EDISON

Newron Pharmaceuticals

Pipeline update

Plans for sarizotan to enter pivotal development

Pharma & biotech

Newron recently announced detailed plans for the sarizotan pivotal trial in Rett Syndrome (RS), which could allow for first approval by end 2017 if initiated in Q116. With RS an orphan indication, we believe Newron could commercialise alone in key regions (US and major EU). The planned NW-3509 Phase II trial has now started prior to partnering. Separately, Newron has decided to terminate sNN0031 and sNN0029 owing to issues with the delivery device (third-party supplier). The Xadago US decision is now at end March (from end Dec). Our updated valuation is CHF522m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/13	3.5	(7.7)	(0.62)	0.0	N/A	N/A
12/14	1.6	(10.7)	(0.79)	0.0	N/A	N/A
12/15e	3.0	(15.1)	(1.11)	0.0	N/A	N/A
12/16e	4.1	(15.0)	(1.06)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items.

Pivotal sarizotan trial in RS planned

Newron is planning to initiate a pivotal Phase II/III study in RS in coming months to assess sarizotan's efficacy in treating fatal-breathing disorders associated with RS. RS is a genetic neurodevelopmental disorder that generally affects girls and leads to difficulty in breathing, swallowing, movement and speaking. Newron estimates that there around 36,000 RS patients in the US and Europe. Sarizotan has been shown in preclinical RS models to reduce apnoea. We continue to forecast potential first approval by year-end 2017 and peak sales of €260m. Given the size of the indication, Newron could commercialise in RS alone with a small salesforce.

NW-3509 Phase II starts ahead of potential partnering

As expected, Newron has now started the Phase II proof-of-concept trial with NW-3509 as an add-on to antipsychotics. NW-3509 is a partnering candidate, given the potential size of the indication. Phase II data are expected in Q416 but a deal could be agreed sooner if suitable terms are offered.

Xadago: Inaugural sales; US decision now in March

With H115 financial results, Newron reported first Xadago-related royalties from sales of Xadago in Germany by commercial partner Zambon. Xadago has now been approved in Switzerland and we expect further launches across Europe by partner Zambon in coming months. The Xadago (safinamide) US PDUFA decision date was recently extended by three months to 29 March 2016. This is for the FDA to process recent non-data related submissions.

Valuation: rNPV of CHF522m or CHF36.8/share

Our updated Newron valuation is CHF522m (from CHF526m). Both sNN0031 and sNN0029 have been removed. We have slightly delayed initial US Xadago sales, while maintaining our peak €450m in PD. Our valuation also includes risk-adjusted contributions for Xadago in dyskinesia, sarizotan in Rett syndrome and NW-3509. We have included proceeds from the November CHF5.4m US private placement.

18 December 2015

Price	**CHF26.55**
Market cap	**CHF378m**
	€0.92/CHF
Net cash (€m) at end June 2015	43.1
Shares in issue	14.2m
Free float	77%
Code	NWRN
Primary exchange	SIX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(3.1)	1.1	15.7
Rel (local)	0.2	3.4	17.3
52-week high/low	CHF35.0	CHF23.1	

Business description

Newron Pharmaceuticals is an Italian CNS-focused biotechnology company. Safinamide/Xadago for Parkinson's disease has been approved in mid-late PD in Europe and launched in Germany; the US PDUFA date is 29 March 2016. Safinamide is partnered with Zambon and Meiji Seika.

Next events

Start of sarizotan pivotal trial	Q116
US safinamide FDA approval decision (PDUFA 29 March)	Q116
NW-3509 Phase II data	Q416
Partnering agreements for safinamide and/or NW-3509	2016

Analysts

Dr Philippa Gardner	+44 (0)20 3681 2521
Susie Jana	+44 (0) 20 3077 5700
Christian Glennie	+44 (0)20 3077 5727

healthcare@edisongroup.com

Edison profile page

Overview of sarizotan and Rett syndrome

Rett Syndrome (RS) is a genetic neurodevelopmental disorder that generally affects girls, and arises from a non-inherited genetic mutation (MECP2 mutation on the X chromosome). The mutation leads to central nervous system disorders, including impaired brain function, leading to issues with a number of functions, including breathing, swallowing, movement and speaking.

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 1-2 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.

