7 June 2017

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VALUATIONLAB
FINANCIAL ANALYSIS

NEWRON PHARMACEUTICALS

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

KEY DATA			SIX: NWRN
MARKET CAPITALIZATION (CHF MN)	**330**	**PRICE ON JUNE 07, 2017**	**20.9**
ENTERPRISE VALUE (CHF MN)	**279**	**RISK-ADJUSTED NPV PER SHARE** * (CHF)	**45**
CASH (31 DECEMBER 2016) (CHF MN)	**51**	**UPSIDE/DOWNSIDE** (%)	**114%**
MONTHLY OPERATING EXPENSE (CHF MN)	**2.8**	**RISK PROFILE**	**HIGH RISK**
CASH LIFE (YEAR)	**2019**	**SUCCESS PROBABILITY LEAD PIPELINE DRUG**	**25%**
BREAK-EVEN (EXCL. MILESTONES) (YEAR)	**2019**	**EMPLOYEES** (GROUP)	**24**
FOUNDED (YEAR)	**1998**	**LISTED** (YEAR)	**2006**

KEY PRODUCTS:	STATUS	MAJOR SHAREHOLDERS:	(%)
- XADAGO (PARKINSON'S DISEASE)	APPROVED	- DUBA AB (INVESTOR AB)	11.2
- SARIZOTAN (RETT SYNDROME)	PHASE III	- ZAMBON GROUP	8.3
- EVENAMIDE (SCHIZOPHRENIA)	PHASE II	- AVIVA	8.3
		- EXECUTIVE MANAGEMENT	0.5
		- FREE FLOAT	**99.5**
		- AVERAGE TRADING VOLUME (30-DAYS)	53,352

UPCOMING CATALYSTS:	DATE	ANALYST(S):	BOB POOLER
- XADAGO - US LAUNCH	JULY 2017		BP@VALUATIONLAB.COM
- EVENAMIDE - NEXT STEPS TO MAXIMIZE VALUE	H2 2017		+41 79 652 67 68
- SARIZOTAN - TOPLINE RESULTS "STARS"	MID 2018		

* NOTE: BASED ON DILUTED NUMBER OF SHARES TO RAISE FUNDS FOR PHASE IIB DEVELOPMENT EVENAMIDE
ESTIMATES AS OF 7 JUNE, 2017

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Persistence beats resistance

Xadago approved in the US; positive evenamide POC

Newron Pharmaceuticals has a product pipeline that targets diseases of the central nervous system (CNS) and rare diseases. The company's key value driver is Xadago, a once daily oral add-on therapy for Parkinson's disease with a unique dual mechanism of action. Xadago was first launched in the EU in Q2 2015, with a US launch expected in July 2017 following the FDA approval last March. Xadago was licensed to Meiji Seika (Japan & Asian markets) and Zambon (worldwide excluding Meiji Seika territories) in 2012. Substantial revenues are expected from sub-licensing, milestone and royalty payments from Xadago sales. With cash of CHF 51 mn (December 31st, 2016) and increasing Xadago revenues, Newron has a cash runway into 2019, and is adequately funded to advance sarizotan for Rett syndrome (in pivotal development), and is evaluating a fund raise for a potentially pivotal phase IIb/III study with evenamide in schizophrenia. We derive a risk-adjusted NPV value of CHF 45 per share (assuming an 8% dilution to raise EUR 25 mn for the potentially pivotal phase IIb/III trial of evenamide in schizophrenia), with 47% of the value related to Xadago, 32% to sarizotan, 15% to evenamide, and 7% to cash. Newron's risk profile is currently High Risk as the company is loss making and product revenues stem solely from Xadago. A re-rating should occur once profitability is reached in the next 2 years.

Key catalysts:

1) **Xadago US launch (July 2017):** US approval added CHF 3/share and triggered a total of EUR 11.3 mn milestone payments; more than 60 sales representatives will initially support US launch by US WorldMeds, a US specialty pharmaceutical company.
2) **Next steps to maximize value of evenamide (H2 2017):** Positive POC (proof-of-concept) results in Q1 2017 added CHF 7/share; Newron is seeking to raise EUR ~25 mn to fund a potentially pivotal potentially pivotal phase IIb/III trial planned to start in H1 2018 to maximize evenamide's long-term value.
3) **Topline results sarizotan "STARS" trial (mid 2018):** On positive topline results, our risk-adjusted NPV will jump by CHF 23/share (65% phase III success probability) from currently CHF 15/share (25% phase II/III orphan drug probability).

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 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). In 2014 Newron opened a US office in Morristown, New Jersey, USA. Currently the group has 24 employees. The present clinical focus is on Parkinson's disease (safinamide, branded "Xadago"), schizophrenia (evenamide, previously named NW-3509) and rare diseases such as Rett syndrome (sarizotan). In October 2015, Newron decided to discontinue two orphan drug projects, sNN0031 (severe Parkinson's disease) and sNN0029 (ALS), stemming from the NeuroNova AB acquisition in 2012, due to ongoing problems and delays of a critical investigational delivery catheter from a third party supplier.

Newron's current therapeutic focus is a result of:

1) The company's expertise in ion channel research, an important class of CNS drugs (e.g. Xadago, evenamide)
2) 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, 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.

Persistence beats resistance – US approval of Xadago in March 2017

After several setbacks at the FDA spanning more than two years, and thanks to Newron's persistence, Xadago was approved in the US as add-on therapy to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes in March 2017. US launch of Xadago is expected in July 2017 by US WorldMeds with the support of more than 60 sales representatives. US WorldMeds is a US specialty pharmaceutical company that licensed the US commercialization rights from partner Zambon in March 2016. The company sells specialty pharmaceuticals in the US including the Parkinson's drug Apokyn (apomorphine hydrochloride) that is used to treat acute "wearing-off" episodes (muscle stiffness, loss of muscle control and movement) in patients with advanced Parkinson's disease. Xadago nicely complements their Parkinson's product offering. The FDA approval triggered a total of EUR 11.3 mn milestone payments for Newron. The company will also receive a share of sales milestone payments and royalty payments on US sales made by US WorldMeds to Zambon.

European launch of Xadago is well on its way with more to countries to follow

Xadago was already approved in the EU in Q2 2015 to treat mid to late stage Parkinson's patients in combination with mainstay levodopa or other Parkinson medications (~80% of treated patients) with Germany being the first country where Xadago was launched. Xadago has now been launched in twelve European countries, including Switzerland,

Spain, Italy, the Benelux, Denmark, Sweden, Norway, the UK, and Portugal with more countries to follow soon, including France. This year, 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. Further launches of Xadago are expected in territories such as South and Latin America.

Key priorities in 2017 include the successful launch of Xadago …
Newron's key priorities for 2017 include supporting Zambon and its sublicensing partners with the rollout of Xadago in the EU and the US launch in July, and supporting Meiji Seika with the Japanese/Asian clinical development of Xadago. In October 2015 partner Meiji Seika started the Japanese phase II/III confirmatory and long-term trials in Parkinson's disease, making a potential launch in Japan in early 2019 likely.

… and advancing its two core pipeline projects up to new value inflection points
With sufficient financial resources available, Newron has stepped up clinical development of its two core pipeline projects: **1) sarizotan**, which targets disordered breathing in Rett syndrome, a rare disease that causes severe disability and reduced life expectancy in girls, and **2) evenamide** (formerly NW-3509), a novel add-on therapy to current antipsychotic treatments to address poorly responding patients with schizophrenia/mania.

Newron plans to:

1. Continue to see Xadago launched by its partners in new areas (US in July 2017) and see commercial partners for Xadago being signed on in new territories (throughout 2017)
2. Determine the next steps to maximize the value of evenamide by either raising EUR ~25 mn to fund a potentially pivotal phase IIb/III trial in schizophrenia or sign on a lucrative licensing agreement with a major CNS player (H2 2017)
3. Start a potentially pivotal phase IIb/III trial of evenamide as an add-on to current antipsychotic therapy in schizophrenia (H1 2018)
4. Announce topline results of the single, potentially pivotal phase III "STARS" trial of sarizotan in Rett syndrome as well as the results of the international Burden of Disease study in Rett syndrome" (mid 2018)

More than EUR 240 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. The company raised EUR 243 mn, of which EUR 91 mn in several private placements, most recently in early October 2016, raising EUR 24 mn (CHF 26 mn) with existing and new investors.

