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

KEY DATA		SIX: NWRN	
MARKET CAPITALIZATION (CHF MN)	105	PRICE ON JULY 03, 2013	9.0
ENTERPRISE VALUE (CHF MN)	69	RISK-ADJUSTED NPV PER SHARE (CHF)	14.6
NET CASH (YE 2012) (CHF MN)	35	UPSIDE/DOWNSIDE (%)	62%
MONTHLY OPERATING EXPENSE (CHF MN)	1.2	RISK PROFILE	HIGH
CASH LIFE	2015	SUCCESS PROBABILITY LEAD PIPELINE DRUG	65%
BREAK-EVEN (YEAR)	2016	EMPLOYEES (GROUP)	23
FOUNDED (YEAR)	1998	LISTED (YEAR)	2006
<b>KEY PRODUCTS:</b>		<b>MAJOR SHAREHOLDERS:</b>	(%)
- SAFINAMIDE (PARKINSON'S DISEASE)	STATUS	- INVESTOR AB (SHAREHOLDER AGREEMENT)	13.1
- SARIZOTAN (RETT'S SYNDROME)	PHASE II/III	- ZAMBON GROUP (SHAREHOLDER AGREEMENT)	12.8
- SNN0031 (PARKINSON'S DISEASE)	PHASE II/III	- AVIVA	6.2
- SNN0029 (AMYOTROPHIC LATERAL SCLEROSIS)	PHASE II	- EXECUTIVE MANAGEMENT	0.7
- NW-3509 (SCHIZOPHRENIA)	PHASE I	- FREE FLOAT	73.4
<b>UPCOMING CATALYSTS:</b>		<b>ANALYST(S):</b>	<b>BOB POOLER</b>
- SARIZOTAN (RETT'S) START PHASE II/II TRIAL	DATE		BP@VALUATIONLAB.COM
- SNN0031 (PD) START PHASE II/III TRIAL	2013		+41 79 652 67 68
- US/EU FILING SAFINAMIDE (PARKINSON'S)	2013		
	Q4 2013		

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

# Persistence pays off

## Substantial revenues from safinamide ahead

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, potentially the first once a day oral add-on therapy for all stages of Parkinson's disease. The company has successfully completed pivotal phase III trials for safinamide and plans to file for approval in the US and the EU in Q4 2013. 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 of EUR 29 mn (plus EUR 11 mn commitments) Newron is funded halfway into 2015, and is sufficiently financed to advance other pipeline assets including rare diseases drugs for Rett's syndrome, ALS and severe, treatment resistant, Parkinson's disease. We derive a risk-adjusted NPV value of CHF 14.6 per share with a 65% success probability for lead pipeline project safinamide. Because Newron has no sustainable revenues from products on the market yet, we qualify the risk profile as high.

### Key catalysts:

- 1) Global filing safinamide in Q4 2013.** Newron and partner Zambon plan to file safinamide for approval in Parkinson's disease in the US and EU at the end of 2013. A successful filing should raise our success probability to 80% (from 65%) leading to a 28% jump of our risk-adjusted NPV to CHF 18.6 (from CHF 14.6).
- 2) US partner for safinamide.** Newron expects that its partner Zambon will sub-license safinamide in the US (and potentially other territories), which should trigger substantial upfront milestone payments and royalties on future sales.
- 3) Start clinical trials of four new drugs.** In 2013 Newron plans to start clinical trials for sNN0031 (severe, treatment resistant, Parkinson's disease), sNN0029 (ALS/Lou Gehrig's), sarizotan (Rett's syndrome) and 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). This therapeutic focus is a result of: 1) the company's expertise in ion channel research, an important class of CNS drugs, 2) a development agreement signed with Merck KGaA in 2011 and 3) the acquisition of NeuroNova AB with two promising orphan drug candidates in 2012.

## **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 now close to filing and market launch**

Newron, together with its global partner Zambon (ex-Japan & Asian markets), is currently preparing the US and EU filing for its lead pipeline project safinamide for the treatment of Parkinson's disease. Filing should occur in Q4 2013 with first launches expected roughly a year later. Safinamide is a once a day oral add-on to dopamine agonists (early stage Parkinson's) and levodopa and other Parkinson's medications in patients with motor fluctuations (mid to late stage disease), and could become the first add-on therapy to treat all disease stages from early to late. This could position the drug as the new cornerstone treatment in Parkinson's disease.

## **Safinamide - the comeback kid**

The development of safinamide up to filing was far from easy. At times it led to quite some turmoil with a change of partners and concerns of sufficient funding for the company. Importantly, the clinical development program remained unchanged and was executed flawlessly. The persistence and belief of Newron's management team, together with a handful of stakeholders, in the value of safinamide was relentless. Thanks to their dedication, and a bit of luck, safinamide is now close to filing and market launch.

## **From preclinical epilepsy project to a new treatment for Parkinson's disease**

Safinamide started as a spinout of an early preclinical project for epilepsy from Pharmacia & Upjohn. Newron spent most of its pre-IPO money on successfully developing safinamide to a first positive phase III trial for early stage Parkinson's disease.

Around the time of the IPO in late 2006 Newron licensed the global rights of safinamide to Serono, which was just acquired by Merck KGaA. This initially caused investor uncertainty as Merck KGaA had its own Parkinson's disease projects, also in an advanced stage. Luckily, the new Merck Serono division decided to continue development of safinamide in Parkinson's according to Newron's original plan.

### **Ralfinamide setback followed by Merck Serono returning safinamide rights**

After the failure of Newron's second key drug ralfinamide in neuropathic low back pain in early 2010, the company was forced to reorganize and reduce costs by cutting staff and reconsider all strategic options. In September 2011, Biotie a Finnish biopharmaceutical company announced the friendly acquisition of Newron to increase its critical mass and broaden its portfolio with safinamide. Only a month later Merck Serono, in a surprise move, decided to give back the global rights of safinamide to Newron due to a strategic portfolio re-prioritization. As a result Biotie abandoned the acquisition, with Newron having to explore all strategic options, again.

### **All turned positive in 2012**

Fortunately, in January 2012 Newron was able to sign on Meiji Seika for the Japanese and Asian rights for safinamide. And in April 2012 Newron and Zambon entered into a strategic collaboration and license option for safinamide in the EU and US with Zambon making an initial investment of EUR 20 mn partially in equity and covering further development and registration costs for safinamide. And that all ahead of the phase III "SETTLE" and "MOTION" pivotal trial results! In May 2012 Newron reported both trials met their primary endpoints. The trials were presented at the American Academy of Neurology in March 2013.

### **NeuroNova acquisition strengthens Newron pipeline and provides cash into 2015**

2012 was an important transition year for Newron with the company reporting positive phase III results for safinamide and the signing on of strategic partner Zambon and Meiji Seika. The transition also includes the acquisition of NeuroNova, a privately held Swedish biopharmaceutical company. After two failed attempts by Newron earlier in the year, the acquisition was completed at the end of 2012 and at better terms. The NeuroNova acquisition was important to Newron because it: 1) provided cash until 2015, with no need for Newron to go back to the financial markets in the near term with the risk of dilution, 2) added two complimentary orphan CNS drugs close to major milestones, 3) provided surplus cash to support further development of two Newron drugs, NW-3509 and sarizotan, to reach new value inflection points, and 4) broadened Newron's knowledge and investor base with two renowned life science investors, Investor AB and Healthcap.

