Good afternoon and thank you for joining us here today. This is the beginning of my 10th year with Neuren and, from my perspective – and hopefully yours – this is the most exciting time in the company’s history. We are truly on the cusp of realising the tremendous potential value of our technology both for shareholders and for patients. I’d like to begin by recognising the enlightened stewardship and guidance of our Directors, the dedication and enthusiasm of our staff and the patience and commitment of our shareholders. Without these, we would not be where we are today.

My objective today is to give you a comprehensive overview of the company and to share some of the reasons for my excitement. Of course, you are all mindful of the risks inherent in this industry as summarised in the Forward Looking Statement provided in Neuren’s announcements and reports.

Neuren was created by the merger of two companies that were formed to develop and commercialize intellectual property from the University of Auckland. The company listed on the ASX in 2005. Since then, the company’s headquarters has been in Auckland with clinical development and operations spread between Auckland and the US. As Richard mentioned, we have recently decided to move shareholder relations and certain administrative functions to Melbourne. We believe that this will improve our communications with shareholders and accessibility to the Australian capital market and investment community. We also are consolidating clinical development and operations in the US where virtually all of our clinical trials are run. This will streamline the operation and we believe will result in increased cost-effectiveness as we move into new clinical arenas. Both of these changes respond to the growing
demands on the company as we expand the portfolio of trials and clinical targets and
the consequent need to utilise resources efficiently and responsibly.

The people who will lead the company as we execute on the plans that I’ll describe
include Richard Treagus, the Executive Chairman, myself, a CFO who will join Neuren
in a new Melbourne-based role and Joe Horrigan who serves as VP for Clinical
Development and Medical Affairs. Richard is trained as a physician and brings over
20 years of operational and strategic experience in the international pharmaceutical
industry, most recently as CEO of Acrux which, under his leadership, completed the
largest product licensing deal in the history of the Australian biotech sector, a deal with
Eli Lilly worth $335m plus royalties. I originally trained as an epidemiologist and have
more than 30 years of experience in the sector. Before I joined Neuren, I was CEO of
a contract research organization that supported pharmaceutical and biotechnology
companies, the NIH and the US Army in biomedical research and product
development. Joe is a neuropsychiatrist and internationally-recognised expert in
clinical trial design. He joined Neuren last year from Autism Speaks, the largest
research and advocacy organization in the autism field, where he served as Assistant
VP and Head of Medical Research. Previously, he coordinated paediatric drug
development in the Neurosciences Medicines Development Center at GlaxoSmithKline where he worked for nine years.

Neuren enjoys three highly productive and critically important strategic relationships.
These include:

- A collaborative relationship with the US Army Medical Research & Materiel
  Command (USAMRMC) and the Walter Reed Army Institute of Research
  (WRAIR) which began in 2004. WRAIR conducted much of the ground-
  breaking work to define the pharmacology and mechanisms of action of NNZ-
  2566, our lead clinical candidate, elaborating its effects on neuroinflammation
  and microglial activation as well as its effects in models of TBI and non-
  convulsive seizures. The USAMRMC also has provided regulatory support,
  technical advice and more than $26 million in non-dilutive grants to Neuren and
  our collaborators to support development of NNZ-2566 for TBI and concussion
  as well as development of the oral formulation.

- The International Rett Syndrome Foundation (IRSF) has provided advice on
  clinical trial strategy, introductions to leading clinical investigators and a
  $600,000 grant to cover part of the cost of the first Rett Syndrome trial. Support
from an advocacy organisation such as IRSF in our discussions with the FDA and communications with patients, families and investigators is extremely important and will continue to be critical to successful implementation of our programmes.

- The Fragile X Drug Validation Initiative (FraX-DVI) is a non-profit research organisation committed to developing novel therapies for Fragile X Syndrome by translating scientific discoveries into practical applications. Funded by FRAXA, the Fragile X Research Foundation, FraX-DVI is a multidisciplinary laboratory with internationally recognised capabilities in preclinical research including the animal model used to test NNZ-2566.

