Neuren delivers its 2nd CY21 tick in a watershed year

NNZ-2591 receives its second tick for CY21

- NEU has reported positive results of its Phase 1 safety trial of NNZ-2591 which is being developed for Phelan-McDermid, Angelman and Pitt Hopkins syndromes. The success paves the way to submission of an Investigational New Drug (IND) application to the US Food and Drug Administration (FDA) to begin Phase 2 trials, planned to start in H2CY21.

- In January 2021, the company received a positive decision on its applications to the European Medicines Agency (EMA) for NNZ-2591 Orphan Designation in its three targeted syndromes. Orphan drug status carries a number of benefits including 10 year market exclusivity, +2 years if granted paediatric use extension of patent life. FDA Orphan drug status of 7 years +6 month paediatric extension has also been granted.

CY21 to crystallise trofinetide value

- Topline Phase 3 results of trofinetide in Rett Syndrome are expected to be announced in late CY21. MST estimates that positive results will lead to US$25m milestone payment from its partner, ACAD Pharmaceuticals (NASDAQ:ACAD) over CY22. The licensing deal includes potential US$455m in milestone payments and 10+% sales royalties for Rett and Fragile X Syndromes for the North American market (NAM).

- Over CY21, MST assumes that NEU will confirm licensing arrangements for the ex NAM rights including Europe and major Asian markets. MST estimates a US$15m upfront payment over CY21. Positive results of the ACAD trials are expected to drive further milestones and royalty flows with the progression to EU and other market approvals.

- MST estimates assume that positive results in trofinetide's Phase 3 trials and NNZ-2591's Phase 2 trial will trigger milestone payments over CY21-CY23 of ~A$146m, almost equal to its current market cap.

Valuation Uplift

MST valuation of the NEU pipeline is based on a risk adjusted DCF. Progression to Phase 2 sees the probability increase to 25%, (previously 19%) taking the NEU valuation to A$433m from A$398m ($3.68ps fully diluted). Including cash of $24m, a value of A$457m is almost 3X the current market cap of $165m. In MST's view, CY21 potential news flow including the start of Phase 2 NNZ-2591 trials, positive topline Phase 3 trial results and licensing deal/s for exNAM trofinetide rights in Rett/Fragile X syndromes will close the valuation gap. Risks include clinical trial timing, demonstration of drug safety & efficacy to support key global markets approvals and trigger licensing agreements with milestone payments/ sales royalties from both ACAD and expected new licensing partners.

Neuren Pharmaceuticals is an ASX listed biotechnology company developing drugs for debilitating neurodevelopmental disorders.

Trofinetide and NNZ-2591 are targeting five disorders for which there are no approved therapies. Trofinetide Phase III trial results in Rett Syndrome are expected in late CY21, NNZ-2591 to enter Phase 2 trials over CY21.

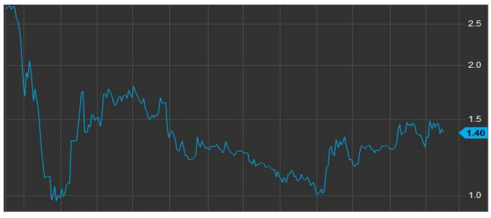
Board and management are well-credentialled with in-depth experience in drug development and commercialisation.

Company data	
Stock	ASX: NEU
Primary Exchange	ASX
Price	A$1.40
Market cap	A$165m
Valuation (per share)	A$3.68 diluted
Net cash (31/12/20)	A$24.1m
Shares on issue	114.6m
Options/Rights	3m

Next steps

- H1CY21 Submit IND for Phase 2 trials of NNZ-2591
- H2CY21 Commence Phase 2 trial
- Late CY21 Topline Phase III results trofinetide in Rett Syndrome

Share Price Performance (12 months)



Source: FactSet.

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Investment Thesis

Crystallising portfolio value CY21/CY22

In MST's view, there is a disconnect between the stage of development and market potential of NEU's assets and its current valuation (See NEU report Nov 5 2020). Continued positive newsflow of significant near term milestones is likely to see a material re assessment.

