EDISON

Newron Pharmaceuticals

Corporate update

Back on track

Pharma & biotech

Xadago (safinamide) for Parkinson's disease (PD) is back on track in the US as the FDA has informed the company and its partners, Zambon and US WorldMeds, that no further clinical studies will be required following the 29 March complete response letter. Newron will re-submit Xadago's NDA by end November and now anticipates US approval mid-2017. In Europe the Xadago roll-out is ongoing, with commercial partner Zambon having launched the product in multiple European countries. We value Newron at CHF494m or CHF34.7/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/14**	1.6	(8.6)	(0.63)	0.0	N/A	N/A
12/15	2.4	(18.3)	(1.17)	0.0	N/A	N/A
12/16e	2.1	(23.3)	(1.64)	0.0	N/A	N/A
12/17e	6.4	(11.3)	(0.80)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments. ** FY14 PBT is restated

Xadago US back on track for NDA resubmission

The FDA no longer requires any extra clinical studies on Xadago's potential abuse liability or dependence/withdrawal effects; thus Newron will expedite the NDA resubmission. This removes uncertainty surrounding Xadago's US future filing. We have re-instated our forecasts and now anticipate US launch in H217. Importantly, partner Zambon continues its roll-out of the drug across Europe; it is now available in 11 European countries and further launches are expected this year.

Evenamide schizophrenia Phase II data due Q416

The US Phase II proof-of-concept trial is ongoing, assessing the novel mechanism of action drug, evenamide (NW-3509) as an add-on to antipsychotics in patients with positive symptoms of schizophrenia. Phase II data are expected in Q416. NW-3509 is a partnering candidate, given the potential size of the indication and its differentiating mode of action. Partnering activities could provide upside.

Sarizotan potentially written in the STARS

Sarizotan remains a priority given the potentially rapid clinical development path in addition to the size of the Rett syndrome (RS) market (c 36,000 patients in the US/EU). STARS, the potentially pivotal clinical trial evaluating breathing disorders associated with RS, has now begun. We forecast potential first approval and launch in 2018 and peak sales of €260m; given the size of the indication, Newron could commercialise in RS alone with a small salesforce.

Valuation: Risk-adjusted NPV of €376m/CHF494m

Our updated Newron valuation is CHF494m (from CHF504m) or CHF34.7/share, reflecting primarily a push back to US Xadago launch by six months. Our valuation includes risk-adjusted contributions for Xadago in PD and dyskinesia indications, sarizotan in RS and evenamide in schizophrenia and reflects 2015 year-end net cash of CHF44.1m.

21 July 2016

Price	**CHF24.6**
Market cap	**CHF355m**
	€/CHF 1.1
Net cash (€m) at 31 December 2015	40.2
Shares in issue	14.4m
Free float	77%
Code	NWRN
Primary exchange	SIX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	24.0	48.8	(5.2)
Rel (local)	23.8	49.6	0.4
52-week high/low	CHF30.8	CHF13.9	

Business description

Newron Pharmaceuticals is an Italian CNS-focused biotechnology company. Xadago (safinamide) for Parkinson's disease has been launched in Europe; Xadago is partnered with Zambon (EU), Meiji Seika (Japan); and US Worldmeds (US).

Next events

Xadago US NDA re-submission	By end Nov 16
Evenamide Phase II data	Q416
Sarizotan Phase III STARS data	Q417

Analysts

Dr Susie Jana +44 (0) 20 3077 5700

Daniel Wilkinson +44 (0)20 3077 5734

healthcare@edisongroup.com

Edison profile page

Investment summary

Newron is an Italian company focused on CNS (central nervous system) disorders. Lead product Xadago/safinamide for the treatment of PD has been launched in multiple European countries by commercial partner Zambon and is under regulatory review in the US. Safinamide is partnered with Meiji Seika in Japan/Asia, Zambon in the rest of the world with a sub-licence agreement for the US granted to US WorldMeds. Newron also has a pipeline of earlier-stage products, including orphan drug candidate sarizotan for the genetic disorder RS, which could represent the first product for Newron to commercialise alone and Phase II asset evenamide (NW-3509), an entirely novel mechanism action antipsychotic drug for schizophrenia. Evenamide is a partnering candidate given the potential size of the indication.

Newron floated on the SIX at the end of 2006, raising CHF118m (€74.3m) at CHF55/share. In 2008 it acquired UK-based Hunter-Fleming and at the end of 2012 acquired NeuroNova. During 2014 Newron raised CHF22.2m gross proceeds (CHF3.6m at CHF17/share in January and CHF18.6m at CHF15.75/share in April). It is headquartered in Bresso, Italy, and employs around 25 people, including in its operations in Stockholm, Sweden, and Morristown, NJ, US.