Looking back briefly at 2012 and the first part of this year, Neuren had a number of notable achievements including a positive review of safety in the first 80 subjects in the INTREPID trial, enrolment of the 100th subject in that study, approval by the US Defence Department to enrol under Exception from Informed Consent (EFIC), a Phase 1 study with the oral formulation of NNZ-2566 that showed the drug to be very well tolerated with no indications of safety concerns, a grant awarded to Baylor College of Medicine to help support the first Rett trial, a remarkably compelling result in a preclinical model of Fragile X Syndrome and issuance of a second US patent covering oral formulations of NNZ-2566. These accomplishments reinforce the value of our science and technology and reflect our ongoing commitment to the highest level of execution against the backdrop of the challenges that will always be part of this industry.

**Strategy.** Overall, the company’s strategy is to maximise shareholder value and to minimise the risk, cost and time to bring safe, effective, life-changing medicines to patients. At its core is leveraging the unique biology of NNZ-2566 across a number of different indications. A key part of our strategy is to expand Neuren’s pipeline from acute, generally one-time treatments into chronic conditions where treatment is likely to be long-term, possibly for life. In chronic conditions – even those like Rett Syndrome that affect a relatively small number of patients – long-term use will result in large commercial opportunities. Similarly, targeting multiple, distinct conditions provides multiple opportunities for success with the same compound. The risk of a setback in any one area is mitigated and potential for multiple wins is heightened.

Our selection of therapeutic targets is neither opportunistic nor “follow the leader” – it’s part of a calculated strategy with fundamental criteria underpinning it. All of the clinical targets we’ve chosen to pursue meet these criteria:
• Significantly under-treated medical needs with no currently approved therapies
• Legitimate opportunity to be first in class with a treatment that fundamentally alters the course of the disease or its core symptoms
• Eligible for regulatory advantages which come with Fast Track, Orphan Disease or Breakthrough Therapy designation that can significantly reduce the cost and time of bringing a new medicine to the market and provide additional clarity around the path to approval
• Financial and organisational support from advocacy groups and other stakeholders
• Clinical endpoints that are directly related to the biology of our molecules and the disorder, have been confirmed in validated animal at doses believed to be safe and feasible in the clinic, and that we believe are approvable as clinically meaningful.

With respect to partnering, we believe that thoughtful, efficient and well-executed product development of candidates with strong commercial potential is the key both to obtaining meaningful partnerships and to value creation in general. We maintain relationships with a wide range of potential partners both through traditional business development approaches and in scientific venues. These professional exchanges help us to understand the priorities and objectives of potential partners and their perspectives on value. Addition of new therapeutic targets – particularly indications for chronic oral therapy – has generated a significant increase in interest as has our continuing progress in elucidating the biology of our lead molecules.

At this stage, our goal is to add value to the portfolio by obtaining a positive signal in the clinic while working in parallel to increase the commercial potential of the lead compound. We are actively engaged in efforts to reduce the cost of goods by increasing batch size and simplifying drug product manufacturing as well as reducing special handling requirements for storage and shipping. These objectives will increase the profitability of a marketed product, which in turn will increase the value of the product in the hands of potential partners. We also continue to actively pursue avenues to expand our already strong patent estate, which, of course, further increases the value for a partner.

**Scientific Foundation.** I pointed out earlier that the unique biology of NNZ-2566 is at the core of our corporate strategy. The foundation of that biology is based on IGF-1 and its derivatives. IGF-1 is one of the primary growth factors in the CNS and is essential for growth and development of the human brain. A small piece at the end of
IGF-1 called Glypromate or, more formally, (1-3)IGF-1 is a naturally occurring derivative of IGF-1 which is a central part of the brain’s response to injury and stress. NNZ-2566 is an analogue of Glypromate, modified so that it has a longer half-life and oral availability.