MONEY RAISED	EUR MN
PRE-IPO	62
IPO	74
PRIVATE PLACEMENTS	91
NEURONOVA ACQUISITION	16
TOTAL RAISED	**243**

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

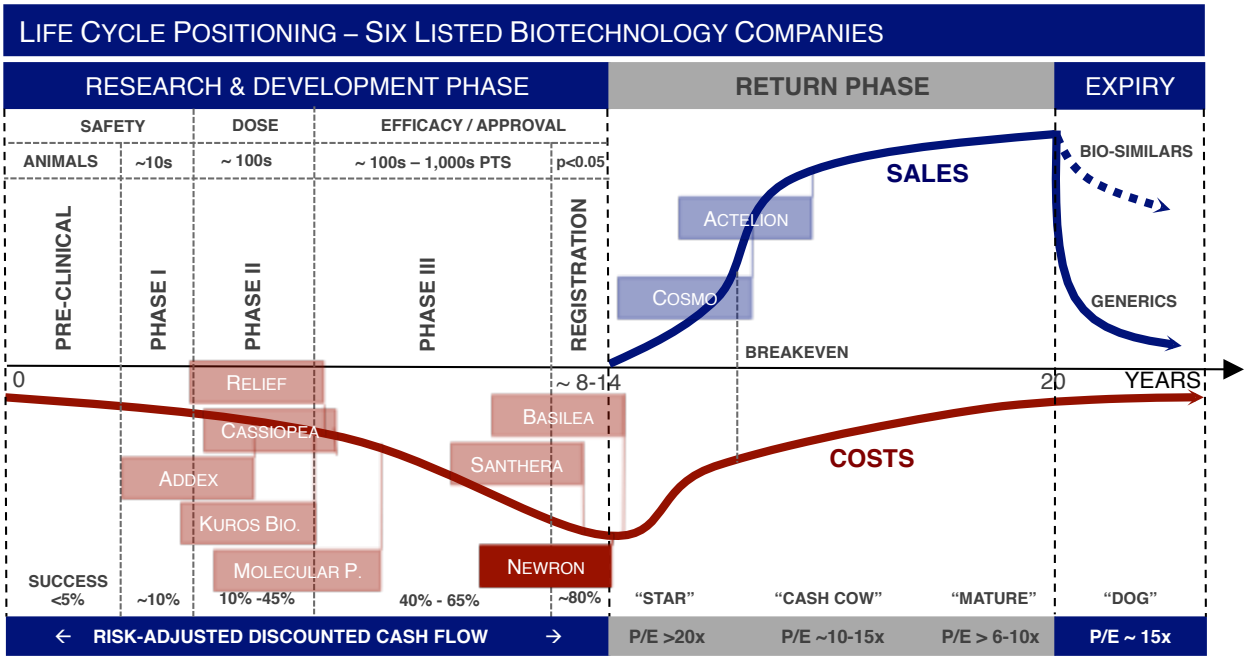
a EUR 25 mn B round (3i, Atlas, Apax) and a EUR 30 mn C round (3i, Atlas, Apax, HBM, TVM). Newron had one of the largest biotech IPO's in 2006 that provided the company with sufficient funds to develop ralfinamide up to phase IIb dose ranging trials in neuropathic low back pain. The NeuroNova acquisition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

Newron comfortably funded to approach profitability in 2019

Newron had EUR 46.5 mn (CHF 51 mn) in cash and short-term investments at hand at year-end 2016. The company received a EUR 11.3 mn milestone payment triggered by the US approval of Xadago in Q1 2017. Together with increasing royalty payments on Xadago sales and assuming EUR 25 mn raised for a potentially pivotal phase IIb/III trial for evenamide in schizophrenia, 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 71 mn for the next two years to fully develop sarizotan in Rett syndrome and complete a potentially pivotal potentially pivotal phase IIb/III trial of evenamide in schizophrenia before licensing the compound to a major CNS player for higher upfront, development and sales milestones and royalties on sales. 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. Therefore, we believe Newron is comfortably funded to successfully execute its development plans and reach profitability in 2019.

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 the next two years and successful development of sarizotan in Rett syndrome and completion of the potentially pivotal potentially pivotal phase IIb/III trial of evenamide in schizophrenia, 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 45 per share

We derive a risk-adjusted NPV of CHF 45/share, conservatively assuming an 8% dilution per share to raise EUR 25 mn for the potentially pivotal phase IIb/III trial of evenamide in schizophrenia, with cash of CHF 3/share (December 31st, 2016), overhead of CHF 2/share, using a WACC of 7.0% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT NAME	INDICATION	PEAK SALES (EUR MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE (CHF)	SUCCESS PROBABILITY	RISK-ADJUSTED NPV/SHARE (CHF)	PERCENTAGE OF TOTAL
XADAGO (SAFINAMIDE)	PARKINSON'S DISEASE	671	2015(EU) / 2017(US)	22	100%	22	47%
SARIZOTAN	RETT SYNDROME	455	2019	59	25%	15	32%
EVENAMIDE	SCHIZOPHRENIA	1,354	2024	46	15%	7	15%
RALFINAMIDE	NEUROPATHIC PAIN	NON CORE		7			
RDPPR VOUCHER ** (ON US APPROVAL OF SARIZOTAN)		155		10			
NET CASH POSITION (31 DECEMBER 2016)		46		3		3	7%
TOTAL ASSETS				**149**		**47**	**100%**
OVERHEAD EXPENSES				-2		-2	
NPV/SHARE (CHF)				147		**45**	
SHARE PRICE ON JUNE 07, 2017						20.9	
PERCENTAGE UPSIDE / (DOWNSIDE)						114%	

* PER SHARE DATA BASED ON DILUTED NUMBER OF SHARES TO RAISE CHF 25 MN FOR PHASE IIB EVENAMIDE; ** RDPPR VOUCHER = RARE DISEASE PEDIATRIC PRIORITY REVIEW VOUCHER PROGRAM

ESTIMATES AS OF 7 JUNE, 2017 SOURCE: VALUATIONLAB ESTIMATES

Newron's key value drivers, include:

Xadago (Parkinson's disease) - risk-adjusted NPV of CHF 22 per share

Xadago is Newron's first ever drug to be approved and launched. In 2015 the drug was approved and launched in the EU to treat mid-to-late stage Parkinson's disease and is now available in more than ten European countries, with more to come. After several setbacks at the FDA, Xadago was approved in the US in March 2017 (triggering a total of EUR 11.3 mn milestones) with launch by US WorldMeds planned for July. We assume Newron will receive up to EUR 32 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, 7-8% in the US, and <5% in Japan. We calculate a risk-adjusted NPV of CHF 22 per share with peak sales of EUR 650+ mn for Xadago.

Sarizotan (Rett syndrome) – risk-adjusted NPV of CHF 15 per share

The potentially pivotal "STARS" trial evaluating sarizotan in Rett syndrome was started in July 2016 with results expected mid 2018. We forecast peak sales of EUR 455 mn with a conservative 25% success probability (phase II/III orphan drug). 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 market exclusivity from approval in the EU (12 years) and US (7 1/2 years). Newron might qualify to receive a valuable RDPPR voucher on US approval (not in forecasts).

Evenamide (schizophrenia) – risk-adjusted NPV of CHF 7 per share

Evenamide, a proprietary discovery project for treating schizophrenia, targets a global USD 12 bn antipsychotic market opportunity peak sales potential of EUR 1.3+ bn. Newron reported positive proof-of-concept (POC) results in schizophrenia in January 2017 adding CHF 7 per share. Newron is reviewing the next steps to maximize the value of evenamide, which include funding a potentially pivotal phase IIb/III trial in schizophrenia (EUR ~25 mn needed) or licensing the compound to a strong CNS player in return for substantial upfront, development and sales milestone payments and royalties on sales.

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. To fund a potentially pivotal phase IIb/III trial of evenamide is schizophrenia, Newron will need to raise EUR ~25 mn, with the potential of share dilution (we assume 8% based on the current market capitalization). Successful completion will boost the long-term value of evenamide.

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 will be established in July, while Xadago continues to be rolled out in the EU.

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-licensers 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 (we assume 7-8%).

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, which potentially could require additional funding.

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 (which includes 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. In 2015, a voucher was sold by another company for USD 350 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, while data protection provides 10 years exclusivity in the EU.

Catalysts

Newron had an excellent start of the year with solid FY 2016 results, sufficient cash to develop its key pipeline projects up to targeted value inflection points, positive evenamide POC trial results in schizophrenia (adding CHF 7 per share to our risk-adjusted NPV), and US approval of Xadago (adding another CHF 3 per share), which triggered a total of EUR 11.3 mn milestone payments from Zambon.

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT PER SHARE
2017					
3 JAN	EVENAMIDE	SCHIZOPHRENIA	RESULTS PHASE IIA	POSITIVE IIA PROOF-OF-CONCEPT RESULTS WITH GOOD TOLERABILITY, SAFETY AND PRELIMINARY EVIDENCE OF EFFICACY	
10 JAN	XADAGO	PARKINSON'S	PARTNERSHIP	ZAMBON ENTERS PARTNERSHIP WITH SEQIRUS FOR COMMERCIALIZATION OF XADAGO IN AUSTRALIA & NEW ZEALAND	
2 MAR			FY 2016 RESULTS	CASH: EUR 46.5 MN; FUNDED WELL INTO 2018 BEYOND VALUE INFLECTION POINTS; XADAGO ROYALTIES OF EUR 1.7 MN FROM ~EUR 20 MN XADAGO SALES	
21 MAR	XADAGO	PARKINSON'S	US APPROVAL	FDA APPROVES XADAGO AS ADD-ON THERAPY TO LEVODOPA/CARBIDOPA IN PARKINSON'S DISEASE - TRIGGERS EUR ~10 MN MILESTONE PAYMENT	
24-28 MAR	EVENAMIDE	SCHIZOPHRENIA	RESULTS PHASE IIA	DETAILED RESULTS OF POSITIVE POC TRIAL PRESENTED AT INTERNATIONAL CONFERENCE ON SCHIZOPHRENIA RESARCH IN SAN DIEGO	
28 MAR			AGM	ANNUAL GENERAL MEETING IN MILAN, ITALY; ALL MOTIONS ACCEPTED	
5-11 APR	XADAGO	PARKINSON'S	PARTNERSHIP/LAUNCH	EISAI ACQUIRES EXCLUSIVE RIGHTS FROM MEIJI SEIKA FOR JAPAN & ASIA (5 APR); ZAMBON LAUNCHES XADAGO IN PORTUGAL (10 APR); VALEO AND ZAMBON FORM PARTNERSHIP FOR XADAGO IN CANADA (11 APR)	
12 MAY	XADAGO	PARKINSON'S	MILESTONE	TOTAL MILESTONE PAYMENTS OF EUR 11.3 MN RECEIVED FROM ZAMBON ON US APPROVAL	
17 MAY	SARIZOTAN	RETT SYNDROME	EXPANSION "STARS"	"STARS" TRIAL TO BE EXPANDED TO PATIENTS UNDER 13 YEARS OF AGE	
JUNE	SARIZOTAN	RETT SYNDROME	HEOR TRIAL	HEALTH ECONOMIC OUTCOME RESEARCH (HEOR) "INTERNATIONAL BURDEN OF DISEASE IN RETT SYNDROME" STUDY STARTED	
THROUGHOUT 2017	XADAGO	PARKINSON'S	PARTNERSHIP/LAUNCH	FURTHER EU LAUNCHES EXPECTED INCLUDING FRANCE; OTHER AREAS SUCH AS SOUTH AMERICA, LATIN AMERICA	
JUL	XADAGO	PARKINSON'S	US LAUNCH	US WORLDMEDS KICKS OFF US LAUNCH WITH >60 DEDICATED SALES REPS	
H2	EVENAMIDE	SCHIZOPHRENIA	FUND RAISING	POTENTIAL FUND RAISING (UP TO EUR ~25 MN) TO FINANCE POTENTIALLY PIVOTAL 'PHASE IIB TRIAL TO MAXIMIZE LUCRATIVE PARTNERING DEAL WITH MAJOR CNS PLAYER	
14 SEP			H1 2017 RESULTS	PUBLICATION OF HALF-YEAR REPORT 2017	
2018					
H1	EVENAMIDE	SCHIZOPHRENIA	PHASE IIB/III	START OF FIRST PHASE IIB/III TRIAL IN SCHIZOPHRENIA PATIENTS	+ CHF 7
H1	SARIZOTAN	RETT SYNDROME	"STARS" TRIAL	COMPLETION SINGLE POTENTIALLY PIVOTAL PHASE III "STARS" TRIAL	
MID	SARIZOTAN	RETT SYNDROME	"STARS" TRIAL RESULTS	TOP LINE RESULTS SINGLE POTENTIALLY PIVOTAL PHASE III "STARS" TRIAL AT WEEK 24	+ CHF 23
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"	
H2	XADAGO	PARKINSON'S	PHASE II/III JAPAN	TOP LINE RESULTS JAPANESE PHASE II/III CONFIRMATORY TRIAL	
H2	SARIZOTAN	RETT'S SYNDROME	FILING US & EU	FILING IN THE EU AND US (6-MONTH PRIORITY REVIEW)	+ CHF 9

