Neuren Pharmaceuticals Limited

CEO Presentation to the Annual Shareholders Meeting

31 May 2012

The logic that has driven the company since the beginning is the same logic that drives us now. Twenty years ago, Professor Peter Gluckman (now Professor Sir Peter Gluckman), Neuren's scientific founder, published a paper highlighting the role of IGF-1 in neurology[1]. NNZ-2566 is a direct, linear descendent of that work and the succeeding two decades of international research on IGF-1 and its derivatives. Across our neurology portfolio, the drugs that we're developing are improved versions of naturally occurring molecules – molecules produced by the brain in response to acute and chronic injury. We don't start with a molecular target then screen large numbers of compounds to find which ones interact with the target. We start with molecules that result from millions of years of evolution, that we know work, then modify them only to the extent necessary to make them suitable drug candidates.

During 2011 and the first part of 2012, we made significant strides, advancing our product portfolio by relying on the same logic that provided the impetus for founding the company. These advances have created substantial new opportunities for Neuren and its shareholders. The pipeline is deeper and represents a dramatically enhanced value proposition compared to this time last year. Much of the incremental value derives from continued development of the oral form of NNZ-2566 and progress toward important clinical trials in two new indications: concussion and Rett Syndrome. With the steps we've taken since last year, Neuren has clearly emerged as the leading company in the industry targeting these indications. These are very different conditions – one rare, the other common; one

[1] Gluckman et al. A role for IGF-1 in the rescue of CNS neurons following hypoxic-ischemic injury. Biochemical and Biophysical Research Communications Volume 182, Issue 2, 31 January 1992; 593–599

acute, the other chronic – but, as I'll discuss a bit later, there are common features that make both valid targets for NNZ-2566 and commercially attractive opportunities.

The new opportunities related to NNZ-2566 oral result from the confluence of a large number of accomplishments and studies:

- Brilliant work by US Army scientists has shed new light on the fundamental mechanisms of action of the drug, elucidating the critical role that inhibiting neuroinflammation plays in preventing secondary brain injury by reducing pathological microglial activation and cell death or apoptosis.
- Rapidly expanding understanding of the cellular and molecular basis of neurological diseases and conditions and the extent to which common pathological processes (especially inflammatory cytokines) are involved in many acute and chronic CNS indications – TBI, stroke, autism spectrum disorders, Alzheimer's and Parkinson's diseases, even normal aging.
- The rational modification of the native molecule by Prof. Margaret Brimble and her team in the Organic and Medicinal Chemistry program at the University of Auckland. These simple modifications resulted in oral bioavailability and dramatically improved the half-life of the drug.
- Our finding that a simple aqueous formulation yields a superior pharmacokinetic profile compared to more complicated and expensive formulations has saved time and money and will help keep our manufacturing costs down. In addition, the stability of oral NNZ-2566 after reconstitution with water – at least 5 days – means more convenience for patients and simpler logistics for clinical trials.
- The excellent safety profile that NNZ-2566 has shown, both in animals and people, gives us more latitude in selecting doses and should mitigate against testing sub-optimal doses. There are many potentially valuable and effective drugs that have been abandoned because they couldn't be or simply weren't given at efficacious levels.
- We have worked very hard to ensure that our intellectual property rights are robust and well-protected. And they are. We now have issued patents for composition of matter, oral formulation and broad utility claims as well as a number of pending patent applications.

These will not only protect our rights, they will enhance the potential value of the NNZ-2566 franchise in partnering negotiations.

So, how are these new opportunities different and why do we believe that they add so much value?

