BELL POTTER

7 December 2015

Speculative
See Key risks on Page 9 & Biotechnology Risk Warning on Page 11
Speculative securities may not be suitable for Retail clients

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Neuren (NEU)

Trofinetide shines in Phase II Fragile X trial, licensing prospects improved

Recommendation
Buy (unchanged)
Price
$0.12
Valuation
$0.28 (previously $0.25)
Risk
Speculative

GICS Sector

Pharmaceuticals & Biotechnology

Expected Return	
Capital growth	**133.3%**
Dividend yield	**0.0%**
Total expected return	**133.3%**
Company Data & Ratios	
Enterprise value	**$183.5m**
Market cap	**$205.0m**
Issued capital	**1708.6m**
Free float	**100%**
Avg. daily val. (52wk)	**$340,674**
12 month price range	**$0.074- $0.185**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.09	0.09	0.12
Absolute (%)	33.33	37.93	4.35
Rel market (%)	34.90	36.61	6.42

Trofinetide successful in Phase II again

NEU has reported positive results from its Phase II Fragile X Syndrome (FXS) trial. The trial met its primary end-point of safety and tolerability with strong efficacy signals. A consistent pattern of clinical benefit of trofinetide (high dose) in improving core symptoms of the disease was observed, similar to that seen in the Phase II Rett trial last year. Importantly, the improvement was in both the clinician as well as caregiver assessments. NEU has Fast Track and orphan drug designation from the FDA for FXS and orphan drug designation from the EMA. NEU will hold end-of Phase II meeting with the FDA to discuss results and development path forward for FXS in 1H16. The company envisages following a similar development path to Rett for FXS.

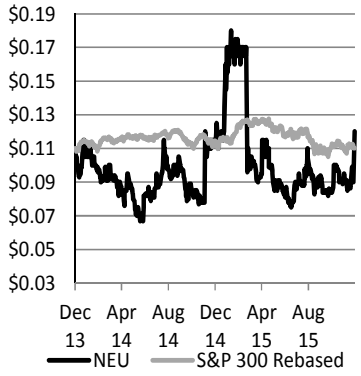
It's time to start paying attention to Neuren

Licensing and M&A activity has heated up in the orphan drug space in recent years, with large companies paying multi-billion dollars to acquire smaller companies with one or more orphan drugs nearing commercialization. NEU is particularly well positioned to benefit from this. In our view, the Phase II results provide proof-of-concept (POC) for trofinetide in FXS and more broadly in neurodevelopmental disorders with benefits seen across two different indications now, which significantly de-risks the company. FXS represents one end of the autism spectrum disorders (ASDs) while Rett represents the other. Success in both of these indications now positions trofinetide to be tried across other ASDs and therefore strengthens its value proposition and increases its licensing prospects. We believe that the POC in FXS, coupled with the positive results seen in Rett, will inject additional impetus into NEU's partnering discussions. We assume trofinetide gets licensed for US$680m in 2HCY16.

Valuation lifted to $0.28/sh, Maintain Buy rating

We have increased the probability of success assigned to FXS (25% vs. 14.5%) and trofinetide's market penetration for FXS, partially offset by revised launch timeline for it (FY20 vs. FY19). Our DCF valuation has lifted by 12% to $0.28/sh (was $0.25/sh). We retain Buy on NEU. Key catalyst: results from the Phase II trial for TBI in early 2016.

Absolute Price



SOURCE: IRESS

Earnings Forecast

Year end 31st December	2013A	2014A	2015E	2016E	2017E
Revenue (A$m)	4.8	2.9	2.3	128.8	57.7
EBITDA (A$m)	-5.6	-8.7	-12.6	118.7	55.1
NPAT (reported) (A$m)	-10.4	-8.3	-13.0	82.7	39.4
NPAT (adjusted) (A$m)	-7.1	-7.3	-11.8	83.6	39.8
EPS (reported) (cps)	-0.8	-0.5	-0.8	4.6	2.1
EPS (adjusted) (cps)	-0.6	-0.5	-0.7	4.7	2.2
EPS growth (%)	N/A	N/A	N/A	NM	NM
PER (x)	N/A	N/A	N/A	2.6	5.5
EV/EBITDA (x)	-33.0	-21.1	-14.6	1.5	3.3
Dividend (¢ps)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
ROE (%)	-29.0%	-38.0%	-80.6%	84.3%	28.3%

NOTE: FY16/17 REVENUE INCLUDES EST. UPFRONT AND MILESTONES FROM POTENTIAL PARTNERS. SOURCE: BELL POTTER SECURITIES ESTIMATES

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DISCLOSURE: BELL POTTER SECURITIES ACTED AS LEAD MANAGER IN THE JULY 2011 AND OCTOBER 2013 PLACEMENT AND RECEIVED FEES FOR THAT SERVICE.