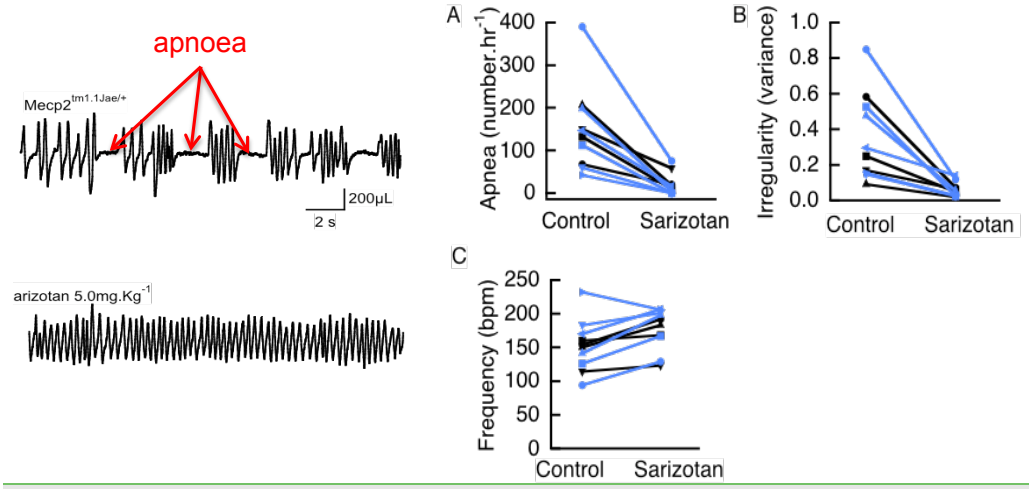
According to the IRSF (International Rett Syndrome Foundation) sudden death occurs in around 25% of RS patients, with studies speculating that possible causes could include respiratory failure and apnoea, owing to an underlying disorder in the heart's electrical activity. Research suggests that RS is associated with a prolonged QT interval[1] (a measure of the heart's electrical activity).

Sarizotan is not being developed to address the underlying cause of RS, but rather as a potential treatment for these life-threatening breathing disorders. Sarizotan, which modulates the activity of serotonin and dopamine receptors in the brain was in-licensed from Merck KGaA in 2011. Sarizotan was previously examined as a treatment for Parkinson's disease (PD) by Merck KGaA but failed in two Phase III trials in 2006.

In preclinical studies, sarizotan has demonstrated reduced apnoea and corrected irregular breathing in RS mouse models. These data are shown in Exhibit 1. 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; the study plans are described in more detail below.

Exhibit 1: Sarizotan reduced apnoea and breathing irregularities in preclinical studies

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



Source: Newron

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

Phase II/III sarizotan study

The planned Phase II/III pivotal study will recruit around 90 RS patients at least 13 years old. 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 apnoea 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. Assuming the study commences during Q116 and allowing around six months for recruitment, top-line primary endpoint data (based on 24 weeks of treatment) could become available during H117.

Given there is already a substantial safety database accumulated with prior development in PD, the planned 90-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 H217, 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 sarizotan 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.

Newron could be eligible to qualify for an FDA 'Rare Paediatric Disease Priority Review Voucher', a transferable voucher that allows for an accelerated FDA approval process. The voucher does not have to be used for sarizotan or by Newron and can be sold to a third party (for example, priority review vouchers either for paediatric or for tropical diseases have been purchased for $67-350m, the most recent being the United Therapeutics rare paediatric voucher, which it sold to AbbVie in August 2015 for $350m).

There is some uncertainty around the future availability of these vouchers. The current 'Food and Drug Administration Safety and Innovation Act' limits the period during which these can be awarded to one year after issuance of the third voucher; this was awarded in March 2015. Extending the current system for a further three years is under consideration.

NW-3509 enters Phase II ahead of partnering

In-line with previously announced plans, Newron has announced initiation of a Phase II study with NW-3509 as a potential add-on therapy to antipsychotics for the treatment of schizophrenia. Newron anticipates initial efficacy data could become available in Q416. Given the potential size of the addressable market, Newron plans to out-license NW-3509. Availability of efficacy data could help to maximise deal terms, although we believe Newron would be prepared to partner NW-3509 sooner if favourable terms were offered.