- Our decision to target these indications coincides with dramatically increased public and government awareness of the incidence or prevalence of autism spectrum disorders and concussion and their impact on patients, families, public health and health care expenditures.
- It also coincides with an increasing interest in rare, genetic and niche indications among big pharma and big biotech companies.
- For some indications, treatment would be chronic, possibly for life, rather than a single short course of therapy. That means even relatively rare conditions like Rett Syndrome represent large potential markets.
- Rare diseases, pediatric target populations and serious diseases or conditions with unmet medical need come with significant advantages including Fast Track designation during development, accelerated review of NDAs, lower or waived FDA registration fees, longer periods of market exclusivity, US tax credits equal to 50% of the cost of human trials, premium pricing and fewer reimbursement hurdles.
- Drug development for these sorts of indications also takes place within a more flexible regulatory environment that can support use of non-standard endpoints, more reliance on surrogate measures, smaller numbers of patients, fewer placebo controls and single pivotal trials.
- The clinical trials for Rett Syndrome and concussion will be easier to manage. Patients are more concentrated, our investigators already have good access to patients, infrastructure for clinical research is in place and the tools that the investigators are already using in patient care and research will qualify as endpoints for the trials.

- For Rett Syndrome, we have support and encouragement from the International Rett Syndrome Foundation and Autism Speaks – highly motivated advocacy organizations with grant programs and established connections to families and leading clinical researchers.
- For concussion, we have financial and scientific support from another highly motivated partner – the US Army.
- We have world-class academic partners in the Blue Bird Circle Rett Center at Baylor and the Sports Medicine Concussion Program at the University of Pittsburgh, both with strong experience in clinical research and proven capabilities in running trials.

With that introduction, let me provide an overview of our ongoing R&D efforts.

INTREPID[-2566]

Overall, the trial is progressing well although enrollment continues to be very slow. Unfortunately, we don't control enrollment at active sites since TBI is not a chronic condition where we can go out and recruit patients. Slower than forecast enrollment is reportedly being experienced by the progesterone trials as well. Whether this reflects lower incidence during winter months, a slow economy or some other factor is unclear. We've recently brought in a new CRO (Jubilant ClinSys) with a mandate to bring on 15 new sites. The sites that ClinSys has proposed have all been pre-qualified in terms of both patient flow and clinical trial capabilities. Payments to ClinSys are based on enrollment milestones to provide strong and continuing incentives. We also are nearing completion of a feasibility assessment of sites in Russia, where the incidence of TBI is very high, and expect to bring at least six sites there into the study in the second half of this year.

The Exception from Informed Consent or EFIC process is well underway. Five of the 7 current sites that will be participating in the EFIC protocol have IRB approval for the Community Consultation and Public Disclosure program that precedes final approval. The first fully approved site is presently undergoing Army review which is required for all clinical trials funded by the Army. For trials conducted under EFIC, the study has to be approved by the Secretary of Defense or his designee.

Because of slow enrollment, we're now projecting completion of enrollment in the second half of 2013. We realize that this delay is disappointing and, believe me, we share your frustration but we're doing everything we can to remedy the situation without in any way jeopardizing the integrity or uniqueness of the trial. On a positive note, the incidence of serious adverse events or SAEs continues to be very low as does mortality. We recently completed the reproductive toxicology studies that are necessary to initiate a pivotal trial and found no effects whatsoever on male or female fertility or reproductive fitness.

Oral NNZ-2566 in concussion

As I mentioned earlier, public awareness of the potentially devastating impact of concussion in sports, combat and other activities is growing very quickly. Concussion represents at least 75% of all traumatic brain injury in both civilian and military populations. I'm sure you've all read or watched recent stories about concussion in athletes here, in the US and elsewhere. Even with a single concussion, a significant proportion of patients – up to 30% in some studies – continue to have symptoms a month or more later. These symptoms can include trouble with memory and thinking, attention, depression, irritability, problems sleeping, dizziness and headaches. With multiple concussions, the persistence of symptoms increases dramatically and, in some patients, a neurodegenerative condition called chronic traumatic encephalopathy or CTE develops. CTE can result in symptoms of dementia including memory loss, confusion, aggressiveness, and depression. An article in *Science Magazine* a couple of weeks ago titled "Afghanistan, Like Football, May Be Bad for the Brain" reported on a paper by Lee Goldstein and his colleagues from Boston University. The paper was published in *Science Translational Medicine* on 16 May 2012 and reported that the chronic, pathological changes to the brain resulting from blast exposure in military personnel are much the same as those experienced by head injured athletes that can lead to CTE. Nobody says "It's just a concussion" any more.

