can last for years or decades. Prominent features include reduced mobility, curvature of the spine (scoliosis) and muscle weakness, rigidity, spasticity, and increased muscle tone with abnormal posturing of an arm, leg, or top part of the body. Girls who were previously able to walk may stop walking.

Doctors clinically diagnose Rett syndrome by observing signs and symptoms during the child's early growth and development and conducting ongoing evaluations of the child's physical and neurological status. A genetic test is available to complement the clinical diagnosis.

Rett syndrome is caused by a mutation of the MeCP2 gene

Nearly all cases of Rett syndrome are caused by a mutation in the methyl CpG binding protein 2 (MECP2) gene, which is believed to control the functions of many other genes. The MECP2 gene contains instructions for the synthesis of a protein called methyl cytosine binding protein 2 (MeCP2), which is needed for brain development and acts as one of the many biochemical switches that can either increase gene expression or tell other genes when to turn off and stop producing their own unique proteins. Because the MeCP2 gene does not function properly in individuals with Rett syndrome, insufficient amounts or structurally abnormal forms of the protein are produced and can cause other genes to be abnormally expressed.

The MeCP2 gene is in the X chromosome, one of the two sex chromosomes (X and Y) that determine the gender. Rett syndrome almost exclusively affects girls (XX). Boys (XY) have only one X chromosome and if affected they usually do not survive until birth. In girls only one X chromosome is active in any given cell. This means that in a girl with Rett syndrome, only a portion of the cells in the nervous system will use the defective gene. Some of the child's brain cells use the healthy gene and express normal amounts of the protein. The severity of Rett syndrome in girls is in part a function of the percentage of their cells that express a normal copy of the MeCP2 gene. Although Rett syndrome is a genetic disorder, less than 1 percent of recorded cases are inherited or passed from one generation to the next, which means the mutation occurs randomly.

New market entrants expected to spark growth

New compounds that specifically target treating symptoms of the disease should lead to substantial growth in this largely underdeveloped market. These include Newron's **sarizotan** (phase II/III), Neuren Pharma's **trofinetide** (phase IIa POC completed) and Boston Children's Hospital's **IGF-1** (phase IIa POC completed). New genetic treatments that target the underlying cause of the disease, a mutation of the MECP2 gene, are still many years away from market entry.

Income Statement

NEWRON PHARMACEUTICALS								SHARE PRICE (CHF)		11.9	
IFRS											
INCOME STATEMENT (EUR MN)	2017	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
PRODUCT SALES (INCLUDING PARTNERS)	29	95	166	339	525	829	1,162	1,486	1,782	2,004	1,973
CHANGE (%)	43%	228%	74%	105%	55%	58%	40%	28%	20%	12%	-2%
PRODUCT SALES (BY NEWRON)	0	0	15	90	192	284	341	364	383	396	220
CHANGE (%)				515%	113%	48%	20%	7%	5%	4%	-45%
ROYALTIES	3	10	16	27	35	78	139	208	272	320	352
CHANGE (%)	68%	234%	70%	67%	31%	122%	78%	50%	30%	18%	10%
LICENCE, UPFRONT & MILESTONE INCOME	10	0	5	81	0	27	0	16	79	0	87
OTHER INCOME & GRANTS	0	0	0	0	0	0	0	0	0	0	0
REVENUES (EXCL. PARTNER SALES)	13	10	36	198	227	390	480	589	734	716	659
CHANGE (%)	100%	-28%	272%	451%	15%	72%	23%	23%	25%	-2%	-8%
COGS	0	0	-2	-13	-23	-28	-34	-36	-38	-40	-22
GROSS PROFIT	13	10	34	185	204	361	446	553	696	676	637
CHANGE (%)	100%	-28%	250%	447%	10%	77%	24%	24%	26%	-3%	-6%
MARGIN	100%	100%	94%	94%	90%	93%	93%	94%	95%	94%	97%
R&D	-9	-15	-16	-20	-13	-10	-11	-11	-12	-13	-13
CHANGE (%)	-31%	76%	8%	22%	-35%	-20%	5%	5%	5%	5%	5%
S,G&A	-9	-10	-37	-41	-73	-98	-108	-108	-100	-99	-64
CHANGE (%)	-5%	9%	272%	11%	77%	34%	11%	0%	-8%	-1%	-35%
OPERATING EXPENSES	-18	-25	-56	-74	-109	-136	-154	-156	-150	-151	-99
CHANGE (%)	-19%	41%	121%	33%	48%	25%	12%	2%	-4%	1%	-34%
AS % REVENUES	132%	260%	155%	37%	48%	35%	32%	26%	20%	21%	15%
EBITDA	-4	-15	-20	124	118	253	327	433	584	565	560
CHANGE (%)	-72%	258%	27%	-735%	-5%	114%	29%	32%	35%	-3%	-1%
MARGIN (%)	-32%	-159%	-54%	63%	52%	65%	68%	74%	80%	79%	85%
DEPRECIATION & AMORTISATION	0	0	0	0	0	0	0	0	0	0	0
AS % REVENUES	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%
EBIT	-4	-15	-20	124	118	253	327	433	584	565	560
CHANGE (%)	-72%	255%	27%	-733%	-5%	114%	29%	32%	35%	-3%	-1%
MARGIN (%)	-32%	-160%	-55%	63%	52%	65%	68%	74%	80%	79%	85%
NET FINANCIAL INCOME/(EXPENSE)	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
PROFIT BEFORE TAXES	-5	-16	-21	123	117	252	326	432	583	564	559
MARGIN	-39%	-170%	-57%	62%	52%	65%	68%	73%	79%	79%	85%
TAXES	0	0	0	-27	-22	-86	-109	-143	-190	-184	-183
TAX RATE (%)	0%	0%	2%	22%	18%	34%	33%	33%	33%	33%	33%
NET PROFIT/LOSS	-5	-16	-20	96	96	166	217	289	393	380	376
CHANGE (%)	-65%	210%	23%	-578%	-1%	74%	30%	34%	36%	-3%	-1%
MARGIN (%)	-39%	-170%	-56%	49%	42%	43%	45%	49%	54%	53%	57%
NET PROFIT/LOSS (EXCLUDING MILESTONES)	-16	-16	-25	15	96	139	217	273	314	380	289
MARGIN (%)	-117%	-170%	-70%	8%	42%	36%	45%	46%	43%	53%	44%
PROFIT/(LOSS) PER SHARE (IN EUR)	-0.32	-0.92	-1.13	5.39	5.36	9.32	12.16	16.23	22.04	21.28	21.07
PROFIT/(LOSS) PER SHARE (IN CHF)	-0.39	-1.08	-1.33	6.36	6.32	11.00	14.34	19.15	26.00	25.11	24.86