Trofinetide shines in Fragile X Trial

Neuren has reported promising Top-line results from its Phase II Fragile X Syndrome (FXS) Trial. The trial met its primary end-point of safety and tolerability with strong efficacy signals. Results warrant further development of trofinetide for Fragile X Syndrome.

The results show that trofinetide compared to placebo was safe and well-tolerated at both the low dose and high dose treatment groups and also gave compelling evidence of efficacy with the higher dose (70mg/kg) exceeding the pre-specified efficacy success criteria of improvement across core outcome measures of Fragile X.

Trofinetide (high dose) demonstrated a consistent pattern of clinical benefit across 5 core efficacy measures, using both clinician and caregiver assessments. We were looking at overall effect of trofinetide in ameliorating multiple functional and behavioural symptoms which could potentially improve the quality of life of patients. The improvement seen with trofinetide in the trial is across a broad range of such functional and behavioural measures where clinical benefit thresholds were pre-specified. Improvements were seen across core symptoms of Fragile X, including higher sensory tolerance, reduced anxiety, better self-regulation and more social engagement.

A dose response was observed, with high dose being more efficacious than the low dose. Results provide a rationale to explore a longer duration of treatment, higher doses and benefits in younger patients.

Neuren will hold end-of Phase II meeting with the FDA in 1HCY16 to discuss the results from the trial as well as development path forward for trofinetide in Fragile X Syndrome.

Announcement suggests that Neuren will pursue a similar path forward for Fragile X as they did for Rett. Depending on the outcome of the FDA meeting in 1HCY16, they could decide to run a Phase II open label paediatric trial to explore benefits of giving higher dose than 70mg/kg used in the current Phase II trial, giving it for longer duration than 4 weeks and in a younger patient population. We anticipate that a Phase II paeditric trial for Fragile X syndrome could start in 2HCY16.

Licensing and M&A activity has heated up in the orphan drug space in recent years, with large companies paying multi-billion dollars to acquire smaller companies with one or more orphan drugs nearing commercialization. NEU is particularly well positioned to benefit from this.

In our view, the Phase II results provide proof-of-concept (POC) for trofinetide in FXS and more broadly in neurodevelopmental disorders with benefits seen across two different indications now, which significantly de-risks the company.

Results from the FXS trial strengthens trofinetide's licensing package. We have always maintained that the key attraction to a licensee for trofinetide would be its potential applicability across multiple autistic disorders. Rett Syndrome represents one end of the Autism spectrum disorders where the neurons have too few connections and Fragile X syndrome represents the other end of the Autism spectrum disorders where the neurons have too many connections. **Success in both of these indications now positions trofinetide to be tried across other ASDs and therefore strengthens its value proposition and increases its licensing prospects.** We believe that the POC in FXS, coupled with the positive results seen in Rett, will inject additional impetus into NEU's partnering discussions. We continue to expect trofinetide to be licensed in 2HCY16, before initiation of Phase 3 trials for trofinetide.

We discuss and analyse the reported results from the trial in our note ahead.

Phase II Fragile X Syndrome trial summary

Start Date: Neuren initiated the trial with trofinetide in males (adolescents and adults) suffering from Fragile X Syndrome in January 2014 after IND approval from the US FDA.

Top Line Results Date: 7th December, 2015

Trial Protocol:

- Randomized, double-blind, placebo-controlled, parallel group, fixed dose Phase II study, to evaluate safety and tolerability of treatment with oral administration of trofinetide of 35 mg per kg of body weight (twice daily) and 70 mg per kg of body weight (twice daily) in adolescent or adult females (age 12 to 45 years) with Fragile X Syndrome.
- Trofinetide was administered as a powder (2g in 50ml vials or 3g in 30ml bottles) mixed in a strawberry flavoured solution. Placebo was just a strawberry flavoured solution.
- 70 subjects received randomized treatment in 3 treatment groups: placebo (25 subjects), 35 mg/kg twice per day (24 subjects) and 70 mg/kg twice per day (21 subjects).
- Dosing was 28 days, with follow-up after ~14 days post-treatment.

Sites: The trial was conducted at 16 sites in the US.

Primary end-point: Evaluation of safety and tolerability of trofinetide in adolescent and adult male Fragile X syndrome subjects (compared with placebo).