ESTIMATES AS OF 7 JUNE, 2017

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Key catalysts include:

- **Xadago US launch (July 2017):** US approval added CHF 3/share and triggered a total of EUR 11.3 mn milestone payments; more than 60 sales representatives will initially support US launch by US WorldMeds, a US specialty pharmaceutical company.
- **Next steps to maximize value of evenamide (H2 2017):** Positive POC (proof-of-concept) results in Q1 2017 added CHF 7/share; Newron is seeking to raise EUR ~25 mn to fund a potentially pivotal phase IIb/III trial planned to start in H1 2018 to maximize evenamide's long-term value.
- **Topline results sarizotan "STARS" trial (mid 2018):** On positive topline results, our risk-adjusted NPV will jump by CHF 23/share (65% phase III success probability) from currently CHF 15/share (25% phase II/III orphan drug probability).
- **Start phase IIb/III trial results evenamide (H1 2018):** The start of the potentially pivotal phase IIb/III trial in schizophrenia results in an increase of the risk adjusted NPV to CHF 7/share with a 30% phase IIb success probability (from 15%)
- **Out license evenamide (2019):** Out-license evenamide to a major CNS player to fully develop and commercialize the drug in schizophrenia/mania and potentially other CNS disorders.

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), 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	EU: LAUNCHED US: APPROVED	EU: H1 2015 US: JULY 2017	ZAMBON/MEIJI SEIKA/ EISAI/US WORLDMEDS	EUR 650+ MN
SARIZOTAN	DOPAMINE RECEPTOR BLOCKER	RETT SYNDROME (ORPHAN INDICATION)	PHASE III PIVOTAL TRIAL	2019	ESTABLISH A SMALL TEAM OF MEDICAL LIAISON MANAGERS	EUR 450 MN
EVENAMIDE (NW-3509)	ION CHANNEL BLOCKER	SCHIZOPHRENIA	PHASE IIB	2024	PARTNER AFTER PHASE IIB	EUR 1.3+ BN
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 7 JUNE, 2017

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

Xadago generating product sales in the EU and soon in 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, where it has been launched in Switzerland, Spain, Italy, the Benelux, Denmark, Sweden, Norway, the UK with more European country launches expected, including France in 2017. 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 plans a US launch for July 2017. With sufficient cash secured, Newron has stepped up its development plans for sarizotan in Rett syndrome and evenamide in schizophrenia.

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. Successfully developed compounds should attract much interest from Big Pharma, Big Biotech and specialty pharmaceutical companies, seeking profitable new compounds to offset generic sales erosion.

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 (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 amount 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, evenamide as an add-on therapy for schizophrenia, and sarizotan for treating breathing disorders in Rett syndrome.

Forecasts & Sensitivity Analysis

Xadago (Parkinson's Disease)

Product Analysis

Parkinson's peak sales of EUR 671 mn - Risk-adjusted NPV of CHF 22 per share

We forecast peak sales of EUR 671 mn for Xadago, based on a strong EU sales uptake, a US launch in July 2017 and Japanese launch in 2019. 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), which could prove to be conservative considering Xadago's unique dual mechanism of action, and a market penetration peaking at around 9-10%. Our risk-adjusted NPV amounts to CHF 370 mn, or CHF 22 per share, assuming Newron receives a total of EUR 33 mn milestone payments, royalties on sales ranging between <5% (Japan), 7-8% (US) and 10-15% (EU/ROW), with a 100% success probability and a WACC of 7.0% (reflecting the low Swiss interest environment).

Xadago – A successful end to a long odyssey at the FDA

In March 2017 Xadago was finally approved in the lucrative US market after an odyssey of more than 2 years at the FDA, thanks to the perseverance of Newron's management team. The US approval triggered a total of EUR 11.3 mn milestone payments from Zambon. Commercialization partner US WorldMeds plans to launch Xadago in the US in July. The launch in Europe is well underway where Xadago is available in more than ten countries with more to come. In FY 2016 Newron reported royalties of EUR 1.7 mn (+69%), despite the Italian AIFA imposing a ceiling for 2016 and 2017 sales, impacting royalties by EUR 0.3 mn. These royalties translate to approximately EUR 20 mn of product sales for Xadago in FY 2016, largely from Germany where the product was first launched in 2015. We expect FY 2017 sales of Xadago to amount to EUR 55 mn, boosted by the US launch and the continued roll out in Europe and other regions such as South and Latin America. Launch in Japan and Asia is expected to occur in 2019, where Eisai recently acquired the exclusive rights for this region from development and commercialization partner Meiji Seika.

US launch planned for July by US WorldMeds supported by more than 60 reps

Xadago was approved in the US as add-on therapy to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes, similar to the EU label. These are basically mid to late stage Parkinson's disease patients representing roughly 80% of patients. US WorldMeds plans to focus more than 60 sales representatives when it launches Xadago in the US in July. US WorldMeds already sells Apokyn (apomorphine) in the US. Apokyn is an injectable rescue medication for the acute, intermittent treatment of hypomobility (patient can barely move or not at all) associated with advanced Parkinson's disease. Xadago fits nicely in US WorldMed's product portfolio that has an extensive reach to physicians that treat Parkinson's disease.

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)

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 "STUDY 3" (+ L-DOPA); 26 WEEKS			XADAGO "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 surpass Azilect as the leading MAO-B inhibitor

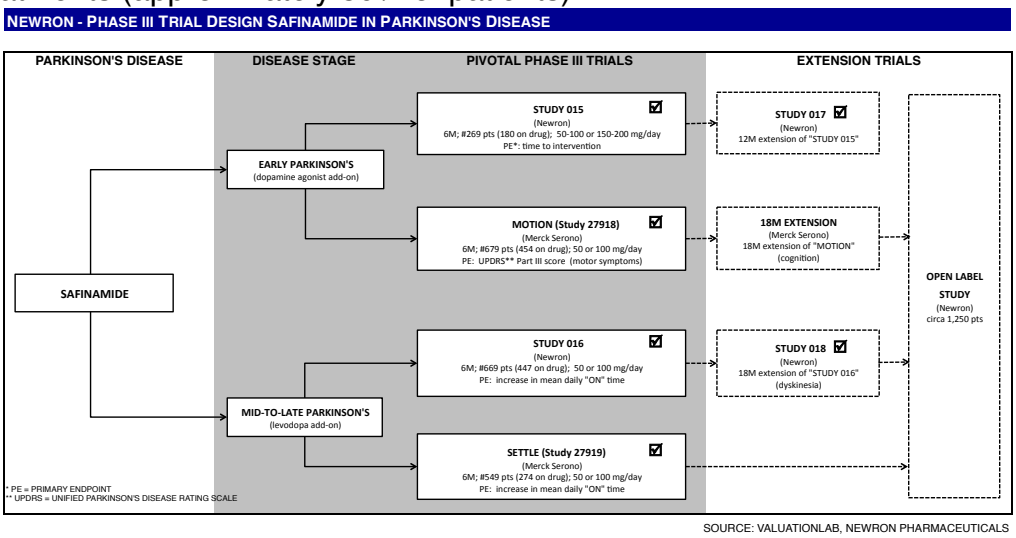
Therefore, we believe Xadago has the potential to surpass Azilect as the leading MAO-B inhibitor in treating Parkinson's patients with mid to late stage disease thanks to its superior safety and tolerability profile and proven long-term efficacy up to 2 years of treatment. Moreover, Xadago has the potential to reduce dyskinesia in Parkinson's patients with moderate dyskinesia (DRS>4) as seen in "Study 016/018 (see page 17). Currently there are no drugs on the market that have shown reducing dyskinesia over such a period. However, Newron would have to prove this important finding in a prospective phase III trial. This would add significantly to our sales forecasts for Xadago.