ESTIMATES AS OF 2 MAY, 2018

SOURCE: VALUATIONLAB ESTIMATES

NOTE: At the end of FY 2017 Newron had a total of EUR 175.1 mn tax loss carryforwards. Due to the uncertainties as to whether Newron can use these, we have excluded them from our forecasts.

Ratios & Balance Sheet

NEWRON PHARMACEUTICALS									SHARE PRICE (CHF)		11.9	
RATIOS		2017	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
P/E			-11.0x	-8.9x	1.9x	1.9x	1.1x	0.8x	0.6x	0.5x	0.5x	0.5x
P/S			18.7x	5.0x	0.9x	0.8x	0.5x	0.4x	0.3x	0.2x	0.3x	0.3x
P/NAV			3.5x	5.7x	1.4x	0.8x	0.5x	0.3x	0.2x	0.1x	0.1x	0.1x
EV/EBITDA			-7.8x	-6.1x	1.0x	1.0x	0.5x	0.4x	0.3x	0.2x	0.2x	0.2x
PER SHARE DATA (CHF)		2017	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
EARNINGS		-0.39	-1.08	-1.33	6.36	6.32	11.00	14.34	19.15	26.00	25.11	24.86
CHANGE (%)		-69%	178%	23%	-578%	-1%	74%	30%	34%	36%	-3%	-1%
CASH		4.40	2.66	1.09	9.01	16.54	32.98	54.44	83.06	121.80	159.40	196.77
CHANGE (%)		17%	-40%	-59%	725%	84%	99%	65%	53%	47%	31%	23%
DIVIDENDS		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PAYOUT RATIO (%)		0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE		4.96	3.38	2.07	8.42	14.74	25.74	40.08	59.23	85.23	110.34	135.20
CHANGE (%)		23%	-32%	-39%	307%	75%	75%	56%	48%	44%	29%	23%
BALANCE SHEET (EUR MN)		2017	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NET LIQUID FUNDS		60	40	17	136	250	499	823	1,256	1,841	2,410	2,975
TOTAL ASSETS		73	53	29	149	263	512	836	1,269	1,854	2,423	2,988
SHAREHOLDERS' EQUITY		68	51	31	127	223	389	606	895	1,289	1,668	2,044
CHANGE (%)		36%	-24%	-39%	307%	75%	75%	56%	48%	44%	29%	23%
RETURN ON EQUITY (%)		-8%	-32%	-64%	75%	43%	43%	36%	32%	31%	23%	18%
FINANCIAL DEBT		1	1	1	1	1	1	1	1	1	1	1
FINANCIAL DEBT AS % OF TOTAL ASSETS		1%	1%	2%	0%	0%	0%	0%	0%	0%	0%	0%
EMPLOYEES		24	24	25	25	26	26	27	28	28	29	29
CHANGE (%)		4%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
CASH FLOW STATEMENT (EUR MN)		2017	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E
NET PROFIT / (LOSS) BEFORE TAX		-5	-16	-21	123	117	252	326	432	583	564	559
DEPRECIATION & AMORTIZATION		0	0	0	0	0	0	0	0	0	0	0
OTHER NON-CASH ITEMS		-2	-2	-2	-2	-2	-2	-2	-2	-2	-2	-2
CASH FLOW		-7	-19	-23	121	115	250	324	430	581	562	556
NET INCREASE/(DECREASE) IN WORKING CAPITAL		-1	-1	-1	-1	-1	-1	-1	-1	-1	-1	-2
OPERATING FREE CASH FLOW		-8	-20	-24	120	114	248	323	430	583	564	560
NET CASH FLOWS FROM INVESTING ACTIVITIES		0	0	0	0	0	0	1	2	3	4	5
NET CASH USED IN OPERATING ACTIVITIES		-9	-20	-24	120	114	249	324	433	586	568	565
NET CASH FLOWS FROM FINANCING ACTIVITIES		22	0	0	0	0	0	0	0	0	0	0
NET INCREASE/(DECREASE) IN CASH AND CASH EQUIVALEN		13	-20	-24	120	114	249	324	433	586	568	565
ESTIMATES AS OF 2 MAY, 2018									SOURCE: VALUATIONLAB ESTIMATES			