### **A total of EUR 209.7 mn raised since inception from various channels**

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 almost EUR 210 mn.

<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		18.5
NEURONOVA ACQUISITION		16.0
<b>TOTAL RAISED</b>		<b>209.7</b>

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

Prior to the IPO in 2006, management raised EUR 62.2 mn in three financing rounds. The company 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,

Please see important research disclosures at the end of this document

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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. With net cash of EUR 29.2 mn at the end of 2012, Newron's average annual cash burn since inception amounts to EUR 13.7 mn.

### Global filing and sub-licensing safinamide #1 priority in 2013

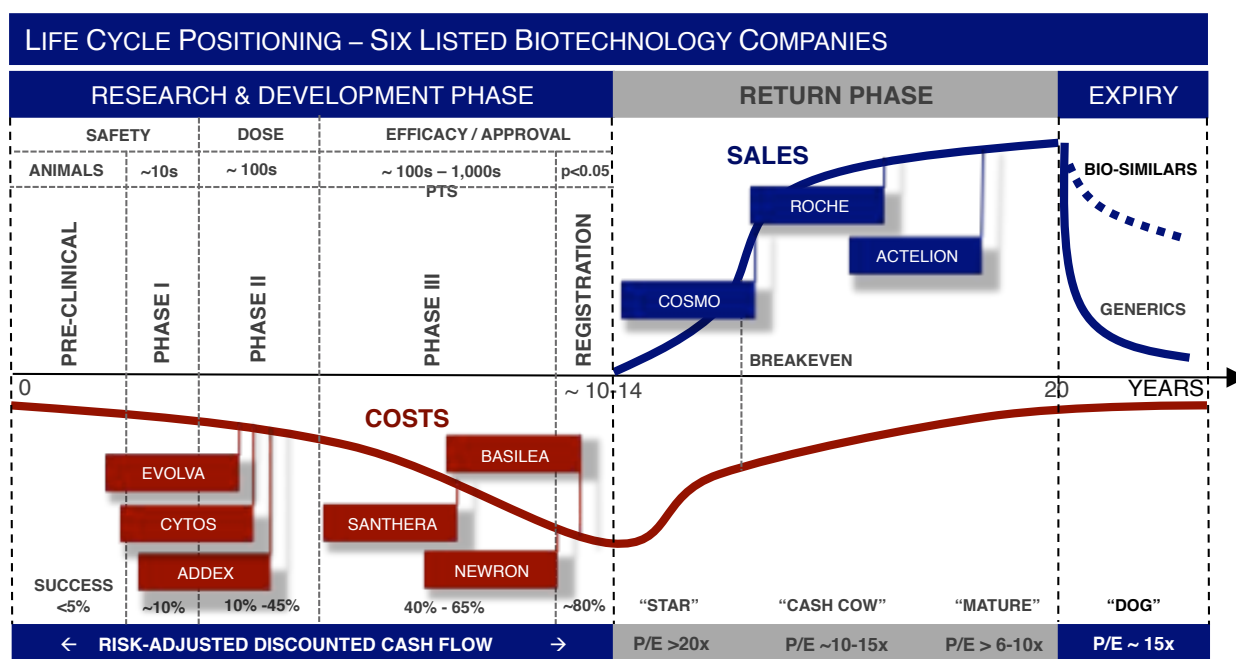
Newron's number one priority for 2013 is finalizing the US and EU regulatory submission of safinamide in Parkinson's disease in Q4. The company is supporting its partner Zambon in seeking for commercialization partners for safinamide in those territories where Zambon has no or a low presence. The lucrative US market has the first 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.

### Newron comfortably funded halfway into 2015

At the end of FY 2012 Newron reported it has EUR 29.2 mn in cash plus EUR 11 mn in additional commitments. Assuming operating expenses of around EUR 50 mn and no other revenues for the next three years, the company should be funded halfway into 2015.

### Life Cycle Positioning - High Risk

We qualify Newron as high risk, because the company currently has no products on the market that can provide sustainable revenue streams, with cash life reaching into 2015. First material cash flows from safinamide are expected around the end of 2014 with a potential "sustainable" breakeven, where the company is no longer dependent on new partnering milestones, to be reached in 2016. (See Income Statement)



SOURCE: VALUATIONLAB

# Valuation Overview

## Risk-adjusted sum-of-parts NPV points to a fair value of CHF 14.6 per share

We derive a risk-adjusted NPV of CHF 14.6 per share with net cash of CHF 4.3 per share (YE 2012) and overhead expenses of CHF 7.4 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	497	2014	27.2	65%	17.7	80%
sNN0031	PARKINSON'S DISEASE	225	2016	8.4	0%	0.0	0%
sNN0029	ALS (LOU GEHRIG'S DISEASE)	261	2017	14.0	0%	0.0	0%
NW-3509	SCHIZOPHRENIA	794	2019	18.8	0%	0.0	0%
SARIZOTAN	RETT'S SYNDROME	230	2016	9.1	0%	0.0	0%
RALFINAMIDE	NEUROPATHIC PAIN	264	2017	10.7	0%	0.0	0%
HF 1020 (TRIDENT SPV)	ASTHMA	N.M.	N.M.	0.4	0%	0.0	0%
NET CASH POSITION (YE 2012)		29		4.3		4.3	20%
<b>TOTAL ASSETS</b>				<b>92.9</b>		<b>22.0</b>	<b>100%</b>
OVERHEAD EXPENSES				-7.4		-7.4	
<b>NPV/SHARE (CHF)</b>				<b>85.5</b>		<b>14.6</b>	
SHARE PRICE ON JULY 03, 2013						9.0	
PERCENTAGE UPSIDE / (DOWNSIDE)						62%	

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

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

### Safinamide (Parkinson's disease) - risk-adjusted NPV of CHF 17.7 per share

Safinamide is Newron's first drug ever drug to be filed for approval with first launches expected at the end of 2014. The filing is based on positive pivotal trials presented in 2013 for early (as an add-on to dopamine agonists) and mid to late stage Parkinson's disease (as an add-on to levodopa and other dopaminergic treatments). We assume Newron will receive up to EUR 61 mn in milestone payments from its partners Zambon, Meiji Seika 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 17.7 per share for safinamide in Parkinson's disease with peak sales amounting to EUR 500 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 provides a "sneak preview" on what the value could amount to if our assumptions were reached.

**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 2013 with results at the end of 2015. Peak sales could reach EUR 225 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 is planned for 2015 with results in 2016. Peak sales could reach EUR 260 mn.

**Sarizotan** targets respiratory disturbances in Rett's syndrome, a rare disease affecting primarily girls. A phase II/III single pivotal trial should start in 2013 with results in 2015. Peak sales could reach EUR 230 mn. Merck KGaA has a buy-back option.

**NW-3509** targets schizophrenia and therefore presents a blockbuster sales opportunity. Phase I trials have started in 2013. Newron plans to out-license the drug after successful phase I/Ib development, which could occur around the end of 2014.

# Catalysts

The year started well with the presentation of the phase III "MOTION" and "SETTLE" trials at the American Academy of Neurology in March. Both trials met their primary endpoints as well as several secondary endpoints. Safinamide was well tolerated in both early stage and mid to late stage Parkinson's patients.