NNZ-2566 addresses critical pathology underlying many acute and chronic CNS conditions and disorders. What’s important is that we’re directly targeting core aspects of the biology of these disorders, not just symptoms. At the cellular and molecular level, the pathology that NNZ-2566 targets includes inflammation, dysregulation of microglia which play a major role in maintenance of the connections between neurons, impaired communication between neurons called “synaptic plasticity”, loss of neurons due to programmed cell death or apoptosis and abnormal electrical activity that often manifests as convulsive or non-convulsive seizures. These pathologies are primary features of many acute and chronic CNS conditions including TBI, stroke, neurodevelopmental disorders such as Rett and Fragile X Syndromes and neurodegenerative diseases such as Alzheimer’s disease, Parkinson’s disease and even so-called “normal” aging. More and more, NNZ-2566 seems to be one molecule that can potentially treat a wide range of poorly treated CNS conditions at the level of disease causation. By analogy, aspirin treats pain, inflammation and fever regardless of the aetiology – a sinus infection, a strained back, osteoarthritis – because its mechanism of action targets a common pathological phenomenon. Some individuals have taken to calling NNZ-2566, “aspirin for the brain”.

Therapeutic target selection. Getting back to selection of therapeutic targets, I want to specifically address the rationale for selecting TBI and concussion, Rett Syndrome and Fragile X Syndrome keeping in mind the criteria I discussed a few minutes ago. The three indications meet all of the criteria that we have established.

TBI and concussion. In animal models, NNZ-2566 inhibits inflammatory cytokines, pathological microglial activation, apoptosis and necrosis, key features of the biology of TBI and concussion. As a result, it improves functional recovery, preserves cognitive function and inhibits post-injury seizures, addressing symptoms that are of primary concern in TBI and concussion patients. There are more than 1.5 million head injuries per year in the US alone, with more than 75% being classified as mild. TBI is a leading cause of death and disability around the world, particularly in young people and the aging population. Our partnership with and funding from the US Army have made it feasible for Neuren to target this difficult indication in which the only late-stage competition is progesterone for moderate to severe TBI. We are not aware of any
sponsor-led clinical trials in concussion. The potential global market for TBI and concussion is estimated at more than $4 billion.

**Rett Syndrome.** At the cellular level, Rett Syndrome is characterized by impaired development of dendrites, the connections between neurons. In a mouse model of Rett Syndrome, NNZ-2566 increases dendritic length and branching, signal transmission between neurons and survival in the “knock-out” group of mice. Rett Syndrome is a cause of profound intellectual and functional impairment and huge financial burden for more than 50,000 patients and their families worldwide. There are presently no other sponsor-led trials in Rett Syndrome. Sagient Research, a subsidiary of Informa, estimates the market potential for a Rett Syndrome drug at between $1.3 billion and $2 billion per year in the US.

**Fragile X Syndrome.** Fragile X Syndrome is also characterized by impaired interneuronal signal transmission although, in contrast to Rett Syndrome, exhibits an excess of dendrites which are immature and not fully functional. In a mouse model of Fragile X Syndrome, NNZ-2566 normalized activation of molecular pathways that control signal transmission between neurons and reversed all of the core molecular, cellular, anatomic and behavioural deficits in the knock-out animals at a statistically significant level. There are no approved drugs although Roche, Novartis, Seaside Therapeutics, Marinus Pharmaceuticals and Forest Laboratories have compounds in Phase 2 or 3 clinical trials. Fragile X Syndrome affects 100,000 or more people worldwide and is a leading genetic cause of intellectual disability (the leading cause among males). Sagient Research estimates the addressable market at more than $5 billion dollars per year.

All of the indications that we’ve selected are expected to be eligible for Fast Track designation (which has already been issued for NNZ-2566 in TBI) and both Rett Syndrome and Fragile X Syndrome are potentially eligible for Orphan Drug designation and possibly Pediatric Exclusivity. With strongly positive Phase 2 results, all would be expected to qualify for Breakthrough Therapy designation as well.