Secondary end-point: A number of physiological, behavioural and functional measures to ascertain the potential pattern of efficacy of trofinetide in Fragile X Syndrome including pharmacokinetics.

Outcome measures: The outcome measures were pre-specified and included 5 core measures. Clinical benefit was measured on a subject level for each individual from their baseline and also on a dose group level.

Figure 1 - Core efficacy measures in Trofinetide's Phase II Fragile X Syndrome trial

Core measure	Type of measure
Fragile X Syndrome Rating Scale	Clinician-completed syndrome-specific
Fragile X Domain Specific Concerns	Clinician-completed syndrome-specific
Clinical Global Impression - Improvement Scale (CGI-I)	Clinician-completed syndrome-specific global
Caregiver Top 3 Concerns	Caregiver-completed syndrome-specific
Aberrant Behavior Checklist (ABC) Total Score	Caregiver-completed non-syndrome specific

SOURCE: COMPANY DATA

The analyses compared the mean clinical responses in the 3 treatment groups for each core measure, as well as comparing the collective clinical responses in all the core measures for each subject individually. The individual analysis was designed to confirm that the treatment benefit shown by the group mean responses was broadly evident and not simply due to a few large outlier responses.

The targeted magnitude of improvement over placebo required to demonstrate clinical benefit (clinically meaningful threshold) was pre-specified in the analysis plan.

Permutation test was performed to estimate the probability of obtaining the predefined clinical benefit by chance alone. The probability that the observed clinical improvement in both the group-level and subject-level analyses was observed purely by chance was determined as only 4.5% (p=0.045).

Instruments and scales used to measure the severity and improvement (outcome) in various parameters: Neuren has used both well-established instruments already reported in published literature and widely used in a variety of trials (including that for Fragile X syndrome and autism spectrum disorders) as well as two novel rating scales developed in consultation with Fragile X syndrome clinical experts and specific to the symptoms of

Fragile X Syndrome. In our view, using the well-established instruments reduces data subjectivity. Using multiple instruments to measure outcomes enhances the validity of the results.

Top-line results from the Phase II Fragile X Syndrome trial

- **Primary end-point met:** Trial met its primary end-point showing that both the doses of trofinetide were safe and well tolerated with no serious adverse events. The adverse events (AEs) did not display dose-dependent or time-dependent trends, were not significant and did not lead to discontinuation of treatment.
- **Consistent pattern of clinical benefit observed in high dose group:** The trial exceeded the clinical benefit requirement for group-level analysis in the high dose group. Improvement was seen in the 70mg/kg group in 3 core outcome measures i.e. the Fragile X Syndrome Rating Scale, the Fragile X Syndrome Domain Specific Concerns and the Aberrant Behaviour Checklist (ABC) Total Score. Across the remaining 2 core outcome measures also a consistent pattern of clinical benefit vs. placebo was observed.

  In the high dose (70mg/kg) group the pre-specified criterion of benefit was achieved in the subject-level efficacy analysis. Mean efficacy scores for each subject based on combined changes across the 5 outcome measures were compared with placebo.
- **Permutation analysis shows low probability of positive trial results being due to chance alone:** The results of the permutation analysis suggest that the clinical improvement observed with trofinetide in the study is unlikely to be the result of chance alone. This increases the robustness and validity of the results.
- **Low dose also shows improvement trends although did not achieve pre-defined clinical benefit threshold:** The lower dose level (35mg/kg twice daily) exhibited improvement in a number of core outcome measures, however it was not as consistent as the high dose and the magnitude of improvement did not meet the targets pre-specified in the analysis plan. This clear stronger effect seen with high dose with no dose-dependent trend seen in safety will allow NEU to explore a higher dose than 70mg/kg in future trials. We note that similar dose response was seen in the Rett Phase II trial and based on it NEU will explore higher doses in the paediatric trial in Rett expected to initiate in 1QCY16.
- **Both caregiver and clinician assessments show clinical benefit:** The improvement was observed both in the clinician as well as caregiver (parent) assessments. This is encouraging since normally inconsistencies between caregiver and clinician assessments are expected to be seen in neurodevelopmental disorder trials.
- **Placebo response occurred but was well managed:** As expected there was placebo response seen in the trial with even the placebo group showing improvement. Neuren had accounted for it in their analyses and seem to have managed the placebo response well.

