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

KEY DATA			SIX: NWRN
MARKET CAPITALIZATION (CHF MN)	216	PRICE ON SEPTEMBER 16, 2014	16.6
ENTERPRISE VALUE (CHF MN)	178	RISK-ADJUSTED NPV PER SHARE (CHF)	22.8
NET CASH (END H1 2014) (CHF MN)	38	UPSIDE/DOWNSIDE (%)	38%
MONTHLY OPERATING EXPENSE (CHF MN)	1.6	RISK PROFILE	SPECULATIVE
CASH LIFE (YEAR)	2016	SUCCESS PROBABILITY LEAD PIPELINE DRUG	72.5%
BREAK-EVEN (YEAR)	2016	EMPLOYEES (GROUP)	23
FOUNDED (YEAR)	1998	LISTED (YEAR)	2006
<b>KEY PRODUCTS:</b>	<b>STATUS</b>	<b>MAJOR SHAREHOLDERS:</b>	<b>(%)</b>
- SAFINAMIDE (PARKINSON'S DISEASE)	FILED	- INVESTOR AB (SHAREHOLDER AGREEMENT)	12.8
- SARIZOTAN (RETT'S SYNDROME)	PHASE II	- ZAMBON GROUP (SHAREHOLDER AGREEMENT)	11.4
- SNN0031 (PARKINSON'S DISEASE)	PHASE II	- AVIVA	8.0
- SNN0029 (AMYOTROPHIC LATERAL SCLEROSIS)	PHASE II	- EXECUTIVE MANAGEMENT	0.2
- NW-3509 (SCHIZOPHRENIA)	PHASE I	- FREE FLOAT	75.6
<b>UPCOMING CATALYSTS:</b>	<b>DATE</b>	<b>ANALYST(S):</b>	BOB POOLER
- SAFINAMIDE - US RE-FILING	Q4 2014		BP@VALUATIONLAB.COM
- SAFINAMIDE - EU APPROVAL	Q4 2014		+41 79 652 67 68
- SAFINAMIDE - US APPROVAL	H2 2015		

ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

# Safinamide: Prepare to launch

## Substantial revenues from safinamide starting in 2015

Newron Pharmaceuticals has a product pipeline that targets diseases of the central nervous system and rare diseases. The company's key value driver is safinamide, a once daily oral add-on therapy for all stages of Parkinson's disease with a unique dual mechanism of action. Safinamide was filed in key markets with approval expected in the EU in Q4 2014 and the US in H2 2015. Safinamide 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. With cash and short-term investments of EUR 31.4 mn, Newron is funded well into 2016 when we expect the company to reach breakeven, irrespective of milestone payments, and is sufficiently financed to advance other pipeline assets including orphan drugs for Rett's syndrome, ALS, severe treatment-resistant Parkinson's disease; and NW-3509 for schizophrenia. We derive a risk-adjusted NPV value of CHF 22.8 per share with a 72.5% success probability for lead project safinamide. Because Newron has no sustainable revenues from products on the market yet, we qualify the risk profile as Speculative.

### Key catalysts:

- 1) US re-filing and partnering for safinamide.** US re-filing should occur in Q4 2014, which would raise our risk-adjusted NPV by CHF 2.6/share. Shortly after, we expect Zambon to sub-license safinamide in the US (and potentially other territories), which should trigger substantial upfront milestone payments and royalties on future sales.
- 2) EU approval of safinamide.** EU approval expected in Q4 2014 would lead to a jump of CHF 3.4/share in our risk-adjusted NPV for safinamide.
- 3) Start clinical trials of four new drugs.** By the end of 2014 Newron plans to start clinical trials for: 1) sarizotan (Rett syndrome), 2) sNN0031 (severe treatment-resistant Parkinson's disease), 3) sNN0029 (ALS/Lou Gehrig's disease), and 4) NW-3509 (schizophrenia).

# 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). Currently the group has 23 employees. The present clinical focus is on Parkinson's disease (safinamide and sNN0031) and rare diseases such as Rett's syndrome (sarizotan) and Lou Gehrig's disease (sNN0029).

## **Newron's therapeutic focus is a result of:**

- 1) The company's expertise in ion channel research, an important class of CNS drugs (e.g. safinamide, NW-3509)
- 2) A development agreement signed with Merck KGaA in 2011 (e.g. sarizotan)
- 3) The acquisition of NeuroNova AB in 2012 with two promising orphan drug candidates (sNN0031, sNN0029)

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

Newron's strategy is to develop drugs stemming from earlier discovery capabilities, acquire or in-license CNS or rare disease drugs and develop them to their optimal value. Where necessary, 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.

## **Lead project safinamide has been filed and is now close to market in the EU and US**

Newron, together with its global partner Zambon (ex-Japan & Asian markets), has filed for approval of its lead pipeline project safinamide for the treatment of Parkinson's disease in the EU (December 2013) and in the US (May 2014). In July 2014 the company received a Refusal to File letter from the FDA based on technical issues with the document. A US re-filing is expected in Q4 2014. Safinamide is a once daily oral add-on to dopamine agonists (in early stage Parkinson's), and to levodopa and other Parkinson's medications in patients with motor fluctuations (mid-to-late stage disease). Safinamide has demonstrated efficacy in the short (6 months primary endpoints in pivotal trials) and long-term (18/24 months extension trials) in early and mid-to-late stage disease. We believe, this would position the drug as the new cornerstone treatment in Parkinson's disease. EU approval could occur by the end of 2014 with first member state launches in early 2015, while US approval and launch could take place in the second half of 2015.

## **Number one priority is EU & US approval and US sub-licensing of safinamide**

Newron's number one priority for the next 12 months is securing EU and US approval of safinamide, and supporting its partner Zambon in finding commercialization partners for safinamide in those territories where Zambon has no or a low presence. The lucrative US market is key and has the highest priority. Big Pharma companies with presence in CNS or Parkinson's disease are likely candidates, as well as mid-sized specialty pharmaceutical companies. Next to marketing muscle and financial terms, we believe a candidate that is willing to invest further in a clinical trial investigating the anti-dyskinetic effects of safinamide will be highly considered. Furthermore, Newron will continue to support partner

Meiji Seika with the Japanese/Asian clinical development of safinamide. The first human (phase I) trial has been completed in Japan.

### **Next priority is to step up clinical development of four pipeline projects**

With sufficient financial resources available, Newron will now step up clinical development of its promising pipeline of orphan drugs (sarizotan, sNN0031 and sNN0029); and its schizophrenia drug NW-3509.

### **By the end of the year Newron plans to start a:**

- 1) Phase II pilot efficacy study of sarizotan in Rett syndrome
- 2) Phase II safety and exploratory efficacy study of sNN0031 in severe treatment-resistant Parkinson's disease
- 3) Phase II safety and exploratory efficacy study at a higher dose of sNN0029 in ALS (Lou Gehrig's disease)
- 4) Phase IIa proof-of-concept trial of NW-3509 as an add-on to current antipsychotic therapy in schizophrenia.

The phase II (pilot) trials of the three orphan drug projects will determine their timing and final phase III development. Newron believes it is likely that regulators will accept a single pivotal phase III trial for approval for all three orphan drugs, given the difficulty of finding and enrolling sufficient patients in these rare life-threatening diseases. The company plans to partner or sign on a co-development partner for NW-3509 on positive proof-of-concept.

### **EUR 226 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 safinamide in Parkinson's disease and ralfinamide in neuropathic low back pain. In total the company raised EUR 226.1 mn, of which EUR 18.2 mn in two private placements, including JP Morgan Asset Management (EUR 2.9 mn) and existing shareholders, in H1 2014.

<b>MONEY RAISED</b>	<b>EUR MN</b>
PRE-IPO	62.2
IPO	74.3
GRANTS	13.7
UPFRONT & MILESTONE PAYMENTS	25.0
PRIVATE PLACEMENTS	34.9
NEURONOVA ACQUISITION	16.0
<b>TOTAL RAISED</b>	<b>226.1</b>

ESTIMATES AS OF 16 SEPTEMBER, 2014

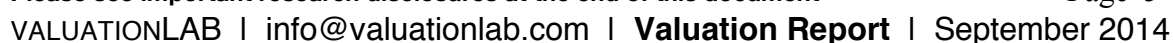
SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Prior to the IPO in 2006, management raised EUR 62.2 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 proof-of-concept in neuropathic low back pain. The company was also doing well in attracting scientific grants and private placements, while the re-partnering of safinamide resulted in EUR 25 mn additional revenue streams. The NeuroNova acquisition added another EUR 16 mn to the cash position and committed cash-inflows in 2012.

Newron currently has EUR 31.4 mn in cash and short-term investments at hand. Assuming operating expenses of around EUR 36 mn for the next two years, the company is funded halfway into 2016. This is a conservative estimate that does not include any revenues or milestones, which can be substantial. For instance, approval and launch of safinamide in the EU and US could trigger milestone payments of up to EUR 38 mn in the next two years, next to royalties on sales, in our view. Furthermore, Newron wants to partner or monetize non-core assets such as ralfinamide (neuropathic pain), HF0220 (Alzheimer's), and its Trident equity holding (HF0120 for asthma); the company plans to attract further investment by leading institutional investors; and finally patient organizations may be willing to participate in co-funding some of the orphan drug studies.

## Life Cycle Positioning - Speculative

We qualify Newron as Speculative, because the company currently has no products on the market that can provide sustainable revenue streams, yet. First material cash inflows from safinamide are expected to start in 2015 with a potential "sustainable" breakeven - where the company is no longer dependent on partnering milestones - to be reached in 2016. Newron would then qualify for a substantial risk profile re-rating (see Important Disclosures for our Risk Qualification).



# Valuation Overview

## Risk-adjusted sum-of-parts NPV points to a fair value of CHF 22.8 per share

We derive a risk-adjusted NPV of CHF 22.8 per share with net cash of CHF 2.9 per share and overhead expenses of CHF 5 per share, assuming a WACC of 8.5%.