Exhibit 1: Newron pipeline

Product	Indication		Stage	Comments
Safinamide	Parkinson's disease	Partnering	Approved (EU); Filed (US)	Formally approved in Europe; US NDA resubmission November 2016
Sarizotan	Rett syndrome	Orphan	Phase III	STARS potentially pivotal study started July 2016
Evenamide	Schizophrenia	Partnering	Phase II	Data expected Q216; Newron seeking to partner

Source: Edison Investment Research, Newron

Valuation: Risk-adjusted NPV of CHF494m or CHF34.7/share

Our updated Newron valuation is CHF494m (from CHF504m) or CHF34.7/share, reflecting primarily a push back to US Xadago launch by six months. Our valuation includes risk-adjusted contributions for Xadago in PD and dyskinesia indications, sarizotan in RS and evenamide in schizophrenia and reflects 2015 year-end net cash of CHF44.1m. We have made only minor changes to our underlying assumptions for other assets; notably we expect sarizotan launch in H218 from mid-2018.

Sensitivities: Safinamide US approval and pipeline evolution

The main near-term sensitivities for Newron relate to safinamide (Xadago) and the ongoing US regulatory process. In the US, safinamide NDA is expected to be re-filed in November 2016. We anticipate approval in H117 and launch in H217. Failure of approval remains a substantial risk given US sales represent c 60% of our total Xadago peak sales estimates. Newron has two earlier-stage programmes (NW-3509, sarizotan) that it is advancing into later-stage development and clinical data could become available in the next 4-18 months, which will help to shape future development plans or to crystallise value through partnering. Success or failure with any of these compounds could have an impact on our valuation and financial forecasts.

Financials: Cash runway to late 2017

Newron has sufficient cash and equivalents to fund operations into late 2017 according to our model. We do include royalty income in our future forecasts and note that this cash reach does include the milestone payment due from partner Zambon for the US approval of Xadago, which we forecast to be €9m in 2017. Any further sub-licencing deals could extend the cash runway. Current cash should be sufficient to fund ongoing clinical development (Phase III trials for sarizotan and Phase II POC for Evenamide). However, partnering activity will be required to take evenamide's development further.

Xadago back on track in the US

Xadago (safinamide) for PD is back on track in the US as the FDA has informed the company and its partners Zambon and US WorldMeds that no further clinical studies will be required for Xadago's US NDA resubmission. A complete response letter issued by the regulators on 29 March had requested clinical evaluation of the possible effect of safinamide on potential abuse liability and dependence/withdrawal effects as required by the Controlled Substance Staff (CSS) in the Center for Drug Evaluation and Research (CDER) at the FDA; no further efficacy or safety data for Xadago in patients with PD has been requested. Newron had subsequently submitted additional preclinical abuse liability studies and additional analyses of the clinical data as requested by CSS following on-going dialogue with the agency.

Newron now aims to re-submit Xadago's NDA by end November and anticipates US approval mid 2017. This outcome is positive in our view as we had raised concerns that additional trials could be required and, as such, had placed our valuation under review while we awaited further clarity from the company post discussions with CSS on the revised approval timelines for Xadago in the US, to understand the magnitude of the slippage. Our concerns have now abated but we have revised our US Xadago expectations to a launch mid-2017 from H216 to reflect the need to re-submit the NDA file.

Safinamide is a reversible MAO-B inhibitor

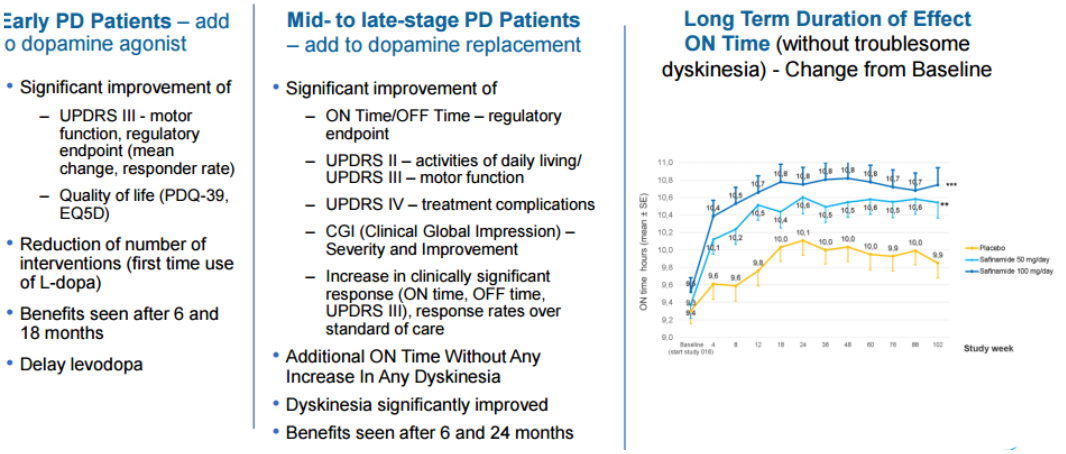
Safinamide has multiple mechanisms of action, with reversible inhibition of MAO-B (monoamine oxidase), which blocks the enzyme responsible for breaking down dopamine, inhibition of dopamine uptake, and inhibition of glutamate release. PD is characterised by progressive loss of dopaminergic neurons within the basal ganglia in the brain, leading to a decline in dopamine levels. Since dopamine plays a critical role in movement and co-ordination, a reduction in its levels leads to the characteristic and progressive features of PD; tremor, slowness of movement and rigidity. The current mainstay of drug treatment is limited to oral therapies such as levodopa (L-DOPA), dopamine agonists (DA) and monoamine oxidase-B inhibitors (MAOI), which aim to increase or substitute for dopamine. However, over time the benefits of drug treatment diminish (L-DOPA provides symptomatic relief of around three to five years. Importantly treatment with L-DOPA can lead to the unpleasant axillary effects of motor fluctuations (ON/OFF effect) and involuntary movements known as L-DOPA induced dyskinesia (LD). Safinamide helps to restore dopamine levels in the brain (by inhibiting dopamine enzymatic breakdown), thereby improving the patient's symptoms.