ESTIMATES AS OF 2 MAY, 2018

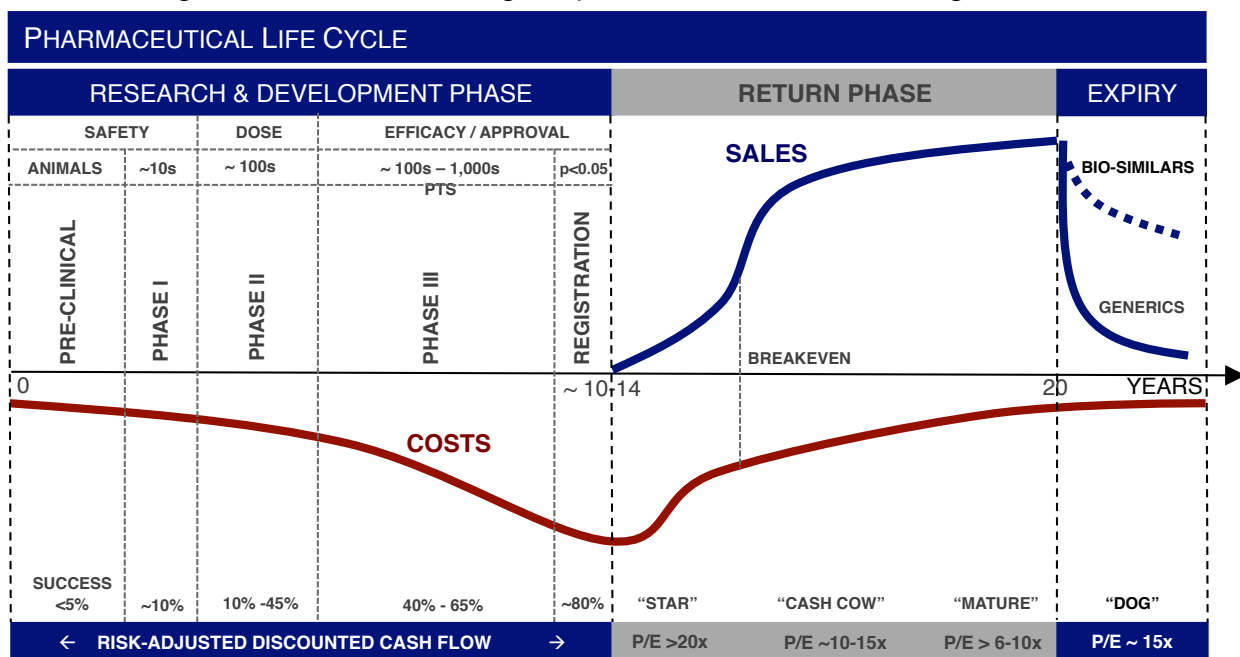
SOURCE: VALUATIONLAB ESTIMATES

NOTE: With cash and cash equivalents of EUR 60.1 mn (31 December 2017), increasing milestone and royalty payments from Zambon on Xadago sales, Newron has sufficient cash to complete full development of sarizotan in Rett syndrome with the pivotal “STARS” trial and prepare commercialization; and complete a potentially pivotal development of evenamide in schizophrenia and CTRS to maximize the long-term value.

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. The average Research & Development Phase takes 10-14 years, leading to an effective Return Phase of 6-10 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.GO.V

Important Research Disclosures

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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.

Purpose of the Research

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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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