Strategic partners Zambon and Investor entered into a long-term shareholders commitment.

The Wellcome Trust awarded EUR 2.5 mn for further development of sNN0029 in ALS.

At the AGM, long-time chairman Rolf Stahel stepped down with Ulrich Köstlin, a Bayer Schering executive, taking over his responsibility. Robert Leslie Holland, a CNS expert, and Bo Jesper Hansen, an orphan drug expert, strengthened the board.

CATALYST TIMELINES					
TIME LINE	PRODUCT	INDICATION	MILESTONE	COMMENT	IMPACT
<b>2013</b>					
28 JANUARY			SHAREHOLDER AGREEMENT	ZAMBON AND INVESTOR SIGN A LONG-TERM SHAREHOLDER AGREEMENT	
4 FEB	sNN0029	ALS	WELLCOME TRUST AWARD	EUR 2.5 MN STRATEGIC TRANSLATION AWARD RECEIVED FROM WELLCOME TRUST TO HELP FUND PHASE I/II TRIALS IN ALS	
18 MARCH	SAFINAMIDE	PARKINSON'S	PRESENTATION PIVOTAL TRIALS AT AAN MEETING	PHASE III "MOTION" AND "SETTLE" TRIAL MEET PRIMARY ENDPOINTS, SAFINAMIDE WELL TOLERATED IN BOTH TRIAL GROUPS	
19 MARCH			FY 2012 RESULTS	WELL FUNDED INTO 2015 WITH EUR 29.2 MN OF CASH AND EUR 11 MN IN COMMITMENTS - POSITIVE PIVOTAL SAFINAMIDE TRIALS PRESENTED TO INVESTMENT COMMUNITY	
18 APRIL			AGM	ANNUAL SHAREHOLDER'S MEETING BRESSO (MILAN), ITALY - CHAIRMAN ROLF STAHEL STEPPING DOWN AFTER >9 YEARS ON BOARD, ULRICH KÖSTLIN (BAYER SCHERING EXECUTIVE) ACCEPTED AS NEW CHAIRMAN, ROBERT LESLIE HOLLAND (CNS EXPERT), BO JESPER HANSEN (ORPHAN DRUG EXPERT) JOIN BOARD	
Q2	NW-3509	SCHIZOPHRENIA	START PHASE I	PLANNED AS ADD-ON THERAPY TO ANTIPSYCHOTICS FOR PATIENTS WITH PSYCHOSIS	
	SAFINAMIDE	PARKINSON'S	PARTNERING	ZAMBON TO SEEK PARTNERING AGREEMENTS FOR THE US AND SELECTED EU MARKETS (TRIGGERS MILESTONES PAYMENTS)	
	sNN0029	ALS	START PHASE I/II	START OF PHASE I/II TRIAL WITH 6 MONTHS OF TREATMENT TO EVALUATE SAFETY & EFFICACY HIGHER DOSES IN ALS PATIENTS - FUNDED BY WELLCOME TRUST GRANT (EUR 2.5 MN)	
	sNN0031	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)	
	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)	
10 SEP			H1 2013 RESULTS		
Q4	SAFINAMIDE	PARKINSON'S	FILING	US AND EU FILING - SUCCESS PROBABILITY JUMPS TO 80% (FROM 65%)	+CHF 4.1

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

For the remainder of the year the company will start clinical trials of **sNN0029** in ALS (Lou Gehrig's disease), **sNN0031** in severe treatment-resistant Parkinson's disease, and **NW-3509** in schizophrenia.

## Upcoming key catalysts for the year include:

- 1) **The US and EU filing of safinamide in Parkinson's in Q4.** Our current success probability of 65% (phase III completion) would rise to 80% (filing) with our risk-adjusted NPV for Newron jumping by 28%, or CHF 4.1, to CHF 18.6 per share.
- 2) **Sub-licensing agreements for safinamide in the US and selected EU markets.** These should trigger milestone and royalty payments, thereby further validating safinamide's value proposition.

# Technology & Pipeline

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

Prior to the acquisition of NeuroNova, 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, and 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. Nevertheless, the medical need is great and currently unmet. 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.

PRODUCT PIPELINE						
PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH DATE (EXPECTED)	PARTNER	PEAK SALES
SAFINAMIDE	ALPHA-AMINOAMIDE	PARKINSON'S DISEASE	FILING	Q4 2014	ZAMBON/MEIJI SEIKA	EUR 500 MN
SARIZOTAN	DOPAMINE RECEPTOR BLOCKER	RETT SYNDROME (ORPHAN INDICATION)	PHASE II/POC	2016	MERCK KGAA	EUR 230 MN
sNN0031	PLATELET-DERIVED GROWTH FACTOR	SEVERE NON-RESPONDING PARKINSON'S DISEASE (ORPHAN INDICATION)	PHASE II/POC	2016	NEURONOVA	EUR 225 MN
sNN0029	VASCULAR ENDOTHELIAL GROWTH FACTOR	AMYOTROPHIC LATERAL SCLEROSIS (ORPHAN INDICATION)	PHASE II/POC	2017	NEURONOVA	EUR 260 mn
NW-3509	ION CHANNEL BLOCKER	SCHIZOPHRENIA	IND	2019	TO BE PARTNERED AFTER PHASE I/IB	EUR 800 MN
RALFINAMIDE	ION CHANNEL BLOCKER	NON-RESPONDING SEVERE NEUROPATHIC PAIN (ORPHAN INDICATION)	POC	2018	2ND PRIORITY - PARTNER BEFORE STARTING TRIALS	EUR 260 mn

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

## 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 diseases. These are rare diseases with less than 200,000 people affected.

### Key advantages for orphan drugs include:

- High unmet medical need for a relatively small patient population
- Faster speed to market
- Lower development costs, lower regulatory hurdles
- Higher selling prices and gross profit
- Additional market protection up to 7 (US) and 10 years (EU)

### 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. 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.

## **R&D pipeline a nice mix of CNS & orphan drugs**

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's syndrome), and the two NeuroNova drugs sNN0029 (ALS) and sNN0031 (severe resistant Parkinson's). A fourth drug could be added once Newron finds a partner for ralfinamide in orphan neuropathic pain indications.

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

### **NW-3509 - the next proprietary CNS drug addressing a large market 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. NW-3509 would become a first-in-class voltage gated, selective sodium channel blocker being specifically developed for schizophrenia therapy. The drug is targeted as the first 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. Now with sufficient funds available, the company will start the first phase I safety trial in Q2 2013. Newron plans to develop NW-3509 up to phase I/Ib and then seek a partner in return for milestone and royalty payments. This could occur in 2014/15. 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 enjoys an extensive patent life beyond 2028 and could become a blockbuster-selling drug.

### **sNN0031 - the natural complement to safinamide in Parkinson's disease**

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. sNN0031 is designed to act on neural stem and progenitor cells in the brain and is given through intracerebroventricular (ICV) delivery. This involves the administration of the drug through a pump and a surgically implanted catheter directly into the ventricular system of the brain. In animal 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.