Our comments on the Results

We are highly encouraged by the results seen with trofinetide in Fragile X Syndrome and view the outcome of the trial as a success in view of the following:

- The core outcome measures on which trofinetide has shown benefits include multiple subsets of functional, motor, communication and behavioural symptoms which in our view will be important from the point of view of improving the overall quality of life of patients. **Improvements were seen across core symptoms of Fragile X, including higher sensory tolerance, reduced anxiety, better self-regulation and more social engagement.** We also note here that some of the symptoms tend to form part of more

than 1 outcome measure and hence improvement trend seen using different measurement scales further enhances the validity of these results.

- The dose dependent relation in efficacy identified gives NEU the scope to increase dosage to potentially increase the benefits seen in the study.
- The trial recruited adolescents and adults suffering from Fragile X Syndrome Syndrome. Adult patients tend to have more debilitated symptoms and thus are harder to treat.
- The trial recruited patients with Clinical Global Impression - Severity (CGI-S) score of 4 or greater and a total score of 30 or greater on the Aberrant Behavior Checklist (ABC).
- Patients recruited were on stable concomitant medication. No drug drug interactions were seen as far as we know in these patients.
- Generally high placebo effect is seen in trials targeting neurodevelopmental disorders. Large profile trials in Fragile X by Big Pharma companies have failed due to results showing similar efficacy as placebo. Keeping this in mind, based on the results seen with trofinetide, Neuren has managed to control the placebo effect well and shown a consistent pattern of clinical benefit across 5 core outcome measures, which is remarkable.
- Neuren has used robust data analysis methods and both novel as well as validated rating scales which accounts for the diversity in symptoms and severity between individuals.
- Being a small trial it was not powered for statistical significance in terms of p values on individual endpoints but had predetermined thresholds to meet clinical benefit criteria. Permutation testing results however gives comfort that the positive results seen in the trial is unlikely to be due to chance alone.
- Path forward will be discussed with the FDA at end of Phase II meeting in 1H16. However, the company envisages following a similar development path to Rett for FXS. Therefore it is likely that they will run a small, open label, paediatric trial to explore the benefits of a longer duration of treatment, higher doses and benefits in younger patients.

In summary, the results show that trofinetide was safe and well-tolerated and also gives compelling evidence of efficacy of trofinetide in improving core symptoms of the disease.

Neurodevelopmental disorders such as Fragile X Syndrome which Neuren is targeting are traditionally hard indications to crack, with no current approved treatments. This makes it risky but also extremely valuable if success is achieved.

For a drug to be finally approved for Fragile X Syndrome, the key requirement will be to provide evidence that the overall effect of the drug in ameliorating multiple symptoms of the disease, improves the quality of life of patients. However, given the lack of any treatment alternative for this debilitating disease and small patient population, we expect the regulatory hurdles to be lower.

The results seen in the Fragile X Syndrome trial are similar to the pattern of clinical benefit observed in the Rett Phase II trial last year and most importantly are across multiple core outcome measures of the disease. The proof-of-concept (POC) for trofinetide in Fragile X and more broadly in neurodevelopmental disorders with benefits seen across two different indications now, in our view, significantly de-risks the company.

Licensing and M&A activity has heated up in the orphan drug space in recent years, with large companies paying multi-billion dollars to acquire smaller companies with one or more orphan drugs nearing commercialization. NEU is particularly well positioned to benefit from this. We note that one of the key attractions for a licensee for trofinetide is the potential applicability of trofinetide across multiple neurodevelopmental disorders. Success in both

Rett and Fragile X indications has now positioned trofinetide to be tried across the other autism spectrum disorders and has improved the drugs licensing prospects.We believe that the POC in FXS, coupled with the positive results seen in Rett, will inject additional impetus into NEU's partnering discussions.

Results from the Phase II Traumatic Brain Injury (TBI) trial are expected to be released in 1QCY16. Though TBI is not an orphan indication, it is still attractive as nothing is approved for it as yet.

We continue to assume that trofinetide gets licensed for a multi-million dollar deal in 2HCY16.

Earnings and Valuation Changes

We have revisited our assumptions for NEU based on the release of positive results from Fragile X Syndrome trial which have impacted our valuation.

Key assumption change

- We have increased our assumed probability of success for Fragile X Syndrome to 25% (from 14.5%).
- We have increased our peak market share penetration rate for trofinetide for Fragile X Syndrome to 30% (was 25%), only for the US market. Our peak sales forecasts have accordingly increased. We choose to keep the Ex-US penetration for Fragile X unchanged at 20% for now, given it is harder to navigate the different regulatory pathways existing in those markets.
- NEU envisages following a similar development path to Rett for Fragile X. Subject to discussions with the FDA in 1HCY16, the company will most likely run a brief paediatric trial in Fragile X Syndrome prior to a Phase III trial. We expect the paediatric trial to start potentially in 4QCY16. Based on this, our forecast launch timeline for Fragile X has moved to FY20 (was FY19).
- At this stage we assume that NEU will license trofinetide prior to initiation of a potential paediatric trial for Fragile X Syndrome in 2HCY16. Hence, we assume that a partner will assume the cost of the Fragile X paediatric trial and therefore do not include the related expenditure in our forecasts.