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
SAFINAMIDE	PARKINSON'S DISEASE	618	2015	34.3	73%	24.9	89%
SARIZOTAN	RETT'S SYNDROME	481	2017	18.0			
sNN0031	PARKINSON'S DISEASE (SEVERE)	236	2017	15.6			
sNN0029	ALS (LOU GEHRIG'S DISEASE)	384	2017	21.9			
NW-3509	SCHIZOPHRENIA	783	2019	19.5			
RALFINAMIDE	NEUROPATHIC PAIN	NON CORE		5.8			
HF1020 (TRIDENT SPV)	ASTHMA	NON CORE		0.3			
HF0220	ALZHEIMER'S/RA	NON CORE		1.2			
NET CASH POSITION (END H1 2014)		31		2.9		2.9	11%
<b>TOTAL ASSETS</b>				<b>120.5</b>		<b>27.8</b>	<b>100%</b>
OVERHEAD EXPENSES				-5.0		-5.0	
<b>NPV/SHARE (CHF)</b>				<b>115.5</b>		<b>22.8</b>	
SHARE PRICE ON SEPTEMBER 16, 2014						16.6	
PERCENTAGE UPSIDE / (DOWNSIDE)						38%	

ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

## Safinamide is currently Newron's key value driver and cash generator:

### Safinamide (Parkinson's disease) - risk-adjusted NPV of CHF 24.9 per share

Safinamide is Newron's first drug ever drug to be filed for approval with first launches in early and mid-to-late Parkinson's disease expected in the EU (early 2015), followed by the US (H2 2015). We assume Newron will receive up to EUR 58 mn in milestone payments from its partner Zambon (and sub-licensors) with royalties on sales ranging from 10-15% in EU/ROW, 15% in the US, and 10% in Japan. We calculate a risk-adjusted NPV of CHF 24.9 per share for safinamide with peak sales amounting to EUR 600+ mn.

### No value contributed to early stage pipeline projects that lack proof-of-concept

We have not accounted for Newron's early stage pipeline focused on schizophrenia and rare diseases due to the current lack of proof-of-concept. However, these projects could provide substantial upside when developed successfully. The unadjusted NPV above provides a "sneak preview" on what the value could be if our assumptions are reached.

**Sarizotan** targets respiratory disturbances in Rett syndrome, a rare disease affecting primarily girls. A phase II/III single pivotal trial should start in 2015 with results in 2016. Peak sales could reach EUR 450+ mn. Merck KGaA has a buy-back option.

**sNN0031** targets severe treatment-resistant Parkinson's disease and complements safinamide. A EUR 6 mn EU grant will support a single phase IIb/III potential pivotal trial to start in 2015 with results in 2016. Peak sales could reach EUR 200+ mn.

**sNN0029** targets ALS (Lou Gehrig's). A EUR 2.5 mn grant from the Wellcome Trust will support a phase I/II safety and efficacy trial at a higher dose. A phase II/III single potential pivotal trial could start in 2015 with results in 2016. Peak sales could reach EUR 350+ mn.

**NW-3509** targets schizophrenia and therefore presents a blockbuster sales opportunity. Preliminary phase I results were announced in 2014. Newron plans to out-license the drug after successful phase IIa development, with trials starting in Q4 2014 and results in H2 2015.

## Sensitivities that can influence our valuation

**Regulatory approval:** EU and US filings are based on an extensive clinical development program that included over 1,500 patients. Safinamide demonstrated significant benefits as: 1) an add-on to a stable dose of a single dopamine agonist in patients with early disease, and 2) an add-on to levodopa and other Parkinson's medications at stable doses in patients with motor fluctuations (mid-to-late stage patients). The EMA (European Medicines Agency) and FDA (Food and Drug Administration) will base their approval on the perceived risk-benefit of safinamide in early and in mid-to-late stage disease. Each regulator can independently approve both indications (early and mid-to-late disease), a single indication, and none at all. We assume an 80% likelihood of the EMA and FDA approving safinamide in both indications once successfully filed.

**Pricing and reimbursement:** Following an FDA or EMA approval, safinamide must be priced and reimbursed by local health care providers. In the US pricing and reimbursement is typically quite straightforward. 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. We conservatively assume safinamide pricing in the range of in-market branded Parkinson's drugs.

**Partnering:** In 2012 Newron out-licensed safinamide 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 market, and will need to secure commercialization partners in these regions. Consequently, there is limited visibility on the timing and terms on which these sub-licensors will be contracted. We assume a US partner at the end of 2014 or early 2015 and Newron to split the milestones and royalty payments evenly with partner Zambon.

**Commercialization:** With no own sales force, Newron's revenues and earnings will be entirely dependent on its commercialization partners to successfully position and market safinamide against existing Parkinson's treatments, in particular against Teva's Azilect (rasagiline).

**Patent and market exclusivity:** Safinamide'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 assume patent protection for safinamide until 2029 (which includes extension).

### Other sensitivities

- **External sourcing:** Newron does not have own manufacturing facilities and is dependent on external sourcing to manufacture safinamide according to strict regulatory specifications.
- **Unexpected side effects:** Although safinamide has been exposed to over 1,500 patients of who around 1,000 were treated more than one year, unexpected side effects could still occur with widespread and long-term use.
- **New market entrants:** No new market entrants have been identified in the medium term. But commercial success of safinamide could spur outside research efforts in this area.



# Catalysts

By raising EUR 18.2 mn through two private placements in early 2014, Newron now has sufficient funds to develop its orphan drug portfolio up to pivotal results, and schizophrenia drug NW-3509 up to phase IIa proof-of-concept, with a cash runway well into 2016.

In July, Newron established a US organization to interact with the FDA and support future clinical trials. Unfortunately, the FDA's Refusal to File letter for safinamide leads to a delay in the US, with a re-filing expected in Q4 2014.

## CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT
<b>2014</b>					
31 JAN			PRIVATE PLACEMENT	CHF 3.6 MN RAISED BY PRIVATE PLACEMENT OF 211,473 SHARES AT J.P. MORGAN ASSET MANAGEMENT	
4 MAR			FY 2013 RESULTS	NEWRON WELL FUNDED INTO 2015 WITH A TOTAL OF EUR 25.2 MN OF FUNDS, OF WHICH EUR 18.4 MN CASH	
7 APR			PRIVATE PLACEMENT	CHF 18.6 MN RAISED BY PRIVATE PLACEMENT OF 1,183,597 NEWLY ISSUED SHARES WITH EXISTING & NEW SHAREHOLDERS	
8 APR	NW-3509	SCHIZOPHRENIA	PHASE I RESULTS	SAFE & WELL TOLERATED WITH ACTIVITY IN BEHAVIORAL STUDIES	
29 MAY	SAFINAMIDE	PARKINSON'S	US FILING	US FILING TRIGGERS MILESTONE PAYMENT FROM ZAMBON	
8 JUL			US OPERATIONS	NEWRON ESTABLISHES US OPERATIONS TO INTERACT WITH FDA AND SUPPORT CLINICAL INVESTIGATIONS OF COMPOUNDS	
29 JUL	SAFINAMIDE	PARKINSON'S	REFUSAL TO FILE	RTF LETTER DUE TO TECHNICAL DOCUMENTATION ISSUES	
14 SEP			H1 2014 RESULTS	EUR 31.4 MN CASH AND SHORT TERM INVESTMENTS	
	sNN0031	SEVERE PARKINSON'S	FDA MEETING	MEETING TO DETERMINE FINAL SPECIAL PROTOCOL AGREEMENT	
Q4	NW-3509	SCHIZOPHRENIA	START PHASE IIA	PHASE IIA PROOF-OF-CONCEPT TRIAL IN SCHIZOPHRENIC'S WHO ARE POOR RESPONDERS TO CURRENT TREATMENT	
Q4	sNN0029	ALS (LOU GEHRIG'S)	START PHASE II	TRIAL TO EVALUATE SAFETY & EFFICACY HIGHER DOSES & 6 MONTHS TREATMENT - FUNDED BY WELLCOME TRUST GRANT (EUR 2.5 MN)	
Q4	sNN0031	SEVERE PARKINSON'S	START PHASE II	PHASE II SAFETY AND EXPLORATORY EFFICACY STUDY	
Q4	SAFINAMIDE	PARKINSON'S	US RE-FILING	RE-FILING AFTER ADDRESSING TECHNICAL ISSUES	+CHF 2.6
Q4	SAFINAMIDE	PARKINSON'S	PARTNERING	ZAMBON TO SEEK PARTNERING AGREEMENTS FOR THE US AND SELECTED EU MARKETS (TRIGGERS MILESTONES PAYMENTS)	
Q4	SAFINAMIDE	PARKINSON'S	EU APPROVAL	FIRST LAUNCHES TRIGGER MILESTONE PAYMENT FROM ZAMBON	+CHF 3.4
END	SARIZOTAN	RETT'S SYNDROME	START PILOT TRIAL	SMALL PILOT TRIAL BEFORE SINGLE PIVOTAL PHASE II/III TRIAL	
<b>2015</b>					
Q2	SARIZOTAN	RETT'S SYNDROME	RESULTS PILOT TRIAL	DATA DETERMINES FINAL SINGLE PIVOTAL PHASE II/III TRIAL	
MID	sNN0029	ALS (LOU GEHRIG'S)	RESULTS PHASE II	HIGHER DOSE TRIAL DETERMINES SINGLE PIVOTAL PHASE II/III TRIAL	
H2	SARIZOTAN	RETT'S SYNDROME	START PHASE II/III	POTENTIALLY ONLY A SINGLE PHASE II/III, 40 PATIENT TRIAL, WILL BE NEEDED FOR REGISTRATION IN RETT'S SYNDROME (ORPHAN DISEASE)	+CHF 4.5
H2	sNN0031	SEVERE PARKINSON'S	START PHASE II/III	POTENTIALLY ONLY A SINGLE PHASE II/III TRIAL WILL BE NEEDED FOR REGISTRATION IN SEVERE, TREATMENT RESISTANT PARKINSON'S DISEASE (ORPHAN DISEASE)	+CHF 3.9
H2	sNN0029	ALS (LOU GEHRIG'S)	START PHASE II/III	POTENTIALLY ONLY A SINGLE PHASE II/III TRIAL WILL BE NEEDED FOR REGISTRATION IN AMYOTROPHIC LATERAL SCLEROSIS (ORPHAN DISEASE)	+CHF 5.5
H2	NW-3509	SCHIZOPHRENIA	DATA PHASE IIA	POSITIVE PHASE IIA PROOF-OF-CONCEPT TRIAL COULD TRIGGER PARTNERSHIP	
H2	SAFINAMIDE	PARKINSON'S	US APPROVAL	US APPROVAL POTENTIALLY TRIGGERS MILESTONE US PARTNER	+CHF 3.4
H2	sNN0031	SEVERE PARKINSON'S	START PHASE II/III	START SINGLE PIVOTAL PHASE II/III TRIAL UNDER S.P.A.	

ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

## Upcoming key catalysts for the next 18 months include:

- 1) **US re-filing and partnering for safinamide.** US re-filing should occur in Q4 2014, which would raise our risk-adjusted NPV by CHF 2.6/share. Shortly after, we expect Zambon to sub-license safinamide in the US (and potentially other territories), which should trigger substantial upfront milestone payments and royalties on future sales.
- 2) **EU approval of safinamide.** EU approval, expected in Q4 2014, would lead to a jump of CHF 3.4/share in our risk-adjusted NPV for safinamide.
- 3) **Start clinical trials of four new drugs.** By the end of 2014 Newron plans to start clinical trials for: 1) sarizotan (Rett syndrome), 2) sNN0031 (severe treatment-resistant Parkinson's disease), 3) sNN0029 (ALS/Lou Gehrig's disease), and 4) NW-3509 (schizophrenia).
- 4) **Start pivotal trials orphan portfolio.** Each orphan drug that starts pivotal trials in 2015 will be included in our risk-adjusted NPV for Newron with a 25% success probability.