The probability of a drug receiving approval increases as it progresses along the development path. With the announcement of the positive Phase 1 trials of NNZ-2591 and its likely progression to Phase 2 trials, MST DCF valuation has been adjusted to reflect a higher probability of success (from 19% to 25%) of NNZ-2591 in the three targeted syndromes. The uplift sees a DCF valuation of $433m (previously $398m). Including cash of $24m, the updated valuation of A$457m is almost 3X NEU's current market cap of $165m.

Over the period of CY21-CY23, by MST estimates positive results in trofinetide's Phase 3 trials and NNZ-2591's Phase 2 trial will trigger milestone payments over CY21-CY23 of ~A$146m, almost equal to its current market cap.

Other CY21 Potential Value Drivers

The results of the Phase 3 trial NEU'S other drug candidate, trofinetide are expected in late CY21. ACAD has licensed the NAM rights of trofinetide in both Rett and Fragile X syndrome with milestone payments of up US$4455m and royalties of 10%+. Positive topline data results in CY21 are expected to lead FDA approval in CY22 and trigger a milestone payment of MSTe US$25m over CY22.

NEU retains the rights of trofinetide for ex NAM markets. Over CY21, licensing deal/s for these markets are expected to be confirmed with an estimated upfront payment of US$15m. Release of positive topline Phase 3 data may deliver a higher payment.

CY21/22 Potential Value Drivers

Significant value-adding events are expected over the next two years

- CY21 Positive Phase 3 results of trofinetide in Rett Syndrome
- CY21/22 Licensing agreements/upfront payments for trofinetide ex NAM
- CY22 FDA approval of trofinetide in Rett syndrome
- CY22 US market entry of trofinetide in Rett syndrome
- CY22 ACAD announce plans for development of trofinetide in Fragile X Syndrome
- CY22 Release of Phase 2 results for NNZ-2591 in the three conditions
- CY22 Licensing agreement for NNZ-2591 post positive Phase 2 trials

CY21 – a watershed year

NNZ-2591 Phase 1 results pave the way to Phase 2

NEU has announced positive results in its first clinical trial of NNZ-2591. Two double-blind placebo-controlled cohorts of eight healthy adult volunteers were dosed orally twice per day for seven days. In each cohort, six subjects received NNZ-2591 and two subjects received placebo. Each cohort was titrated up to the target dose, with the target dose in the second cohort double the target dose in the first cohort.

The twice daily oral dosing for seven days was well tolerated at all dose levels tested and importantly at doses expected to be within the effective therapeutic range. All subjects completed dosing, apart from one subject on lowest dose. There were no clinically significant findings with respect to safety laboratory tests, vital signs, or cardiac tests. The pharmacokinetic analyses are ongoing. All adverse events (AEs) were mild or moderate and resolved during the trial with no Serious Adverse Events.

The data will now form part of the Investigational New Drug (IND) application to the US FDA to support approval to commence Phase 2 trials in children Phelan-McDermid, Angelman and Pitt Hopkins syndromes.

Steps to Phase 2 trials

NEU plans to undertake a Type C meeting with the FDA to discuss requirements prior to lodging its IND submission. The steps to trial commencement include;

- ***EU Orphan Drug decision for NNZ-2591 √***
- ***Results Phase I clinical trial of NNZ-2591 healthy adult volunteers √***
- Drug substance for trials completed and released
- Type C Meeting with FDA to discuss IND submission
- Submit IND application to FDA
- Drug product for trials completed and released
- IND approval from FDA
- Commence Phase 2 trials in H2CY21 with results in CY22

From a funding perspective, NEU had a cash balance of A$24.1m as of 31 December 2020. With ACAD funding the Phase 3 Rett Syndrome trials, NEU believes it has funding to continue development over the Phase 2 trial to the release of the Phase 2 data.

Trofinetide Phase 3 Trial Results

Positive Phase 3 Rett syndrome data are expected to trigger two revenue streams for NEU.

