Giaconda Milestones

Careful Fiscal Management

In February Giaconda announced its half year results for the 6–months ending 31 December 2006 to the market. While achieving significant milestones in bringing Myoconda® towards the clinic Giaconda demonstrated excellent cash management recording a reduced loss before tax of $0.56M compared to $0.83M for the 6-months ending 31 December 2005.

Advancing Myoconda® Development

In April, the moment that Giaconda has been keenly awaiting arrived. The US Food and Drug Administration (FDA) approved the Company's Investigational New Drug application (IND) for the clinical development of Myoconda® to treat patients with Crohn's Disease infected with *Mycobacterium avium spp paratuberculosis* (MAP).

This is a key milestone for Giaconda and the IND approval allows the Company to commence the next clinical trial of Myoconda® The Company is continuing preparations for the multi-centre, double blind, placebo controlled, Phase II/III trial. Before the trial commences the Company will conduct pharmacokinetics investigations, test the drug manufacturing for the trial and make ethics submissions to the various clinical trial centres.

It is anticipated that the trial will commence before the end of 2007.

MAP is considered to be the most likely infectious cause of Crohn's Disease. Current treatments on the market are indicated for symptomatic treatment of the disease. On the basis of clinical experience, Giaconda believes that by treating and controlling the underlying MAP infection, Myoconda® will offer a valuable therapy to patients who do not respond to currently available therapies. Current research indicates that between 40 – 50% of Crohn's patients are MAP positive.

The Company understands that its lead product, Myoconda®, is the first therapy to be submitted to the FDA for this indication. There are no anti-MAP therapies approved for use in Crohn's Disease.

The granting of the IND followed the publication of a groundbreaking paper by Professor Borody in March. The leading peer reviewed journal, Digestive and Liver Disease, supported the comment that "longitudinal scarring and consequent healing with normal histology should become a standard treatment goal for Crohn's Disease". This comment was made about Professor Borody's paper on the role of Anti-mycobacterial ("Anti-MAP") therapy, in profound healing of ulcerating Crohn's Disease. Myoconda®, Giaconda's lead product, is the patented commercial version of the Anti-MAP therapy discussed in the research paper.

The paper entitled "Anti-mycobacterial therapy in Crohn's Disease heals mucosa with longitudinal scars" reported on 39 patients who have received Anti-MAP treatment for 6 months to 9 years. Scarring is an essential part of the healing process in ulcerating Crohn's Disease. Scarring is part of the natural healing process to close a wound.

While standard anti-inflammatory and immunosuppressant drugs can reduce symptoms and inflammation, complete healing of ulcerations and other wounds of the colon appears to be rare for these therapies. The presence of scarring fading to normal mucosa on Anti-MAP therapy implies a more profound healing.

This paper encourages Giaconda in its belief that Myoconda® is likely to set a new standard for achieving complete healing in the treatment of Crohn's Disease and the Company is continuing its efforts to make the therapy available to patients in the shortest possible time.

Patents – An essential part of a biotech business

Patents or intellectual property provide the life blood of any biotech or pharmaceutical business. Without them the products can be copied by anyone and you cannot protect the investment your company has made in developing the products.

In November Giaconda was granted a patent in Europe for Heliconda®, the Company's product for treating resistant Helicobacter Pylori infection. This patent is part of a wider global patent application that has already been granted in Australia and the United States. The issued patent entitled "Improved Method for Eradication of H. pylori" (European patent no: 1073436) provides further protection for Heliconda®. Heliconda® is a combination of three compounds, rifabutin, amoxicillin and a stomach acid suppressant known as a proton pump inhibitor.

In December Giaconda was granted a European patent for Ibaconda, the Company's Irritable Bowel Syndrome therapy. The patent entitled "Novel therapy for constipation" (European patent no: EP0980246) provides further protection for Ibaconda®. This patent is part of a wider global patent application that has already been granted in Australia, South Africa and the United States. The therapy is a combination of two compounds, olsalazine and colchicine.

The patents for Giaconda's products cover Professor Borody's inventions that arose due to his work at the Centre for Digestive Diseases. The securing of patent protection in key territories is a major priority as Giaconda advances its development and licensing activities.

So, all in all, it has been an exciting time for Giaconda; regulatory advances, scientific publications and patent approvals bringing effective treatments for many patients closer to realization.