# Technology & Pipeline

## Blockbuster safinamide close to market and an attractive orphan drug pipeline

Currently, Newron has two drugs addressing multibillion dollar markets including safinamide (Parkinson's) and NW-3509 (schizophrenia), and three drugs addressing orphan drug indications, including sarizotan (Rett syndrome), and the two NeuroNova drugs sNN0029 (ALS) and sNN0031 (severe treatment-resistant Parkinson's). Safinamide has been filed in the EU and the US (re-filing expected in Q4 2014) with first EU launches expected in early 2015. With sufficient cash, Newron now plans to step up the development efforts for its orphan drug projects, with all three starting further pilot studies this year and single potentially pivotal trials in 2015. Schizophrenia drug NW-3509 has completed phase I successfully and a phase IIa proof-of-concept trial will start in Q4 2014 to attract a large CNS player for further development and commercialization.

### PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
SAFINAMIDE	ALPHA-AMINOAMIDE	PARKINSON'S DISEASE	FILED	EU: Q4 2014 US: H2 2015	ZAMBON/MEIJI SEIKA	EUR 600+ MN
SARIZOTAN	DOPAMINE RECEPTOR BLOCKER	RETT SYNDROME (ORPHAN INDICATION)	PHASE II/POC	2017	MERCK KGAA	EUR 450+ MN
sNN0031	PLATELET-DERIVED GROWTH FACTOR	SEVERE NON-RESPONDING PARKINSON'S DISEASE (ORPHAN INDICATION)	PHASE II/POC	2017	TO BE DETERMINED	EUR 200+ MN
sNN0029	VASCULAR ENDOTHELIAL GROWTH FACTOR	AMYOTROPHIC LATERAL SCLEROSIS (ORPHAN INDICATION)	PHASE II/POC	2017	TO BE DETERMINED	EUR 350+ mn
NW-3509	ION CHANNEL BLOCKER	SCHIZOPHRENIA	PHASE IIa/POC	2019	TO BE PARTNERED AFTER PHASE I/IB	EUR 800 MN
RALFINAMIDE	ION CHANNEL BLOCKER	NON-RESPONDING SEVERE NEUROPATHIC PAIN (ORPHAN INDICATION)	POC		PARTNER BEFORE STARTING TRIALS	NON-CORE
HF0220	HUMAN STEROID	ALZHEIMER'S / RHEUMATOID ARTHRITIS	PHASE II/POC		PARTNER OR MONETIZE	NON-CORE
HF1020 (TRIDENT SPV)		ASTHMA	PHASE I		MONETIZE	NON-CORE

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SOURCE: VALUATIONLAB ESTIMATES, NEWRON PHARMACEUTICALS

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

Three pipeline projects are considered non-core that the company wants to partner or monetize including, ralfinamide (neuropathic pain) stemming from Newron's own ion channel blocker discovery platform, and HF0220 (Alzheimer's) and HF1020 (asthma) that were acquired with the Hunter-Fleming acquisition in 2008.

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

Prior to the acquisition of NeuroNova in 2012, Newron's research programs were primarily focused on the selection of 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.

## NeuroNova acquisition complements CNS portfolio with rare disease opportunities

With the acquisition of the privately held Swedish NeuroNova AB at the end of 2012,

Newron has expanded its development focus beyond CNS disorders with so-called orphan or rare diseases. These 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. Sarizotan for treating breathing difficulties for girls with Rett syndrome and sNN0029 for treating ALS qualify and have been granted orphan drug designation. sNN0031 for treating severe treatment-resistant Parkinson's disease targets the same patient population as Abbvie's Duodopa, and therefore should also qualify for orphan drug designation.

**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 (Rett) or limited (ALS, treatment-resistant Parkinson's)
- 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 expiries. 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 will provide an in-depth analysis and forecasts for Newron's key driver safinamide in:**

- 1) Early stage Parkinson's disease (as an add-on to dopamine agonists)
- 2) Mid-to-late stage Parkinson's disease (as an add-on to levodopa)

# Forecasts & Sensitivity Analysis

## Safinamide (Parkinson's Disease)

### Product Analysis

#### Parkinson's peak sales of EUR 600+ mn - Risk-adjusted NPV of CHF 24.9 per share

We forecast peak sales of EUR 600+ mn for safinamide, assuming first market launches in early 2015, global patent protection until 2029 (including patent extensions), a daily treatment cost between USD 7 (US) and EUR 3 (EU/ROW), which could prove to be conservative considering safinamide's unique dual mechanism of action, and a market penetration peaking at 10-11%. Our risk-adjusted NPV amounts to CHF 324 mn, or CHF 24.9 per share, assuming Newron receives a total of EUR 58 mn milestone payments, royalties on sales ranging between 10-15%, with a success probability of 72.5% (the average of EU (80% filed) and US (65% to be re-filed)), and a WACC of 8.5%.

### Safinamide – the comeback kid is close to market

Safinamide was filed for approval for the treatment of all stages of Parkinson's disease in key markets such as the EU and US in December 2013 and May 2014, respectively. In the US, Newron will have to re-file safinamide after it received a Refusal to File letter in July 2014 caused by technical issues in the documentation. This should occur in Q4 2014. The filings 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.

Safinamide demonstrated significant benefits in Parkinson's patients with:

- 1) **Early stage disease** as an add-on to a stable dose of a single dopamine agonist
- 2) **Mid-to-late stage disease** as an add-on to levodopa and other Parkinson's medications at stable doses in patients with motor fluctuations

### US re-filing and acceptance of filing ("74-Day Letter") next critical milestone

On July 29<sup>th</sup> 2014 Newron announced that, upon preliminary review of safinamide, the FDA identified some organizational and navigation problems, relating to hyperlinking of tables, folders and the organization of the table contents in the filing, as well as the conformation of the Package Insert to FDA guidelines, resulting in a Refusal to File letter. Recently, the company has discussed these technical documentation issues with the FDA and a re-filing should occur in Q4 2014. Once re-filed, the FDA will start its preliminary review again to determine if the filing is sufficiently complete to conduct a complete review. The FDA will communicate any significant review deficiencies identified by the filing review by day 74 of the review cycle. The FDA considers the so-called "74-Day Letter" a preliminary review, but does not consider this review to be comprehensive nor indicative of deficiencies that may be identified later in the review cycle.

### Announcement of a US partner a major catalyst for Newron

We believe the issuance of the "74-day Letter", with no issues identified in the preliminary review, represents a key milestone to conclude a commercialization agreement with a US partner. Although we have factored a US commercialization partner in our forecasts, we

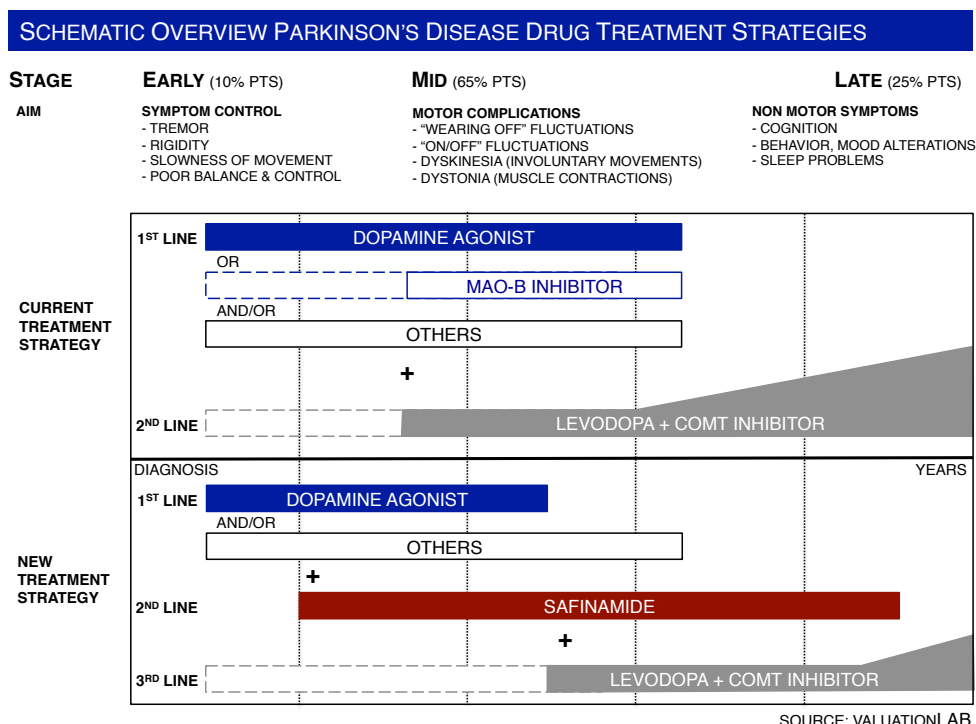
believe the announcement of the partner will be a major catalyst for Newron. Importantly, the marketing muscle of the US partner as well as the commercialization terms will be of special interest. The announcement of a US partner will significantly improve the visibility of safinamide's commercial value in this critical and lucrative market.

### Next safinamide catalysts will be EU and US approvals

The EMA and FDA base their approval on the perceived risk-benefit of safinamide in early disease (add-on to dopamine agonists) and mid-to-late stage disease (add-on to levodopa). Each regulator can independently approve both indications, a single indication or none at all. The EMA is advised by the CHMP (Committee for Medicinal Product for Human use), while an Advisory Panel of independent experts often advises the FDA. The product label describes how and to whom safinamide may be prescribed and ultimately determines patient penetration. Approval in the EU is expected in Q4 2014, and in the US in H2 2015. Following EU approval, the company will have to negotiate on a country-by-country base pricing and reimbursement. Depending on the member state, this can be a matter of weeks to many months. Pricing and reimbursement in the US is a more straightforward and prompt process.

## Potential to become a new cornerstone treatment

We believe safinamide has a promising profile in that it has the potential to enhance the efficacy of existing Parkinson's treatments over a longer course of treatment, thereby increasing patients' quality of life and daily activities, and potentially reducing dyskinesia and increasing longevity (further study needed). Safinamide can be given to patients early in disease with dopamine agonists. As the disease progresses and patients are switched to levodopa, safinamide can continue to be given in combination with it. Safinamide will complement rather than compete against dopamine agonists and levodopa. Moreover, safinamide as a combination treatment pushes back the need and reduces the required dose of levodopa, whose highly effective early outcomes usually wear off with prolonged use. The majority of patients on levodopa develop a number of progressive and severe side effects, primarily daily motor fluctuations and dyskinesia.