The Phase II trial will recruit at least 60 schizophrenic patients who have breakthrough symptoms despite being on a stable dose of current available therapy. NW-3509 is administered orally twice per day and patients will receive 5-25mg/day. Symptoms will be measured over four weeks, which will be compared to placebo.

At this stage, we have made no changes to our key underlying assumptions for NW-3509, which conservatively assume, in the absence of efficacy data, that NW-3509 could achieve peak sales of c €380m, representing only around 2% of the estimated $23bn antipsychotic market (Newron estimate). We also continue to include standard deal 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, NW-3509's potential could be significantly larger than our current estimate.

Valuation

With sarizotan plans now in place and this progressing to a pivotal study, we have increased the probability of success to 30% (from 20%). This remains conservative, given the pivotal nature of the trial. However, to date there is limited efficacy data in the proposed target group of patients, with only data from preclinical models available; this makes assessing the likelihood of success in RS more challenging, and hence why we apply a heavy risk-adjustment to this programme.

We have removed both sNN0031 and sNN0029 from our sum-of-the-parts valuation, following Newron's decision to terminate both projects. For Xadago in the US, we have slightly delayed initial sales following the extended FDA review process, and have also pushed out the potential approval milestone to 2016 (from 2015) in our valuation forecasts. Our Xadago forecasts continue to include €450m of peak sales in PD. We have made no other major changes to the remainder of our valuation assumptions, which include risk-adjusted contributions for Xadago in dyskinesia, sarizotan in Rett syndrome and NW-3509, which Newron is planning to partner.

Our valuation has been rolled forward in time and updated for net cash (which comprises last reported gross cash of €44m, last reported total debt of €0.9m relating to an Italian government loan, and incorporates the CHF5.4m gross proceeds from the private placement, we estimate CHF5.1m net), equating to €47.8m/CHF52.0m at current FX rates (€0.92/CHF). Our updated valuation is therefore CHF522m (from CHF526m), or CHF36.8/share.

Exhibit 2: Newron rNPV valuation

Product	Indication	Launch	Peak sales (€m)	NPV (CHFm)	Probability	rNPV (CHFm)	NPV/share (CHF/share)
Xadago	Parkinson's Disease	2015	450	344.3	90-100%	327.2	23.0
	Dyskinesia	2018	390	151.6	40%	60.6	4.3
Sarizotan	Rett syndrome	2018	260	251.0	30%	67.9	4.8
NW-3509	Schizophrenia	2019	380	91.5	20%	14.7	1.0
sNN0031	Severe PD	2018	200	147.3	0%	0.0	0.0
sNN0029	ALS	2018	250	192.8	0%	0.0	0.0
Net cash at end June 2015				52.0	100%	52.0	3.7
Valuation				**890.4***		**522.4**	**36.8**

Source: Edison Investment Research. Note: Products in shaded rows have been terminated and are left in for illustrative purposes only to give an overview of our key prior assumptions. *Our total NPV does not include the terminated products sNN0031 and sNN0029.

Financials

Our financial forecasts have been updated to incorporate H115 results, in addition to changes arising from the termination of sNN0029 and sNN0031 and the recent US private placement. The main changes to our forecasts are in Exhibit 3. Although the Xadago FDA extended review has

pushed back any potential milestone due from partner Zambon on approval to 2016, this has no impact on our financial forecasts, as we did not include this milestone in our revenue forecasts (we generally do not include uncertain/unknown milestones in our financial forecasts). However, the slightly later launch has led us to lower expected royalty income in 2016. Our updated 2016 revenue forecast of €4.1m is based purely on royalty income related to Xadago sales in Europe and does not include any potential milestone related income. If Xadago is approved in the US, we believe Newron will be eligible to receive a milestone payment from Zambon (we estimate around €9m). Furthermore, if Zambon successfully sub-licenses Xadago in the US, which could be facilitated once US approval is granted, Newron is entitled to receive a portion of any upfront or milestones; we estimate this is around 25% of income that Zambon negotiates (and around 50% of any royalties that Zambon receives).