Safinamide is used as an add-on to L-DOPA therapy

Safinamide is being positioned as an add-on rather than a monotherapy treatment in PD, given that it can be used in combination with DA's in early PD and with L-DOPA in mid- to late-stage patients. This means patients can remain on safinamide throughout their life, without physicians having to switch treatment with disease progression, which in our view would facilitate its use. Exhibit 2 highlights the clinical impact of safinamide as an add-on therapy at various stages of PD.

Both DAs and L-DOPA are now generic, hence expensive drug combinations should not be an issue or barrier to safinamide's use. Both DAs and L-DOPA are well established in treating PD, hence the biggest competition to safinamide, in our view, will likely be new drugs with unique or novel mechanisms of action; however, the majority of such candidates are at an earlier stage of development.

Exhibit 2: Xadago offers benefits in PD across the disease spectrum as add on therapy



Source: Newron presentation

Regional partnerships in place to maximise value

Safinamide was partnered with Meiji Seika in Japan/Asia, with Zambon in all other regions during 2012 and with US WorldMeds as a sublicence from Zambon for the US market in 2016. Zambon is a private Italian company with 2014 reported group turnover of €601m, with the pharmaceutical division contributing 88% and the chemicals division 12%. The main focus of the pharma division is respiratory, pain management and women's health. Zambon does not have a significant pharmaceutical sales presence in the US and hence the drug was sub-licensed to US WorldMeds in the US to maximise safinamide's potential. Newron is eligible for regulatory related milestone payments from Zambon (we assume US approval) and for double-digit royalties on sales. As part of any sub-licensing, Newron could be eligible for around 25-30% of milestone payments and 50% of royalties. Financial terms with Meiji Seika have not been disclosed; the Phase III study has been initiated in Japan. To date, partner Zambon has launched Xadago in nine EU countries (Germany, Spain, Italy, Belgium, Denmark, Sweden, the UK, the Netherlands, Luxembourg) and Norway and Switzerland. We expect further launches in Europe in 2016.

US WorldMeds: Xadago a neat fit into the portfolio

Commercial partner, Zambon, has sublicensed the US commercialisation Xadago (safinamide) to US WorldMeds. Under the agreement's terms, Zambon will give Newron a share of undisclosed upfront, milestone and royalty payments made by US WorldMeds in addition to a milestone payment on FDA approval (we estimate €9m, which we include in our 2017 forecasts).

US WorldMeds is a Kentucky-based pharmaceutical company that markets a number of specialty products including a treatment for PD (notably Apokyn) for the acute treatment of intermittent 'off' episodes). If approved, Xadago would fit neatly into WorldMeds' portfolio as it would be indicated for use as add on to levodopa in mid- to late-stage PD. WorldMeds plans to focus more than 60 sales representatives on launching Xadago in the US, which we now assume in H217 on the basis of an approval in H117.

We forecast global peak sales of €450m in PD

In the US there are 1-1.5 million PD patients; we estimate around 80% of PD patients receive treatment, suggesting a total treated PD patient population of around one million (taking the mid-way point). There is a similar-sized market in Europe and a smaller market of around 250,000 in Japan. Safinamide could be used to treat all stages of PD and we assume can reach peak penetration of 10% of treated PD patients six years after launch. We assume a price of $7/day in the US and €3.7/day in Europe and Japan (around a 20% discount to the US price assumption),

which compares favourably to other PD products, including rasagiline (which will go generic in 2017). We continue to forecast peak Xadago sales of €450m in PD, which comprises ex-US peak sales of €200m based on use only in the mid-late stage PD patients, a group which represents 75-80% of the PD market. In the US, our peak sales are €250m where we continue to include both the early and mid- to late-stage patients. Our royalty rate forecasts are around 12-13%.

In our view, the closest comparable (and competitor) for Xadago/safinamide is Azilect (rasagiline), an MAO-B inhibitor that is used as monotherapy and as an add-on to L-DOPA. Azilect is sold by Teva and Lundbeck and generated sales of $650m in 2014; it will go generic in 2017. In contrast to other MAO-B inhibitors, safinamide does not appear to have a tyramine interaction, hence avoiding any dietary restrictions (such as cheese and red wine).