**Intellectual property.** Supporting the science behind our molecules and the rationale behind the selection of lead therapeutic targets is a robust intellectual property portfolio. With no royalty burden on lead compounds, there are seven issued patents and seven pending applications covering composition of matter, oral formulations and methods of use for NNZ-2566 across a wide range of possible uses. Remaining patent life is between 9 and 15 years not including any possible extensions of market exclusivity. For NNZ-2591, there are three issued patents and three pending
applications covering composition of matter, formulation and methods of use with remaining patent life (without extensions) between 11 and 15 years.

**Investment thesis.** I’ve spoken now about Neuren’s commercial strategy, the company’s scientific foundation, our rationale for selection of the lead therapeutic targets and the IP that protects our exclusive rights to the compounds and their use. Summarising these points essentially reinforces the investment thesis:

- A lead clinical-stage molecule with unique biology directly applicable to many critically underserved CNS conditions
- $26 million in non-dilutive funding and a productive partnership with the US Army to support development of NNZ-2566 for TBI and concussion including development of the oral formulation
- A robust patent estate covering composition of matter, formulation and methods of use with no royalties due to third parties
- Targeting rare and orphan conditions with no approved therapies that will be accorded regulatory flexibility with an accelerated path to approval
- Development costs that are lower for rare and orphan conditions with fewer and smaller trials and a shorter timeline to achieve clinical proof of concept
- Execution risk that has been reduced by virtue of the organisational restructuring and increased efficiency in utilisation of resources
- Our ability to wait for optimum timing on a partnership should increase shareholder value considerably

**Expected news flow.** With that background and logic, I’d like to share the expected news flow around key milestones that we forecast through the end of 2014.

- Initiate the first Phase 2 trial in Fragile X Syndrome: 2H-2013
- Complete enrolment in the Phase 2 trial in Rett Syndrome: 1H-2014
- Top-line results for the Phase 2 trial in Rett Syndrome: 2H-2014
- Complete enrolment in the Phase 2 trial in Fragile X: 2H-2014
- Complete enrolment in the INTREPID\(^{2566}\) trial: 2H-2014
- Top-line results for the Phase 2 trial in Fragile X: 1H-2015
- Top-line results for the INTREPID\(^{2566}\) trial: 1H-2015

**Shareholding and financial position.** Before I get into the details of our clinical trials and other programmes, I’d like to give you a brief overview of the company’s current shareholding and financial position. There are presently 1.18 billion shares
outstanding and 274 million options. With a closing price of $0.051 on Friday 17 May, the market capitalization is approximately A$60 million. As you know, the most recent capital raise was at $0.013 in 2011. The top 20 shareholders hold approximately 57% of outstanding shares with the top 50 holding approximately 68%. Among all shareholders, 9% of shares are held by institutions, 6% by directors, 65% by retail investors, and 20% by a substantial shareholder. Over the past 12 months, share price has ranged from a low of $0.021 to a high of $0.054.

At 30 April, Neuren’s cash position was NZD4.24m. As Richard noted, with the current programmes and new initiatives over the next 18 months, we are considering a range of funding alternatives, including additional funding from the US Army, other sources for non-dilutive grants and the possibility of introducing strategic investors. If additional equity funding becomes necessary, we are confident that we have the support and commitment of our major shareholders.

Programmes. Moving now to our ongoing and planned programmes, I’d like to give you an update on each project. I’m going to focus predominantly on NNZ-2566 but will say a quick word about Perseis and Motiva before I do.

Motiva (nefiracetam) A Phase 2 trial of Motiva in stroke patients with apathy but not depression is presently enrolling subjects at the Freemantle and Royal Perth Hospitals in Western Australia in a study funded by the National Health and Medical Research Council to Professor Sergio Starkstein. This trial is intended to differentiate the effect of Motiva on depression versus apathy. Enrolment has been slow as approximately 60% of eligible subjects decline to participate. An interim analysis will be conducted when 20 subjects have completed follow-up which we believe will occur in 2H-2013.