Manufacturing Myoconda®

centre for digestive diseases

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THE Inside Story

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Crossing over to Excellence

We are celebrating 12 months at the new Centre for Digestive Diseases. The new specialist facility features many quality improvements from spacious patient bays, consultation rooms and procedural theatres. The patient accommodation features improved privacy, comfortable new beds and recliners with the best nursing care provided.

The Centre provides the latest in electronic patient information system allowing rapid access to medical history including pathology results.

At CDD, we compliment the modern patient facilities with the latest in medical equipment including the latest series of endoscopes, sterilising and anaesthetic equipments.

Human Bowel Flora changing paradigms

There is a "sea change" occurring in the importance of the human bowel flora and its power to make people healthy or ill.

The change in the perception of the importance of the bowel flora among world Gastroenterology leaders was fuelled in part by an epidemic of a mutant *Clostridium difficile* bacterium. Since drugs fail to cure this condition in many cases doctors in the US and Canada have turned to human probiotic infusions (HPI) i.e. faecal bacteriotherapy. Our clinic has carried out over 900 infusions and our recent publication demonstrates a cure rate of 99% in recurrent or chronic *C. difficile* infection. Indeed, as a result of this HPI has now become 'standard of care' therapy for recalcitrant *C. difficile* in North America.

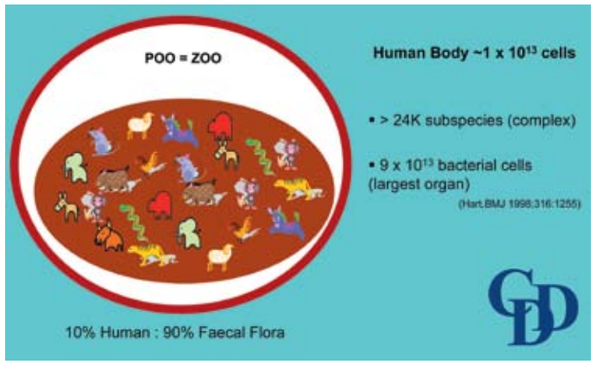
The next breakthrough at CDD in this paradigm is the recognition that *C. difficile* can markedly aggravate severe Inflammatory

> CDD has been leading the world in using HPI for *C. difficile* and other conditions of bowel flora overgrowth.

Bowel Disease (IBD) and make it so severe that it can lead to resection of the bowel. Quite dramatic improvement of symptoms can occur after HPI –with more formed stools, fewer diarrhoea episodes, weight gain and improvement in blood markers such as CRP and ESR. At CDD, 9 patients have been treated with HPI to date for eradication of their chronic *C difficile* infection. Of those 7/9 have achieved a virtually immediate positive response.

The third aspect of the changing paradigm worldwide in the last 12 months is that Irritable Bowel Syndrome is seen as the result of 'bacterial overgrowth'. Indeed, it is quoted now that it is "indefensible to call IBS a functional bowel disorder".

World scientists in the field have finally recognised that occult bacteria can overgrow our normal flora - the largest organ of the body with huge numbers of bacteria – and this is the cause of Irritable Bowel Syndrome. Reminiscent of the *C difficile* story above? More to follow in the coming years.



Endoscopes *of the future*

Often the demands of medical practice have driven scientific development, sometimes it is a new discovery of science that quickly finds an application in every day medicine. In the case of the new Pentax 90i series of endoscopes, the development story has been a bit of both.

The Pentax 90i series are known as the "mega scopes".For the first time, science has provided engineers with technology to install a tiny video camera with more than 1 million pixels in the confines of a standard endoscope. The results are fully digital images never before achievable, this is the result of 25 years of development.

With each advance in endoscope design the specialists using them became more skilled and in turn demanded more from their instruments. Where once the endoscope was used to hopefully give a glimpse of a problem in the stomach or colon, today it can also show the formation of cells and provides a system through which the treatment and often the eradication of the disease can be achieved.

The endoscope is one of the great success stories of modern medicine.

It provides today's endoscopists with a tool for diagnosis and treatment; it has minimised many surgical procedures and in some cases turned weeks of hospitalization into a visit of only a few hours. The Centre for Digestive Diseases has played it's own part in this development process. In a partnership with Pentax of almost two decades there has been a two way sharing of ideas. The Centre has assisted CR Kennedy & Co the Australian representative for Pentax in the pre-release trials of the new 90i series.
CDD has always pursued the highest standard of excellence in all it's endeavours.