Development aim was to limit or delay the onset of levodopa-related complications

The EU and US approvals were based on an extensive clinical development program that included over 1,500 patients of who around 1,000 were treated for at least one year, and many for over 4 years. Efficacy was derived from five placebo-controlled studies including assessments performed under double-blind conditions for two years.

Xadago was developed for all disease stages of Parkinson's disease:

1) **Early disease** as an add-on to dopamine agonists (approximately 20% of patients)
2) **Mid-to-late stage disease** as an add-on to levodopa and other dopaminergic treatments (approximately 80% of patients)



SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

This is reflected in the phase III trial design with all 4 phase III trials reaching their primary endpoint. Newron has also performed extension trials. Although they are not necessary for approval, they provide an important insight into the long-term impact of Xadago, including demonstrating long-term efficacy and anti-dyskinetic properties.

Statistically significant results in early Parkinson's disease...

Xadago demonstrated statistically significant results as an add-on to a single dopamine agonist, in three placebo-controlled trials in early Parkinson's disease. Note that the positive effects seen are on top of dopamine agonists that already provide efficacy in early Parkinson's disease. Roughly 30% of Parkinson's patients are on dopamine agonists.

UPDRS II/III primary endpoint met in "Study 015" and "MOTION"

The primary endpoint of both studies was the so-called UPDRS, the Unified Parkinson's Disease Rating Scale, Part II and III. This is a rating tool used to follow the longitudinal course of Parkinson's disease. It is made up of 5 sections with **Part II** being a self-reported evaluation of activities of daily living (ADL) and **Part III** a clinician scored motor evaluation.
In the first pivotal phase III **"Study 015"** the low dose range (50-100 mg/day) showed a mean change from baseline of -2.2 (p=0.0248) for UPDRS II and -6.00 for UPDRS III at 6 months. In the 12 month extension "Study 017" there was a mean change from baseline of -4.7 for UPDRS III and a responder rate of 18.1% difference from placebo at 18 months, as well as statistically significant benefits on UPDRS II and EuroQoL (quality of life).

In the second pivotal phase III **"MOTION"** trial the 100 mg/day dose showed a -2.06 (p=0.0396) mean change from baseline on UPDRS III at week 24, which was statistically significant (p=0.040) compared to the placebo group that showed a mean change from baseline of -1.04 in the DA-ITT (dopamine agonist intent-to-treat) population. The 50 mg/day showed a -1.93 mean change from baseline that did not reach statistical significance compared to placebo.

Patients and physicians see improvements in quality of life scores

In two other secondary endpoints, the **EQ-5D** (patient scored European Quality of Life index) and the **PDQ-39** (patient scored Parkinson's Disease Quality of Life index), the 100 mg/day dose of Xadago reached statistical significance as well.

So in early Parkinson's disease adding 100 mg of Xadago on top of a dopamine agonist statistically improves motor fluctuations and activities of daily living (physician rated), and several quality of life scores recorded in both caregiver and patient evaluations.

Xadago was well tolerated with the majority of patients completing the trials

In both phase III trials Xadago was well tolerated with most side effects similar to placebo with almost all patients (approximately 90%) completing the trials. In the "MOTION" trial nausea (9.7% vs. 6.7%) at the 100 mg/day dose occurred more frequently in the Xadago group compared to the placebo group and dizziness (8.0% vs. 6.2%) at the 50 mg/day dose. Drowsiness and back pain (4.8% vs. 8.0%) were lower than placebo with Xadago 100 mg/day.

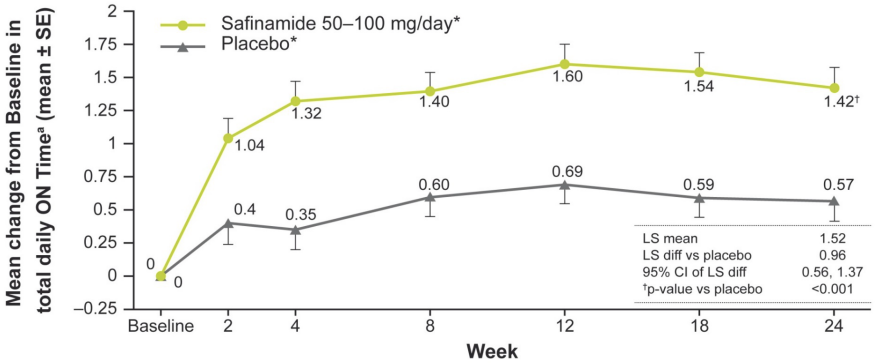
...as well as in mid to late stage Parkinson's disease

Xadago also showed statistically significant results in its two pivotal phase III trials as an add-on to stable doses of levodopa and/or other stable dose dopamine agonists/anticholinergics in mid to late stage Parkinson's disease. Roughly 70-80% of PD patients are on levodopa regimens.

Daily ON time primary endpoint met in "Study 016" and "SETTLE"
The primary efficacy endpoint was to evaluate the change from baseline to week 24 in daily ON time (ON time without dyskinesia plus ON time with non-troublesome dyskinesia)

In the first pivotal phase III **"Study 016"** both the 50 and 100 mg dose met the primary endpoint of improving ON time (+0.6 hours vs. placebo, p=0.02 at 50 mg, p=0.013 at 100 mg). Importantly, the increase in ON time was not associated with any increase in troublesome dyskinesia. Key secondary endpoints were also met, including **OFF time**, **UPDRS III**, and **PDQ-39** at 6 months.

A consistent result occurred in the second pivotal phase III **"SETTLE"** trial where Xadago showed a significant improvement in its primary endpoint of ON time of almost an hour (+0.96 hours vs. placebo, p<0.001).

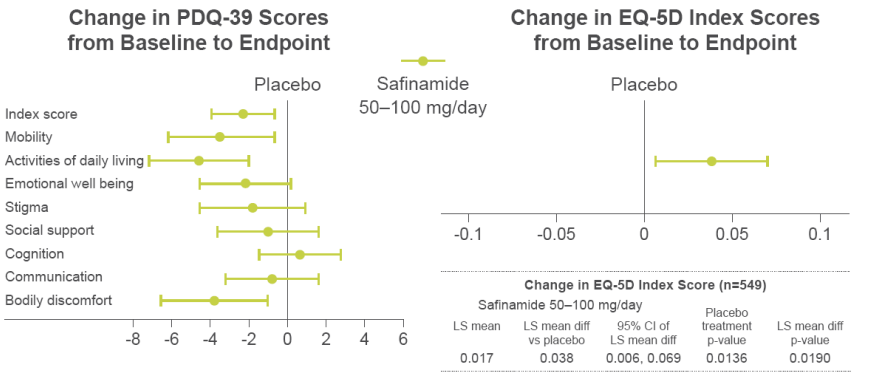


[a]ON Time is defined as ON Time without dyskinesia plus ON Time with non-troublesome dyskinesia
*As add-on to L-dopa and PD medication

SOURCE: NEWRON PHARMACEUTICALS

In the graph above one can clearly see that adding Xadago (safinamide) on top of levodopa therapy adds approximately one hour ON time, already after 2 weeks and this statistically significant effect is continued throughout the trial. Importantly, the increase in ON time was not associated with any increase in troublesome dyskinesia.

...and patients and physicians see improved quality of life scores and less OFF time
Statistically significant results in secondary endpoints were also reported, including total daily **OFF time** (-1.03 hours vs. placebo, p<0.001), mean change from baseline in **UPDRS III** during ON phase (-1.82 vs. placebo, p=0.003), **PDG-39** (-2.33, p=0.006) and **EQ-5D** (0.06, p<0.001) scores, and in **OFF time post morning dose of levodopa**. The latter is important for patients and caregivers as PD patients are often "frozen" in the morning requiring immediate-release levodopa.



SOURCE: NEWRON PHARMACEUTICALS

In the graphs above one can clearly see that adding Xadago (safinamide) to levodopa therapy improves a broad range of scores that improve patients' quality of life and daily activities.

"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. Currently there are no drugs on the market that have shown reducing dyskinesia over such a period. However, Newron would have to prove this important finding in a prospective phase III trial. This would add significantly to our sales forecasts for Xadago.

Xadago has a peak sales potential of EUR 671 mn

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 281 mn assuming a daily treatment price of EUR 2.80 and a peak penetration rate of ~9%. We assume a tiered royalty rate from 10% to 15%.
2) **US (US WorldMeds):** peak sales could amount to around EUR 350 mn assuming a launch in July 2017 with a conservative daily treatment price of USD 9. US approval triggered a total of EUR 11.3 mn milestone payments from Zambon. We assume further sales milestones of up to EUR 28 mn, and royalties of 7-8%.
3) **Japan/Asia (Meiji Seika & Eisai):** we forecast a launch in early 2019 with peak sales amounting to almost EUR 40 mn. We assume a EUR 5 mn milestone payment on Japanese approval and royalties on sales to amount to <5%.