The Phase I safety and pharmacokinetic study is underway. The first cohort has been completed. No adverse events were reported during the specified follow-up period. Dosing of the second cohort was initiated this week. We are expecting to complete the Phase I study by the end of July. Neuren is

planning to start a Phase II trial in Q4 this year, in time for high school and college football and soccer seasons in the US. The study will be led by the University of Pittsburgh Sports Medicine Concussion Program, one of the leading centers for research in concussion. The direct costs of the trial will be funded by the US Army which has committed approximately US$3.8m for the study and for development of NNZ-2566 oral. Patients enrolled in the trial will be athletes who are already enrolled in a screening program called Immediate Post-Concussion Assessment and Cognitive Testing or ImPACT®. People enrolled in ImPACT® have baseline, pre-injury neurocognitive assessments completed such that each subject will essentially serve as his or her own control. This design increases the statistical power and decreases sample size requirements, allowing us to use return to baseline as the measure of efficacy which is much more sensitive than comparison with normative, general population-based data.

Potential subjects will be identified by personnel trained by the UPMC group at the sports field rather than waiting for them to show up at the emergency department. All patients will have an MRI with Diffusion Tensor Imaging or DTI to help identify patients with specific types of brain injury which will be part of the analysis at the end of the study. DTI is particularly useful for imaging injuries in the axons that make up the white matter of the brain. So-called diffuse axonal injury or axonal shearing often occurs as a consequence of acceleration – deceleration injuries which are common among athletes and blast-injured soldiers. We are forecasting that enrollment in the Phase II trial will be completed within a year.

Oral NNZ-2566 in Rett Syndrome

Rett Syndrome is a profoundly disabling neurological condition that occurs almost exclusively in girls following apparently normal development for the first six months of life. Typically, between 6 to 18 months of age, patients experience a period of rapid decline with loss of purposeful hand use and the ability to speak. Many patients have recurrent seizures. They experience a variety of motor problems including increased muscle tone (spasticity) and abnormal movements as well as cardiac, respiratory, gastrointestinal and sometimes orthopedic problems. They are never able to provide for their own needs. Although it is a rare disorder, it is believed to be second only to Down Syndrome as a cause

of chronic neurological problems that include severe communication, motor disabilities and epilepsy. Rett Syndrome is caused by mutations on the X chromosome on a gene called MECP2. There are more than 200 different mutations found on the MECP2 gene. Rett Syndrome affects all racial and ethnic groups and occurs worldwide in 1 of every 10,000 to 23,000 female births. Patients with Rett Syndrome can live for 40 years or more.

Importantly, it is no longer considered to be a neurodevelopmental disorder because experiments in a mouse model of Rett Syndrome in which the normal MECP2 gene was added back showed that the phenotype can actually be reversed. Experiments conducted at MIT with the n-terminal tripeptide of IGF-1 or IGF-1(1-3) – what we call Glypromate, the parent compound of NNZ-2566 – also showed that symptoms can be partially reversed with therapy. Following on from the MIT experiments, a Phase I/II clinical trial of Increlex® (recombinant human IGF-1) has been initiated at Boston Children's Hospital. That trial is being supported by the International Rett Syndrome Foundation and Autism Speaks. Increlex® is approved for severe IGF-1 deficiency, a cause of growth failure. Because it induces rapid bone growth, however, it cannot be administered to adults or older children whose epiphyses – the growth plates at the end of the long bones – are closed.