With H115 results, Newron reported first Xadago-related royalties of €93k to end June 2015, following launch by partner Zambon in mid-May. Based on our assumed 12% royalty rate (we assume a tiered royalty starting at 12% with a step-up to 18%), this suggests initial sales of €775k in the six weeks since mid-May launch to 30 June period-end. If sales continue at the current run rate, Germany alone could contribute nearly €7m of sales in the first 12 months of launch. Newron also reported milestone income of €1.8m for the European approval (versus our forecast of €6m). With the European approval milestone below our previous forecast, we have lowered our 2015 revenue forecast by around €4m.

Underlying H115 R&D spend was €7.6m, offset by €2.8m of grant and expense reimbursement by Zambon, with Newron reporting H115 R&D costs of €4.7m (compared to our last published FY15 forecast of €11.5m). G&A was €4.1m (compared to our last published FY15 forecast of €7.1m). Our last published 2015 forecast for total operating expenses of €18.6m is broadly in line with €8.8m reported with H115 (allowing for an uptick in R&D with the start of further trials including NW-3509 and with sarizotan) and we have made no changes to our total operating expenses forecast. However, within this we have increased G&A by €1m, while reducing R&D spend by a similar amount, reflecting the H115 trends.

Our R&D forecast in 2016 has been increased to reflect the size of the planned sarizotan study; our previous forecasts assumed a trial in around 60 patients; with the planned trial now in 90 patients we have raised R&D spend in 2016 to reflect this.

Despite the higher G&A base in 2015, there are limited changes in future years owing to the restructuring in Sweden (discussed in more detail below).

Our previous R&D forecasts for the now terminated sNN0029 and sNN0031 only included costs of the current pilot clinical trials and did not include future costs of any pivotal development, hence there are only limited changes to our underlying R&D spend estimates with the termination of these projects. We assume there will be some residual costs associated with the ongoing pilot studies to bring these to a complete close, so have not removed all associated spend immediately from our future forecasts.

The book value for sNN0029 and sNN0031 at the end of 2014 was €6.8m and we assume Newron will record the bulk of this as an impairment charge of €6m during 2015. The termination of these programmes will also lead to a restructuring in Sweden, affecting up to six employees. Our forecasts now include a €0.6m restructuring charge in 2015, in addition to a corresponding decrease in future G&A spend. These are our preliminary estimates, which will be subject to change when the accounting treatment and impact are disclosed in the future. We allocate both the impairment and restructuring charge to exceptional items.

Newron reported cash and equivalents of €44m at end June 2015 and has debt of €0.9m relating to an Italian government grant, for net cash at end June of €43.1m. This has been boosted by CHF5.4m gross proceeds from a private placement with a US biotechnology/healthcare specialist

fund (issuing 209k shares at CHF25.60/share), we estimate CHF5.1m net proceeds, or €4.7m at current FX, for total estimated net cash of around €47.8m (CHF52m at current FX). We continue to estimate that this should be sufficient to fund operations for the foreseeable future.

Exhibit 3: Key changes to financial forecasts

€m	2015 Old	2015 New	% change	2016 Old	2016 New	% change
Revenue	7.130	3.016	-58	5.822	4.127	-29
Research and development	(11.500)	(10.000)	-13	(10.000)	(12.000)	+20
Selling, general and administration	(7.090)	(8.095)	+14	(7.442)	(7.553)	+1
Operating profit (reported)	(11.460)	(21.680)	+89	(11.620)	(15.426)	+33
Profit before tax (reported)	(11.104)	(21.699)	+95	(11.123)	(15.040)	+35
Profit after tax (reported)	(11.104)	(21.711)	+96	(11.123)	(15.040)	+35