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

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), LEVADOPA +/- 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 & US UNTIL 2029: 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: PHASE II/III CONFIRMATORY TRIAL RESULTS H2 2018E, APPROVAL 2019E
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)	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
NUMBER OF PATIENTS (MN)	3.5	3.6	3.6	3.7	3.8	3.9	3.9	4.0	4.1	4.2	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 (MN)	2.4	2.5	2.5	2.6	2.6	2.7	2.8	2.8	2.9	2.9	3.0
PENETRATION (%)	1%	2%	4%	5%	6%	6%	7%	7%	8%	8%	8%
NUMBER OF PATIENTS (MN)	0.0	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
COST OF THERAPY PER YEAR (EUR)	1,278	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022	1,022
SALES (EUR MN)	**20**	**55**	**95**	**123**	**153**	**170**	**187**	**205**	**224**	**236**	**247**
CHANGE (%)	388%	170%	73%	30%	24%	11%	10%	10%	9%	5%	5%
ROYALTY (%)	10%	12%	14%	15%	15%	15%	15%	15%	15%	15%	15%
ROYALTIES (EUR MN)	2	7	13	18	23	25	28	31	34	35	37
UPFRONT & MILESTONE PAYMENTS (EUR MN)	3										
PROFIT BEFORE TAX (EUR MN)	**5**	**7**	**13**	**18**	**23**	**25**	**28**	**31**	**34**	**35**	**37**
TAXES (EUR MN)	0	0	-3	-3	-7	-8	-9	-10	-11	-11	-12
PROFIT (EUR MN)	**5**	**6**	**11**	**16**	**16**	**17**	**19**	**21**	**23**	**24**	**25**

UNITED STATES (ZAMBON PARTNER US WORLDMEDS)	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
NUMBER OF PATIENTS (MN)	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.3	1.3	1.3	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)	0.9	0.9	0.9	1.0	1.0	1.0	1.0	1.0	1.1	1.1	1.1
PENETRATION (%)	0%	0.5%	3%	5%	7%	8%	8%	9%	9%	9%	9%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1
COST OF THERAPY PER YEAR (EUR)	2,878	3,022	3,022	3,022	3,022	3,022	3,022	3,022	3,022	3,022	3,022
SALES (EUR MN)	**0**	**14**	**85**	**144**	**192**	**225**	**245**	**266**	**287**	**299**	**312**
CHANGE (%)			512%	70%	33%	18%	9%	8%	8%	4%	4%
ROYALTY (%)	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
ROYALTIES (EUR MN)	0	1	6	11	14	17	18	20	22	22	23
UPFRONT & MILESTONE PAYMENTS (EUR MN)		11			9				18		
PROFIT BEFORE TAX (EUR MN)	**0**	**12**	**6**	**11**	**24**	**17**	**18**	**20**	**40**	**22**	**23**
TAXES (EUR MN)	0	-1	-1	-2	-7	-5	-6	-6	-13	-7	-7
PROFIT (EUR MN)	**0**	**12**	**5**	**9**	**16**	**12**	**13**	**14**	**27**	**15**	**16**

JAPAN (MEIJI SEIKA PARTNER EISAI)	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
NUMBER OF PATIENTS (MN)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
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)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3
PENETRATION (%)	0%	0%	0%	2%	5%	7%	8%	9%	9%	10%	9%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
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**	**7**	**17**	**25**	**29**	**32**	**34**	**37**	**37**
CHANGE (%)					155%	43%	17%	8%	8%	8%	1%
ROYALTY (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
ROYALTIES (EUR MN)	0	0	0	0	1	1	1	2	2	2	2
UPFRONT & MILESTONE PAYMENTS (EUR MN)				5							
PROFIT BEFORE TAX (EUR MN)	0	0	0	5	1	1	1	2	2	2	2
TAXES (EUR MN)	0	0	0	-1	0	0	0	0	-1	-1	-1
PROFIT (EUR MN)	**0**	**0**	**0**	**5**	**1**	**1**	**1**	**1**	**1**	**1**	**1**

	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
GLOBAL SALES (EUR MN)	**20**	**69**	**180**	**275**	**362**	**420**	**461**	**503**	**545**	**572**	**596**
CHANGE (%)	388%	238%	162%	53%	32%	16%	10%	9%	8%	5%	4%
GLOBAL PROFIT (EUR MN)	**5**	**18**	**16**	**29**	**32**	**30**	**33**	**36**	**52**	**41**	**43**
CHANGE (%)	114%	279%	-11%	83%	11%	-8%	10%	9%	44%	-21%	4%

WACC (%)	7.0%
NPV TOTAL PROFIT (CHF MN)	**370**
NUMBER OF SHARES (MN)	17.0 = DILUTED NUMBER OF SHARES TO RAISE FUNDS FOR 1ST PHASE IIB/III TRIAL OF EVENAMIDE IN SCHIZOPHRENIA
RISK ADJUSTED NPV PER SHARE (CHF)	**22**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	800	30	29	28	27	26	25	24
	750	28	27	26	25	24	24	23
	700	26	25	24	23	23	22	21
PEAK SALES	650	24	23	23	**22**	21	20	20
	600	22	22	21	20	19	19	18
	550	20	20	19	18	18	17	17
	500	19	18	17	17	16	16	15

ESTIMATES AS OF 7 JUNE, 2017

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 has to be further established in blinded clinical trials.

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: Approved and launched in the EU in early 2015 with more than ten county launches to date. Approved in the lucrative US market in March 2017 after a delay at the FDA of almost 3 years. US launch by US WorldMeds is planned for July. Topline results of the Japanese phase II/III confirmatory trial conducted by partner Meiji Seika are expected in H2 2018 with a potential launch in 2019 by Eisai, which acquired exclusive rights for Japan and Asia in April 2017.

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 (needs further study in blinded clinical trials).

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.

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 STRATIAL 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 **ND0611/0612**, a carbidopa/levodopa subcutaneous patch pump (phase II), and Mylan’s/US WorldMeds’ Apokyn, a non-ergoline dopamine agonist for the treatment of acute hypomobility.

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 Nouriast) and Acorda's **tozadenant** (phase III), and Addex's **dipraglurant** (phase II), which targets metabotropic glutamate receptor 5 (mGluR5).

Evenamide (Schizophrenia)

Product Analysis

Schizophrenia peak sales of EUR 1.3+ bn - Risk-adjusted NPV of CHF 7 per share

We forecast peak sales of EUR 1.3+ bn for evenamide as an add-on to existing schizophrenia therapies, assuming a potentially pivotal phase IIb/III trial to start in H1 2018 with headline results due in 2019. 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 2024 and global patent protection until 2033 (including patent term extensions), 10-years data exclusivity on approval in the EU (2034), a daily treatment cost of between USD 15 (US) and EUR 10 (EU/ROW), and a target market penetration peaking at around 20%. Our risk-adjusted NPV amounts to CHF 118 mn, or CHF 7 per share, assuming Newron receives a total of EUR 204 mn of upfront and milestone payments, royalties on sales of 20% from its partner(s) with a success probability of 15% (proof-of-concept completed) and a WACC of 7.0% (reflecting the low Swiss interest environment).

Evenamide (NW-3509) – The next CNS blockbuster opportunity

Evenamide (previously named NW-3509) 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). Newron has successfully completed a phase IIa proof-of-concept (POC) trial of evenamide in schizophrenia and is currently exploring options to maximize the compound's long-term value. The company could raise EUR 25 mn (at an 8% dilution) to complete a potentially pivotal phase IIb/III trial to boost future upfront, development and sales milestones and royalties on sales from a partnership with a major CNS player in 2019 (our assumption). Alternatively, Newron could out license evenamide now on the positive POC results, although at lower terms. 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.

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. 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. 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 ON 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 0F 34 (3%)	2 OF 103 (2%)
ADVERSE EVENTS (MILD SEVERITY)	58 OF 69 (84%)	30 OF 34 (88%)	88 0F 103 (85%)
ADVERSE EVENTS (MODERATE SEVERITY)	9 OF 69 (13%)	4 0F 34 (12%)	13 OF 103 (13%)

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

SOURCE: VALUATION LAB, 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)

	BASELINE VALUE				CHANGE FROM BASELINE TO DAY 28			
	EVENAMIDE (N=44)		PLACEBO (N=39)		EVENAMIDE (N=44)		PLACEBO (N=39)	
SCALE	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)	N	MEAN (SD)
PANNS 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.

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

	CHANGE FROM BASELINE				DIFFERENCE EVENAMIDE VS. PLACEBO		
	EVENAMIDE (N=44)		PLACEBO (N=39)				
DAY 28	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
CGI-C (PATIENT'S OVERALL CONDITION)	RATING OF 1 (VERY MUCH IMPROVED), 2 (MUCH IMPROVED) OR 3 (MINIMALLY IMPROVED)	50	26 OF 48 (54.2%)	39	14 OF 39 (35.9%)
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%)

* STATISTICALLY SIGNIFICANT WITH P-VALUE OF 0.0043

SOURCE: VALUATION LAB, 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.

Next steps: potentially pivotal phase IIb/III trial design – partner now or later?
Based on the positive findings of the POC trial, Newron is scheduling meetings with regulatory authorities to obtain feedback on plans for future development of evenamide in schizophrenia. The company expects the next clinical trial to be a global phase IIb/III, potentially pivotal trial requiring approximately 360 patients randomized (1:1:1) to evenamide 15 and 30 mg twice daily or placebo for a duration of 12 weeks. The cost of this trial is estimated at around EUR 25 mn. Two of such studies are expected to be needed to obtain approval in the US and three for approval in the EU/ROW. Upon raising sufficient funds for the potentially pivotal phase IIb/III trial, Newron would consider to conduct this trial before signing on a partnering agreement with a major CNS player to maximize the long-term value of evenamide. On positive results Newron could achieve far higher milestone payments and royalties on sales than partnering on the positive POC trials. However, if an attractive proposal were offered, Newron would consider partnering this year on the positive POC trial results.

Evenamide has a 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 raise EUR 25 mn in 2017 to complete a potentially pivotal Phase IIb/III trial of evenamide in schizophrenia and to out license the drug in 2019 to a strong CNS player in return for substantial upfront, development and sales milestone payments and royalties on sales. First launches are expected in 2024.

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

1) **Europe/ROW:** we forecast peak sales to amount to EUR 828 mn assuming a conservative daily treatment price of EUR 10, 10 years data exclusivity until 2034, and a peak penetration rate amounting to 20%. 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 538 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 20%. We assume total milestone payments of up to EUR 74 mn, and royalties on sales of 20%.