1. Acadia Pharmaceuticals NAM Licensing Agreement Milestone/Royalty payments

In total, NEU's agreement with ACAD includes milestone payments of US$455m for both Rett and Fragile X syndromes. US$105m are based on developmental milestones with some US$350m contingent on sales performance. MST's sales royalty estimates range from 10% to 12%.

The MST model assumes a total of US$50m milestones for Rett Syndrome on FDA approval and market entry. Sales revenues are expected to trigger 10% royalty payments on net sales.

ACAD also holds the rights for trofinetide in Fragile X syndrome in NAM markets. Post the Rett Syndrome results' read out, management is likely to announce its development plans, creating further interest.

2. ex NAM Licensing Milestones /Royalties Rett and Fragile X Syndromes

NEU retains the rights for trofinetide in ex-NAM markets. Its agreement with ACAD allows the use of all the trofinetide technical, clinical, and regulatory data to seek approval and commercialise the drug in countries outside North America for both Rett Syndrome and Fragile X.

Prior to or on positive topline Phase 3 trials in the US, the MST valuation assumes NEU will finalise a licensing deal that will include both Rett syndrome and Fragile X syndromes for rest of world markets. ACAD trials have only been conducted in the US. The terms of the deal are likely to vary depending on the timing of the deal. Regulatory authorities such as the EU and Japan may require additional data or bridging studies. The MST valuation model assumes an agreement is negotiated prior to the Phase 3 results readout, with an upfront payment of US$15m. The uncertainty of the results and the potential for further trials are likely to see an agreement that is weighted to achievement of later milestones such as approval in the key exNAM markets, market entry and sales performance. If NEU awaits the Phase 3 data read out, a higher upfront payment would be likely.

Market advantages for potential suitors of trofinetide and NNZ-2591

Both drugs offer advantages that are likely to be of interest to potential partners. From a market competitive position, there are no approved treatments for the targeted conditions. From a regulatory perspective, trofinetide and NNZ-2591 are targeting rare paediatric conditions. Trofinetide has US and EU Orphan Drug status in Rett Syndrome and NNZ-2591 has US and EU Orphan Drug status for all three conditions. The classification offers a number of advantages including extended market exclusivity of 7 years and 10 years with extensions of 6 months and 2 years respectively in paediatric conditions. ACAD is a likely suitor.

Risks, Sensitivities & Valuation

The valuation of NEU has been derived from a risk adjusted DCF. The investment case is based on the use of trofinetide and NNZ-2591 in the nominated indications. No value has been ascribed to other potential clinical indications. The valuation is subject to the usual sensitivities and risks of new drug development and commercialisation of its two drug candidates. These include confirmation of drug safety and efficacy in the nominated conditions, clinical trial timing and regulatory approval in the key global markets, confirmation licensing agreements and milestone payments/ sales royalties from both ACAD and expected new licensing partners. The COVID pandemic has resulted in clinical trial delays and in some circumstances abandonment of the trial. ACAD and potential new partners may experience delay.

ACAD's Phase 3 trofinetide trial is only being conducted in the US. There is risk that the European Medicines Agency and other regulatory bodies may require European / local clinical trial data, adding cost and delay to market entry.

The expected commercial performance is based on a number of assumptions such as market entry, pricing, market penetration, sales royalties. The assumptions present upside and downside risk. The failure to secure partners may see NEU assume the regulatory filings and marketing/distribution role which is likely to see an extension of the forecast timelines, additional costs and changes to the revenue forecasts.

MST's risk adjusted DCF presents a valuation of NEU at A$433m, A$3.68ps fully diluted. With cash reserves of A$24.1m the implied enterprise value of A$457m compares to a market capitalisation of A$165m, share price of A$1.40. MST believes that positive Phase 3 trial results and other expected news will result in a significant re-rating of the stock over CY21.