We value NEU at A$0.28/sh

The above changes to our model, have resulted in a modest lift in our valuation for Neuren to A$0.28/sh (was A$0.25/sh). **There were no changes to our FY15-17 earnings forecasts.** We retain our Buy recommendation.

Our DCF valuation model is based on a WACC of 18% and a terminal growth rate of 1%.

Table 1 - Summary of Valuation

Revised Forecasts	Base case
Enterprise value from DCF (AUDm)	494.4
Add: Cash at end FY15E (AUDm)	17.4
Less: Debt at end FY15E	0.0
Equity value (AUDm)	511.8
Total diluted shares (million)	1,845.7
Value per share (AUD)	**$0.28**
Current Share price (AUD)	$0.120
Expected Capital Growth	133.3%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Table 2 - NEU -Probability-Weighted Sum-of parts Base Case Valuation Summary

Asset	Stage	First Fiscal Year of sales (Est.)	Peak Market share	Peak Global Sales (US$m)	Probability of success	Probability adjusted NPV (A$m)	Value per share (A$)	% Mix
Trofinetide (IV) - Severe Traumatic Brain Injury	Phase II	2020	12.0%	$1,172	14.5%	$82	**$0.04**	16.1%
Trofinetide (oral) -Concussion	Phase II	2021	12.0%	$1,065	14.5%	$80	**$0.04**	15.6%
Trofinetide (oral)- Rett Syndrome	Phase II Top-line results reported	2019	50.0%	$1,377	30.0%	$163	**$0.09**	31.8%
Trofinetide (oral)- Fragile X Syndrome	Phase II Top-line results reported	2020	30% (US), (20% Ex-US)	$1,713	25.0%	$172	**$0.09**	33.6%
Other Pipeline/Non-allocated	NA	NA	NA	NA	NA	-$3	**$0.00**	-0.5%
Cash (EOY 2015E)	NA	NA	NA	NA	NA	$17	**$0.01**	3.4%
Equity Value						**$511.8**	**$0.28**	**100%**

GLOBAL PEAK SALES ARE PRE-RISK ADJUSTMENT AND ROYALTIES.

SOURCE: BELL POTTER SECURITIES ESTIMATES

Risk to our valuation

We currently assign only a 14.5% probability of success to each of the 2 ongoing trofinetide Phase II trials. We envisage that completion of Phase II trials with positive results will allow us to assign a higher probability of success and therefore will lead to material upgrades in our numbers.

We currently assume a licensing deal for trofinetide in CY2H16. If trofinetide gets licensed prior to our estimates, it will be an upside to our valuation.

At this stage, we do not value Neuren's second asset NNZ-2591 as it is yet to enter the clinic. Progress of this compound into the clinic will represent an upside to our current valuation.

Deal assumptions for trofinetide

Looking at deals in the orphan space, we believe that the structure of the trofinetide deal will be more front loaded in terms of a hefty upfront payment receivable by Neuren from the licensee. We expect average deal size in the orphan drug space to be over $350m.

Table 3 –Licensing deals in the orphan drug space

Date	Company	Product	Indication	Stage at licensing	Licensee	Total deal value in USDm (upfront plus milestones)	Upfront (USDm)	Milestones (USDm)	Note
CNS Indications									
Aug-10	Knopp Neurosciences	KNS-760704	Amyotrophic Lateral Sclerosis/ Lou Gehrig's disease	Phase II complete	Biogen Idec	345	20	325	Plus $60m equity stake
Nov-11	PTC Therapeutics	3 compounds	Spinal Muscular Atrophy	Pre-clinical	Roche	490	30	460	
Oct-09	Prosensa	4 RNA-based products	Duchenne's Muscular Dystrophy	Phase II complete	GSK	665	25	640	
Sep-10	Acceleron Pharma	ACE-031	Duchenne's Muscular Dystrophy	Phase II	Shire	498	45	453	Ex-US rights only
Jan-12	Isis Pharmaceuticals	ISIS-SMNRx	Spinal Muscular Atrophy	Phase II/III	Biogen Idec	299	29	270	
Apr-13	Isis Pharmaceuticals	Antisense compounds	Huntington Disease	Pre-clinical	Roche	392	30	362	
Other Indications									
Nov-07	Amicus Therapeutics	Amigal/Pilcera/duvoglustat	Fabry disease/Gaucher Disease/Pompe Disease	Phase II/Phase II/Phase I	Shire	440	50	390	
Oct-11	GlycoMimetics	GMI-1070	vaso-occlusive crisis associated with sickle cell disease	Phase II	Pfizer	340	NA	NA	
Oct-10	Amicus Therapeutics	Amigal	Fabry disease	Phase III	GSK	230	30	200	Plus $30m equity stake
Nov-09	Protalix	Elelyso	Gaucher disease	Phase III complete	Pfizer	115	60	55	Revenue expense share for Pfizer Protalix on a 60/40 basis respectively
					Average	381			