A EUR 6 mn EU grant will support the next development steps. This will be a global trial of 12 months intermittent treatment in patients with debilitating symptoms on optimized oral Parkinson's treatment and is planned to start this year with results expected in 2015. Licensing and filing in key territories should occur around the same time. Newron is currently in discussion with the regulatory authorities including the FDA on the design of the study and the primary efficacy measure. The drug should qualify as an orphan indication, 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). With around 180,000 patients in the US and Europe and an assumed treatment cost of USD

40,000 per patient, sNN031 could address a large market opportunity. However uptake should be limited by the cumbersome delivery.

### **sNN0029 - targeting ALS a fatal disease with virtually no treatment options**

This is the second drug candidate stemming from the NeuroNova acquisition and is targeted for the treatment of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. This is a 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 several months.

In preclinical animal trials, sNN0029 has demonstrated 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. The patients have by now been followed for up to three years. A EUR 2.5 mn grant obtained from the Wellcome Trust will support a phase I/II safety and efficacy trial at a higher dose, to start in 2013 with results expected in 2014. Patients will be given 6 months permanent treatment. sNN0029 is also given through intracerebroventricular (ICV) delivery. A phase II/III single potential pivotal trial is planned for 2015 with results in 2016.

### **Sarizotan - potential to restore disordered breathing in girls with Rett's syndrome**

Sarizotan, in-licensed from Merck KGaA in March 2011, is targeted for the treatment of breathing disturbances in girls with Rett's syndrome. This is a severe neuro-development disorder primarily affecting females with approximately 16,000 patients in the US and 20,000 in the EU. 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 and disordered breathing. 26% of deaths in girls with Rett's syndrome are attributed to sudden disordered breathing. There is no specific cure for Rett's syndrome.

Sarizotan has demonstrated positive preclinical data in a genetic knockout model, and there is a strong rationale for restoring the regular respiratory rhythms through the modulation of the medullar respiratory network with the drug. Newron plans to start a phase II/III single potentially pivotal study in around 40 patients in 2013 with results expected in 2015. This will be a double blind, placebo-controlled, multicenter, randomized, crossover trial with a total duration of 29 weeks. Merck KGaA has a buy-back option.

### **Ralfinamide - second priority, partner needed first**

The development of ralfinamide in orphan neuropathic pain indications is currently on the backburner until a partner is found to fund development in these indications.

In the following section we will provide an in-depth analysis and forecasts for Newron's key driver **safinamide** in Parkinson's disease.

# Forecasts & Sensitivity Analysis

## Safinamide (Parkinson's Disease)

### Product Analysis

#### Parkinson's peak sales of EUR 500 mn - Risk-adjusted NPV of CHF 17.7 per share

We forecast peak sales of EUR 500 mn for safinamide, assuming first market launches at the end of 2014, patent protection until 2024 (EU/ROW) and 2026 (US), 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%. Our risk-adjusted NPV amounts to CHF 205 mn, or CHF 17.7 per share, assuming Newron receives a total of EUR 61 mn milestone payments, royalties on sales ranging between 10-15%, with a success probability of 65% and a WACC of 8.5%.

### It took a lot of nerves to come so far with safinamide

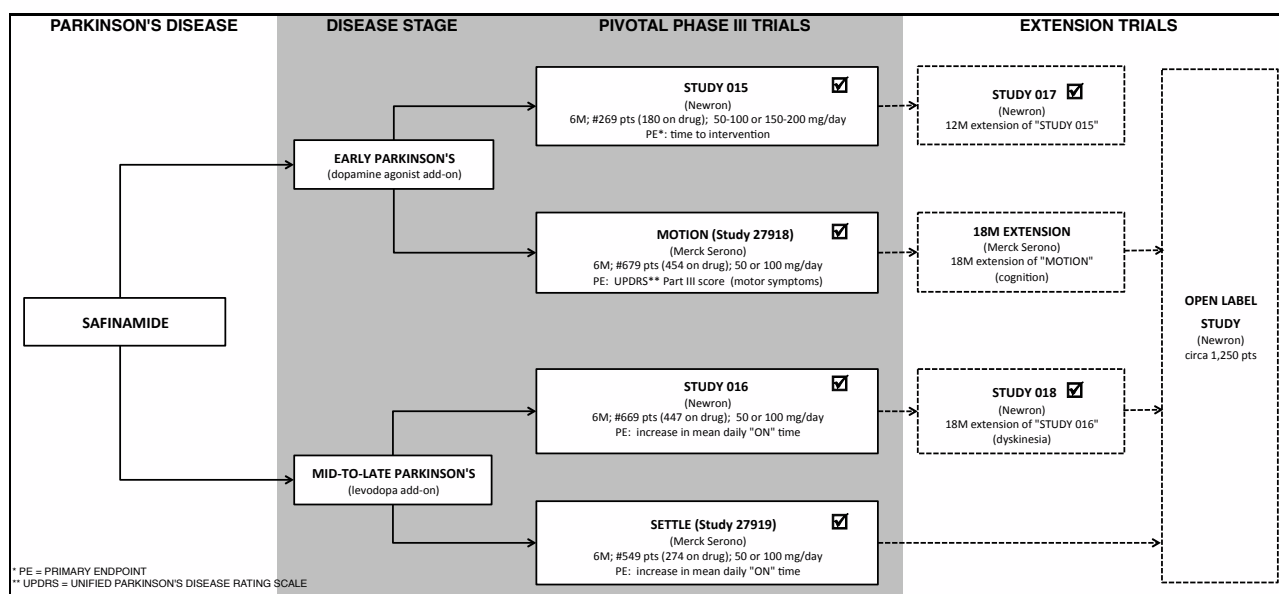
As we discussed earlier it took a lot of nerves for Newron's management and investors to come so far with safinamide. However, this was only related to the uncertainties surrounding the ownership of the safinamide rights and the funding in the final stages. On the bright side, the phase III trial design set out by Newron from the start was executed effortlessly despite all these concerns, with now positive results in all four phase III trials.

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) and, 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).

#### Safinamide 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 SAFINAMIDE IN PARKINSON'S DISEASE



SOURCE: VALUATIONLAB, NEWRON PHARMACEUTICALS

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

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

Safinamide 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

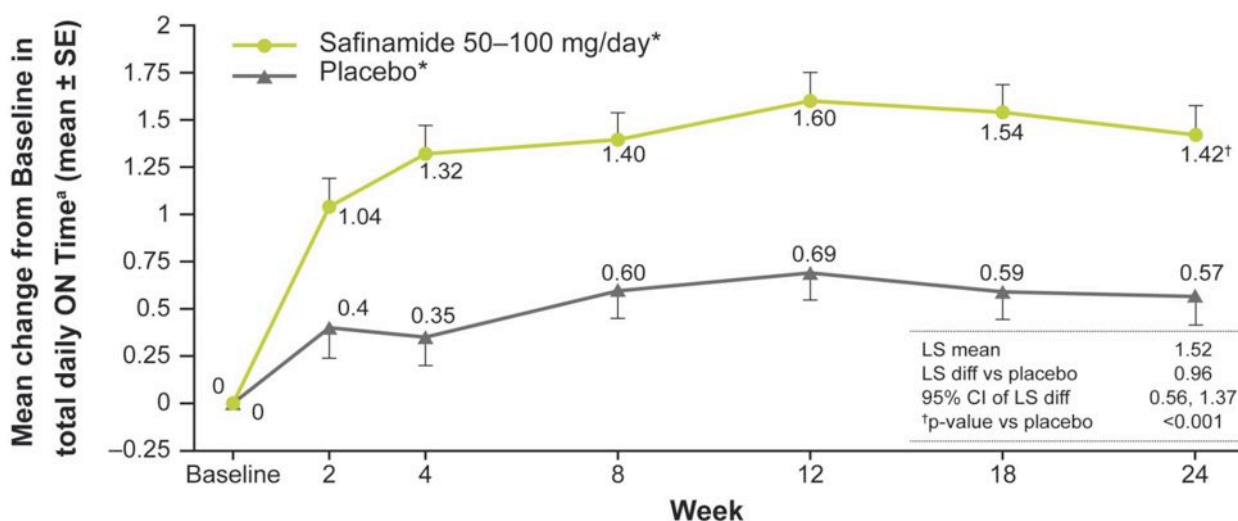
Safinamide also showed statistically significant results in its two pivotal phase III trials as an add-on to stable doses of levodopa and/or other stable dose dopamine agonists/anticholinergics in mid to late stage Parkinson's disease. Roughly 70% of PD patients are on levodopa regimens.