While it may not be intuitively obvious that a drug being evaluated as a therapy for TBI may also be applicable to Rett Syndrome, the underlying pathologic processes in Rett Syndrome and TBI show a remarkable degree of overlap. These include increased neuroinflammation, pathological microglial activation, increased extracellular glutamate levels, decreased dendritic spine density and convulsive and non-convulsive seizures. Dr. Steven Kaminsky, Chief Scientific Officer for IRSF, former VP of Research at the Uniformed University of the Health Sciences (the military's medical school) and former Vice Chairman of the Department of Molecular and Human Genetics at Baylor, has advocated that the pathology of TBI and that of Rett Syndrome have so many mechanisms in common that development of therapeutics for both conditions should be integrated. When he was with the military, Dr. Kaminsky was a member of the committee that reviewed and approved Neuren's first grant application for NNZ-2566 in TBI. He has commented that the mechanisms of action of NNZ-2566 are directly relevant to both TBI and Rett Syndrome.

In TBI, the therapeutic goal is to prevent secondary brain injury caused primarily by the acute neuroinflammatory cascade. In Rett Syndrome, the therapeutic goal is to restore neuronal function as a way of reducing the symptoms of the condition. Neurons in Rett Syndrome patients have not died or atrophied; they exist in an immature state with impaired intra-neuronal communication, called synaptic plasticity. Deficits in synaptic plasticity are a feature of other autism spectrum disorders as well which could eventually create additional opportunities for NNZ-2566.

Neuren is planning to initiate a Phase II proof of concept trial in adolescents and adults with Rett Syndrome late this year pending completion of the Phase I study. Drs. Daniel Glaze and Jeffrey Neul, Director and Assistant Director, respectively, of the Blue Bird Circle Rett Center at Texas Children's Hospital, one of the world's leading clinical centers, will lead the trial.

We held a very productive and informative pre-IND meeting with the FDA in early May. We're presently modifying the protocol based on the FDA's feedback and plan to submit the IND in June. A second study in pediatric patients is planned for 2013. Both studies are expected to take approximately 1 year to complete. If the results of the Phase II trials are positive, we believe that a single pivotal trial in adolescents and adults and one in children would be required to submit an NDA for approval.

Perseis

Neuren's Perseis Therapeutics subsidiary, a joint venture with the New Zealand Breast Cancer Research Trust, is developing monoclonal antibodies against two trefoil factors, TFF-1 and TFF-3, proteins expressed by a wide range of cancers that increase the spread of the tumor, decrease its susceptibility to therapy and are associated with more metastatic disease and poorer survival in patients. Our first target is TFF-1 in breast cancer which we are targeting with human monoclonal antibodies produced from antibody fragments selected from a fragment library licensed from the University of California San Francisco. The fragments were first selected by screening them for binding against the TFF protein then testing them against a human breast cancer cell line in vitro. The best were selected for testing in a xenograft model where human breast cancer cells are

implanted into immunocompromised mice and allowed to become established before treatment begins.

The first xenograft experiment has been now been completed. Of the two monoclonal antibodies we tested (identified as TFF1.1 and TFF1.4), following 8 weeks of treatment, TFF1.4 resulted in a statistically significant reduction in tumor volume (approximately 35%) compared to a vehicle control as well as 3-fold higher survival at the end of the experiment. Xenograft experiments typically also include an antibody control – an antibody raised against a target that is unrelated to the disease target – in order to differentiate between any possible non-specific antibody effect and the specific effect of the antibody being tested. A technical error on the part of a supplier resulted in our using an antibody that had been raised against a known cancer antigen which meant that it wasn't a true control. TFF1.4 outperformed that antibody as well but the study will need to be repeated with a valid control antibody. Despite this, we now know what we hoped for but didn't know before – that anti-TFF MAbs significantly inhibit proliferation of human cancer cells in vivo.

Based on the results from the xenograft study, we are moving forward with the program and have entered into a relationship with a company in Maryland called Noble Life Sciences to develop a stable cell line that will produce TFF1.4 antibodies fully capable of going from lab to patient to market. Noble estimates that producing the cell line and antibody and completion of the next xenograft study will be completed in Q1 2013. Noble specializes in development of drugs and biologics for cancer and was founded by former senior staff from Human Genome Sciences, MedImmune and other companies. They have capabilities from discovery through clinical trials (including partnering) and will help us ensure that development of TFF1.4 is accelerated and that all facets of the program meet full industry standards. We are prioritizing the anti-TFF project as a core Neuren program and I will be managing it personally. We will continue to pursue partnering in parallel with internal development alternatives.

