



30 January 2004



Securities and Exchange Commission  
Judiciary Plaza,  
450 Fifth Street,  
Washington DC 20549

SUPPL

**Re: Bionomics Limited - File number 82-34682**

Please see attached provided pursuant to Section 12g3-2(b) file number 82-34682.

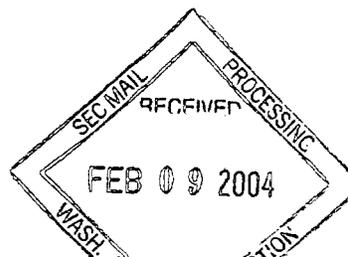
Yours sincerely

A handwritten signature in black ink, appearing to be "Jill Mashado".

Per: Jill Mashado  
Company Secretary

PROCESSED  
FEB 13 2004  
THOMSON  
FINANCIAL

A handwritten signature in black ink, appearing to be "Jill Mashado".



82-34682

# inSIGHT



The Bionomics' Shareholders Newsletter

January 2004



**Dr Deborah Rathjen**  
Chief Executive Officer  
and Managing Director

## Spotlight on Epilepsy

Welcome to this first edition of "Insight" the Bionomics' shareholder newsletter. My hope is that this new form of communication with our shareholders will provide an informative update on the progress of Bionomics.

This issue of the newsletter will focus on our epilepsy research program which has made considerable progress through 2003.

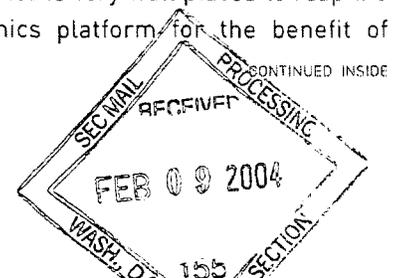
The many gene discoveries in epilepsy achieved in collaboration with The University of Melbourne and the Adelaide Women's and Children's Hospital have advanced the understanding of the causes of this debilitating and serious condition. These discoveries have also provided the impetus for Bionomics epilepsy drug discovery program which is funded by a \$2.9 million R&D Start Grant and for the development of specific gene-based tests for the different forms of epilepsy in collaboration with Nanogen, Inc. Recent significant developments in the program include funding by the US National Institutes of Health to the team led by Dr Steven Petrou and a new collaboration with researchers based at the Brigham and Women's Hospital, a teaching hospital of Harvard University.

### TOWARDS NEW DRUGS TO TREAT EPILEPSY

Epilepsy affects approximately 8 million people in the major pharmaceutical markets and in 1996 approximately 71,200 Australians suffered from epilepsy. The epilepsy drug market was estimated to be US\$6 billion in 2003 and with around a third of epilepsy sufferers unable to gain adequate control of their seizures using currently available medications there exists considerable unmet need in this market.

Bionomics has discovered that changes in an ion channel - the GABA receptor - which plays a major role in regulating electrical stimulation in the brain is responsible for a common form of epilepsy. Demonstration of the critical role this genetic change plays in epilepsy came through the development of Bionomics' proprietary animal model of epilepsy which shows aspects of absence epilepsy as well as tonic-clonic seizures induced by noise. This is the first animal model of absence epilepsy to demonstrate the same EEG brain patterns of human absence epilepsy sufferers. In people, absence epilepsy is often displayed as staring spells. Using this animal model we will be able to test for the first time drug candidates by looking at their impact on the same clinical measures that are observed in humans. This should lead to improved ability to identify treatments which will be more effective.

During 2003 we started building our drug discovery team to capitalize on the advantage of this unique model of epilepsy and we were able to attract our third successful R&D Start Grant to assist in this initiative. We believe that Bionomics is very well placed to reap the promise of its genomics platform for the benefit of epilepsy patients.





**Dr Steven Petrou**  
**Vice President**  
**of CNS Research**

Dr Steven Petrou is Bionomics' Vice President of CNS Research. In his role with Bionomics, Steve works with Bionomics' scientists and collaborators on the company's CNS program, which includes developing Bionomics' animal model of inherited human epilepsy. Steve also holds the position of Senior Research Fellow at the Howard Florey Institute for Experimental Physiology in Melbourne, which is one of Australia's premier neurosciences research institutions. In this article, Steve provides a background to the genetics of epilepsy and the role that Bionomics' CNS research may play in the development of new drugs and diagnostic products.

Epilepsy is more prevalent than commonly thought. Estimates suggest that at any given time some 0.5-1% of the world's population is afflicted and that the lifetime incidence is 3%. Epilepsy results from uncontrolled electrical activity in the brain. In primary generalized epilepsy, the most common form, there is no brain focus and it appears that abnormal electrical activity strikes the entire brain at the one instance. This has made it difficult to diagnose and treat epilepsy effectively in the past.