### 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

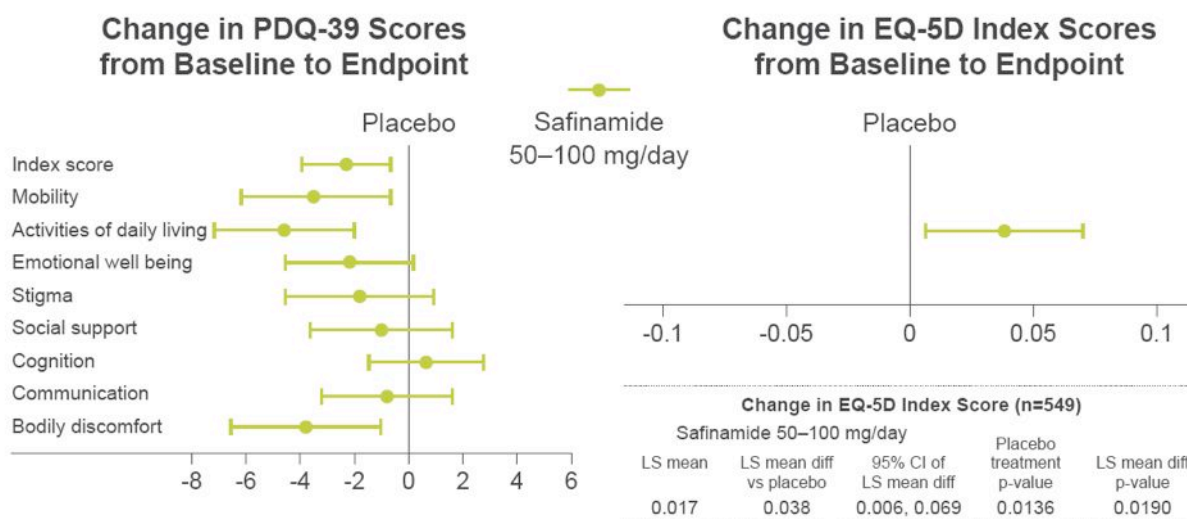
\*As add-on to L-dopa and PD medication

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,  $p=0.003$ ), **PDQ-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 sildenafil 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 sildenafil 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 sildenafil 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 sildenafil 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 sildenafil 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	-0.7	-1.22
- P-VALUE VS. PLACEBO	N/A	0.1999	0.0317

SOURCE: NEWRON PHARMACEUTICALS

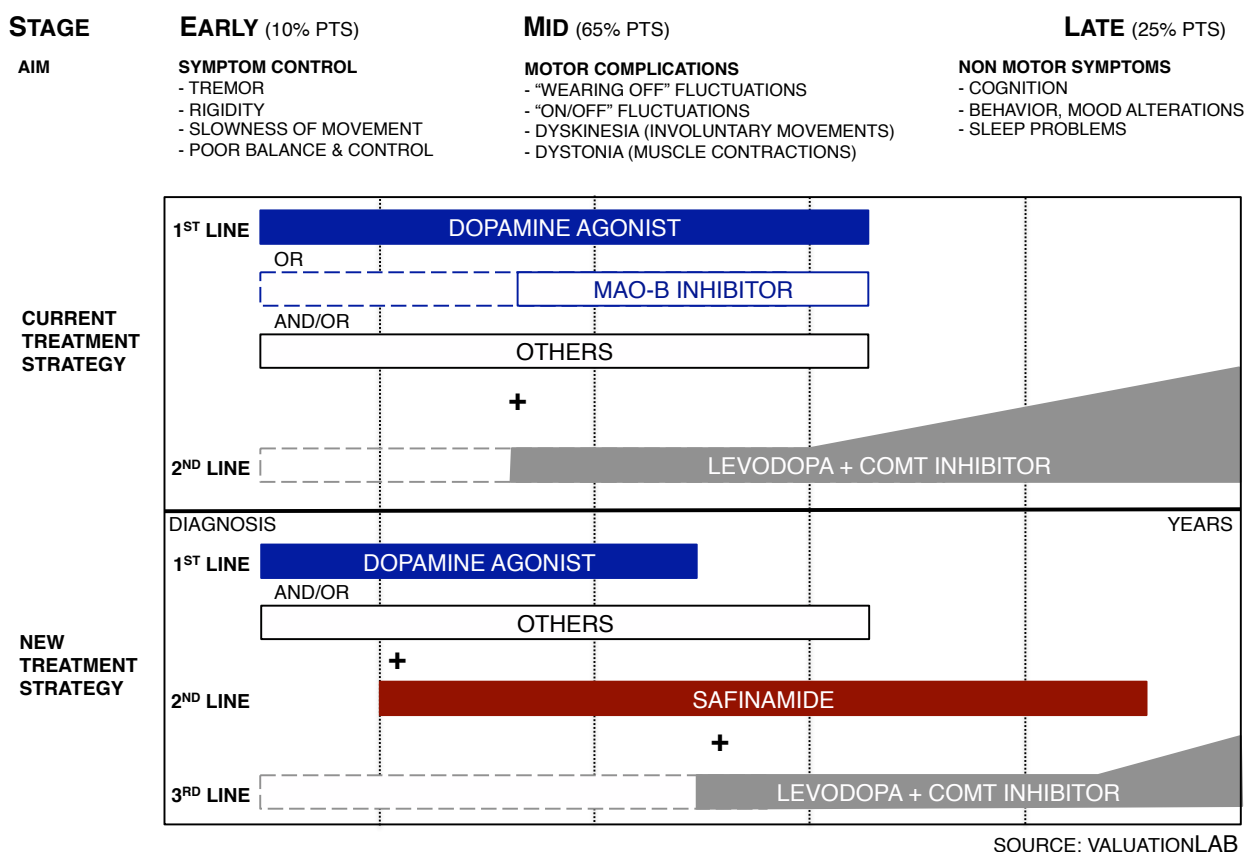
Importantly, in Parkinson's patients with moderate dyskinesia (DRS>4) at baseline "Study 016/018" showed under double-blind, placebo-controlled conditions that sildenafil 100 mg/day reduces dyskinesia. Currently there are no drugs on the market that have shown reducing dyskinesia over such a period. However, Newron would have to prove this important finding in a prospective phase III trial. This would add significantly to our sales forecasts for sildenafil.