Exhibit 1 - MST Forecast Financial Summary

NEUREN PHARMACEUTICALS						
Year ending 31 December	A$000					
STATEMENT OF COMPREHENSIVE INCOME	**2018A**	**2019A**	**2020E**	**2021E**	**2022E**	**2023E**
Revenue						
Liceninsg Revenue	13,544			21,750	58,000	65,833
Australian R&D tax incentive	446	495	591	931	2,793	2,793
Gross Profit	**13,098**	**300**	**591**	**22,681**	**60,793**	**68,626**
Expenses						
R&D	-6,101	-9,858	-6,583	-10,000	-10,000	
Administration	-2,074	-1,713	-1,480	-1,421	-1,463	-1,507
Other	-3,921	-261				
Amortisation of intangibles	-72	-72	-72	-72	-72	-72
Depreciation	-6	-6	-6	-6	-6	-6
Operating profit (loss)	**1,002**	**-12,686**	**-7,550**	**11,182**	**49,252**	**67,041**
Interest received	218	389	164	242	357	854
Interest Paid						
Net Interest Received	218	389	164	242	357	854
Profit (loss) before income tax	3,073	-10,816	-7,386	11,424	49,609	67,895
Income tax expense						
Total comprehensive profit (loss) attributable	3,073	-10,816	-7,386	11,424	49,609	67,895
Marginal tax rate						
Profit after tax	3,073	-10,816	-7,386	11,424	49,609	67,895

STATEMENT OF FINANCIAL POSITION	**2018A**	**2019A**	**2020E**	**2021E**	**2022E**	**2023E**
Current Assets						
Trade and other receivables	942	522	522	522	522	522
Cash and cash equivalents	23,576	13,844	24,188	35,690	85,377	153,350
Other	2,121		2,516	2,097	2,360	2,282
Total current assets	26,639	14,396	27,226	38,309	88,259	156,154
Non-Current Assets						
Property, plant and equipment	2	10	10	10	10	10
Intangible Assets	1					
Total non-current assets	3	10	10	10	10	10
Total Assets	26,639	14,406	27,236	38,319	88,269	156,164
Current Liabilities						
Trade and other payables	1,973	559	559	559	559	559
Total current liabilities	1,973	559	559	559	559	559
Non-Current Liabilities						
Total Liabilities	1,973	559	559	559	559	559
Net Assets	24,669	13,847	26,677	37,760	87,710	155,605
Minority Interst						
Net assets attributable	24,669	13,847	26,677	37,760	87,710	155,605
Equity	126,426	126,426	146,642	146,642	146,642	146,642
Other Reserves	-8,497	-8,503	-8,503	-8,503	-8,503	-8,503
Accumulated Deficit	-93,260	-104,076	-111,462	-100,038	-50,429	17,466
Total Equity	24,669	13,847	26,677	38,101	87,710	155,605

STATEMENT OF CASH FLOWS	**2018A**	**2019A**	**2020E**	**2021E**	**2022E**	**2023E**
License Agreement Receipts	13,544			21,750	58,000	65,833
Tax paid						
Australian R&D Tax Incentive Receipts	631	450	591	931	2,793	2,793
Interest Received	165	413	164	242	357	854
GST Refunded	95	102				
Payments for Employees and Admin,Corp Costs	-1,909	-1,742	-2,250	-1,421	-1,463	-1,507
R&D and Other Payments	-6,118	-10,942	-6,583	-10,000	-10,000	0
Net Cash Flow from Operating Activities	6408	-11719	-8,078	11,502	49,687	67,973
Net Cash Flow from Investing Activities						
Cash Flows from Financing Activities						
Proceeds from Issue of Shares	11,730	1,860	20,216			
Payments of Shares Issue Expenses	-16		-1,075			
Net Cash Provided from Financing Acitivites	11,714	1,860	19,141			
FX changes			-719			
Net Increase/Decrease in cash	18,122	-9,871	10,344	11,502	49,687	67,973
Cash equivalents at beginning of year	4,706	23,576	13,844	24,188	35,690	85,377
Cash & equivalents at end of year	23,576	13,844	24,188	35,690	85,377	153,350

Source: Company reports, MST assumptions

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