Perseis Therapeutics is developing monoclonal antibodies which target Trefoil Factors (TFFs) 1 and 3. Preclinical R&D has been outsourced to Noble Life Sciences which created five new cell lines based on sequences licensed from the University of California San Francisco that are now producing antibody. The antibodies have been screened in vitro for biological activity and binding to TFF and are undergoing final characterisation prior to progressing into an in vivo cancer model. The in vitro screening has taken somewhat longer than anticipated five antibodies rather than the original two being evaluated. Results from the in vivo experiments are now expected in Q3-2013.

Moving on now to NNZ-2566:

**INTREPID**2566
The **INTREPID** study is a randomised, double-blind, placebo-controlled, dose escalation trial to test intravenous NNZ-2566 as a treatment for acute, moderate to severe TBI. 260 subjects between 16 and 75 years of age will be enrolled in one of three, sequential dose cohorts (30 subjects at 1 mg/kg/hr, 30 subjects at 3 mg/kg/hr and 200 subjects at 6 mg/kg/hr, all administered for 72 hours by continuous infusion following a bolus loading dose of 20 mg/kg) with 2:1 randomisation of active to placebo. Study endpoints include safety, a global functional measure (the Glasgow Outcome Scale Extended) a measure of activities of daily living (the Mayo Portland Adaptability Inventory), incidence of non-convulsive seizures and a battery of standardised neuropsychological tests. Safety is assessed through 30 days or discharge for AEs and through 90 days for SAEs. EEG data are collected for 120 hours post start of infusion. Functional and neuropsychological efficacy measures are assessed at 30 and 90 days.

All study sites are Level I or II trauma centres in the US. Test article administration is begun within 8 hours of injury which requires obtaining informed consent and randomisation within ~6 ½ hours to enable preparation of the infusion solution. As essentially all subjects are unconscious in the immediate post-injury period, a Legally Authorized Representative (LAR) must sign the consent form. LARs are frequently not able to reach the hospital within the prescribed period which has resulted in not being able to enrol approximately 35% of otherwise eligible subjects.

109 subjects have now been enrolled in the study. The three best performing sites have collectively enrolled 68 (66%) of subjects. All three of those centres are participating in the EFIC protocol.

While the FDA approved enrolment under EFIC in July 2011, separate approval is required for clinical trials utilizing Department of Defense (DOD) funding. Final DOD approval for the EFIC protocol and for the first site participating under EFIC was received in January 2013. Five of the current sites have obtained local IRB approval and two have now been approved by the Army. Five new sites are currently completing the EFIC process. Once these have local IRB approval, their application packages will be submitted for DOD review and approval.

The rationale for seeking authorisation to enrol under EFIC was that more than 30% of otherwise eligible patients were not enrolled due to a legally authorised representative not being available within the 8 hour window between injury and initiation of drug or placebo administration. As the EFIC protocol is rolled out, we expect a significant increase in enrolment by participating sites. Further, 10 new sites
are in the process of being activated and are expected to receive DOD approval in Q3 of this year which would mean that 18 sites will be actively screening and enrolling, 10 under the EFIC protocol. We are forecasting completion of enrolment in 2H-2014 with top-line results in 1H-2015.

The total value of Neuren’s Army grant is US$21m which includes funding for INTREPID as well as oral formulation development, the Phase 1 oral PK/safety trial and the Phase 2 mTBI/concussion trial. Separate funding of US$3.6m (net of overhead) is in place through a grant to the Geneva Foundation.

Rett Syndrome

In 2009, a group at MIT published a paper showing that IGF-1 and, more particularly, (1-3)IGF-1 (Glypromate) reversed key symptoms and improved survival in a mouse model of Rett Syndrome (MeCP2 knockout model). Subsequently, we were approached by the Rett Syndrome Research Trust and entered into a collaboration to test NNZ-2566 in the MeCP2 model. The initial effort was a preliminary study but showed positive effects on synaptic plasticity, dendritic morphology and survival. We believe that the mechanism of action is inhibition of neuroinflammatory cytokines and normalization of microglial function. Comparable measurements in the Army’s TBI model strongly support this and results from the Fragile X model confirm it as well. Because we already had an IND open for oral NNZ-2566, the company, in consultation with the IRSF and Baylor, decided to initiate a Phase 2 trial rather than spend additional time and money on further preclinical work.