### **Aim is to limit or delay the onset of levodopa-related complications**

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. 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.

### **Teva's Azilect now also competing for cornerstone therapy position**

Teva's Azilect (rasagiline), a selective irreversible MAO-B inhibitor, belongs to the same drug class as Newron's safinamide. Azilect was approved in 2005 (EU) and 2006 (US) as a mono-therapy in early stage Parkinson's disease and as an add-on to levodopa in mid-to-late stage disease. In 2013 Teva reported global in-market sales of USD 493 mn (+17%). Lundbeck has commercialization rights in Europe and some markets outside Europe including six Asian countries. We consider Azilect to be safinamide's main rival. In particular, because Teva has recently developed Azilect as an add-on therapy to dopamine agonists in early stage Parkinson's, following Newron's positioning of safinamide. Azilect announced positive results in the "ANDANTE" study where Azilect significantly improved total Unified Parkinson's Disease Rating Scale (UPDRS) scores compared to placebo. In June 2014 the FDA expanded Azilect's US label with this indication, giving it a head start in the US. Teva's plans in the EU/ROW are still unclear.

### **Safinamide is a MAO-B inhibitor with unique qualities**

Although Azilect and safinamide both belong to the MAO-B inhibitor class, we believe safinamide has distinct properties, which can position the compound as the new cornerstone therapy in treating Parkinson's disease across all disease stages.

Safinamide is 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 safinamide, making comparisons difficult. However, certain observations can be made.

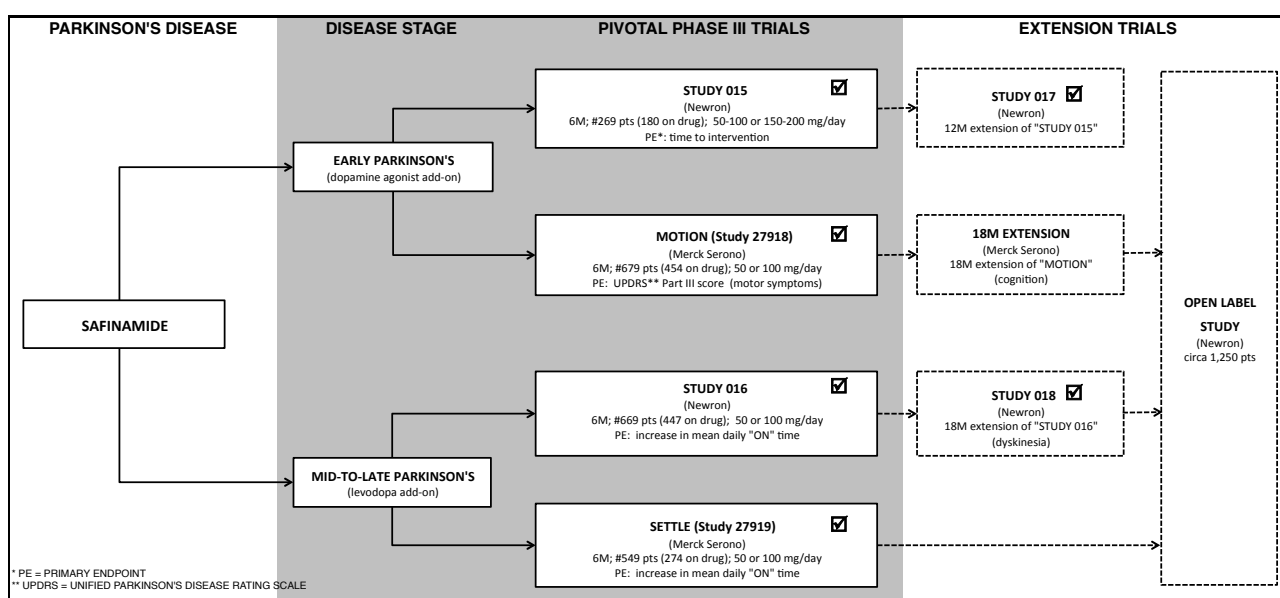
- Safinamide is a reversible MAO-B inhibitor, whereas Azilect is an irreversible MAO-B inhibitor given its long half-life. This can be an important safety aspect in case of serious side effects caused by e.g. drug interactions; safinamide is cleared faster out of the body
- Safinamide has unparalleled 18/24 months clinical data backing long-term efficacy and safety

- Saffenamide 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
- Saffenamide has a fast onset of action, which lasts up to 2 years (backed by double-blinded clinical trials)
- Saffenamide has the potential to reduce (levodopa-induced) dyskinesia due to its unique ability to reduce glutamatergic activity (needs to be further investigated)
- Saffenamide has the potential to reduce depression due to its unique ability to reduce glutamatergic activity (needs to be further investigated)

### Saffenamide has been developed for all disease stages of Parkinson's disease:

- 1) **Early disease** as an add-on to dopamine agonists
- 2) **Mid to late stage disease** as an add-on to levodopa and other dopaminergic treatments.

#### NEWRON - PHASE III TRIAL DESIGN SAFFENAMIDE IN PARKINSON'S DISEASE



SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

This is reflected in the phase III trial design with all four 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 saffenamide, including demonstrating long-term efficacy and anti-dyskinetic properties.

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

Saffenamide 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 safinamide reached statistical significance as well.

So in early Parkinson's disease adding 100 mg of safinamide 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.

### **Safinamide was well tolerated with the majority of patients completing the trials**

In both phase III trials safinamide 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 safinamide 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 safinamide 100 mg/day.

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

Safinamide 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% of PD patients are on levodopa regimens.

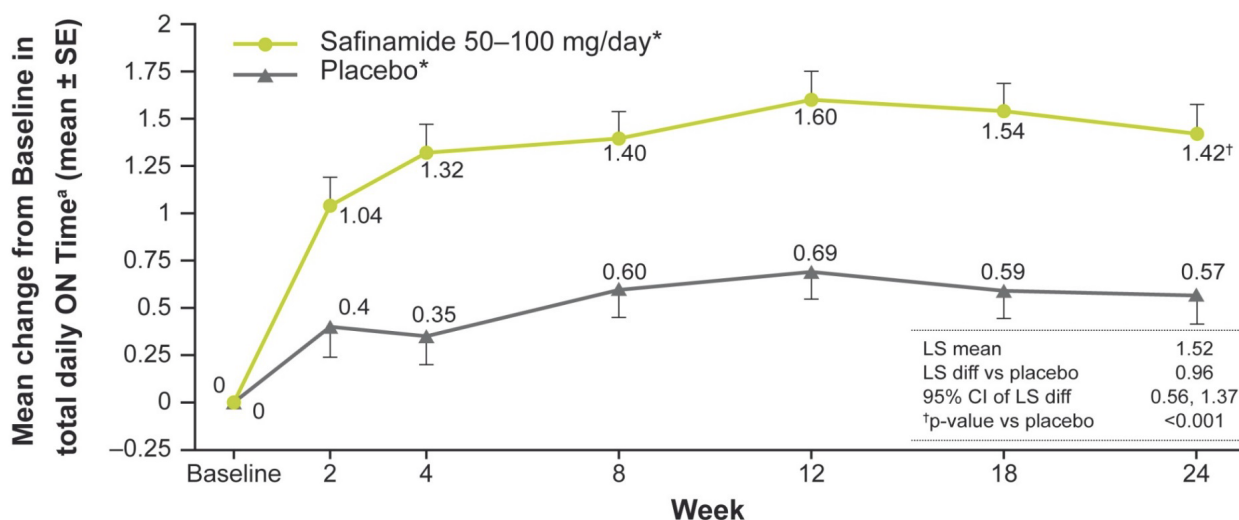
### **Daily ON time primary endpoint met in "Study 016" and "SETTLE"**

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 safinamide showed a significant improvement in its primary endpoint of ON time of almost an hour (+0.96 hours vs. placebo,  $p < 0.001$ ).



\*ON Time is defined as ON Time without dyskinesia plus ON Time with non-troublesome dyskinesia

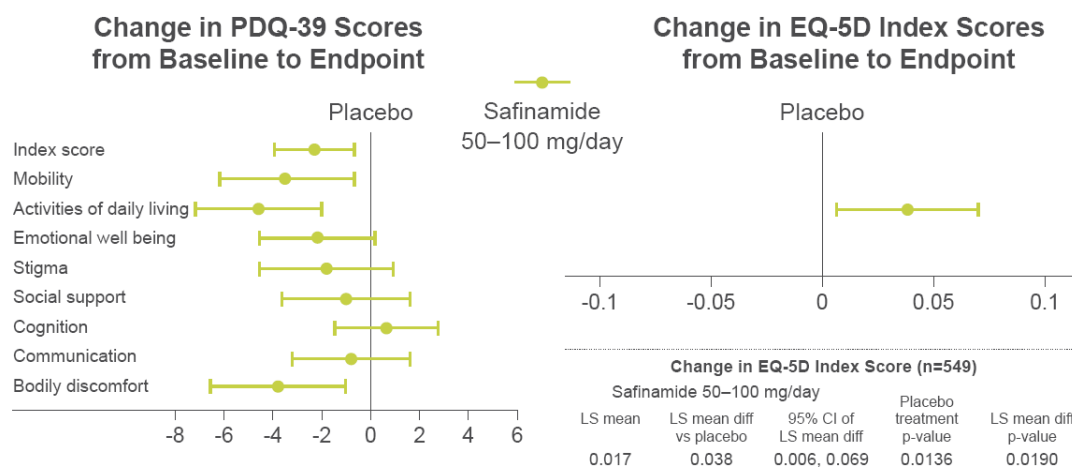
\*As add-on to L-dopa and PD medication

SOURCE: NEWRON PHARMACEUTICALS

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

**Well tolerated with slight transient dyskinesia seen at start of therapy**

In both trials safinamide was well tolerated with most side effects similar to placebo and almost all patients (approximately 90%) completing the trials. In "SETTLE" dyskinesia (14.6% vs. 5.5%) was seen more frequently in the safinamide group than in the placebo group, but was this not a reason for patients to stop treatment, nor to reduce the treatment dose. Dyskinesia occurred at the start of treatment but this was mostly transient and mild. Fall (6.6% vs. 3.6%) and urinary tract infection (6.2% vs. 4.4%) were also slightly higher than placebo, while headache (4.4% vs. 6.2%) and back pain (3.3% vs. 5.1%) occurred less in the safinamide group compared to placebo.