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

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

Forecasts & Sensitivity Analysis

EVENAMIDE - FINANCIAL FORECASTS FOR SCHIZOPHRENIA

INDICATION	ADD-ON THERAPY TO ANTIPSYCHOTICS FOR REDUCING POSITIVE SYPMTOMS 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	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
NUMBER OF PATIENTS (MN)	5.2	5.2	5.3	5.4	5.5	5.6	5.6	5.7	5.8	5.9	6.0
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)	3.6	3.7	3.7	3.8	3.8	3.9	3.9	4.0	4.1	4.1	4.2
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED (MN)	0.9	0.9	0.9	0.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0
PENETRATION (%)	0%	0%	0%	0%	0%	0%	0%	0%	2%	5%	9%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1
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**	**0**	**0**	**0**	**74**	**188**	**344**
CHANGE (%)										154%	83%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	0	0	0	0	15	38	69
UPFRONT & MILESTONE PAYMENTS (EUR MN)				30					50		
R&D COSTS	-6	-7	-12	-6	0	0	0	0	0	0	0
PROFIT BEFORE TAX (EUR MN)	**-6**	**-7**	**-12**	**24**	**0**	**0**	**0**	**0**	**65**	**38**	**69**
TAXES (EUR MN)	0	0	0	0	0	0	0	0	-20	-12	-21
PROFIT (EUR MN)	**-6**	**-7**	**-12**	**24**	**0**	**0**	**0**	**0**	**45**	**26**	**47**

UNITED STATES	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
NUMBER OF PATIENTS (MN)	2.4	2.4	2.5	2.5	2.6	2.6	2.6	2.7	2.7	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	1.7	1.8	1.8	1.8	1.8	1.9	1.9	1.9	2.0
COMPLIANCE RATE (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
PATIENTS TREATED (MN)	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5
PENETRATION (%)	0%	0%	0%	0%	0%	0%	0%	0%	3%	7%	11%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1
COST OF THERAPY PER YEAR (EUR)	4,797	5,037	5,037	5,037	5,037	5,037	5,037	5,037	5,037	5,037	5,037
SALES (EUR MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**72**	**170**	**271**
CHANGE (%)										137%	60%
ROYALTY (%)	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
ROYALTIES (EUR MN)	0	0	0	0	0	0	0	0	14	34	54
UPFRONT & MILESTONE PAYMENTS (EUR MN)	0	0	0	28	0	0	0	0	46	0	0
PROFIT BEFORE TAX (USD MN)	**0**	**0**	**0**	**30**	**0**	**0**	**0**	**0**	**66**	**37**	**59**
TAXES (EUR MN)	0	0	0	0	0	0	0	0	-19	-11	-17
PROFIT (EUR MN)	**0**	**0**	**0**	**28**	**0**	**0**	**0**	**0**	**42**	**23**	**37**

	2016E	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**146**	**358**	**615**
CHANGE (%)										145%	72%
GLOBAL PROFIT (EUR MN)	**-6**	**-7**	**-12**	**52**	**0**	**0**	**0**	**0**	**86**	**49**	**85**
CHANGE (%)	20%	17%	71%	-530%	-100%					-43%	72%

WACC (%)	7.0%	
NPV TOTAL PROFIT (CHF MN)	**787**	
NUMBER OF SHARES (MN)	17.0	= DILUTED NUMBER OF SHARES TO RAISE FUNDS FOR 1ST PHASE IIB/III TRIAL OF EVENAMIDE IN SCHIZOPHRENIA
NPV PER SHARE (CHF)	**46**	
SUCCESS PROBABILITY	15%	= PROOF-OF-CONCEPT COMPLETED
RISK ADJUSTED NPV PER SHARE (CHF)	**7**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	30%	17	16	15	14	13	12	12
	25%	14	13	12	12	11	10	10
	20%	11	10	10	9	9	8	8
SUCCESS PROBABILITY	15%	8	8	7	**7**	7	6	6
	10%	6	5	5	5	4	4	4
	5%	3	3	2	2	2	2	2
	0%	0	0	0	0	0	0	0

ESTIMATES AS OF 7 JUNE, 2017

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. 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 2024, 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. Including evenamide in our forecasts added CHF 7/share. Next step is a potentially pivotal phase IIb/III trial requiring approximately 360 patients treated for 12 weeks, which Newron plans to conduct itself if it successfully raises the EUR 25 mn needed for the trial in H2 2017.

Pathway: To gain approval in the US and EU, Newron will have to submit two pivotal phase IIb/III trials as an add-on to other antipsychotics; grant of a breakthrough designation may reduce this to one trial. In the EU, a relapse prevention trial is also required for monotherapy drugs. 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 patients 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: Newron is assessing whether to raise EUR 25 mn to complete a potentially pivotal phase IIb/III trial in 2019 and then seek a development and commercialization partner for better terms or sign on a partner based on the positive POC trial results of evenamide in schizophrenia. We assume Newron will raise EUR 25 mn, complete the potentially pivotal phase IIb/III trial and then seek a major CNS player in return for upfront, development and sales milestones of up to CHF 204 mn with 20% royalties on sales.

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	- "POSITIVE" SYMPTOMS, INCLUDING: - DELUSIONS (OF REFERENCE, PARANOID, SOMATIC, GRANDEUR) - HALLUCINATIONS (VISUAL, AUDITORY, TACTILE, OLFACTORY, GUSTATORY) - DISORGANIZED SPEECH - GROSSLY DISORGANIZED OR CATATONIC BEHAVIOUR - "NEGATIVE SYMPTOMS" INCLUDING: - LACK OF EMOTION/INTEREST - LOW ENERGY - AFFECTIVE FLATTENING - SOCIAL ISOLATION
DRUG CLASS (KEY BRANDS)	- TRADITIONAL, 1ST GEN. ANTIPSYCHOTICS: (HALDOL, THORAZINE, STELAZINE) - ATYPICAL, 2ND GEN. ANTIPSYCHOTICS: (CLOZARIL, GEODON, SEROQUEL, RISPERDAL, ZYPREXA, SYMBYAX, ABILIFY, INVEGA, SAPHIRIS)
MAJOR PLAYERS (KEY BRANDS)	- 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-HT2A receptor antagonists (**lumateperone**, **MIN-101**), 5-HT6 receptor antagonists (**Lu AF35700, AVN-211)**, and alpha7 nicotinic acetylcholine receptor modulators (**AVL-3288)**, among others.

Sarizotan (Rett syndrome)

Product Analysis

Rett syndrome peak sales of EUR 455 mn - Risk-adjusted NPV of CHF 15 per share

We forecast peak sales of EUR 455 mn for sarizotan, assuming first market launches in 2019, 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 70% 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 249 mn or CHF 15 per share with a conservative success probability of 25% (phase II/III orphan drug), and a WACC of 7.0% (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 in Rett syndrome health economic outcome research study 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 build up 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 2019 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

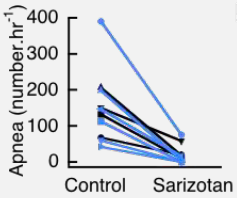
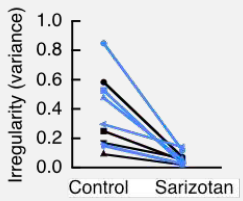
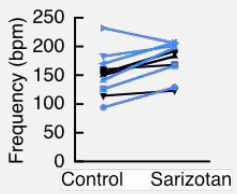
abnormalities in the MeCP2 (methyl CpG-binding protein 2) gene, which has important information for the normal functioning of nerve cells. This gene is in the X chromosome, one of the two sex chromosomes (X and Y) that determine the gender. Rett syndrome almost exclusively affects girls (XX). Boys (XY) 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) D_2 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 (D_2 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 $^{BIRD/+}$)

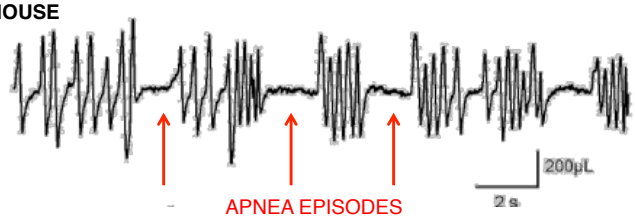
OUTCOMES DEFINITION AND UNITS	MEAN BASELINE DATA IN VEHICLE TREATED RETT MICE	MEAN DATA IN SARIZOTAN TREATED RETT MICE	DATA FROM INDIVIDUAL MICE	CHANGE VS. BASELINE
APNEA INCIDENCE (NUMBER OF APNEAS PER HOUR)	**143** +/- 31	**20** +/- 8		**REDUCED BY 86%** (P=0.001)
IRREGULARITY SCORE (VARIANCE)	**0.34** +/- 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 medullar 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.

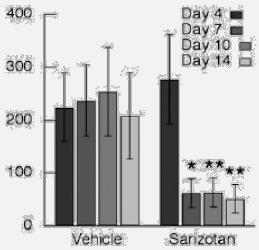
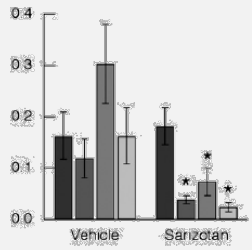
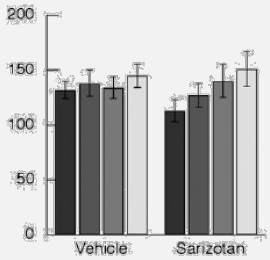
REGULAR BREATHING PATTERN RESTORED

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)		**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 single, potentially pivotal, phase II/III trial in Rett syndrome patients

In July 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 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 the trial is expected in H1 2018 with top line results due in mid 2018. Assuming priority review (6-months), first country launches of sarizotan are expected to occur in 2019.

"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 – build up of own sales force pays off
Peak sales for sarizotan in Rett syndrome are estimated to amount to EUR 455 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 70% 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 455 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 build up 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, now the "STARS" trial has kicked off in the US. Typically a 50-65% success rate would apply for a trial in this stage. 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 249 mn or CHF 15 per share.