Although great strides in diagnosis and treatment have been made over recent years, the choice of drugs to treat epilepsy is limited and they produce a number of side effects, from mild sedation and cognitive impairment to the serious problem of birth defects. Many current antiepileptic drugs are old and off patent. The industry response has been the creation of second generation anti epileptic compounds. Unfortunately, many of the side effects persist and the proportion of patients unable to achieve adequate control of their epilepsy with the currently available medications remains alarmingly high at around 30%.

In retrospect it may not be all that surprising that these second generation drugs have fallen short of expectations and needs. Their discovery has relied heavily on model systems that have been in use for decades. These models do not reliably mimic the human condition and likely only model the symptoms of epilepsy but not the cause. Drug discovery efforts have been handicapped for this reason.

Bionomics' approach is to identify the genes that cause epilepsy, and create new diagnostic products and treatments utilizing those gene discoveries.

Working with eminent epileptologist and clinical geneticist, Prof Samuel Berkovic (Director, Epilepsy Research Collaborating Centre, Austin & Repatriation Medical Centre), and the Women's and Children's Hospital in Adelaide, our team at Bionomics has successfully identified a number of genes that have been linked to human epilepsy. At the Howard Florey Institute, my research group has been focused on providing functional validation of these epilepsy linked gene mutations. This entails work in cell systems as well as creation of mouse models harboring identical gene mutations to those found in patients with epilepsy. Together with Bionomics we successfully created the worlds first knockin mouse model of an inherited epilepsy syndrome with several more on the horizon. With our R&D Start Grant-funded drug discovery program, we are working towards our goal creating new drug treatments that are more effective with reduced side effects.

Why should this approach succeed where others have not? First, we are taking an approach driven by gene discoveries in humans, utilizing the ion channel genes we identify in humans as our drug targets. Second, our mouse models are being established as relevant to the human disease – a first in this field. Early indications are that clinical features, such as EEG properties, are emerging in our mouse models with striking resemblance to those seen in patients with epilepsy, which means that our models may be better tools for developing effective drugs than current models. We also have the potential to test our drugs in other CNS disorders that are related to our ion channel drug targets, which include anxiety, depression and pain.

The opportunity to use our gene discoveries to better diagnose and treat epilepsy is being developed by Bionomics Ltd and its commercial collaborator, Nanogen. Full development of diagnostic and theranostic products will provide physicians with new tools for accurate diagnosis and deciding therapy, reducing or eliminating the need for trial and error in searching for the best available drugs for a given patient.

With our combination of gene discoveries, diagnostic product development and drug discovery, we are making strong ground towards our objective of creating new, more effective and safer treatments and diagnostic products for epilepsy and other CNS disorders.

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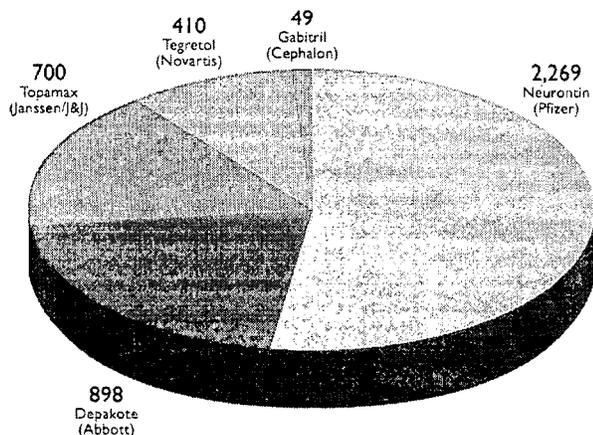
**TOWARDS ACCURATE DIAGNOSIS OF EPILEPSY**

Bionomics initial focus in epilepsy diagnostic product development together with that of partner Nanogen, Inc. is on the development of a test for Severe Myoclonic Epilepsy of Infancy (SMEI). SMEI, one of the severest forms of epilepsy in infancy, is currently difficult to diagnose and may be mistaken for febrile convulsions and other forms of epilepsy. It is also difficult to treat since it is in most cases resistant to current anti-epileptic drug treatment.

The clinical studies undertaken by Bionomics' collaborators have been amongst the largest clinical studies in the world. In 2004 we anticipate the completion of a clinical study of over 100 patients with SMEI. This study will be the largest single study of patients with this form of epilepsy undertaken to date and the outcomes will greatly assist the development and marketing of gene-based diagnostic tests for SMEI.

In the US alone there are approximately 2 million people diagnosed with epilepsy with an additional 180,000 diagnosed with epilepsy each year. Currently there are no gene-based tests for the different forms of epilepsy. Earlier and more accurate diagnosis of epilepsy will in many cases improve treatment outcomes for sufferers of epilepsy.