**"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 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)
<b>DYSKINESIA RATING SCALE</b>			
- VALUE AT MONTH 24	7.0 +/- 3.53	6.6 +/- 3.54	6.4 +/- 4.45
- LS DIFFERENCE VS. PLACEBO	0.0	<b>-0.7</b>	<b>-1.22</b>
- P-VALUE VS. PLACEBO	N/A	0.1999	<u>0.0317</u>

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 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 safinamide.

# Forecasts & Sensitivity Analysis

## SAFINAMIDE - FINANCIAL FORECASTS FOR PARKINSON'S DISEASE

<b>INDICATION</b>	ADJUNCT TO DOPAMINE AGONISTS AND LEVODOPA IN ALL STAGES OF PARKINSON'S DISEASE (PD)
<b>DOSAGE</b>	50 OR 100 MG / DAY
<b>PRICE</b>	US: USD 7 PER DAY; JAPAN: EUR 3 PER DAY; EUROPE/ROW: EUR 3 PER DAY - NOTE: PRICING COULD BE TOO CONSERVATIVE DUE TO THE UNIQUE DUAL MECHANISM OF ACTION
<b>STANDARD OF CARE</b>	DOPAMINE AGONISTS (EARLY PD), LEVADOPA (MID-TO-LATE PD)

**UNIQUE SELLING POINT** ONCE DAILY ADD-ON THERAPY FOR ALL STAGES OF PARKINSON'S DISEASE WITH A UNIQUE DUAL MECHANISM OF ACTION WITH POTENTIAL ANTI-DYSKINETIC PROPERTIES

### 7Ps ANALYSIS

<b>PATENT</b>	PROTECTION IN EU & US UNTIL 2029: LEVODOPA COMBINATION PATENT 2026 (US) / 2024 (EU) + UP TO 5 YEAR EXTENSION   SYNTHESIS PATENT: 2027
<b>PHASE</b>	EU: FILED DEC 2013; CH: FILED MAR 2014; US: FILED MAY 2014, REFUSAL TO FILE JULY 2014, RE-FILING Q4 2014; JAPAN: PHASE I TRIALS STARTED IN 2013
<b>PATHWAY</b>	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
<b>PATIENT</b>	IMPROVING QUALITY OF LIFE IN EARLY DISEASE AND DELAYING IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA RELATED TO LONG-TERM LEVODOPA USE
<b>PHYSICIAN</b>	HELPS DELAY USE OF MAINSTAY LEVODOPA TREATMENT THAT LEADS TO IRREVERSIBLE SIDE EFFECTS SUCH AS DYSKINESIA AND "WEARING OFF"
<b>PAYER</b>	DELAYS SIGNIFICANT COSTS RELATED TO DYSKINESIA AND "WEARING OFF" WHERE PATIENTS NEED EXTENSIVE CARE OR HAVE TO BE INSTITUTIONALIZED
<b>PARTNER</b>	ZAMBON (WORLDWIDE EXCL. JAPAN & KEY ASIAN MARKETS), MEIJI SEIKA PHARMA (JAPAN & KEY ASIAN MARKETS) - NEWRON SHARES IN MILESTONE & ROYALTY PAYMENTS

### REVENUE MODEL

EUROPE / REST OF WORLD	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
NUMBER OF PATIENTS (MN)	3.3	3.4	3.4	3.5	3.6	3.6	3.7	3.8	3.9	3.9	4.0
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)	2.3	2.3	2.4	2.4	2.5	2.5	2.6	2.6	2.7	2.8	2.8
PENETRATION (%)	0.0%	0.0%	2.5%	4.5%	5.5%	6.5%	7.0%	7.5%	8.0%	8.5%	9.0%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.3
COST OF THERAPY PER YEAR (EUR)	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095
<b>SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>66</b>	<b>120</b>	<b>150</b>	<b>181</b>	<b>199</b>	<b>217</b>	<b>236</b>	<b>256</b>	<b>277</b>
CHANGE (%)				84%	25%	21%	10%	9%	9%	8%	8%
ROYALTY (%)	10.0%	10.0%	10.0%	10.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
ROYALTIES (EUR MN)	0	0	7	12	23	27	30	33	35	38	41
UPFRONT & MILESTONE PAYMENTS (EUR MN)	3	10	10								
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>3</b>	<b>10</b>	<b>17</b>	<b>12</b>	<b>23</b>	<b>27</b>	<b>30</b>	<b>33</b>	<b>35</b>	<b>38</b>	<b>41</b>
TAX RATE (%)	0%	0%	0%	0%	30%	30%	30%	30%	30%	30%	30%
TAXES (EUR MN)	0	0	0	0	-7	-8	-9	-10	-11	-12	-12
<b>PROFIT (EUR MN)</b>	<b>3</b>	<b>10</b>	<b>17</b>	<b>12</b>	<b>16</b>	<b>19</b>	<b>21</b>	<b>23</b>	<b>25</b>	<b>27</b>	<b>29</b>

UNITED STATES	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
NUMBER OF PATIENTS (MN)	1.1	1.1	1.1	1.1	1.1	1.2	1.2	1.2	1.2	1.3	1.3
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)	0.8	0.9	0.9	0.9	0.9	0.9	1.0	1.0	1.0	1.0	1.0
PENETRATION (%)	0.0%	0.0%	0.5%	4.0%	6.0%	7.5%	8.5%	9.5%	10.0%	10.5%	11.0%
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)	1'952	1'872	1'872	1'872	1'872	1'872	1'872	1'872	1'872	1'872	1'872
<b>SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>8</b>	<b>67</b>	<b>103</b>	<b>132</b>	<b>152</b>	<b>173</b>	<b>186</b>	<b>199</b>	<b>213</b>
CHANGE (%)				716%	53%	28%	16%	14%	7%	7%	7%
ROYALTY (%)	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
ROYALTIES (EUR MN)	0	0	1	10	15	20	23	26	28	30	32
UPFRONT & MILESTONE PAYMENTS (EUR MN)			7	11							
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>9</b>	<b>21</b>	<b>15</b>	<b>20</b>	<b>23</b>	<b>26</b>	<b>28</b>	<b>30</b>	<b>32</b>
TAX RATE (%)	0%	0%	0%	0%	30%	30%	30%	30%	30%	30%	30%
TAXES (EUR MN)	0	0	0	0	-5	-6	-7	-8	-8	-9	-10
<b>PROFIT (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>9</b>	<b>21</b>	<b>11</b>	<b>14</b>	<b>16</b>	<b>18</b>	<b>20</b>	<b>21</b>	<b>22</b>

JAPAN	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
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	0.2	0.2	0.2	0.3
PENETRATION (%)	0.0%	0.0%	0.0%	0.0%	2.0%	5.0%	7.0%	8.0%	8.5%	9.0%	9.5%
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)	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095	1'095
<b>SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>10</b>	<b>27</b>	<b>38</b>	<b>44</b>	<b>48</b>	<b>52</b>	<b>56</b>
CHANGE (%)						155%	43%	17%	8%	8%	8%
ROYALTY (%)	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
ROYALTIES (EUR MN)	0	0	0	0	1	3	4	4	5	5	6
UPFRONT & MILESTONE PAYMENTS (EUR MN)					20						
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1</b>	<b>3</b>	<b>4</b>	<b>4</b>	<b>5</b>	<b>5</b>	<b>6</b>
TAX RATE (%)	0%	0%	0%	0%	20%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	0	0	0	0	-1	-1	-1	-1	-1	-1
<b>PROFIT (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>4</b>	<b>4</b>	<b>4</b>

	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
<b>GLOBAL SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>74</b>	<b>188</b>	<b>264</b>	<b>339</b>	<b>389</b>	<b>435</b>	<b>471</b>	<b>507</b>	<b>546</b>
CHANGE (%)				154%	40%	29%	15%	12%	8%	8%	8%
<b>GLOBAL PROFIT (EUR MN)</b>	<b>3</b>	<b>10</b>	<b>25</b>	<b>33</b>	<b>27</b>	<b>35</b>	<b>40</b>	<b>45</b>	<b>48</b>	<b>52</b>	<b>56</b>
CHANGE (%)		211%	151%	32%	-17%	27%	14%	12%	8%	8%	8%
WACC (%)	8.5%										
<b>NPV TOTAL PROFIT (CHF MN)</b>	<b>447</b>										
NUMBER OF SHARES (MN)	13.0										
<b>NPV PER SHARE (CHF)</b>	<b>34.3</b>										
SUCCESS PROBABILITY	72.5%										
<b>RISK ADJUSTED NPV PER SHARE (CHF)</b>	<b>24.9</b>										

### SENSITIVITY ANALYSIS

	CHF/SHARE	WACC (%)							
		7.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5
SUCCESS PROBABILITY	100%	38.3	36.9	35.6	34.3	33.1	32.0	30.9	29.9
	95%	36.4	35.0	33.8	32.6	31.5	30.4	29.4	28.4
	90%	34.4	33.2	32.0	30.9	29.8	28.8	27.8	26.9
	85%	32.5	31.3	30.2	29.2	28.1	27.2	26.3	25.4
	80%	30.6	29.5	28.4	27.4	26.5	25.6	24.7	23.9
	75%	28.7	27.7	26.7	25.7	24.8	24.0	23.2	22.4
	72.5%	27.7	26.7	25.8	24.9	24.0	23.2	22.4	21.7
	68%	25.8	24.9	24.0	23.2	22.3	21.6	20.9	20.2
	63%	23.9	23.0	22.2	21.4	20.7	20.0	19.3	18.7

ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES

## Unique Selling Point

Once daily oral add-on therapy together with dopamine agonists in early stage Parkinson's disease and in combination with levodopa in mid-to-late stage disease, with a unique dual mechanism of action. Delays introduction of levodopa in early Parkinson's, while in mid-to-late stage disease, safinamide reduces levodopa dose and increases "on-time" without troublesome dyskinesia. There is a potential to reduce dyskinesia owing to safinamide's unique dual mechanism that has to be further established in blinded clinical trials.

## 7P's Analysis

**Patent:** Granted combination patents protect safinamide 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. Assuming first product launches to start in 2015, the drug has an effective patent life of approximately 14 years.

**Phase:** Successfully filed in the EU, while re-filing in the US is expected in Q4 2014, currently resulting in a 72.5% success probability (the average of 80% (filed in EU) and 65% (to be re-filed in US)). EU approval is expected in Q4 2014 followed by the US in H2 2015.

**Pathway:** To receive approval, safinamide needs 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 safinamide 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 safinamide, including over 1,000 patients treated for at least one year and several hundred treated for four years, we believe Newron comfortably fulfills these requirements.