The Phase 2 Rett Syndrome trial is actively recruiting and 3 subjects have now been enrolled. Approximately 120 families of patients who meet the key inclusion criterion have been identified by Baylor and are being screened for enrolment and randomisation. The trial will enrol up to 60 subjects from 16-40 years of age, allowing for some early discontinuation, in order to have 48 who complete all dosing and assessments. The study will involve two dose cohorts stratified by type of mutation which correlates with symptom severity. A DSMC review will be conducted on completion of the lower dose cohort. Assessments include safety, autonomic measures (respiratory function, heart rhythm and rate), EEG abnormalities, behaviour and global and functional measures out to day 28.

The study is forecast to complete enrolment and follow-up in 1H 2014 with top-line results announced in 2H 2014. We are adding a second site (University of Alabama) to ensure that the enrolment target is met. Baylor and University of Alabama are
leading the NIH-funded Rett Syndrome Natural History Study which is following approximately 2000 Rett Syndrome patients.

If the results of the Phase 2 trial are positive, we intend to request an end of Phase 2 meeting with FDA to discuss requirements for a pivotal trial and registration under provisions of Fast Track and potentially Breakthrough Therapy designation. We are expecting that a pivotal trial would be same size as the Phase 2 trial and could be completed within one year.

Fragile X Syndrome

Neuren and our colleagues have shown that NNZ-2566 regulates microglial and synaptic function. The initial results in the Rett Syndrome model provided reasonable preliminary evidence; the results in the Fragile X Syndrome model provided more conclusive evidence. All autism spectrum and related neurodevelopmental disorders involve problems with the number and quality of synaptic connections between neurons. Approximately 70% involve too many connections, of poor quality, while 30% involve too few connections. Fragile X Syndrome has too many; Rett Syndrome has too few. In both cases, the neurological and behavioural consequences are similar with regard to the pervasive detrimental impact on neurological development and functioning. The core logic of our approach to autism spectrum and neurodevelopmental disorders has been to target both “ends” of the neuronal connection continuum in order to create a wedge that could potentially offer clinical benefits in the more common category of idiopathic autism, thought to affect at least 1 out of 88 individuals worldwide.

The preclinical study in the Fragile X Syndrome model was intended to provide an opportunity to show an effect on the “too many” end of the spectrum. What we frankly did not anticipate was that the results of the preclinical FXS model would be so overwhelmingly positive and conclusive as to change the calculus of our strategy. At doses directly comparable to those planned for the first Rett trial, NNZ-2566 completely normalized behavioural and anatomic features of Fragile X Syndrome with statistical significance achieved in virtually every measure of effect. The results appear to be among the most profoundly positive results achieved with any molecule in a validated model. Full results were presented at a national neuropsychiatry meeting April and are being prepared for submission as a peer-reviewed paper.

Fragile X Syndrome, while still relatively rare, is the single largest known cause of intellectual disability and autism in males. At least in part because it is a known cause of autism and related neurobehavioural symptoms, it has been selected by a number
of pharmaceutical companies as a key therapeutic target. Roche, Novartis, Seaside, Forest and Marinus have active clinical programmes targeting Fragile X Syndrome. In 2012, Roche acquired rights to a competitive programme being run by Seaside Therapeutics.

NNZ-2566 is viewed as a directly competitive product and also offers the possibility of being an adjunctive medication due to expected compatibility with the existing products in clinical development. NNZ-2566 has the potential to be a disruptive force in the therapeutic area.