## 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). As seen, 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.

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.

### SCHEMATIC OVERVIEW PARKINSON'S DISEASE DRUG TREATMENT STRATEGIES



# 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), LEVODOPA (MID-TO-LATE PD)

**UNIQUE SELLING POINT** FIRST ONCE A DAY ADJUNCTIVE THERAPY FOR ALL STAGES OF PARKINSON'S DISEASE TOGETHER WITH DOPAMINE AGONISTS (EARLY PD) OR LEVODOPA (MID-TO-LATE PD)

### 7Ps ANALYSIS

<b>PATENT</b>	LEVODOPA COMBINATION PATENT: 2026 (US) / 2024 (EU)   SYNTHESIS: 2028 - 5 YEAR PATENT EXTENSION POSSIBLE
<b>PHASE</b>	US & EU FILING Q4 2013E. PHASE I TRIALS IN JAPAN ALREADY 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	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
NUMBER OF PATIENTS (MN)	3.2	3.3	3.4	3.4	3.5	3.6	3.6	3.7	3.8	3.9	3.9
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	2.3	2.4	2.4	2.5	2.5	2.6	2.6	2.7	2.8
PENETRATION (%)	0.0%	0.0%	0.0%	2.0%	4.0%	5.0%	6.0%	6.5%	7.0%	7.5%	8.0%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.2	0.2	0.2	0.2
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>52</b>	<b>107</b>	<b>136</b>	<b>167</b>	<b>185</b>	<b>203</b>	<b>222</b>	<b>241</b>
CHANGE (%)					104%	28%	22%	11%	10%	9%	9%
ROYALTY (%)	10.0%	10.0%	10.0%	10.0%	10.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
ROYALTIES (EUR MN)	0	0	0	5	11	20	25	28	30	33	36
UPFRONT & MILESTONE PAYMENTS (EUR MN)	4	2	10	10							
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>4</b>	<b>2</b>	<b>10</b>	<b>15</b>	<b>11</b>	<b>20</b>	<b>25</b>	<b>28</b>	<b>30</b>	<b>33</b>	<b>36</b>
TAX RATE (%)	-3%	0%	0%	0%	0%	30%	30%	30%	30%	30%	30%
TAXES (EUR MN)	0	0	0	0	0	-6	-8	-8	-9	-10	-11
<b>PROFIT (EUR MN)</b>	<b>4</b>	<b>2</b>	<b>10</b>	<b>15</b>	<b>11</b>	<b>14</b>	<b>18</b>	<b>19</b>	<b>21</b>	<b>23</b>	<b>25</b>

UNITED STATES	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
NUMBER OF PATIENTS (MN)	1.0	1.1	1.1	1.1	1.1	1.1	1.2	1.2	1.2	1.2	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	0.8	0.9	0.9	0.9	0.9	0.9	1.0	1.0	1.0	1.0
PENETRATION (%)	0.0%	0.0%	0.5%	2.5%	5.5%	7.5%	8.5%	9.0%	9.5%	10.0%	10.0%
NUMBER OF PATIENTS (MN)	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1
COST OF THERAPY PER YEAR (EUR)	1,952	1,952	1,952	1,952	1,952	1,952	1,952	1,952	1,952	1,952	1,952
<b>SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>8</b>	<b>43</b>	<b>97</b>	<b>135</b>	<b>156</b>	<b>168</b>	<b>181</b>	<b>194</b>	<b>198</b>
CHANGE (%)				410%	124%	39%	16%	8%	8%	7%	2%
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	6	15	20	23	25	27	29	30
UPFRONT & MILESTONE PAYMENTS (EUR MN)		8	11								
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>0</b>	<b>8</b>	<b>13</b>	<b>6</b>	<b>15</b>	<b>20</b>	<b>23</b>	<b>25</b>	<b>27</b>	<b>29</b>	<b>30</b>
TAX RATE (%)	0%	0%	0%	0%	0%	30%	30%	30%	30%	30%	30%
TAXES (EUR MN)	0	0	0	0	0	-6	-7	-8	-8	-9	-9
<b>PROFIT (EUR MN)</b>	<b>0</b>	<b>8</b>	<b>13</b>	<b>6</b>	<b>15</b>	<b>14</b>	<b>16</b>	<b>18</b>	<b>19</b>	<b>20</b>	<b>21</b>

JAPAN	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
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	0.2
PENETRATION (%)	0.0%	0.0%	0.0%	0.0%	0.0%	3.0%	6.0%	8.0%	9.0%	9.5%	10.0%
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>0</b>	<b>16</b>	<b>32</b>	<b>43</b>	<b>50</b>	<b>54</b>	<b>58</b>
CHANGE (%)							104%	36%	15%	8%	7%
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	0	2	3	4	5	5	6
UPFRONT & MILESTONE PAYMENTS (EUR MN)	5					20					
<b>PROFIT BEFORE TAX (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>5</b>	<b>6</b>
TAX RATE (%)	0%	0%	0%	0%	0%	20%	20%	20%	20%	20%	20%
TAXES (EUR MN)	0	0	0	0	0	0	-1	-1	-1	-1	-1
<b>PROFIT (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>1</b>	<b>3</b>	<b>3</b>	<b>4</b>	<b>4</b>	<b>5</b>

	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
<b>GLOBAL SALES (EUR MN)</b>	<b>0</b>	<b>0</b>	<b>8</b>	<b>96</b>	<b>204</b>	<b>287</b>	<b>354</b>	<b>396</b>	<b>433</b>	<b>469</b>	<b>497</b>
CHANGE (%)				1031%	113%	41%	24%	12%	9%	8%	6%
<b>GLOBAL PROFIT (EUR MN)</b>	<b>4</b>	<b>10</b>	<b>23</b>	<b>22</b>	<b>25</b>	<b>30</b>	<b>36</b>	<b>40</b>	<b>44</b>	<b>48</b>	<b>51</b>
CHANGE (%)		139%	136%	-4%	16%	18%	23%	11%	9%	8%	6%

WACC (%)	8.5%
NPV TOTAL PROFIT (EUR MN)	259
NPV TOTAL PROFIT (CHF MN)	316
NUMBER OF SHARES (MN)	11.6
NPV PER SHARE (EUR)	22.3
NPV PER SHARE (CHF)	27.2
SUCCESS PROBABILITY	65%
<b>RISK ADJUSTED NPV PER SHARE (CHF)</b>	<b>17.7</b>

### SENSITIVITY ANALYSIS

		WACC (%)							
		7.0	7.5	8.0	8.5	9.0	9.5	10.0	10.5
SUCCESS PROBABILITY	100%	30.2	29.1	28.1	27.2	26.3	25.4	24.6	23.8
	95%	28.7	27.7	26.7	25.8	24.9	24.1	23.3	22.6
	90%	27.2	26.2	25.3	24.5	23.6	22.8	22.1	21.4
	85%	25.7	24.8	23.9	23.1	22.3	21.6	20.9	20.2
	80%	24.1	23.3	22.5	21.7	21.0	20.3	19.6	19.0
	75%	22.6	21.9	21.1	20.4	19.7	19.0	18.4	17.8
	70%	21.1	20.4	19.7	19.0	18.4	17.8	17.2	16.6
	65%	19.6	18.9	18.3	17.7	17.1	16.5	16.0	15.4
	60%	18.1	17.5	16.9	16.3	15.8	15.2	14.7	14.3

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB

## Unique Selling Point

First once a day oral add-on therapy together with dopamine agonists in early stage Parkinson's disease and in combination with levodopa in mid and late stage disease. Delays introduction of levodopa in early Parkinson's, while in mid and late-stage disease, safinamide reduces levodopa dose, increasing "on-time" and reducing "off-time". There is a potential to reduce dyskinesia 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 the possibility of a 5-year patent extension. In addition, the drug has a synthesis patent that protects until 2028. We have conservatively factored in patent expiry in the EU until 2024 and in the US until 2026. Assuming first product launches to start in 2014, the drug has an effective patent life of at least 10 years. Additional patent protection through 5-year extension will provide considerable upside to our forecasts.