Dyskinesia could expand the market opportunity

A subset analysis of a previous clinical trial (study 018) found that safinamide could improve dyskinesia in patients with moderate dyskinesia at baseline. This could present an attractive and differentiated market opportunity for safinamide. Safinamide is thought to improve dyskinesia owing to inhibition of glutamate release, with glutamate expression associated with dyskinesia. Although L-DOPA is an effective treatment for PD, its use is associated with the development of dyskinesia. The ability to improve dyskinesia could therefore allow for potentially earlier use of L-DOPA in PD and to expand the market opportunity for safinamide.

The subset analysis revealed that the third of patients who scored a four or higher on the dyskinesia rating scale at the beginning of the study reported an improvement of 24% on 100mg of safinamide (added to L-DOPA) versus placebo. There were no significant differences, however, for patients on 50 mg of safinamide.

Further studies evaluating safinamide's impact on dyskinesia will depend on partner Zambon and sub-licenser US WorldMeds intentions for its development. We believe a single six-month treatment study assessing patients with higher grade dyskinesia could be sufficient to file for a label extension for safinamide. We highlight that the dyskinesia label extension would differentiate safinamide from all other classes of PD drug treatments.

We include a risk-adjusted contribution for safinamide in dyskinesia, assuming peak sales of €350m until there is more clarity on the potential magnitude of benefit. It is estimated that dyskinesia affects around 40% of PD patients treated with L-DOPA for four to six years, with limited treatment options aside from L-DOPA dosing adjustment. With around one million PD patients in each of the US and Europe, this represents a large opportunity. We assume the safinamide label could be expanded to include dyskinesia following a single clinical trial, which could potentially start once approval has been granted in the US and could lead to potential launch in 2020.

Evenamide (NW-3509) Phase II data potential Q416

Evenamide (NW-3509) is an internally developed asset that originates from Newron's ion channel discovery platform. It is a novel, new generation, oral, antipsychotic drug in development for schizophrenia that acts through pathways that are not targeted by available antipsychotic drugs. Given the lack of novel treatments for this chronic, debilitating condition, positive Phase II data confirming proof of concept would be welcomed by the market. Evenamide is being evaluated in the first instance as a potential add-on therapy to antipsychotics for treating schizophrenia.

Schizophrenia is a chronic and severe mental disorder involving a breakdown in the relation between thought, emotion and behaviour, leading to faulty perception and the inability to function normally. Signs and symptoms can vary. Generally symptoms are classified into three categories:

- Positive symptoms include hallucinations, delusions, thought disorders, movement disorders

- Negative symptoms include flat effect (reduced expression of emotion), social withdrawal, lack of interest in everyday activities
- Cognitive symptoms include trouble focusing, poor 'executive functioning' and problems with 'working memory'

Drug treatments for schizophrenia focus on eliminating symptoms; the current mainstay of which are antipsychotic drugs ('typical antipsychotics' were developed in the 1950's examples include haloperidol, chlorpromazine and fluphenazine; 'atypical antipsychotics' were developed in the 1990s, examples include aripiprazole (BMS's Abilify), olanzapine (Lilly's Zyprexa), quetiapine (AstraZeneca's Seroquel) and risperidone (Risperdal). The first generation of typical anti-psychotics were hampered with significant neurological side effects including in some cases non-reversible tardive dyskinesia. The newer generation of 'atypical antipsychotics improved on the side effect profile, however, long-term drug treatment of schizophrenia has its limitations; the NCBI (US National Center for Biotechnology) estimates that 25-33% of patients are treatment resistant.

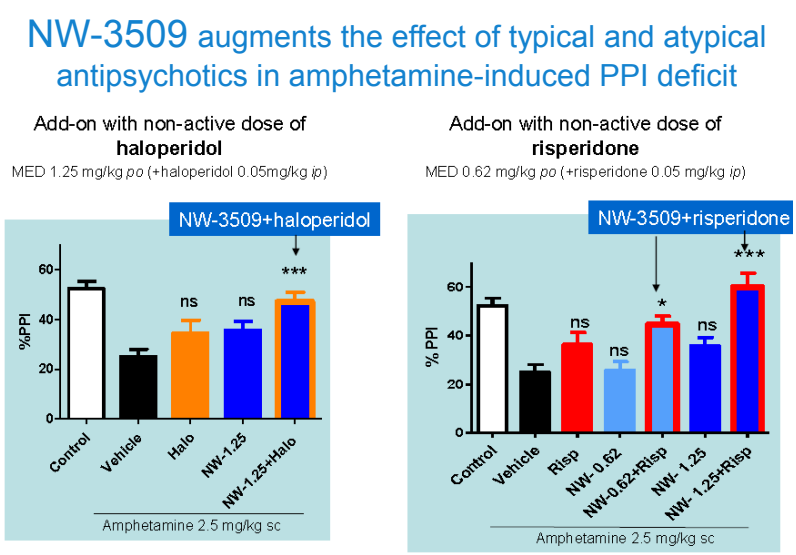
Novel mode of action enables reduced hyper-excited neuronal activity