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

Forecasts & Sensitivity Analysis

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 PHASE II/III "STARS" TRIAL IN ~129 RETT SYNDROME PATIENTS WITH BREATHING DISORDERS - STARTED JULY 2016, RESULTS 2018, LAUNCH 2019
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	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
NUMBER OF PATIENTS	20,400	20,808	21,224	21,649	22,082	22,523	22,974	23,433	23,902	24,380	24,867
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH BREATHING DISORDERS (50%)	10,200	10,404	10,612	10,824	11,041	11,262	11,487	11,717	11,951	12,190	12,434
PERCENTAGE DIAGNOSED (%)	20%	20%	20%	25%	35%	50%	60%	65%	67%	68%	69%
PATIENTS DIAGNOSED	2,040	2,081	2,122	2,706	3,864	5,631	6,892	7,616	8,007	8,289	8,517
PENETRATION (%)	0%	0%	0%	10%	35%	50%	60%	65%	67%	69%	70%
NUMBER OF PATIENTS	0	0	0	271	1352	2815	4135	4950	5365	5720	5962
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**	**0**	**9**	**47**	**99**	**145**	**173**	**188**	**200**	**209**
CHANGE (%)					400%	108%	47%	20%	8%	7%	4%
COGS (%)	0%	0%	0%	14%	12%	10%	10%	10%	10%	10%	10%
COGS (EUR MN)	0	0	0	-1	-6	-10	-14	-17	-19	-20	-21
R&D COSTS (EUR MN)	-6	-10	-10	-2	0	0	0	0	0	0	0
M&S (%)				62%	37%	35%	33%	31%	29%	27%	25%
M&S COSTS (EUR MN)	0	0	0	-15	-18	-34	-48	-54	-54	-54	-52
PROFIT BEFORE TAX (EUR MN)	**-6**	**-10**	**-10**	**-9**	**24**	**54**	**82**	**102**	**115**	**126**	**136**
TAXES (EUR MN)	0	0	2	1	-8	-17	-26	-32	-36	-40	-43
PROFIT (EUR MN)	**-6**	**-10**	**-8**	**-7**	**17**	**37**	**57**	**70**	**79**	**87**	**93**

UNITED STATES	**2016E**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
NUMBER OF PATIENTS	15,300	15,606	15,918	16,236	16,561	16,892	17,230	17,575	17,926	18,285	18,651
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
PATIENTS WITH BREATHING DISORDERS (50%)	7,650	7,803	7,959	8,118	8,281	8,446	8,615	8,787	8,963	9,142	9,325
PERCENTAGE DIAGNOSED (%)	20%	20%	20%	25%	35%	50%	60%	65%	67%	68%	69%
PATIENTS DIAGNOSED	1,530	1,561	1,592	2,030	2,898	4,223	5,169	5,712	6,005	6,217	6,388
PENETRATION (%)	0%	0%	0%	15%	40%	55%	65%	70%	70%	70%	70%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	304.4	1159.3	2322.7	3359.9	3998.3	4203.7	4351.8	4471.5
COST OF THERAPY PER YEAR (EUR)	52,568	55,199	55,199	55,199	55,199	55,199	55,199	55,199	55,199	55,199	55,199
SALES (EUR MN)	**0**	**0**	**0**	**17**	**64**	**128**	**185**	**221**	**232**	**240**	**247**
CHANGE (%)					281%	100%	45%	19%	5%	4%	3%
COGS (%)	0%	0%	0%	14%	12%	10%	10%	10%	10%	10%	10%
COGS (EUR MN)	0	0	0	-2	-8	-13	-19	-22	-23	-24	-25
M&S (%)				35%	33%	31%	29%	27%	25%	20%	20%
M&S COSTS (EUR MN)	0	0	0	-14	-21	-40	-54	-60	-58	-48	-49
PROFIT BEFORE TAX (USD MN)	**0**	**0**	**0**	**1**	**38**	**82**	**123**	**151**	**164**	**183**	**188**
TAXES (EUR MN)	0	0	0	0	-11	-24	-36	-44	-47	-53	-54
PROFIT (EUR MN)	**0**	**0**	**0**	**1**	**24**	**52**	**78**	**95**	**103**	**115**	**119**

	2016E	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
GLOBAL SALES (EUR MN)	**0**	**0**	**0**	**26**	**111**	**227**	**330**	**394**	**420**	**440**	**455**
CHANGE (%)					324%	104%	46%	19%	7%	5%	3%
GLOBAL PROFIT (EUR MN)	**-6**	**-10**	**-8**	**-7**	**41**	**89**	**134**	**166**	**182**	**202**	**212**
CHANGE (%)	7%	56%	-19%	-15%	-689%	119%	51%	23%	10%	11%	5%

WACC (%)	7.0%	
NPV TOTAL PROFIT (CHF MN)	**995**	
NUMBER OF SHARES (MN)	17.0	= DILUTED NUMBER OF SHARES TO RAISE FUNDS FOR 1ST PHASE IIB/III TRIAL OF EVENAMIDE IN SCHIZOPHRENIA
NPV PER SHARE (CHF)	**59**	
SUCCESS PROBABILITY	25%	= PHASE II/III ORPHAN DRUG
RISK ADJUSTED NPV PER SHARE (CHF)	**15**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	40%	27	25	24	23	23	22	21
	35%	23	22	21	21	20	19	18
	30%	20	19	18	18	17	16	16
SUCCESS PROBABILITY	25%	17	16	15	**15**	14	14	13
	20%	13	13	12	12	11	11	10
	15%	10	10	9	9	8	8	8
	10%	7	6	6	6	6	5	5

ESTIMATES AS OF 7 JUNE, 2017

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 about 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 were enrolment of large patient numbers would be difficult.

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 2019, 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-EPILPEPTIC (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 **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)	20.9
IFRS											
INCOME STATEMENT (EUR MN)	**2016**	**2017E**	**2018E**	**2019E**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**
PRODUCT SALES (INCLUDING PARTNERS)	**20**	**69**	**180**	**301**	**473**	**647**	**792**	**896**	**1,111**	**1,370**	**1,666**
CHANGE (%)	388%	238%	162%	67%	57%	37%	22%	13%	24%	23%	22%
PRODUCT SALES (BY NEWRON)	**0**	**0**	**0**	**26**	**111**	**227**	**330**	**394**	**420**	**440**	**455**
CHANGE (%)					324%	104%	46%	19%	7%	5%	3%
ROYALTIES	**2**	**8**	**20**	**30**	**38**	**44**	**48**	**52**	**86**	**131**	**185**
CHANGE (%)	308%	348%	158%	51%	29%	14%	10%	9%	64%	53%	41%
LICENCE, UPFRONT & MILESTONE INCOME	**3**	**11**	**0**	**63**	**9**	**0**	**0**	**0**	**114**	**0**	**0**
OTHER INCOME & GRANTS	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
REVENUES (EXCL. PARTNER SALES)	**7**	**21**	**22**	**121**	**161**	**272**	**380**	**448**	**622**	**574**	**643**
CHANGE (%)	190%	211%	4%	457%	33%	69%	40%	18%	39%	-8%	12%
COGS	**0**	**0**	**0**	**-4**	**-13**	**-23**	**-33**	**-39**	**-42**	**-44**	**-46**
CHANGE (%)					263%	70%	46%	19%	7%	5%	3%
AS % REVENUES	0%	0%	0%	3%	8%	8%	9%	9%	7%	8%	7%
GROSS PROFIT	**7**	**21**	**22**	**117**	**147**	**250**	**347**	**409**	**580**	**530**	**597**
CHANGE (%)	190%	211%	4%	440%	26%	69%	39%	18%	42%	-9%	13%
MARGIN	100%	100%	100%	97%	92%	92%	91%	91%	93%	92%	93%
R&D	**-12**	**-20**	**-25**	**-17**	**-10**	**-10**	**-11**	**-11**	**-12**	**-13**	**-13**
CHANGE (%)	-33%	61%	25%	-32%	-41%	5%	5%	5%	5%	5%	5%
AS % REVENUES	184%	96%	116%	14%	6%	4%	3%	3%	2%	2%	2%
S,G&A	**-10**	**-10**	**-10**	**-39**	**-49**	**-84**	**-112**	**-123**	**-123**	**-112**	**-112**
CHANGE (%)	16%	5%	0%	284%	25%	73%	32%	11%	-1%	-8%	0%
AS % REVENUES	144%	49%	47%	32%	30%	31%	29%	28%	20%	20%	17%
OPERATING EXPENSES	**-22**	**-30**	**-35**	**-60**	**-72**	**-117**	**-156**	**-174**	**-177**	**-169**	**-170**
CHANGE (%)	-18%	37%	17%	70%	21%	63%	32%	12%	1%	-4%	1%
AS % REVENUES	328%	144%	162%	49%	45%	43%	41%	39%	28%	29%	27%
EBITDA	**-15**	**-9**	**-13**	**61**	**89**	**155**	**225**	**274**	**446**	**405**	**472**
CHANGE (%)	-37%	-40%	46%	-552%	45%	75%	45%	22%	63%	-9%	17%
MARGIN (%)	-227%	-44%	-62%	51%	55%	57%	59%	61%	72%	71%	73%
DEPRECIATION & AMORTISATION	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
AS % REVENUES	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
EBIT	**-15**	**-9**	**-14**	**61**	**89**	**155**	**224**	**274**	**446**	**405**	**472**
CHANGE (%)	-37%	-40%	46%	-551%	45%	75%	45%	22%	63%	-9%	17%
MARGIN (%)	-228%	-44%	-62%	51%	55%	57%	59%	61%	72%	71%	73%
NET FINANCIAL INCOME/(EXPENSE)	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
PROFIT BEFORE TAXES	**-15**	**-8**	**-11**	**64**	**93**	**160**	**231**	**281**	**454**	**414**	**482**
CHANGE (%)	-39%	-47%	40%	-662%	45%	73%	44%	22%	61%	-9%	17%
MARGIN	-226%	-39%	-53%	53%	58%	59%	61%	63%	73%	72%	75%
TAXES	**0**	**-1**	**-2**	**-4**	**-34**	**-54**	**-77**	**-92**	**-146**	**-133**	**-155**
TAX RATE (%)	0%	-12%	-16%	7%	36%	34%	33%	33%	32%	32%	32%
NET PROFIT/LOSS	**-15**	**-9**	**-13**	**60**	**59**	**105**	**154**	**189**	**308**	**281**	**328**
CHANGE (%)	-33%	-40%	45%	-552%	-1%	78%	46%	23%	63%	-9%	17%
MARGIN (%)	-227%	-44%	-61%	50%	37%	39%	41%	42%	49%	49%	51%
NET PROFIT/LOSS (EXCLUDING MILESTONES)	**-18**	**-20**	**-13**	**-3**	**50**	**105**	**154**	**189**	**194**	**281**	**328**
MARGIN (%)	-272%	-98%	-61%	-2%	31%	39%	41%	42%	31%	49%	51%
PROFIT/(LOSS) PER SHARE (IN EUR)	**-1.04**	**-0.58**	**-0.84**	**3.79**	**3.75**	**6.69**	**9.77**	**11.98**	**19.53**	**17.79**	**20.79**
PROFIT/(LOSS) PER SHARE (IN CHF)	**-1.14**	**-0.63**	**-0.92**	**4.16**	**4.11**	**7.33**	**10.71**	**13.12**	**21.40**	**19.50**	**22.78**