**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, safinamide 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:** Safinamide 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 safinamide 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 safinamide in May 2012. The company has a strong presence in Southern Europe, France and Latin America, where it will market the drug. In other regions, such as the important US market, Zambon will sub-license safinamide to either a Big Pharma or a specialty pharma company. Newron shares in the 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 STRIATAL NEUROTRANSMITTER DOPAMINE
SYMPTOMS	- TREMOR (SHAKING OF HANDS, ARMS, LEGS, JAW, FACE) - RIGIDITY (LIMBS, TRUNK) - BRADYKINESIA (SLOWNESS OF MOVEMENT) - POSTURAL INSTABILITY (POOR BALANCE AND COORDINATION)
DRUG CLASS (KEY BRANDS)	- LEVODOPA/CARBIDOPA (MADOPAR, SINEMET CR, PARCOPA, STALEVO, DUODOPA) - DOPAMINE AGONIST (MIRAPEX, REQUIP, APOKYN, PARLODEL, NEUPRO PATCH) - MAO-B INHIBITORS (AZILECT, ELDEPRYL, ZELAPAR ODT) - 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) - VALEANT (ZELAPAR ODT, TASMAR) - ABBVIE (DUODOPA) - ENDO PHARMACEUTICALS (SYMMETREL)

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

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 monotherapy 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 include:** XenoPort's **XP21279**, a sustained release levodopa pro-drug (phase II), Abbvie's **Duodopa**, a carbidopa/levodopa intestinal gel (EU/ROW approved, US pending), Impax's **Rytary**, an extended-release capsule formulation of carbidopa/levodopa (US re-filed), and NeuroDerm's **ND0611/0612**, a carbidopa/levodopa subcutaneous patch pump (phase IIa).

**New molecules and novel approaches include:** Newron/Zambon's **safinamide** (filed) a dual mechanism of action drug that provides both MAO-B and glutamate inhibition, adenosine 2a (A2a) agonists such as Kyowa-Kirin's **istradefylline** (US: phase III SPA, Japan approved as Nourias) and Biotie's **tozadenant** (phase III 2015E), and Addex's **dipraglurant** (phase II), which targets metabotropic glutamate receptor 5 (mGluR5), and Santhera's **fipamezole**, an adrenergic alpha2 receptor antagonist (phase II).

## **Pipeline – next step is to capitalize on orphan drugs**

With sufficient funding at hand and safinamide close to market, Newron will now step up the development efforts for its orphan drug compounds and the schizophrenia drug NW-3509. The company wants to develop the orphan drugs up to pivotal phase results before seeking partners to maximize the long-term potential. In the case of NW-3509, Newron will start phase IIa proof-of-concept trials in Q4 2014 and then seek a major player at more attractive terms on positive results.

**NOTE: Only safinamide is in our current valuation, as the other projects have no validated proof-of-concept yet.**

### **1) Sarizotan (Rett syndrome) – Orphan drug with highest priority**

Within Newron's orphan drug portfolio sarizotan has gained highest priority, as it is likely the easiest and fastest drug to develop in a rare disease. The drug is targeted for the treatment of breathing disturbances in girls with Rett syndrome, where there is a high premature mortality rate and no specific cure. Sarizotan was in-licensed from Merck KGaA in March 2011, where it was originally developed for Parkinson's disease, but 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. Merck KGaA has a buy-back option upon completion of proof-of-concept trials, which triggers a co-development option for Newron. Given Merck KGaA's current therapeutic focus, we believe the company will not exercise its option for this niche indication. Orphan drug designation will provide sufficient market exclusivity.

### **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 16,000 patients in the US and 20,000 in the EU, with an incidence of 1 per 10-20,000 people. 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 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). 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<sub>1A</sub> receptors and partial agonist/antagonist at (dopamine) D<sub>2</sub> receptors. These are important receptors implicated in many neurological processes in the body including the regulation of blood pressure and heart beat (5HT<sub>1A</sub> receptors); and mood, cognition, memory and fine movement (D<sub>2</sub> receptors). Hyper-excited expiratory neurons in



the brain stem are believed to be involved in the breathing disturbance in Rett syndrome. 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. Due to its mechanism of action affecting important neurotransmitters, safinamide could have other potential benefits for Rett syndrome patients impacting behavior, cognition and neurological deficits.

#### **Clinical trial program – Pilot trial in 2014 followed by a single pivotal trial in 2015**

- **Small pilot trial in 2014:** Newron will start a small open label pilot trial in around 10 patients focusing on breathing symptoms in the EU and possibly the US, with results expected around the end of 2014. The company is in discussion with regulators to gain acceptance of the CMC (chemistry, manufacturing and controls), preclinical and clinical safety data package of sarizotan (acquired in Parkinson's disease), and to accept a single pivotal trial for approval in Rett syndrome.
- **Single pivotal trial in 2015:** Newron plans to start a phase II/III single potentially pivotal study in around 40 patients with results expected in 2016. This will be a double blind, placebo-controlled, multicenter (EU/US), randomized, crossover trial with a total duration of 29 weeks. Breathing symptoms could potentially be measured by a novel and convenient "life shirt" technology that records for instance apnea episodes. Newron is also interacting with the Rett Foundation for a potential buy-in, funding or co-sponsorship of the trials.

#### **Peak sales of EUR 480 mn in Rett syndrome (not included in valuation)**

In our view, peak sales could amount to EUR 480 mn assuming an annual treatment price of EUR 35,000 in the EU/ROW and USD 60,000 in the US with penetration rates up to 60%. The company will seek commercialization partners in key territories. Currently, we exclude sarizotan in our risk-adjusted NPV calculation for Newron due to the lack of proof-of-concept in humans. On the initiation of the single pivotal trial in 2015 we would conservatively assume a 25% success probability for this high-risk project in Rett syndrome.

## **2) sNN0031 (Parkinson's) - The perfect complement to safinamide**

This is a drug candidate stemming from the NeuroNova acquisition and is targeted for the treatment of Parkinson's disease in patients who no longer respond to oral therapy, and could be an alternative to deep brain stimulation. Therefore, the compound is a natural complement to safinamide. Roughly 4% of Parkinson's patients amounting to around 180,000 patients have become resistant to current oral treatments. sNN0031 should qualify for orphan designation, similar to AbbVie's Duodopa (a levodopa/carbidopa-containing gel given through a pump that is connected with a tube that is placed into the small intestine) that targets these severe treatment-resistant Parkinson's patients and was granted orphan drug exclusivity. sNN0031 was granted a method of use patent in the US and EU that protects beyond 2015, while orphan drug designation provides additional market exclusivity.

### **Potential to restore motor function and improve neuro-chemical deficits**

sNN0031 is a recombinant human Platelet Derived Growth Factor (rhPDGF) and is designed to act on neural stem and progenitor cells in the brain and is given through intracerebroventricular (ICV) delivery at regular intervals. This involves the administration of the drug through an external pump and a surgically implanted catheter directly into the ventricular system of the brain. In animal (primates) models of Parkinson's disease, sNN0031 has been shown to restore motor function and improve neuro-chemical deficits. In a phase I/II trial in patients with Parkinson's disease, the drug was well tolerated and demonstrated preliminary beneficial effects on biochemical markers of the degenerating dopamine system. Long-term follow-up of more than 2 years has not shown safety concerns. The results were presented at the 2013 Movement Disorder Society meeting.

### **Clinical trial program – Pilot trial in 2014 followed by a single pivotal trial in 2015**

- **Pilot trial in 2014:** Newron will start a new pilot trial in treatment-resistant Parkinson's patients to gain additional data and experience with the pump and delivery device and the required dose for the pivotal trial. A EUR 6 mn EU grant will support the next development steps.
- **Single pivotal trial in 2015:** In 2013 the company already had a pre-IND meeting with the FDA that agreed on a phase II/III single potentially pivotal trial with approximately 180 patients. No carcinogenicity or long-term toxicology studies are required. There will be a 6 months primary endpoint with 12 months safety data using an intermittent treatment paradigm in patients with debilitating symptoms on optimized oral Parkinson's treatment. The primary endpoint measure – presumably improvement in "ON time" without troublesome dyskinesia - will be finalized together with the FDA in a Special Protocol Assessment (SPA), and the CHMP in the EU in 2014. Results should be due in 2016 with approval and launch expected in 2017.

### **Peak sales of EUR 250+ mn in severe Parkinson's (not included in valuation)**

With around 180,000 patients in the US and Europe and an assumed annual treatment cost of between EUR 30,000 (in the EU/ROW) and USD 50,000 (in the US) per patient, and a penetration rate up to 4%, peak sales could amount to more than EUR 250 mn. Note that uptake of sNN0031 should be limited by the cumbersome delivery. With only 50 sales representatives needed to cover the US, we believe Newron will expand its US operations into a commercial organization to sell sNN0031, and find licensing partners in other key territories. We currently exclude sNN0031 from our risk-adjusted NPV for Newron due to the lack of proof-of-concept. On the initiation of the single potentially pivotal phase II/III trial in 2015 we would conservatively assume a 25% success probability for this novel but high-risk project.

### **3) sNN0029 (ALS) – Expensive and difficult orphan drug to develop**

sNN0029 is the second drug compound stemming from the NeuroNova acquisition and is targeted for the treatment of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. The compound is probably Newron's most expensive and complex orphan drug to develop. The current clinical development paradigm in ALS is 18 months treatment in 600-800 patients to demonstrate efficacy. Newron cannot afford this and would need a partner to start such a development program. However, the company is discussing alternative clinical trial designs with regulators, such as using responder rates after 6 months treatment with sNN0029 as a primary endpoint, and continued treatment afterwards to determine safety and other efficacy parameters. Given the recent failure of

Biogen Idec's dexamipexole in ALS, limited treatment options for this rapidly fatal disease, and sNN0029 novel approach, we believe such a clinical program would be feasible. sNN0029 is also given through cumbersome intracerebroventricular (ICV) delivery similar to sNN0031, only on a continuous base.

NeuroNova licensed the compound from VIB/Genentech (now Roche) that has an opt-in right for the US, Canada and Mexico. The drug was granted a method of use patent in the US and EU that protects beyond 2025, while orphan drug designation provides additional market exclusivity.

### **ALS – A rapidly fatal motor neuron disease with limited treatment options**

ALS is an orphan disease that affects roughly 20-25,000 people in the US and a similar amount in the EU, usually at the age of 40-60 years. Men are slightly more affected than women. The underlying cause is unknown, but ALS is a so-called motor neuron disease where the motor function of the central nervous system is progressively destroyed. Median survival time from onset to death is approximately 39 months. Patients experience rapidly progressive weakness, muscle wasting, spasticity, and difficulties in breathing, swallowing and speaking. Sanofi-Aventis' Rilutek, now generically available, is the only approved drug for ALS and improves survival by 2-3 months.