Evenamide functions as a sodium channel modulator, which regulates the hyperexcitability of neurons. This means that evenamide may normalise the activity of neurons that are firing too rapidly or at an abnormal rate; many schizophrenia patients exhibit abnormal excitability of neurons in certain regions of the brain. This abnormal excitability translates into high levels of glutamate, which may be responsible for many symptoms of schizophrenia. Thus, modulation of hyperexcitability could reduce psychotic symptoms such as hallucinations and delusions, especially when used as an add-on to available antipsychotic treatments. Importantly the addition of evenamide as an adjunct to antipsychotics could reduce antipsychotic-induced side effects and enable patients to take a lower dose of the concurrent anti-psychotic. Evenamide importantly has a fast onset of action and has demonstrated high bioavailability in the brain. Evenamide is patent protected in the US and other territories until around 2028, excluding any extensions.

Early data show evenamide could have utility as add-on therapy

A Phase I safety study including doses of evenamide up to 30mg has completed in 54 healthy volunteers; the drug was generally well tolerated. Evenamide has shown benefits in preclinical models of psychosis, mania, depression, anxiety and cognition. In particular, improved effects were noted with the combination of evenamide with either haloperidol or risperidone (both typically used to treat schizophrenia) in a preclinical model, shown in Exhibit 3. Evenamide could therefore have utility as an add-on treatment to antipsychotics in patients with schizophrenia who are experiencing breakthrough symptoms despite being on standard of care.

Exhibit 3: Preclinical data demonstrating the improved effect from the combination of NW-3509 with typical antipsychotics



Amph (2.5 mg/kg sc) and NW-3509A (1.25 or 0.62 mg/kg po) were administered 5 min before PPI session. Haloperidol and risperidone were administered ip 30 min before PPI session at 0.05 mg/kg. Statistics: Tukey's multiple comparison test *p<0.05, ***p<0.001 vs Vehicle+Amp (n=6-18 rats per group) (Studies performed by Dr Bortolato, Dept. of Pharm. Sciences, Univ. Cagliari- USCLA)

Source: Newron. Note: PPI or prepulse inhibition deficit is an excessive startle response, which is typically associated with schizophrenia; it results in an inability to recognise weak stimuli which is thought to lead to the typical symptoms of schizophrenia (including hallucinations and delusions).

Phase II POC is expected to read out Q416

A Phase II study is ongoing (enrolment started January 2016), assessing evenamide as an add-on therapy for reducing positive symptoms and psychotic worsening in patients with schizophrenia experiencing breakthrough symptoms while on adequate doses of risperidone or aripiprazole; data could become available in Q416. This is a double-blind, placebo controlled, four-week in/outpatient study evaluating 15-25mg of evenamide (twice daily) in a minimum of 90 patients across study centres based in the US and India.

We forecast conservative evenamide peak sales of €380m

Newron estimates that the antipsychotic market is worth around $23bn, suggesting that evenamide could have significant potential. However, until proof-of-concept data are available, estimating the potential market opportunity for evenamide is not straightforward given its potential would be dependent on the breadth of clinical trials conducted. For the purposes of our valuation, we include base-case assumptions, which conservatively assume that evenamide could achieve peak sales of c €380m, representing only c 2% of the current market. Although we have limited visibility on the timing and terms of any potential out-licensing, we continue to assume standard terms including a double-digit royalty on sales, commensurate with an asset out-licensed with proof-of-concept data. Given the size of this market, evenamide's potential could be significantly larger than our current estimate. Given the potential size of the market and scope of development, Newron plans to out-license this asset and a deal could come after the Phase II is complete; this should maximise deal terms although Newron would be prepared to partner sooner if suitable deal terms were offered.

Sarizotan the first orphan drug for RS

Sarizotan is a highly selective serotonin (5-HT1a) and dopamine (D2) antagonist that in preclinical studies demonstrated activity in normalising the abnormal breathing patterns in animal models of

RS. In July 2015 the FDA designated orphan drug status to sarizotan for the treatment of RS. It was in-licensed from Merck KGaA in 2011 and was previously examined as a treatment for PD by Merck KGaA but failed in two Phase III trials in 2006.

Rett syndrome: A rare genetic disorder

RS is a rare, genetic neurodevelopmental disorder that generally affects girls. This severe brain disorder arises from a non-inherited genetic mutation (X-linked methyl CpG-binding protein 2). The mutation causes severe disability and a reduction life expectancy. Symptoms include impaired brain function, leading to issues with a number of functions, including breathing, swallowing, problems with muscles and co-ordination, and seizures. There is no curative treatment for RS and current treatment is therefore more symptomatic.

RS affects between one in every 10,000 to 15,000 female births (source: US NIH), with Newron estimating that there are around 36,000 RS patients in the US and Europe. Children with RS will generally develop normally until one to two years of age, when development will slow and regress. Given the infrequency of RS, precise mortality rates are difficult to establish. However, life expectancy is generally thought to be less than the general population. According to the IRSF (International Rett Syndrome Foundation) sudden death occurs in around 25% of RS patients, with studies speculating that possible causes could include respiratory failure and apnoea, owing to an underlying disorder in the heart's electrical activity. Research suggests that RS is associated with a prolonged QT interval[1] (a measure of the heart's electrical activity). Boys born with RS usually die shortly after birth; as males have only one chromosome (XY) versus females (XX) and thus the disease is more fatal.