Our partner US company Nanogen Inc. (NASDAQ:NGEN) has a unique and powerful diagnostic platform. As part of our ongoing relationship with Nanogen, which aims to bring the first molecular tests for epilepsy to market, Bionomics will in the current financial year receive database access fees and may also receive development and clinical milestone payments based on the achievement of agreed objectives. Under our arrangements, with successful commercialization of epilepsy diagnostic products by Nanogen, Bionomics will be eligible to receive further milestone payments and a royalty on product sales.

**GABAA Modulating drug sales 2002 (US\$ million)**

Sources: Company annual reports and SEC filings

**US FUNDING AND COLLABORATIONS TO FAST TRACK BIONOMICS' EPILEPSY RESEARCH**

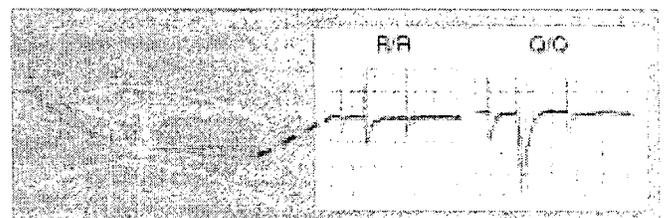
At the end of 2003 Bionomics' secured an additional academic collaboration with a highly regarded US team based at the Brigham and Women's Hospital in Boston. The Brigham and Women's Hospital is a teaching hospital of the Harvard Medical School, and a world leader in patient care, medical education and research. Bionomics will have commercialization rights over the genes identified by the Brigham and Women's Hospital. The Brigham's expertise in gene discovery combined with Bionomics' unequalled understanding of epilepsy genes will strengthen our portfolio of epilepsy gene discoveries and will be important in expanding Bionomics' epilepsy drug discovery program.

This new US collaboration followed the announcement of US funding from the National Institutes of Health to Dr Steven Petrou and colleagues. The funding of US\$1.7 million will cover research using Bionomics' animal model of epilepsy and will identify new approaches for drug discovery. The award of this grant is an endorsement of the quality and innovation inherent in Bionomics' epilepsy program. The impressive work of Steve and the team is further highlighted in this edition of Bionomics' Insight.

Bionomics' continues to look for ways to further increase its presence in the US through collaborations, commercial relationships and other mechanisms.

As we move through 2004 I look forward to reporting further exciting developments in our epilepsy program including further development of animal models, progress in our drug discovery efforts including the initiation of key collaborations and the completion of clinical studies which will assist further commercialization of epilepsy diagnostics incorporating Bionomics' gene discoveries.

**Dr Deborah Rathjen**  
Chief Executive Officer  
and Managing Director



Patch clamp recordings from brain slices of mice containing the normal gene (R/R) and mice containing the epilepsy causing gene (Q/Q).

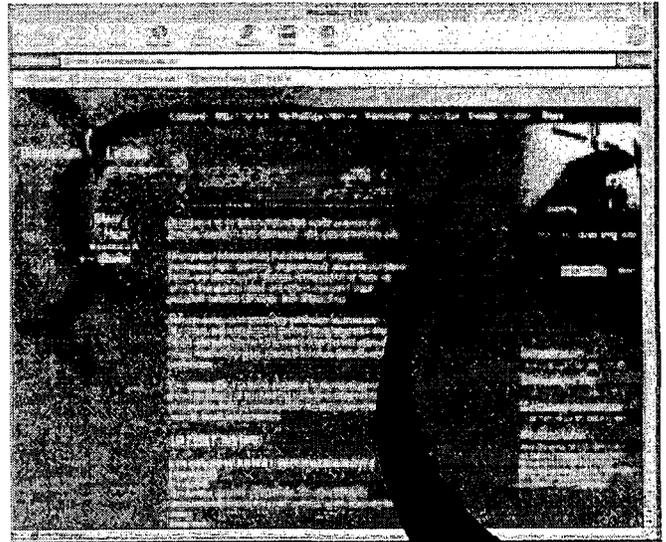
# Scientific Advisory Board Member.



**Professor Samuel Berkovic**  
Epilepsy Program Director

Professor Samuel Berkovic is the Director of the Epilepsy Program at the Austin & Repatriation Medical Centre at the University of Melbourne. He is a clinical neurologist and clinical researcher specialising in the genetics of epilepsy. His research has been recognised internationally by the 1995 Epilepsy Research Recognition Award and the 1998 Lennox Lecture of the American Epilepsy Society. In 1998 he was awarded a personal Chair in Medicine from the University of Melbourne, in 2001 was the recipient of the Novartis prize for Epileptology and in 2002 was awarded the GSK Australia Prize for Excellence in Medical Research.

## ANNUAL GENERAL MEETING



The Annual General Meeting was held in Adelaide on November 6, 2003. The Chairman's address and the Chief Executive Officer's report to the meeting may be found on the Bionomics website at [www.bionomics.com.au](http://www.bionomics.com.au)