NNZ-2591

NNZ-2591 is the lead molecule in Neuren's diketopiperazine or DKP portfolio. DKPs are dipeptides (as opposed to tripeptides like NNZ-2566) and NNZ-2591 comprises two of the three peptides that make up NNZ-2566. NNZ-2591 is 100% orally available and, from the initial tests we've performed, seems to be very safe. It is an extremely promising molecule with strong in vivo results in Parkinson's disease, stroke, cognitive impairment and peripheral neuropathy. At this point, it appears to be a very good candidate for chronic oral administration in a range of neurological conditions. We have committed limited resources to NNZ-2591 to develop a reliable manufacturing process and, as we did with the US Army for NNZ-2566, to elucidate the mechanism of action. These initial steps will inform our future decisions about which indications to pursue and how to position the molecule with respect to commercialization.

Motiva®

Motiva® is the trade name for nefiracetam, a compound for which we acquired certain rights through the acquisition of Hamilton Pharmaceuticals. Motiva® is presently in a Phase IIb trial in patients with post-stroke apathy, a common and highly problematic symptom of stroke and many other acute and chronic neurological conditions. A Phase II trial conducted in the US and Canada by Daiichi, from which Hamilton licensed Motiva®, showed a statistically significant effect of the drug on apathy in patients with co-morbid depression and apathy. The current trial is seeking to assess the efficacy of Motiva® in patients with apathy but not depression in order to clarify future development strategy. The trial is being conducted by Professor Sergio Starkstein at the University of Western Australia under a grant from the National Health and Medical Research Council. Screening, randomization, enrollment and follow-up are ongoing with an interim analysis expected around year end.

Concluding remarks

I'd like to end my statement with a few personal comments about what keeps me up at night and helps me get up in the morning. I've been involved in this industry for better than 30 years and, for most of them, I've been involved in some very challenging areas – HIV/AIDS, hepatitis, emerging infectious diseases and now TBI, concussion and Rett Syndrome. Some of my colleagues say I just like tilting at windmills but the truth is that I know there are real dragons behind those windmills and I would like nothing better than to stick a spear into TBI or concussion or Rett Syndrome.

I grew up around military medicine. My father was an Army doc as was my grandfather. When Neuren first started working on TBI with the Army, I spent some time at Walter Reed Army Medical Center – which is less than a mile from where I live – around wounded warriors suffering from the after-effects of TBI. That experience will always be with me as we move the TBI and concussion programs forward.

As for Rett Syndrome, as I've had a chance to get to know some of the Rett Syndrome families, I've discovered that the strength and grace with which they meet the challenges are profoundly awe-inspiring and humbling. Their love and hope are every bit as important a part of this program as the science and, in the end, are what will make it not just critically important but actually possible to develop an effective therapy. At its best, drug development is a partnership between patients and families, the organizations that advocate for them, companies, the FDA and dedicated physicians and scientists.

Thank you.

Email from mother of Rett Syndrome child (17 May 2012) who serves as Director Family Support and Director of the World Rett Syndrome Congress for the International Rett Syndrome Foundation:

Larry,

Just a quick note to thank you for choosing to work on Rett syndrome. We are a small but very motivated group, and I am happy to help in any way that I can with this proposed trial. I have a personal interest – my eldest daughter [name deleted] is almost 10 yrs old. She has one of the most common mutations (R168X), and is pretty severely affected. Wheelchair bound; g-tube fed; intractable seizures; lost speech; lost functional hand use; braced at ankles, trunk, and elbows to try and slow progression of scoliosis and contractures. Despite all this, she has a smile and attentive eyes that move mountains. She is very slowly learning to communicate through an eye-gaze activated computer. Though RTT is not degenerative, we know time is our enemy in combating these secondary issues. Be safe, but be swift – our hopes and dreams are with you!

Looking forward to our shared success,

Warmly,

[name deleted]