**Phase:** Phase III has been successfully completed resulting in a 65% success probability. In Q4 2013 Newron plans to file for approval in the EU and US. A successful filing leads to an increase of the success probability to 80% and raises our risk-adjusted NPV by 28%.

**Pathway:** To receive approval from the regulatory authorities safinamide needs at least one positive phase III trial for each Parkinson's indication, 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, in early stage patients in combination with dopamine agonists, and in mid to late stage patients with levodopa, and more than 1,700 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)

ESTIMATES AS OF JULY 03, 2013

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 (dopamine agonists, anticholinergics, MAO-B inhibitors) may be required.
- 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 that 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:** Abbvie's **Duodopa**, a carbidopa/levodopa intestinal gel (EU/ROW approved, US pending), XenoPort's **XP21279**, a sustained release levodopa pro-drug (phase 2), Impax/GSK's **Rytary**, an extended-release capsule formulation of carbidopa/levodopa (US pending), and NeuroDerm's **ND0611/0612**, a carbidopa/levodopa subcutaneous patch pump (phase I/II).

**New molecules and novel approaches include:** Newron/Zambon's **safinamide** (global filing Q4/13) a mixed mechanism of action drug that provides both MAO-B and glutamate inhibition (important neurotransmitter), adenosine 2a (A2a) agonists such as Kyowa-Kirin's **istradefylline** (US filing, Japan approved as Nourias) and Biotie/UCB's **tozadenant** (phase II), anti-dyskinesia drugs such as Novartis' **AFQ056** (phase III) and Addex's **dipraglurant** (phase II), which target metabotropic glutamate receptor 5 (mGluR5), and Santhera's **fipamezole**, an adrenergic alpha2 receptor antagonist (phase II).

# Income Statement

## NEWRON PHARMACEUTICALS

SHARE PRICE (CHF) 9.0

IFRS

INCOME STATEMENT (EUR MN)	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
PRODUCT SALES (BY PARTNERS)	0	0	8	96	224	459	664	930	1,375	1,706	1,938
CHANGE (%)				1031%	134%	105%	45%	40%	48%	24%	14%
ROYALTIES	0	0	1	12	28	73	106	145	204	247	278
CHANGE (%)				824%	142%	158%	45%	36%	41%	21%	12%
UPFRONT & MILESTONE PAYMENTS	9	10	21	50	20	20	0	50	0	0	0
CHANGE (%)		8%	123%	133%	-60%	0%	-100%		-100%		
OTHER INCOME & GRANTS	0	0	0	0	0	0	0	0	0	0	0
CHANGE (%)	-100%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
REVENUES (EXCL. PARTNER SALES)	8.9	9.7	22.7	61.7	48.4	93.2	106.4	194.9	203.6	247.0	277.6
CHANGE (%)	108%	8%	136%	171%	-22%	93%	14%	83%	4%	21%	12%
R&D	-3.5	-4.5	-9.0	-9.0	-2.0	-3.0	-4.0	-5.0	-6.0	-7.0	-8.0
CHANGE (%)	-8%	27%	100%	0%	-78%	50%	33%	25%	20%	17%	14%
AS % REVENUES	40%	47%	40%	15%	4%	3%	4%	3%	3%	3%	3%
S,G&A	-8.1	-8.6	-9.1	-9.6	-10.1	-10.6	-11.1	-11.6	-12.1	-12.6	-13.1
CHANGE (%)	16%	6%	6%	6%	5%	5%	5%	5%	4%	4%	4%
AS % REVENUES	91%	89%	40%	16%	21%	11%	10%	6%	6%	5%	5%
TOTAL OPERATING EXPENSES	-11.6	-13.1	-18.1	-18.6	-12.1	-13.6	-15.1	-16.6	-18.1	-19.6	-21.1
CHANGE (%)	8%	13%	38%	3%	-35%	12%	11%	10%	9%	8%	8%
AS % REVENUES	130%	136%	80%	30%	25%	15%	14%	9%	9%	8%	8%
EBITDA	-2.6	-3.4	4.7	43.2	36.4	79.7	91.4	178.4	185.6	227.5	256.6
CHANGE (%)	-59%	28%	-241%	814%	-16%	119%	15%	95%	4%	23%	13%
MARGIN (%)	-30%	-35%	21%	70%	75%	86%	86%	92%	91%	92%	92%
DEPRECIATION & AMORTISATION	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
AS % REVENUES	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%
EBIT	-2.7	-3.4	4.7	43.1	36.3	79.6	91.3	178.3	185.5	227.4	256.5
CHANGE (%)	-58%	27%	-236%	826%	-16%	119%	15%	95%	4%	23%	13%
MARGIN (%)	-30%	-36%	20%	70%	75%	85%	86%	91%	91%	92%	92%
NET FINANCIAL INCOME/(EXPENSE)	0.2	0.7	1.2	1.7	2.2	2.7	3.2	3.7	4.2	4.7	5.2
PROFIT BEFORE TAXES	-2.5	-2.7	5.9	44.8	38.5	82.3	94.5	182.0	189.7	232.1	261.7
CHANGE (%)	-61%	9%	-315%	666%	-14%	114%	15%	93%	4%	22%	13%
MARGIN	-28%	-28%	26%	73%	80%	88%	89%	93%	93%	94%	94%
TAXES	0.1	0.0	0.0	0.0	0.0	-12.5	-16.1	-19.6	-25.1	-28.8	-31.0
NET PROFIT/LOSS	-2.4	-2.7	5.8	44.8	38.5	69.8	78.4	162.3	164.6	203.4	230.7
CHANGE (%)	-63%	15%	-314%	666%	-14%	81%	12%	107%	1%	24%	13%
MARGIN (%)	-27%	-28%	26%	73%	80%	75%	74%	83%	81%	82%	83%
NET PROFIT/LOSS (EXCLUDING MILESTONES)	-11.3	-12.4	-15.6	-5.2	18.5	49.8	78.4	112.3	164.6	203.4	230.7
MARGIN (%)	-127%	-128%	-69%	-8%	38%	53%	74%	58%	81%	82%	83%
PROFIT/(LOSS) PER SHARE (IN EUR)	-0.29	-0.24	0.50	3.86	3.31	6.00	6.74	13.96	14.16	17.49	19.84
PROFIT/(LOSS) PER SHARE (IN CHF)	-0.35	-0.28	0.60	4.63	3.98	7.21	8.10	16.77	17.01	21.01	23.84

ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB

# Ratios & Balance Sheet

## NEWRON PHARMACEUTICALS

SHARE PRICE (CHF) 9.0

RATIOS	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
P/E		-31.8x	14.9x	1.9x	2.3x	1.2x	1.1x	0.5x	0.5x	0.4x	0.4x
P/S		9.0x	3.8x	1.4x	1.8x	0.9x	0.8x	0.4x	0.4x	0.4x	0.3x
P/NAV		3.5x	2.8x	1.2x	0.8x	0.5x	0.3x	0.2x	0.1x	0.1x	0.1x
EV/EBITDA		-17.2x	12.2x	1.3x	1.6x	0.7x	0.6x	0.3x	0.3x	0.3x	0.2x

PER SHARE DATA (CHF)	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
EARNINGS	-0.35	-0.28	0.60	4.63	3.98	7.21	8.10	16.77	17.01	21.01	23.84
CHANGE (%)	-72%	-19%	-314%	666%	-14%	81%	12%	107%	1%	24%	13%
CASH	4.31	3.63	5.17	10.78	15.77	25.34	36.21	56.16	76.97	102.22	130.58
CHANGE (%)	313%	-16%	42%	108%	46%	61%	43%	55%	37%	33%	28%
DIVIDENDS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	4.07	2.57	3.17	7.81	11.78	19.00	27.09	43.87	60.87	81.89	105.73
CHANGE (%)	218%	-37%	24%	146%	51%	61%	43%	62%	39%	35%	29%

BALANCE SHEET (EUR MN)	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
NET LIQUID FUNDS	29.2	35.2	50.1	104.3	152.6	245.2	350.4	543.5	744.9	989.2	1,263.7
TOTAL ASSETS	44.6	50.6	65.5	119.7	168.0	260.6	365.8	558.9	760.3	1,004.6	1,279.1
SHAREHOLDERS' EQUITY	27.6	24.9	30.7	75.6	114.0	183.8	262.2	424.5	589.1	792.5	1,023.1
- CHANGE IN %	319%	-10%	24%	146%	51%	61%	43%	62%	39%	35%	29%
- RETURN ON EQUITY	-9%	-11%	19%	59%	34%	38%	30%	38%	28%	26%	23%
FINANCIAL DEBT	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
- FIN. DEBT % OF TOTAL ASSETS	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
EMPLOYEES	23	24	24	25	26	27	27	28	29	30	31
- CHANGE IN %	5%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%

CASH FLOW STATEMENT (EUR MN)	2012	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
NET PROFIT / (LOSS)	-2.5	-2.7	5.9	44.8	38.5	82.3	94.5	182.0	189.7	232.1	261.7
+ DEPRECIATION & AMORTIZATION	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
+ OTHER NON-CASH ITEMS	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3	1.3
CASH FLOW	-1.2	-1.4	7.2	46.2	39.8	83.7	95.8	183.3	191.1	233.5	263.1
+ NET INCREASE/(DECREASE) IN WORKING CAPITAL	7.0	7.3	7.7	8.1	8.5	8.9	9.4	9.8	10.3	10.9	11.4
OPERATING FREE CASH FLOW	5.8	5.9	14.8	54.2	48.2	92.5	105.1	193.1	201.3	244.2	274.3
+ NET CASH FLOWS FROM INVESTING ACTIVITIES	10.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
NET CASH USED IN OPERATING ACTIVITIES	15.9	5.9	14.9	54.3	48.3	92.6	105.2	193.1	201.4	244.3	274.4
+ NET CASH FLOWS FROM FINANCING ACTIVITIES	8.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NET INCREASE/(DECREASE) IN CASH AND CASH EQUIVALENTS	23.9	5.9	14.9	54.3	48.3	92.6	105.2	193.1	201.4	244.3	274.4

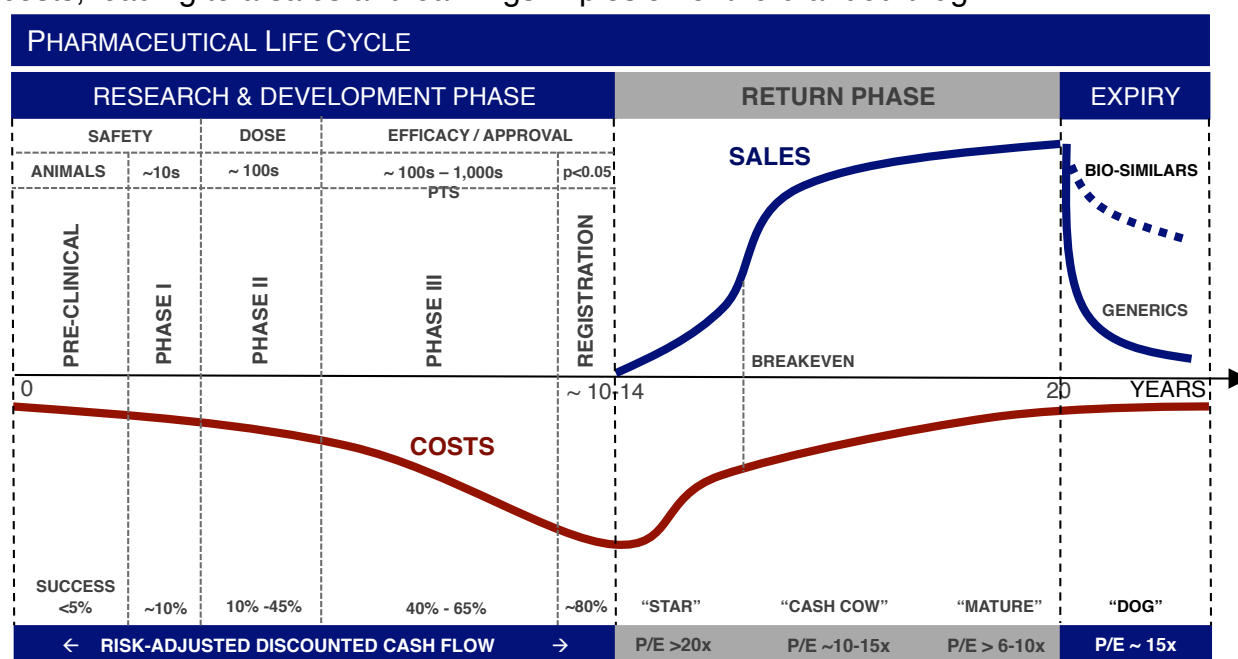
ESTIMATES AS OF 3 JULY, 2013

SOURCE: VALUATIONLAB

# 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: VALUATION LAB

## 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

valuationLAB AG is an independent life science research boutique with no securities or banking services. The company does not hold any positions in the securities mentioned in this report.

**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 Analysis

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)

## Analyst Certification

The research analyst(s) identified on the first page of this research report hereby attest that all of the views expressed in this report accurately reflect their personal views about any and all of the subject securities or issuers. In order to ensure the independence of our research analysts, and their immediate household, are expressly prohibited from owning any securities in the valuationLAB AG research universe, which belong to their sector(s). Neither the research analyst nor his/her immediate household serves as an Officer, Director or Advisory Board Member of **Newron Pharmaceuticals S.p.A.**

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