ESTIMATES AS OF 7 JUNE, 2017 SOURCE: VALUATIONLAB ESTIMATES

FY 2016 results in a nutshell:

- Cash and short-term investments of EUR 46.5 mn (EUR 40.9 mn at YE 2015)
- Cash into 2019, well beyond expected key value inflection points
- Total revenues of EUR 6.7 mn (+183%)
  - EUR 3 mn milestone payments from Zambon (+257%)
  - Xadago royalties of EUR 1.7 mn (+69%), despite Italian AIFA imposing ceiling for 2016 and 2017 sales, impacting royalties by EUR 0.3 mn
- Operating expenses of EUR 22.1 mn (EUR 26.8 mn in FY 2015)
- Net loss of EUR 15.2 mn (EUR 22.8 mn in FY 2015)

NOTE: At the end of FY 2016 Newron had a total of EUR 167.2 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) 20.9

RATIOS	2016	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
P/E		-33.0x	-22.7x	5.0x	5.1x	2.9x	2.0x	1.6x	1.0x	1.1x	0.9x
P/S		14.4x	13.9x	2.5x	1.9x	1.1x	0.8x	0.7x	0.5x	0.5x	0.5x
P/NAV		4.6x	5.7x	2.7x	1.8x	1.1x	0.7x	0.5x	0.3x	0.2x	0.2x
EV/EBITDA		-27.6x	-18.9x	4.2x	2.9x	1.6x	1.1x	0.9x	0.6x	0.6x	0.5x

PER SHARE DATA (CHF)	2016	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
EARNINGS	**-1.14**	**-0.63**	**-0.92**	**4.16**	**4.11**	**7.33**	**10.71**	**13.12**	**21.40**	**19.50**	**22.78**
CHANGE (%)	-37%	-44%	45%	-552%	-1%	78%	46%	23%	63%	-9%	17%
CASH	**3.47**	**4.24**	**3.30**	**7.59**	**13.88**	**24.84**	**40.71**	**60.23**	**91.89**	**120.92**	**154.85**
CHANGE (%)	7%	22%	-22%	130%	83%	79%	64%	48%	53%	32%	28%
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	**3.71**	**4.56**	**3.64**	**7.80**	**11.91**	**19.24**	**29.95**	**43.07**	**64.47**	**83.97**	**106.75**
CHANGE (%)	27%	23%	-20%	114%	53%	62%	56%	44%	50%	30%	27%

BALANCE SHEET (EUR MN)	2016	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
NET LIQUID FUNDS	**46**	**61**	**47**	**109**	**200**	**357**	**586**	**867**	**1,322**	**1,740**	**2,228**
TOTAL ASSETS	**57**	**71**	**58**	**119**	**210**	**368**	**596**	**877**	**1,332**	**1,750**	**2,239**
SHAREHOLDERS' EQUITY	**50**	**66**	**52**	**112**	**171**	**277**	**431**	**620**	**928**	**1,208**	**1,536**
CHANGE (%)	34%	32%	-20%	114%	53%	62%	56%	44%	50%	30%	27%
RETURN ON EQUITY (%)	-31%	-14%	-25%	53%	35%	38%	36%	30%	33%	23%	21%
FINANCIAL DEBT	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
FINANCIAL DEBT AS % OF TOTAL ASSETS	1%	1%	1%	1%	0%	0%	0%	0%	0%	0%	0%
EMPLOYEES	**23**	**24**	**24**	**25**	**25**	**26**	**26**	**27**	**28**	**28**	**29**
CHANGE (%)	0%	4%	2%	2%	2%	2%	2%	2%	2%	2%	2%

CASH FLOW STATEMENT (EUR MN)	2016	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E
NET PROFIT / (LOSS) BEFORE TAX	-15	-8	-11	64	93	160	231	281	454	414	482
DEPRECIATION & AMORTIZATION	0	0	0	0	0	0	0	0	0	0	0
OTHER NON-CASH ITEMS	-5	-3	-3	-3	-3	-3	-3	-3	-3	-3	-3
CASH FLOW	**-20**	**-11**	**-14**	**62**	**90**	**158**	**228**	**279**	**451**	**411**	**480**
NET INCREASE/(DECREASE) IN WORKING CAPITAL	0	0	0	0	0	0	0	0	0	0	0
OPERATING FREE CASH FLOW	**-20**	**-10**	**-14**	**62**	**90**	**158**	**228**	**280**	**453**	**415**	**484**
NET CASH FLOWS FROM INVESTING ACTIVITIES	1	0	0	0	0	0	0	1	2	3	4
NET CASH USED IN OPERATING ACTIVITIES	**-18**	**-10**	**-14**	**62**	**90**	**158**	**228**	**281**	**456**	**418**	**488**
NET CASH FLOWS FROM FINANCING ACTIVITIES	25	25	0	0	0	0	0	0	0	0	0
NET INCREASE/(DECREASE) IN CASH AND CASH EQUIVALENTS	**7**	**15**	**-14**	**62**	**90**	**158**	**228**	**281**	**456**	**418**	**488**

ESTIMATES AS OF 7 JUNE, 2017

SOURCE: VALUATIONLAB ESTIMATES

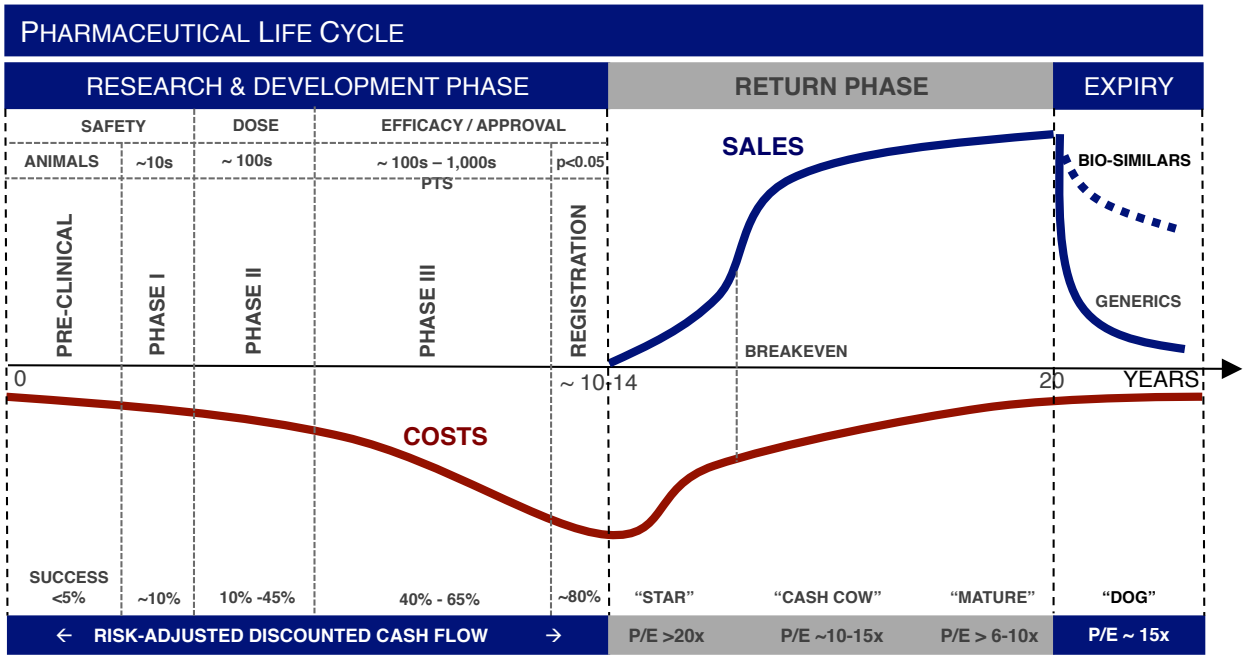
NOTE: With cash and cash equivalents of EUR 46.5 mn (December 31st, 2016), increasing milestone and royalty payments from Zambon on Xadago sales, Newron has sufficient cash to complete full development of sarizotan in Rett syndrome with the pivotal "STARS" trial and prepare commercialization.

An additional EUR 25 mn is needed to complete phase IIb development for evenamide in schizophrenia to maximize long-term value of this potential multi-billion dollar peak sales opportunity before signing on a major CNS player. This would lead to an 8% share dilution based on the current market capitalization, which we assume in our forecasts and per share calculations.

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.GOV

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.

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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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