Source: Edison Investment Research

Exhibit 4: Financial summary

€000s	2010	2011	2012	2013	2014	2015e	2016e
Year-end December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS							
Revenue	806	4,289	8,924	3,539	1,557	3,016	4,127
Cost of Sales	0	0	0	0	0	0	0
Gross Profit	806	4,289	8,924	3,539	1,557	3,016	4,127
Research and development	(15,922)	(3,822)	(3,534)	(4,537)	(6,017)	(10,000)	(12,000)
EBITDA	(21,491)	(6,394)	(2,634)	(7,737)	(11,182)	(15,029)	(15,375)
Operating Profit (before amort. and except.)	(21,613)	(6,465)	(2,684)	(7,766)	(11,202)	(15,056)	(15,402)
Intangible Amortisation	(27)	(17)	(13)	(10)	(13)	(24)	(24)
Exceptionals	0	0	0	0	0	(6,600)	0
Other	0	0	0	0	0	0	0
Operating Profit	(21,640)	(6,482)	(2,697)	(7,776)	(11,215)	(21,680)	(15,426)
Net Interest	(33)	45	200	63	492	(19)	386
Profit Before Tax (norm)	(21,646)	(6,420)	(2,484)	(7,703)	(10,710)	(15,075)	(15,016)
Profit Before Tax (reported)	(21,673)	(6,437)	(2,497)	(7,713)	(10,723)	(21,699)	(15,040)
Tax	1,128	(8)	122	615	628	(12)	0
Profit After Tax (norm)	(20,518)	(6,428)	(2,362)	(7,088)	(10,082)	(15,087)	(15,016)
Profit After Tax (reported)	(20,545)	(6,445)	(2,375)	(7,098)	(10,095)	(21,711)	(15,040)
Average Number of Shares Outstanding (m)	6.6	7.3	8.2	11.5	12.7	13.6	14.2
EPS - normalised (€)	(3.10)	(0.88)	(0.29)	(0.62)	(0.79)	(1.11)	(1.06)
EPS - normalised and fully diluted (€)	(3.10)	(0.88)	(0.29)	(0.62)	(0.79)	(1.11)	(1.06)
EPS - (reported) (€)	(3.11)	(0.89)	(0.29)	(0.62)	(0.80)	(1.59)	(1.06)
Dividend per share (EUR)	0.0	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	100.0
EBITDA Margin (%)	N/A	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	N/A
BALANCE SHEET							
Fixed Assets	6,026	5,937	11,900	9,821	7,686	1,671	1,656
Intangible Assets	5,188	5,171	11,199	9,125	6,993	975	957
Tangible Assets	128	56	72	79	67	70	73
Investments	710	710	629	617	626	626	626
Current Assets	13,106	7,629	32,747	21,797	29,388	42,308	30,018
Stocks	396	246	233	301	102	98	98
Debtors	2,557	1,469	2,811	2,088	3,320	3,719	3,719
Cash	8,087	5,367	29,243	18,426	25,702	38,327	26,037
Other	2,066	547	460	982	264	164	164
Current Liabilities	(4,635)	(2,827)	(11,585)	(6,070)	(4,489)	(3,583)	(5,176)
Creditors	(4,635)	(2,472)	(11,230)	(5,712)	(4,131)	(3,225)	(4,818)
Short term borrowings	0	(355)	(355)	(358)	(358)	(358)	(358)
Long Term Liabilities	(2,306)	(4,154)	(5,454)	(4,458)	(3,324)	(2,966)	(2,608)
Long term borrowings	0	(1,802)	(1,447)	(1,087)	(729)	(371)	(13)
Other long term liabilities	(2,306)	(2,352)	(4,007)	(3,371)	(2,595)	(2,595)	(2,595)
Net Assets	12,191	6,585	27,608	21,090	29,261	37,430	23,890
CASH FLOW							
Operating Cash Flow	(17,973)	(4,884)	6,015	(10,071)	(9,370)	(15,609)	(12,279)
Net Interest	0	0	0	1	107	100	386
Tax	(1,128)	8	(122)	(615)	(628)	148	(3)
Capex	(7)	(1)	(11)	(56)	(22)	(30)	(30)
Acquisitions/disposals	0	0	9,971	301	0	0	0
Financing	3,185	0	8,378	0	17,547	28,379	0
Other	1,602	0	0	(20)	0	(6)	(6)
Dividends	0	0	0	0	0	0	0
Net Cash Flow	(14,321)	(4,877)	24,231	(10,460)	7,634	12,983	(11,932)
Opening net debt/(cash)	(22,408)	(8,087)	(3,210)	(27,441)	(16,981)	(24,615)	(37,598)
HP finance leases initiated	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	(0)
Closing net debt/(cash)	(8,087)	(3,210)	(27,441)	(16,981)	(24,615)	(37,598)	(25,666)

Source: Edison Investment Research, Newron Pharmaceuticals accounts. Note: Newron is based in Italy and reports financials in euros. It is listed in Switzerland on the SIX with the share price quoted in Swiss francs (CHF).

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