SOURCE: COMPANY DATA AND BELL POTTER SECURITIES

We forecast that trofinetide (oral and IV) together can get licensed for a total deal package of US$680m, including US$90m in upfront payment in CY2H16. We also expect tiered double digit royalties could be part of the deal ranging from 15%-25%. For conservatism sake, we model a flat rate of 15% now.

Forthcoming Milestones

In terms of news flow over the next 12 months, we expect the following:

- 1QCY16 -Top-line results from INTREPID Traumatic Brain Injury (TBI) trial;
- 1QCY16 – Initiation of paediatric Rett Syndrome Trial;
- 1HCY16 – End-of Phase II meeting with FDA on Fragile X Syndrome;
- 1HCY16 - Top-line results from Phase II concussion trial;
- 2HCY16 – Top-line results from paediatric Rett Syndrome Trial;
- 2HCY16 – Potential licensing deal for trofinetide (all indications);
- 2HCY16 – Potential initiation of paediatric Fragile X Syndrome trial by a partner.

Neuren Pharmaceuticals (NEU)

COMPANY DESCRIPTION

Neuren Pharmaceuticals (ASX: NEU), registered in Auckland, NZ and with offices in the US and Australia, is a clinical stage drug development company focused on drugs to treat disorders of the Central Nervous System. The company's lead candidate is trofinetide (previously known as NNZ-2566), in Phase II, for the treatment of Traumatic Brain Injury, Concussion and Fragile X Syndrome.The company has reported promising Top-line results from its Rett Syndrome Phase II trial which warrants progress of trofinetide to next stage of development. Neuren is also doing pre-clinical work on NNZ-2591 as a potential treatment for Fragile X Syndrome, Multiple Sclerosis, Parkinson's disease and peripheral neuropathy. Neuren currently has one major shareholder, Walker Corporation, associated with the Sydney businessman Lang Walker, with ~18.6% of the stock after the recent placement.

INVESTMENT STRATEGY

In our view, Neuren's shares are poised to re-rate as the company develops and subsequently commercializes its oral trofinetide product initially in two attractive orphan neurodevelopmental disease markets, Rett Syndrome (RS) and Fragile X Syndrome (FXS), with the potential to be useful in a wide variety of autism spectrum disorders (ASDs). We estimate that at an annual reimbursement of $100,000 per patient, Rett Syndrome would represent a US$1.6bn market and at an annual reimbursement of $125,100 per patient, Fragile X would represent a US$8.7bn market in the US alone.

Neuren is an attractive orphan drug play and is well placed to benefit from the heightened interest by big and specialty pharma in the space from a licensing and M&A perspective. Promising results from Phase II Rett and Fragile X trials serve as proof-of-concept for trofinetide and significantly de-risk the company. Success in both of these indications now positions trofinetide to be tried across other ASDs and therefore strengthens its value proposition and improves its licensing prospects. We also expect considerable upside in the event of clinical success for trofinetide in Traumatic Brain Injury and Concussion. A favourable licensing deal for trofinetide could trigger a significant re-rating.