We are presently preparing to submit an IND and request for Orphan Drug and Fast Track designation to the FDA and are planning to initiate a Phase 2 trial in late 2013. The Phase 2 trial will be a randomised, placebo-controlled, fixed dose, cross-over safety and efficacy study with randomisation set at 1:1:1 for the two doses and placebo. Up to 60 male subjects (allowing for some discontinuation to enable completion of 48) between 16 and 40 years of age will receive 35 or 70 mg/kg twice daily for 28 days. Endpoints for the study include safety, seizure activity, biomarkers of gene activation, and clinician and caregiver assessments of symptom severity and behaviour. Completion of enrolment is forecast for 2H-2014 with top-line results in 2H-15.

Phase 2 Concussion Study

The IND for a Phase 1 study and use of the oral formulation of NNZ-2566 to treat concussion or mild TBI was approved by the FDA at the end of 2011. The Phase 1 clinical protocol was amended during the study to significantly increase the dose administered to support higher dose levels in Phase 2 trials. At the top dose of twice daily 100 mg/kg for five days, oral NNZ-2566 appeared to be safe and well-tolerated. The final Phase 1 study report was received in late October 2012.

During site qualification and feasibility assessments at candidate sites, a number of logistical challenges were identified with respect to enrolling within the 24-hour time window. Standard of care is rest for the first 24 hours prior to evaluation and the majority of sports-related injuries occur on Fridays and Saturdays when the concussion clinics are typically closed. These factors have led us to consider alternative approaches to the trial.

We are currently working with the US Army to finalise a plan to conduct the trial in a military population. The major Army training centres also have dedicated concussion clinics on base and, prior to deployment, all service members have a baseline neuropsychological assessment which is a key part of the protocol’s logic. In the discussions, we have streamlined the trial design to focus on three key outcomes: time
to return to baseline on the neuropsychological assessment at 7 and 28 days, change in the Clinical Global Impression scale from baseline to 28 days and prevalence of post-concussion symptoms at 8 weeks. The dosing regimen will be 35 mg/kg, 70 mg/kg or placebo administered twice daily and randomised 1:1:1.

We believe that, if Neuren and the Army determine that it is feasible to conduct the study at Army training centres, it will make the study more cost-effective and capable of being completed more quickly. We will provide an update when a final decision is made as to when and where the study will be conducted.

**NNZ-2591**

The last program that I want to mention is NNZ-2591, the lead molecule in Neuren’s diketopiperazine (DKP or cyclic dipeptide) portfolio. It is a synthetic analogue of the DKP cyclo-(Gly-Pro) which occurs naturally in the brain and has neuroprotective, anxiolytic and nootropic (memory enhancing) effects in animal models of Parkinson’s disease, cognitive impairment and peripheral neuropathy. Like NNZ-2566, NNZ-2591 inhibits inflammation and attenuates activation of microglia following injury. The molecule has excellent oral bioavailability (~100%) and is currently being assessed as a clinical candidate for treatment of chronic neurological disorders. Preliminary pharmacology and toxicology studies suggest that the molecule has a good safety profile. NNZ-2591 has been protected for composition of matter and therapeutic use in issued patents and pending applications.

The potential value to Neuren of NNZ-2591 is both as a backup to NNZ-2566 and for possible development for other therapeutic targets (e.g., Parkinson’s disease, cognitive impairment, peripheral neuropathy). Its oral bioavailability, apparent potency and stability suggest that it may be suitable for development as a solid oral dosage form. It is important to develop a better understanding of the mechanisms of action as well as relative potency and efficacy compared to NNZ-2566. We have recently entered into a new CRADA with the neurosciences group at WRAIR to assess the effects of orally administered NNZ-2591 on mTOR (a key molecular pathway involved in neuroplasticity and neurite outgrowth that plays a significant role in Rett and Fragile X Syndromes), on the histopathology of neurogenesis and neuroplasticity and on serum-based biomarkers of protein expression and activation. The Army also will identify the pathways which are regulated by NNZ-2591 including neuroinflammatory cytokines and pro- and anti-apoptotic genes. FraX-DVI also will be testing NNZ-2591 in the same *fmr1* mouse model of Fragile X Syndrome in which we tested NNZ-2566.
I want to thank you for the opportunity to provide this review of the company’s operations and for your interest and support of Neuren.