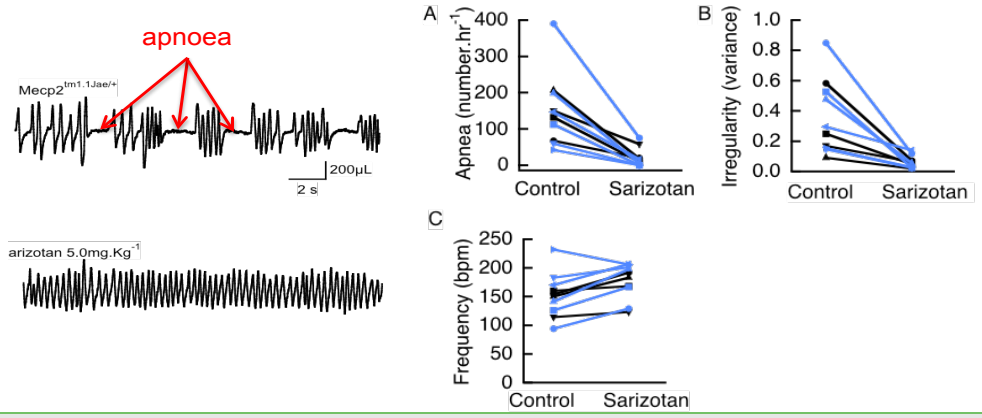
Sarizotan demonstrated utility in RS-related apnoea in animal models

Sarizotan is not being developed to address the underlying cause of RS but as a potential treatment for these life-threatening breathing disorders. Approximately 70% of patients with RS demonstrate respiratory abnormalities (eg apnoea, hyperventilation, respiratory dysrhythmia). It is postulated that the breathing disturbance in RS is related to neuronal hyperactivity in the brainstem. In preclinical studies, sarizotan has demonstrated reduced apnoea and corrected irregular breathing in RS mouse models. These data are shown in Exhibit 4. On the left, the RS mouse model shows recurring instances of apnoea, which are corrected when treated with sarizotan, with apnoea overall reduced by 70-85%. It is this profile which has encouraged Newron to pursue pivotal development of sarizotan in RS. Newron received sarizotan's IND approval by FDA in May 2016.

[1] Ellaway C J, Sholler G, Leonard H. et al Prolonged QT interval in Rett syndrome. Arch Dis Child 1999. 80470–472.472.

Exhibit 4: Sarizotan reduced apnoea and breathing irregularities in preclinical studies

Effect of 5mg/kg ip of sarizotan on respiratory pattern in heterozygous females



Source: Newron

STARS pivotal Phase III sarizotan study has begun

STARS (Sarizostan Treatment of Apneas in Rett Syndrome), a potentially pivotal clinical study to evaluate breathing disorders associated with RS has now begun; the first US study centre initiated is the Rush Medical Center, Chicago. STARS is a global study that will recruit around 129 RS patients (three groups of 43) aged 13 and over. Two doses of sarizotan will be investigated (5mg and 10mg, twice daily), which will be compared to placebo. Efficacy will be assessed via a measure of respiratory function (using an at-home monitor); the primary endpoint of the study is the reduction in the number of clinically significant apnoea (>10seconds) episodes at 24 weeks. After 24 weeks, all patients will be switched to receive sarizotan and will be followed for a further 48 weeks. Newron has sought advice from both regulators and key opinion leaders in the design of this study.

Although RS is a rare condition, diagnosed patients are generally included on patient registries and are known by patient advocacy groups and physicians who work in the RS field. Newron is working with these groups, in particular Rettsyndrome.com, which should help to facilitate recruitment of patients into the planned study. Given the study start date of July 2016 and allowing around six months for recruitment, top-line primary endpoint data (based on 24 weeks of treatment) could become available during the second half of 2017.

Given there is already a substantial safety database accumulated with prior development in PD, the planned 129-patient study could be sufficient to obtain regulatory approvals, particularly given the lack of available treatments in this indication. Our forecasts assume first approval in the US during H218, with launch shortly thereafter, with sarizotan potentially eligible for accelerated review given the unmet medical need.

Given the small size of the indication, we continue to assume that Newron will commercialise sarizotan alone in key markets, including the US and major European countries. We have made no changes to our €260m peak sales forecast, which is based on pricing of €60,000 a year, reflecting the ultra-orphan indication and assumes a 40% penetration of the targeted patients (which we assume is a quarter of the overall market). Pricing and penetration will ultimately depend on sarizotan's magnitude of benefit; if it can command pricing of €80,000 a year with 70% penetration of our assumed target market (one quarter of RS patients) this would suggest peak sales of around €600m.