KEY RISKS

We see the following key stock specific risks to our investment thesis on Neuren:

- **Reliance on partnerships to unlock value:** The success of NEU's business model is underpinned by its ability to ultimately attract a valuable partnering deal for its trofinetide asset. Failure to attract licensees for this drug candidate or to negotiate attractive deal terms as we have postulated will severely impact our forecasts.
- **Clinical risk:** There is a risk that NEU's clinical trials for trofinetide fail to reach their endpoints, which would in turn impact its partnering prospects. Historically trials targeted at CNS (central nervous system) related disorders are more complex and riskier. Also, there have been reports of high placebo effect seen with other competitor trials targeting autism especially in Fragile X Syndrome. In our view, NEU will also not be immune to this risk. We note however that NEU successfully managed this risk in the Phase II Rett and Fragile X Trials.
- **Reliance on one drug class to drive value:** NEU's drug candidate trofinetide for both versions IV and oral and pre-clinical candidate NNZ-2591 are of the same class. This makes them vulnerable to the success/failure of any one trial in any one indication to impact the sentiment of the drug being trialled in any other indication.
- **Funding risk:** Delays in partnering of trofinetide and receipt of upfront/milestone payments from the licensee may impact NEU's funding position in the long term. Although NEU has a high cash balance currently (~A$21.6m), the company may need to raise additional capital if it wishes to self-fund a Phase III trial for trofinetide.

NEU had ~A$15.2m cash at the end of 3Q15 which has been further bolstered by the A$6.35m placement in November

Neuren
as at 7 December 2015

Recommendation	Buy, Speculative
Price	$0.12
Valuation	$0.28

Table 4 - Financial summary

Neuren Pharmaceuticals (NEU) — **Share price (A$) $0.120**
As at 7 December 2015 — **Market cap (A$m) 205.0**

Profit and Loss

Y/e December 31 (A$m)	2013A	2014A	2015E	2016E	2017E
Revenue*	4.8	2.9	2.3	128.8	57.7
EBITDA	**-5.6**	**-8.7**	**-12.6**	**118.7**	**55.1**
Depreciation & Amortisation	-0.4	-0.1	-0.1	-0.1	-0.1
EBIT	**-6.0**	**-8.8**	**-12.7**	**118.5**	**55.0**
Net interest & Other Income/(Expense)	-1.2	1.4	0.9	0.9	1.8
Pre-tax profit	-7.1	-7.3	-11.8	119.4	56.9
Tax	0.0	0.0	0.0	35.8	17.1
NPAT (adjusted) before allocation to Minority Interests	-7.1	-7.3	-11.8	83.6	39.8
Less minority interests	0.0	0.0	0.0	0.0	0.0
NPAT (adjusted)	**-7.1**	**-7.3**	**-11.8**	**83.6**	**39.8**

* FY16/17 revenue numbers comprise of potential upfront and milestone payment receipt forecast from licensee on trofinetide deal in FY2H16

Cashflow

Y/e December 31 (A$m)	2013A	2014A	2015E	2016E	2017E
Reported NPAT plus minority interests	-10.5	-8.3	-13.0	82.7	39.4
Non-cash items	5.0	0.3	0.9	1.0	0.5
Working capital	-1.6	1.6	0.9	-0.3	-0.5
Other operating cash flow	0.0	0.0	0.0	0.0	0.0
Operating cashflow	**-7.1**	**-6.4**	**-11.2**	**83.4**	**39.4**
Capex	0.0	0.0	0.0	0.0	0.0
Investments	0.0	0.0	0.0	0.0	0.0
Other investing cash flow	0.0	0.0	0.0	0.0	0.0
Investing cashflow	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Change in borrowings	0.0	0.0	0.0	0.0	0.0
Equity issued	26.2	2.2	7.4	0.9	1.8
Dividends paid	0.0	0.0	0.0	0.0	0.0
Other financing cash flow	0.0	0.0	0.0	0.0	0.0
Financing cashflow	**26.2**	**2.2**	**7.4**	**0.9**	**1.8**
Net change in cash	**19.1**	**-4.2**	**-3.8**	**84.3**	**41.2**
Cash at end of period*	24.4	20.8	17.4	101.7	142.9
* Includes effect of exchange rate fluctuations on cash balance					
Free cash flow	**-7.1**	**-6.4**	**-11.2**	**83.4**	**39.4**

Balance sheet

Y/e December 31 (A$m)	2013A	2014A	2015E	2016E	2017E
Cash	24.4	20.8	17.4	101.7	142.9
Current receivables	1.6	1.0	0.4	0.4	0.4
Inventories	0.0	0.0	0.0	0.0	0.0
Other current assets	0.0	0.0	0.0	0.0	0.0
Current assets	**26.0**	**21.8**	**17.8**	**102.1**	**143.3**
PPE	0.0	0.0	0.0	0.0	0.0
Non-current receivables	0.0	0.0	0.0	0.0	0.0
Intangible assets	0.4	0.3	0.2	0.1	0.0
Other non-current assets	0.0	0.0	0.0	0.0	0.0
Non-current assets	**0.4**	**0.3**	**0.2**	**0.1**	**0.0**
Total assets	**26.5**	**22.1**	**18.0**	**102.2**	**143.3**
Payables	2.1	3.0	3.4	3.1	2.6
Debt	0.0	0.0	0.0	0.0	0.0
Provisions	0.0	0.0	0.0	0.0	0.0
Other liabilities	0.0	0.0	0.0	0.0	0.0
Total liabilities	**2.1**	**3.0**	**3.4**	**3.1**	**2.6**
Shareholders' equity	24.6	19.3	14.6	99.1	140.7
Minorities	-0.2	-0.2	0.0	0.0	0.0
Total shareholders funds	**24.4**	**19.1**	**14.6**	**99.1**	**140.7**
Total funds employed	**26.5**	**22.1**	**18.0**	**102.2**	**143.3**
W/A Diluted shares on issue	1,261.2	1,552.5	1,713.3	1,796.1	1,839.6