### **Potential to slow disease progression and increase life span**

sNN0029 is a recombinant human Vascular Endothelial Growth Factor 165 (rhVEGF165). There is strong pre-clinical data supporting a role for VEGF in ALS. In an ALS rat model VEGF deficient animals showed ALS-like disease development, while VEGF treatment prolonged life of the animals. sNN0029 is the first treatment targeting motor neurons by blocking activity of apoptotic genes (genes destroyed by programmed cell death). In preclinical animal trials, sNN0029 showed the ability to slow disease progression and increase life span. The drug has also been successfully tested in a three-month phase I/II safety and tolerability study in ALS patients, with a sign for dose dependent efficacy on key variables (ALS Functional Rating Scale, Slow Vital Capacity and Quality of Life). The patients have by now been followed for up to four years without safety concerns.

### **Clinical trial program – Phase I/II trial in 2014, a single pivotal trial in 2015?**

- **FDA meeting / Phase I/II trial in 2014:** Newron has a pre-IND meeting scheduled with the FDA to discuss the clinical development plans for sNN0029. The company will start a phase I/II safety and exploratory efficacy study that will measure motor unit activation after 3 months permanent treatment at a higher dose than in the previous trials. Results are expected in 2014. The trial will be supported by a EUR 2.5 mn grant obtained from the Wellcome Trust.
- **Single pivotal trial in 2015?:** This will be depend strongly on the ongoing discussions with the FDA and the outcomes of the phase I/II safety and exploratory efficacy study. The company plans for a phase II/III single potential pivotal trial to start in 2015 with results in 2016. Patients will be given 6 months permanent treatment through intracerebroventricular (ICV) delivery.

### **Peak sales of EUR 350+ mn in Lou Gehrig's disease (not included in valuation)**

On successful development, we believe peak sales could amount to EUR 350+ mn assuming an annual treatment cost of between EUR 40,000 and USD 60,000 per patient. Cumsome permanent ICV delivery will limit treatment to severely progressed patients (around 20% of ALS patients) with penetration rates reaching up to 60%. Given insufficient

proof-of-concept, we have excluded sNN0029 in our valuation. On the initiation of the single pivotal trial in 2015 we would conservatively assume a 25% success probability for this high-risk project in ALS.

### **NW-3509 - Next CNS drug addressing a blockbuster opportunity**

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. NW-3509 targets a large anti-psychotic market worth more than USD 23 bn with many drugs losing patent protection in the next few years. The drug can be added to current therapy for patients who no longer respond (roughly 65% of patients). Therefore NW-3509 has the potential to be developed in fixed-dose combinations with existing treatments extending their patent life substantially. NW-3509 enjoys an extensive patent life running until at least 2028 (excluding patent term extensions), thanks to the US Patent and Trade Organization that granted a solid composition of matter patent in 2013.

### **Lead indication schizophrenia targets a USD 9 bn market**

The schizophrenia market is currently worth about USD 9 bn, despite low patient compliance and many patients responding poorly to current antipsychotic therapy. NW-3509 would become a first-in-class voltage gated, selective sodium channel blocker specifically developed for schizophrenia therapy. The drug is being developed as an add-on therapy to current antipsychotic medication for schizophrenia patients who respond poorly. In August 2011 Newron received an IND approval from the FDA as an add-on to antipsychotics for patients with psychosis. Results from the ongoing phase I safety trial were disclosed at the SIRS (Schizophrenia International Research Society) meeting in April 2014. NW-3509 was well tolerated, exposure increased with dose, and exposure overlaps with exposure in animals at doses proven to be efficacious.

### **Clinical trial program – Start phase IIa trial in 2014 and seek a strong CNS player**

Now with sufficient funds available, the company will start a phase IIa trial in Q4 2014. Newron plans to develop NW-3509 up to phase IIa proof-of-concept in schizophrenia and then seek a strong CNS player in return for significant milestone and royalty payments. We believe this could occur in 2015/16 presenting a fast value creation step not captured in our risk-adjusted NPV of Newron.

# Income Statement

## NEWRON PHARMACEUTICALS

SHARE PRICE (CHF) 16.6

IFRS

INCOME STATEMENT (EUR MN)	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
<b>PRODUCT SALES (BY PARTNERS)</b>	<b>0</b>	<b>0</b>	<b>74</b>	<b>188</b>	<b>418</b>	<b>857</b>	<b>1'244</b>	<b>1'737</b>	<b>2'080</b>	<b>2'339</b>	<b>2'545</b>
CHANGE (%)				154%	122%	105%	45%	40%	20%	12%	9%
<b>PRODUCT SALES (BY NEWRON)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>2</b>	<b>19</b>	<b>37</b>	<b>46</b>	<b>56</b>	<b>67</b>	<b>78</b>
CHANGE (%)						1022%	95%	26%	22%	18%	16%
<b>ROYALTIES</b>	<b>0</b>	<b>0</b>	<b>8</b>	<b>22</b>	<b>65</b>	<b>132</b>	<b>185</b>	<b>242</b>	<b>281</b>	<b>312</b>	<b>338</b>
CHANGE (%)				184%	192%	104%	40%	31%	16%	11%	8%
<b>UPFRONT &amp; MILESTONE PAYMENTS</b>	<b>3</b>	<b>10</b>	<b>42</b>	<b>11</b>	<b>88</b>	<b>10</b>	<b>50</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
CHANGE (%)	-64%	211%	323%	-74%	701%	-89%	400%	-100%			
<b>REVENUES (EXCL. PARTNER SALES)</b>	<b>3.5</b>	<b>10.3</b>	<b>50.5</b>	<b>33.5</b>	<b>154.6</b>	<b>161.4</b>	<b>271.6</b>	<b>288.5</b>	<b>338.2</b>	<b>379.6</b>	<b>415.6</b>
CHANGE (%)	-60%	192%	389%	-34%	362%	4%	68%	6%	17%	12%	9%
<b>COGS</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>-0.3</b>	<b>-2.8</b>	<b>-5.5</b>	<b>-7.0</b>	<b>-8.5</b>	<b>-10.0</b>	<b>-11.7</b>
CHANGE (%)						1022%	95%	26%	22%	18%	16%
<b>GROSS PROFIT</b>	<b>4</b>	<b>10</b>	<b>50</b>	<b>33</b>	<b>154</b>	<b>159</b>	<b>266</b>	<b>282</b>	<b>330</b>	<b>370</b>	<b>404</b>
CHANGE (%)	-60%	192%	389%	-34%	361%	3%	68%	6%	17%	12%	9%
MARGIN	100%	100%	100%	100%	100%	98%	98%	98%	97%	97%	97%
<b>R&amp;D</b>	<b>-4.5</b>	<b>-8.7</b>	<b>-9.2</b>	<b>-13.0</b>	<b>-8.0</b>	<b>-2.0</b>	<b>-3.0</b>	<b>-4.0</b>	<b>-5.0</b>	<b>-6.0</b>	<b>-7.0</b>
CHANGE (%)	-16%	28%	92%	6%	41%	-38%	-75%	50%	33%	25%	20%
AS % REVENUES	128%	84%	18%	39%	5%	1%	1%	1%	1%	2%	2%
<b>S,G&amp;A</b>	<b>-6.8</b>	<b>-7.3</b>	<b>-7.4</b>	<b>-7.5</b>	<b>-12.2</b>	<b>-16.8</b>	<b>-18.6</b>	<b>-19.9</b>	<b>-21.3</b>	<b>-22.7</b>	<b>-24.3</b>
CHANGE (%)	-16%	41%	2%	1%	62%	38%	10%	7%	7%	7%	7%
AS % REVENUES	192%	70%	15%	22%	8%	10%	7%	7%	6%	6%	6%
<b>OPERATING EXPENSES</b>	<b>-11.3</b>	<b>-16.0</b>	<b>-16.6</b>	<b>-20.5</b>	<b>-20.4</b>	<b>-21.7</b>	<b>-27.1</b>	<b>-30.8</b>	<b>-34.7</b>	<b>-38.8</b>	<b>-43.0</b>
CHANGE (%)	-3%	41%	4%	23%	0%	6%	25%	14%	13%	12%	11%
AS % REVENUES	320%	155%	33%	61%	13%	13%	10%	11%	10%	10%	10%
<b>EBITDA</b>	<b>-7.7</b>	<b>-5.6</b>	<b>33.9</b>	<b>13.0</b>	<b>134.3</b>	<b>139.7</b>	<b>244.6</b>	<b>257.7</b>	<b>303.6</b>	<b>340.9</b>	<b>372.7</b>
CHANGE (%)	194%	-27%	-704%	-62%	931%	4%	75%	5%	18%	12%	9%
MARGIN (%)	-219%	-54%	67%	39%	87%	87%	90%	89%	90%	90%	90%
<b>DEPRECIATION &amp; AMORTISATION</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.1</b>	<b>0.1</b>	<b>0.1</b>	<b>0.1</b>	<b>0.1</b>
AS % REVENUES	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
<b>EBIT</b>	<b>-7.8</b>	<b>-5.7</b>	<b>33.9</b>	<b>13.0</b>	<b>134.2</b>	<b>139.7</b>	<b>244.5</b>	<b>257.7</b>	<b>303.5</b>	<b>340.8</b>	<b>372.7</b>
CHANGE (%)	188%	-27%	-699%	-62%	935%	4%	75%	5%	18%	12%	9%
MARGIN (%)	-220%	-55%	67%	39%	87%	87%	90%	89%	90%	90%	90%
<b>NET FINANCIAL INCOME/(EXPENSE)</b>	<b>0.1</b>	<b>0.6</b>	<b>1.1</b>	<b>1.6</b>	<b>2.6</b>	<b>3.6</b>	<b>4.6</b>	<b>5.6</b>	<b>6.6</b>	<b>7.6</b>	<b>8.6</b>
<b>PROFIT BEFORE TAXES</b>	<b>-7.7</b>	<b>-5.1</b>	<b>34.9</b>	<b>14.5</b>	<b>136.8</b>	<b>143.3</b>	<b>249.1</b>	<b>263.3</b>	<b>310.1</b>	<b>348.4</b>	<b>381.2</b>
CHANGE (%)	209%	-34%	-786%	-58%	841%	5%	74%	6%	18%	12%	9%
MARGIN	-218%	-49%	69%	43%	88%	89%	92%	91%	92%	92%	92%
<b>TAXES</b>	<b>0.6</b>	<b>0.0</b>	<b>0.1</b>	<b>2.3</b>	<b>-37.1</b>	<b>-44.9</b>	<b>-74.9</b>	<b>-80.7</b>	<b>-94.2</b>	<b>-105.5</b>	<b>-115.3</b>
<b>NET PROFIT/LOSS</b>	<b>-7.1</b>	<b>-5.1</b>	<b>35.0</b>	<b>16.8</b>	<b>99.7</b>	<b>98.4</b>	<b>174.2</b>	<b>182.6</b>	<b>215.9</b>	<b>242.9</b>	<b>266.0</b>
CHANGE (%)	198%	-28%	-787%	-52%	494%	-1%	77%	5%	18%	13%	9%
MARGIN (%)	-201%	-49%	69%	50%	64%	61%	64%	63%	64%	64%	64%
<b>NET PROFIT/LOSS (EXCLUDING MILESTONES)</b>	<b>-10.3</b>	<b>-15.1</b>	<b>-7.4</b>	<b>5.8</b>	<b>11.7</b>	<b>88.4</b>	<b>124.2</b>	<b>182.6</b>	<b>215.9</b>	<b>242.9</b>	<b>266.0</b>
MARGIN (%)	-291%	-146%	-15%	17%	8%	55%	46%	63%	64%	64%	64%
<b>PROFIT/(LOSS) PER SHARE (IN EUR)</b>	<b>-0.62</b>	<b>-0.39</b>	<b>2.68</b>	<b>1.29</b>	<b>7.64</b>	<b>7.55</b>	<b>13.36</b>	<b>14.00</b>	<b>16.55</b>	<b>18.62</b>	<b>20.39</b>
<b>PROFIT/(LOSS) PER SHARE (IN CHF)</b>	<b>-0.76</b>	<b>-0.47</b>	<b>3.26</b>	<b>1.56</b>	<b>9.29</b>	<b>9.17</b>	<b>16.23</b>	<b>17.01</b>	<b>20.12</b>	<b>22.64</b>	<b>24.79</b>

ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES

# Ratios & Balance Sheet

## NEWRON PHARMACEUTICALS

SHARE PRICE (CHF) 16.6

RATIOS	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
P/E		-34.9x	5.1x	10.6x	1.8x	1.8x	1.0x	1.0x	0.8x	0.7x	0.7x
P/S		17.2x	3.5x	5.3x	1.1x	1.1x	0.7x	0.6x	0.5x	0.5x	0.4x
P/NAV		11.1x	3.5x	2.6x	1.1x	0.7x	0.4x	0.3x	0.2x	0.2x	0.1x
EV/EBITDA		-26.0x	4.3x	11.2x	1.1x	1.0x	0.6x	0.6x	0.5x	0.4x	0.4x

PER SHARE DATA (CHF)	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
<b>EARNINGS</b>	<b>-0.76</b>	<b>-0.47</b>	<b>3.26</b>	<b>1.56</b>	<b>9.29</b>	<b>9.17</b>	<b>16.23</b>	<b>17.01</b>	<b>20.12</b>	<b>22.64</b>	<b>24.79</b>
CHANGE (%)	116%	-37%	-787%	-52%	494%	-1%	77%	5%	18%	13%	9%
<b>CASH</b>	<b>1.97</b>	<b>2.24</b>	<b>4.82</b>	<b>5.47</b>	<b>17.47</b>	<b>30.03</b>	<b>52.42</b>	<b>76.08</b>	<b>104.06</b>	<b>135.56</b>	<b>170.25</b>
CHANGE (%)	-54%	14%	115%	13%	220%	72%	75%	45%	37%	30%	26%
<b>DIVIDENDS</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>	<b>0.00</b>
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
<b>NET ASSET VALUE</b>	<b>2.25</b>	<b>1.49</b>	<b>4.75</b>	<b>6.31</b>	<b>15.60</b>	<b>24.77</b>	<b>41.01</b>	<b>58.02</b>	<b>78.14</b>	<b>100.78</b>	<b>125.57</b>
CHANGE (%)	-45%	-34%	219%	33%	147%	59%	66%	41%	35%	29%	25%

BALANCE SHEET (EUR MN)	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
<b>NET LIQUID FUNDS</b>	<b>18.4</b>	<b>24.0</b>	<b>51.7</b>	<b>58.6</b>	<b>187.4</b>	<b>322.2</b>	<b>562.4</b>	<b>816.3</b>	<b>1'116.4</b>	<b>1'454.4</b>	<b>1'826.7</b>
<b>TOTAL ASSETS</b>	<b>31.6</b>	<b>37.2</b>	<b>64.9</b>	<b>71.8</b>	<b>200.6</b>	<b>335.4</b>	<b>575.6</b>	<b>829.4</b>	<b>1'129.6</b>	<b>1'467.6</b>	<b>1'839.9</b>
<b>SHAREHOLDERS' EQUITY</b>	<b>21.1</b>	<b>16.0</b>	<b>51.0</b>	<b>67.8</b>	<b>167.4</b>	<b>265.8</b>	<b>440.0</b>	<b>622.5</b>	<b>838.4</b>	<b>1'081.3</b>	<b>1'347.3</b>
CHANGE (%)	-24%	-24%	219%	33%	147%	59%	66%	41%	35%	29%	25%
RETURN ON EQUITY (%)	-34%	-32%	69%	25%	60%	37%	40%	29%	26%	22%	20%
<b>FINANCIAL DEBT</b>	<b>1.4</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>
FINANCIAL DEBT AS % OF TOTAL ASSETS	5%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
<b>EMPLOYEES</b>	<b>24</b>	<b>24</b>	<b>25</b>	<b>26</b>	<b>27</b>	<b>27</b>	<b>28</b>	<b>29</b>	<b>30</b>	<b>31</b>	<b>32</b>
CHANGE (%)	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%

CASH FLOW STATEMENT (EUR MN)	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
<b>NET PROFIT / (LOSS)</b>	<b>-7.7</b>	<b>-5.1</b>	<b>34.9</b>	<b>14.5</b>	<b>136.8</b>	<b>143.3</b>	<b>249.1</b>	<b>263.3</b>	<b>310.1</b>	<b>348.4</b>	<b>381.2</b>
DEPRECIATION & AMORTIZATION	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1
OTHER NON-CASH ITEMS	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
<b>CASH FLOW</b>	<b>-7.0</b>	<b>-4.4</b>	<b>35.6</b>	<b>15.2</b>	<b>137.5</b>	<b>144.0</b>	<b>249.8</b>	<b>264.0</b>	<b>310.8</b>	<b>349.1</b>	<b>382.0</b>
NET INCREASE/(DECREASE) IN WORKING CAPITAL	-4.9	-7.4	-7.8	-8.1	-8.6	-9.0	-9.4	-9.9	-10.4	-10.9	-11.5
<b>OPERATING FREE CASH FLOW</b>	<b>-10.7</b>	<b>-11.9</b>	<b>27.7</b>	<b>7.0</b>	<b>128.8</b>	<b>134.9</b>	<b>240.2</b>	<b>253.9</b>	<b>300.2</b>	<b>338.0</b>	<b>371.3</b>
NET CASH FLOWS FROM INVESTING ACTIVITIES	0.2	-0.1	-0.1	-0.1	-0.1	-0.1	-0.1	-0.1	-0.1	-0.1	0.9
<b>NET CASH USED IN OPERATING ACTIVITIES</b>	<b>-10.5</b>	<b>-11.9</b>	<b>27.7</b>	<b>6.9</b>	<b>128.8</b>	<b>134.8</b>	<b>240.2</b>	<b>253.9</b>	<b>300.2</b>	<b>338.0</b>	<b>372.3</b>
NET CASH FLOWS FROM FINANCING ACTIVITIES	-0.4	17.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
<b>NET INCREASE/(DECREASE) IN CASH AND CASH EQUIVALENTS</b>	<b>-10.8</b>	<b>5.6</b>	<b>27.7</b>	<b>6.9</b>	<b>128.8</b>	<b>134.8</b>	<b>240.2</b>	<b>253.9</b>	<b>300.2</b>	<b>338.0</b>	<b>372.3</b>

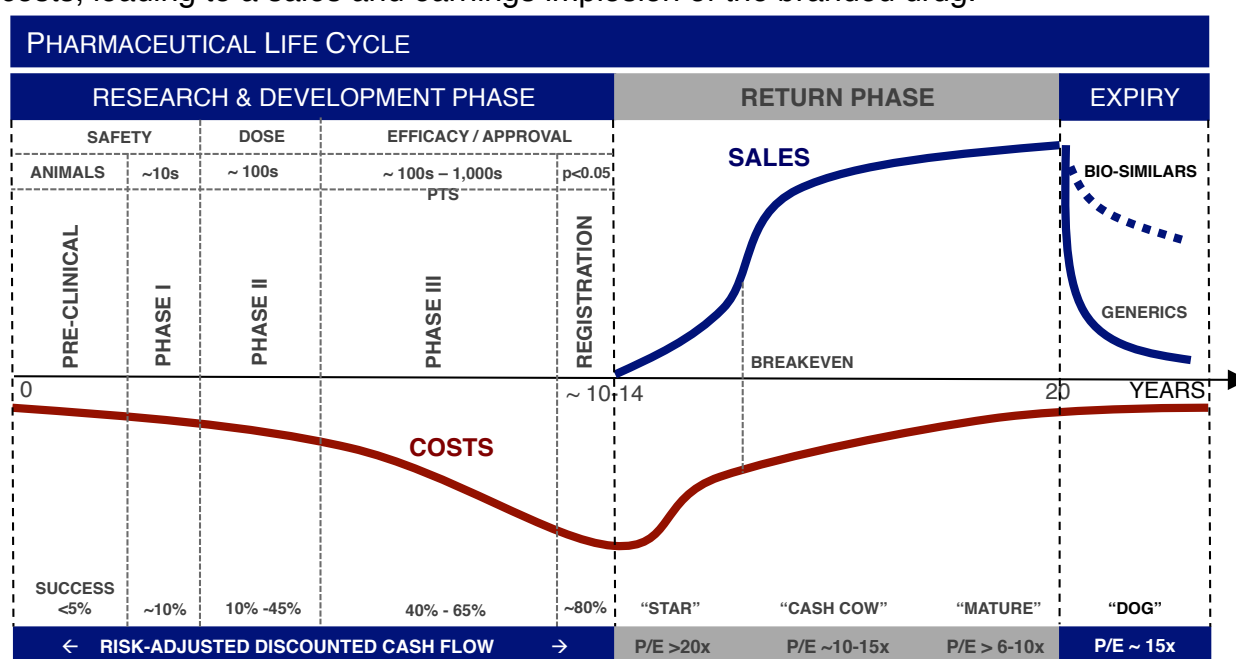
ESTIMATES AS OF 16 SEPTEMBER, 2014

SOURCE: VALUATIONLAB ESTIMATES

# 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)	5-10	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-15		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	10-35	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	less than 2 years cash and sales from 2 or less marketed products
Medium Risk	more than 3 years cash and sales from at least 2 marketed products (patent expiry > 5 years)
Low Risk	self-sustaining cash flows, sales from > 3 marketed products (patent expiry > 5 years)

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