Sensitivities

Newron is subject to the usual biotech risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, financing and commercial risks. With safinamide now approved in Europe the main sensitivity in the near-term will be the launch process, including securing favourable pricing and reimbursement, in addition to the launch trajectory, which will likely be on a country-by-country basis.

In the US, Xadago's NDA will be resubmitted in November 2016; failure of approval remains a substantial risk given US sales represent c 60% of our total Xadago peak sales estimates .Newron has two earlier-stage programmes (evenamide, sarizotan) that it is advancing into later-stage development, and clinical data could become available in the next six to 18 months, which will help shape future developments plans or to crystallise value through partnering. Success or failure with any of these compounds could have an impact on our valuation and financial forecasts.

Valuation

Our updated Newron valuation is CHF494m (from CHF504m) or CHF34.7/share, primarily reflecting a push back to US Xadago launch by six months. Our valuation (see Exhibit 5) includes risk-adjusted contributions for Xadago in PD and dyskinesia indications, sarizotan in RS and evenamide in schizophrenia and reflects 2015 year-end net cash of CHF44.1m. We have made only minor changes to our underlying assumptions for other assets; notably we expect sarizotan launch in H218 from mid-2018. Exhibit 6 highlights key newsflow in the next 12-18 months.

Exhibit 5: Newron rNPV valuation

Product	Indication	Launch	Peak sales (€m)	Value (€m)	Value (CHFm)	Probability	rNPV (€m)	rNPV (CHFm)	NPV/Share (CHF/share)
Xadago	Parkinson's disease	2015	450	256.9	343.7	90-100%	244.6	327.2	23.0
	Dyskinesia	2020	390	77.4	103.5	40%	30.9	41.4	2.9
Sarizotan	Rett syndrome	2018	260	195.1	261.0	30%	51.1	68.4	4.8
NW-3509	Schizophrenia	2019	380	70.9	94.8	20%	9.4	12.6	0.9
Net Cash/(Debt)				40.2	44.1	100%	40.2	44.1	3.1
Valuation				939.5	847.1		376.3	493.7	34.7

Source: Edison Investment Research

Exhibit 6: Key newsflow in the next 12-18 months

News	Period	Comments
Xadago EU next launches	2016	Pricing and uptake rates.
Evenamide/NW-3509 Phase II data	Q416	Will provide first proof of concept data.
Xadago/safinamide US approval	Mid 2017	NDA re-submission expected Nov 2016
Evenamide /NW-3509 partnering	2017	A partnering deal could come after the availability of Phase II data.
Sarizotan PIII data	Q417	24-week potentially pivotal efficacy study.
Sarizotan approval and launch	Mid 18/ H218	

Source: Edison Investment Research, Newron

Financials

Newron reported cash and equivalents of €40.9m at end December 2015 (following two private placements of new shares in FY15 raising net proceeds of €28.4m) and has modest debt of €0.7m relating to an Italian government grant. We continue to expect that current cash resources should be sufficient to fund operations to H217. This should fund ongoing clinical development (Phase III trials for sarizotan and Phase II POC for evenamide). However, partnering activity will be required to take evenamide's development any further.

Our FY16 revenue forecast of €2.1m is based purely on royalty income related to Xadago sales in Europe and does not include any potential milestone-related income given the slippage of the US approval. If Xadago is approved in the US, we believe Newron will be eligible to receive a milestone payment from Zambon (we estimate around €9m) in 2017. Newron is entitled to receive a portion of any upfront or milestone payments; we estimate the payment will be around 25% of the income that Zambon negotiates (and around 50% of any royalties that Zambon receives).

We forecast net R&D for FY16 of €18m, mainly related to the ongoing Phase II evenamide study in schizophrenia and to the start of the pivotal sarizotan Phase II/III trial, which could conclude in Q317. Our forecast €10m in R&D expenses for 2017 reflects the ongoing spend associated with this trial. Any delays to the pipeline development in 2016 could result in a phasing of R&D costs from 2016 to 2017. In addition, if the regulatory bodies request further clinical trials for sarizotan or if Newron decides to progress evenamide alone (beyond the ongoing Phase II), then our 2017 R&D forecasts will need to be materially upgraded. If the latter were to materialise, we would highlight the need for additional capital requirements.

Newron is based in Italy and reports in euros. It is listed in Switzerland on the SIX with the share price quoted in Swiss francs (CHF). Our valuation is based on an FX rate of 1.1€/CHF.