Improved Safety in Endoscopy

Oxygenation in Endoscopy

Given the option most patients are unwilling to undergo gastroscopy or colonoscopy without sedation. Moderate levels of sedation is achieved by administration of a single medication or combination use of benzodiazepines, narcotics and/or propofol.

Complication rates are low, however hypoxemia (lack of oxygen) can still occur during routine endoscopy and can be a potentially life threatening complication. Hence, ensuring airway is open and supplying oxygen is mandatory.

Although clinical vigilance cannot be substituted by mechanical monitoring, early detection allows for timely correction. Monitoring methods of oxygenation and ventilation include the pulse oximeter and capnography.

Over 10 years ago, the Centre for Digestive Diseases developed the Oxyguard™, an oxygenating bite block which has been used for the delivery of oxygen. With an emphasis on improvement of delivery

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and monitoring of oxygenation and ventilation utility a new device Twinguard™, has been developed at CDD with the assistance of an Ausaid Grant.

A clinical trial recently completed at CDD was aimed at examining the different phases of sedation, their associated oxygen requirements and their monitoring parameters in sedated patients.

In a 150 patients who kindly agreed to be in this study we compared Twinguard™ "versus Oxyguard™" looking at; adequacy of oxygen delivery, detection of carbon dioxide levels to assess ventilation and whether trends in carbon dioxide levels correlated with oxygen levels.

The preliminary data analysis thus far shows equivalence in effective oxygen delivery and improved CO2 detection with Twinguard™.


[fig 2] Twinguard™

On the **Research Front**

Trials of new treatments for Erosive Oesophagitis and Ulcerative colitis were completed, along with a trial studying the effectiveness of the new "Twinguard" oxygenating device used during gastroscopy. Ongoing trials include new test devices and methods of the detection of *Helicobacter pylori*. We would like to thank all patients who have participated in any of these trials. Without your positive attitude and added efforts these trials into new and innovative treatments and tests would never be completed!

We are very excited to announce the commencement of a clinical trial into treating chronic Hepatitis C (genotype 1). This trial is testing a treatment called Hepaconda®, a product of Giaconda Ltd. It is the aim of this trial to assess if Hepaconda® can cause a reduction in the viral load of patients with this chronic condition. CDD is working in conjunction with Associate Professor Martin Weltman, a Sydney-based Hepatologist who is associated with the University of Sydney and Nepean Hospital. We would like to thank Prof Weltman for his time and dedication to this project. Recruitment is now open for this trial. For more information please contact the Research Team on (02) 9713 4011, prompt #3.

Other potential upcoming trials include treatments for Ulcerative colitis and proctitis.
For information on trials which we are currently recruiting for please keep an eye on the Research page of the CDD website www.cdd.com.au/research.

your team

The medical team is lead by Prof. Thomas Borody and includes a number of full-time and part-time medical practitioners.
Among them are:

- Emeritus Prof. Robert Clancy, Professor of Pathology in the Faculty of Medicine and Health Sciences at the University of Newcastle, is a Clinical Academic at the Hunter Immunology Unit of John Hunter Hospital
- Dr Andrew Finckh, Staff Specialist at St Vincent's Hospital, holds degrees in Bachelor of Arts from Macquarie University and Medicine from the University of Sydney. He holds the position of Emergency Registrar at Liverpool Hospital
- Dr Sanjay Ramrakha is a graduate in Medicine from the University of NSW in 1986 and a Fellow of the Royal Australian College of General Practioners
- Dr John Saxon is a graduate from the University of NSW in 1985 and has been the Senior Sedationist at CDD since 1995, with some 10,000 patients to date
- Dr Antony Wettstein is a graduate with Honours from the University of NSW. He is a Fellow of the Royal Australian Society of Physicians
- Dr Simon Benstock is a graduate in Medicine from the University of NSW. He is a Fellow of the Royal Australian Society of Physicians
- Dr Ori Ashman is a Registered Psychologist in NSW and holds dual Master's and PhD degrees in Human Development.
- Dr Warwick Adams became a Fellow of the Royal Australian College of Surgeons in 1989. He was selected for the Australasian Colorectal Surgery training programme, which he completed in 1993, before going to Minneapolis, USA, as a visiting Fellow. He completed his Master of Surgery Degree in 1995. He has been a specialist consultant in Colorectal Surgery since 1995.


Dr Warwick Adams