Valuation data

Y/e December 31	2013A	2014A	2015E	2016E	2017E
Adjusted Net profit (A$m)	-7.1	-7.3	-11.8	83.6	39.8
EPS (c)	-0.56	-0.47	-0.69	4.65	2.16
EPS growth (%)	N/A	N/A	N/A	NM	NM
P/E ratio (x)	N/A	N/A	N/A	2.6	5.5
CFPS (c)	-0.6	-0.4	-0.7	4.6	2.1
Price/CF (x)	-21.3	-29.1	-18.4	2.6	5.6
DPS (c)	0.0	0.0	0.0	0.0	0.0
Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	N/A	N/A	N/A	N/A	N/A
EV/EBITDA	-33.0	-21.1	-14.6	1.5	3.3
EV/EBIT	-30.8	-20.9	-14.4	1.5	3.3

Share price now (A$)	$0.120
Valuation (A$):	$0.280
Premium (discount) to price	133.3%
Recommendation:	Buy
Risk Rating	Speculative

Profitability ratios

Y/e December 31	2013A	2014A	2015E	2016E	2017E
EBITDA/revenue (%)	N/A	N/A	N/A	92.1%	95.5%
EBIT/revenue (%)	N/A	N/A	N/A	92.0%	95.3%
Return on assets (%)	-26.8%	-33.1%	-65.5%	81.8%	27.8%
Return on equity (%)	-29.0%	-38.0%	-80.6%	84.3%	28.3%
Return on funds empl'd (%)	-29.1%	-38.4%	-80.6%	84.3%	28.3%
Dividend cover (x)	N/A	N/A	N/A	N/A	N/A
Effective tax rate (%)	0.0%	0.0%	0.0%	30.0%	30.0%

Liquidity and leverage ratios

Y/e December 31	2013A	2014A	2015E	2016E	2017E
Net cash (debt) (A$m)	24.4	20.8	17.4	101.7	142.9
Net debt/equity (%)	N/A	N/A	N/A	N/A	N/A
Net interest cover (x)	N/A	N/A	N/A	N/A	N/A
Current ratio (x)	12.6	7.2	5.3	33.1	55.5

Interims

Y/e December 31 (A$m)	1H14A	2H14A	1H15A	2H15E	1H16E
Revenue	1.4	1.5	2.0	0.3	1.7
EBITDA	**-4.0**	**-4.7**	**-5.5**	**-7.1**	**-3.2**
Depreciation & Amortisation	-0.1	0.0	0.0	-0.1	-0.1
EBIT	**-4.1**	**-4.7**	**-5.5**	**-7.2**	**-3.3**
Net interest & Other Expense	-0.2	1.6	0.8	0.2	0.1
Pre-tax profit	-4.3	-3.1	-4.7	-7.1	-3.2
Tax	0.0	0.0	0.0	0.0	0.0
Adjusted Net Profit	-4.3	-3.1	-4.7	-7.1	-3.2
Less minority interests	0.0	0.0	0.0	0.0	0.0
Net profit to shareholders	**-4.2**	**-3.1**	**-4.7**	**-7.1**	**-3.2**

SOURCE: BELL POTTER SECURITIES ESTIMATES

Recommendation structure

Buy: Expect >15% total return on a 12 month view. For stocks regarded as 'Speculative' a return of >30% is expected.

Hold: Expect total return between -5% and 15% on a 12 month view

Sell: Expect <-5% total return on a 12 month view

Speculative Investments are either start-up enterprises with nil or only prospective operations or recently commenced operations with only forecast cash flows, or companies that have commenced operations or have been in operation for some time but have only forecast cash flows and/or a stressed balance sheet.

Such investments may carry an exceptionally high level of capital risk and volatility of returns.

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