Exhibit 7: Financial summary

€000s	2013	2014	2015	2016e	2017e	2018e
Year-end December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	3,539	1,557	2,380	2,129	6,444	15,948
Cost of Sales	0	0	0	0	0	0
Gross Profit	3,539	1,557	2,380	2,129	6,444	15,948
Research and development (net)	(4,537)	(3,892)	(11,724)	(18,000)	(10,000)	(7,500)
EBITDA	(7,737)	(9,057)	(17,604)	(23,626)	(11,697)	(100)
Operating Profit (before amort. and except.)	(7,766)	(9,077)	(17,668)	(23,647)	(11,719)	(122)
Intangible Amortisation	(10)	(13)	(7)	(24)	(24)	(24)
Exceptionals	0	(2,125)	(6,725)	0	0	0
Other	0	0	0	0	0	0
Operating Profit	(7,776)	(11,215)	(24,400)	(23,671)	(11,743)	(146)
Net Interest	63	492	(583)	386	401	648
Profit Before Tax (norm)	(7,703)	(8,585)	(18,251)	(23,261)	(11,318)	526
Profit Before Tax (reported)	(7,713)	(10,723)	(24,983)	(23,284)	(11,342)	502
Tax	615	628	2,167	0	0	0
Profit After Tax (norm)	(7,088)	(7,957)	(16,084)	(23,261)	(11,318)	526
Profit After Tax (reported)	(7,098)	(10,095)	(22,816)	(23,284)	(11,342)	502
Average Number of Shares Outstanding (m)	11.5	12.7	13.7	14.2	14.2	14.2
EPS - normalised (€)	(0.62)	(0.63)	(1.17)	(1.64)	(0.80)	0.04
EPS - (reported) (€)	(0.62)	(0.80)	(1.66)	(1.64)	(0.80)	0.04
Dividend per share	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET						
Fixed Assets	9,821	7,686	406	425	444	462
Intangible Assets	9,125	6,993	265	245	225	205
Tangible Assets	79	67	79	118	156	194
Investments	617	626	62	62	62	62
Current Assets	21,797	29,388	43,974	22,935	12,200	15,112
Stocks	301	102	38	98	98	98
Debtors	2,088	3,320	3,005	3,883	3,883	3,883
Cash	18,426	25,702	40,931	18,954	8,219	11,131
Other	982	264	0	0	0	0
Current Liabilities	(6,070)	(4,489)	(6,513)	(4,846)	(3,233)	(3,410)
Creditors	(5,712)	(4,131)	(6,151)	(4,488)	(3,220)	(3,410)
Short term borrowings	(358)	(358)	(362)	(358)	(13)	0
Long Term Liabilities	(4,458)	(3,324)	(755)	(404)	(391)	(391)
Long term borrowings	(1,087)	(729)	(364)	(13)	0	0
Other long term liabilities	(3,371)	(2,595)	(391)	(391)	(391)	(391)
Net Assets	21,090	29,261	37,112	18,110	9,019	11,773
CASH FLOW						
Operating Cash Flow	(10,071)	(9,370)	(12,490)	(22,433)	(10,714)	2,340
Net Interest	1	107	48	336	401	648
Tax	(615)	(628)	(299)	542	0	0
Capex	(56)	(22)	(60)	(60)	(60)	(60)
Acquisitions/disposals	301	0	0	0	0	0
Financing	0	17,547	28,392	0	0	0
Other	(20)	0	(4)	(4)	(4)	(4)
Dividends	0	0	0	0	0	0
Net Cash Flow	(10,460)	7,634	15,587	(21,619)	(10,377)	2,925
Opening net debt/(cash)	(27,441)	(16,981)	(24,615)	(40,205)	(18,583)	(8,206)
HP finance leases initiated	0	0	0	0	0	0
Other	0	0	3	(3)	0	0
Closing net debt/(cash)	(16,981)	(24,615)	(40,205)	(18,583)	(8,206)	(11,131)

Source: Edison Investment Research, Newron Pharmaceuticals accounts

Contact details	Revenue by geography
Newron Pharmaceuticals Via Ludovico Ariosto 21 20091 Bresso Italy +39 02 610 3461 www.newron.com	N/A

Management team

Chairman: Dr Ulrich Köstlin	CEO: Stefan Weber
Dr Köstlin was a member of the board of management of Bayer Schering Pharma until 2011. He was responsible for multiple regions globally: Europe, Asia Pacific, Latin America, Japan and North America. He began his pharmaceutical career with Schering. In 1994 he was appointed to the former Schering AG's executive board. He holds a doctorate from Tübingen University and a master of law degree from the University of Pennsylvania Law School.	Mr Weber was appointed CEO in 2012, having been CFO since 2005, successfully executing the 2006 IPO. Mr Weber has more than 25 years' industry experience in general management and finance and has been responsible for numerous equity, debt, mezzanine and grant funding transactions. He holds a master's degree in business management from Fern Universität Hagen.
CMO: Ravi Anand	**VP finance: Roberto Galli**
Mr Anand has been Newron's CMO since 2005. He has over 20 years of experience in drug development, including positions at Roche and Sandoz/Novartis. These were focused on CNS and incorporated all stages of clinical development and post-marketing. He completed his medical training in the US, specialising in psychiatry and neurology.	Mr Galli has held various positions within finance at Newron since joining in 2002 and has more than 16 years of experience in biotech, finance and auditing. He holds a degree in business economics from the University Luigi Bocconi, Milan and he is a chartered auditor.

Principal shareholders	(%)
Investor AB	12.5
Zambon Group	9.2
Aviva	7.6

Companies named in this report

Merck KGaA (MRK GR); Meiji Seika Pharma, part of Meiji Holdings (2269 JP); Zambon Group (private), US WorldMeds (private)

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand