



### Highlights:

**Ongoing Research Activities with Picoconda® and Myoconda®**

**Challenging Accepted Disease Paradigms: An Interview with Professor Tom Borody**

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**G**iaconda has been busy on a number of fronts. In September Giaconda announced its preliminary year end results to the market. The annual report details the year's events and is available at [www.giacondalimited.com](http://www.giacondalimited.com). At the end of October the Company hosted its Annual General Meeting in Sydney. Professor Tom Borody, Giaconda's Chief Medical Officer, gave a presentation entitled "Challenging an Accepted Disease Paradigm" explaining the paradigm that Giaconda was founded on. In this newsletter we interview Professor Borody on this subject.

#### **Myoconda®**

We continue to liaise with potential licensees for our lead product in Europe (excluding UK, Netherlands, Belgium and Luxembourg where Letters of Intent have already been signed) and North America. In addition we are in discussions with those parties who we have signed Letters of Intent (LOIs) with about converting those LOIs into full license agreements. Along with those countries already noted, this will include Australia, South Africa, Namibia and Asia.

In terms of the next clinical trial for Myoconda®, Giaconda has located and tested suppliers for two of the three active pharmaceutical ingredients (API's) in Myoconda® who are willing to supply Giaconda with the APIs required for the next clinical trial. We are currently evaluating a supplier for the remaining API required for the trial. The Company is establishing relationships with the clinical research organizations (CRO's) who will be involved with conducting the next clinical trial in the USA and Canada and we continue to refine the protocol for the trial prior to lodging our IND (Investigational New Drug application) with the US Food and Drug Administration (FDA) and the Therapeutics Product Directorate (TPD) of Canada's Health Protection Branch (HPB).

#### **HELICONDA® PATENT GRANTED IN THE EU**

In November the European Patent Office granted Giaconda's patent for Heliconda® to treat resistant *Helicobacter Pylori* (*H. pylori*) infection. *H. pylori* lives in the mucosal lining of the stomach and causes up to 90% of peptic ulcer disease. With the increased use of antibiotics to treat infections and the resultant prevalence of antibiotic resistance, it has become more difficult to treat *H. pylori* resistant strains. As a result, up to 30% of people fail these treatments.

Heliconda® is a combination of rifabutin, amoxicillin and a proton pump inhibitor. In a Phase II study of 130 patients with resistant *H. pylori* infection, Giaconda demonstrated successful eradication of the infection in 90.9% of patients treated with Heliconda® who had failed one or more *H. pylori* eradication attempts using standard triple antibiotic therapy. The presence of clarithromycin or metronidazole resistant strains had no significant impact on the eradication rates.

Giaconda will validate the patent in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Monaco, Portugal, Spain, Sweden, Switzerland and Liechtenstein, The Netherlands, and the United Kingdom.



## Ongoing Research Activities with Picoconda® and Myoconda®

### Picoconda®

During the last quarter several of Giaconda's products have been featured in poster presentations at key conferences in Australia and the USA. The ongoing research at the Centre for Digestive Diseases with these products has also been published in international peer reviewed scientific journals.

In October Giaconda attended the Australian Gastroenterology Week conference in Adelaide where data on a randomised, single-blinded, comparative Phase II clinical study with Picoconda®, a bowel preparation for gastrointestinal procedures, was announced. The study was also published in the *Journal of Gastroenterology and Hepatology*.

The use of colonoscopic surveillance has increased significantly in recent times as an effective method for detecting colonic polyps and bowel cancer. The effectiveness of this screening relies on an adequately prepared bowel. Preparation of the bowel has been the most poorly tolerated aspect of colonoscopic procedures. Key problems with standard bowel preparations are the volume of the preparation that needs to be consumed, its unpalatability and the effects of purgative solutions administered on the day prior to the procedure which include nausea, vomiting, abdominal pain and headache.

In order to increase patient compliance Giaconda and Pharmatel Ltd developed Picoconda®, a bowel preparation in a capsule form. In order to further reduce the side effect profile a hypertonic salt solution which reduces gas, bloating, nausea and headaches was combined with Picoconda® capsules in this study. This was compared to standard Glycoprep, standard Picosulphate preparations and Picoconda® capsules alone.

Significantly for Giaconda, one outcome of the trial was that the Picoconda® capsules, with or without the hypertonic solution, were found to be the most favoured bowel preparation by patients and in general, resulted in a lower number of mild adverse events than the other preparations.

### Myoconda®

#### Fistulising Crohn's Disease

In late October the results of preliminary research on the therapeutic role of Myoconda®, the company's lead product, in fistulising Crohn's Disease were

presented in a poster at the American College of Gastroenterology meeting in Las Vegas.

The poster reported on fistula healing in patients with severe Crohn's Disease when treated with Myoconda® and optional curetting. The data came from a retrospective review of patients with active fistulae who were treated with Myoconda® and optional curetting. 66.6% of the patients achieved complete fistula healing whilst on Myoconda®. Five patients had been curetted. Of the curetted patients 60% achieved complete fistula healing, 20% achieved partial healing and 20% remained with active fistulae.

In conclusion, the administration of Myoconda® in combination with curetting was found to result in partial or prolonged healing of fistulae for the majority of patients and may present another valuable treatment option.

#### Longitudinal scarring in patients with severe Crohn's Disease

A study on longitudinal scarring in patients with severe Crohn's Disease treated with Myoconda® was published in the *American Journal of Gastroenterology*. In this study, a retrospective review of 52 patients treated with Myoconda®, 53.7% of patients demonstrated longitudinal scarring as evidence of profound healing.

Scarring only takes place once inflamed mucosal tissue begins to heal. 11 of these patients continued on Myoconda® therapy for up to 9 years following the appearance of scarring. Scarring was reduced to almost imperceptible levels in 18.2% of these patients by this time. The existence of scarring fading to normal mucosal tissue state may be indicative of a healing state superior to that found in patients treated with standard immunosuppressive regimens who do not demonstrate longitudinal scarring even in tightly controlled disease states.

#### COLONOSCOPY FACTS

- Due to the high mortality associated with colon cancer and the low risks associated with colonoscopy, it is now also becoming a routine screening test for people aged 50 years or older.
- 14 million colonoscopies are conducted worldwide each year. The United States represented approximately seven million of these. Bowel preparation is required for each procedure.





## Challenging Accepted Disease Paradigms: An Interview with Professor Tom Borody

**Interviewer:** What are you referring to when you speak of “disease paradigms”?

**Prof. Borody:** Disease paradigms in this sense are the accepted, received wisdom approach to the nature of a disease and how it should be treated. For example, today it is accepted that the common cold is caused by a virus and that as such, treatment with antibiotics is not useful (unless there is evidence of a bacterial infection as well).

**Interviewer:** So how is this relevant to your work with Giaconda on Crohn’s Disease?

**Prof. Borody:** It could not be more relevant. The accepted disease paradigm for Crohn’s is that it is an auto-immune disease where an inappropriate immune response causes the inflammation associated with the condition. This is why the standard treatments for Crohn’s are based around anti-inflammatory medications, immunosuppression and surgery. However, we believe that Crohn’s Disease should be treated as an infectious disease because we have a growing body of evidence linking the bacterium, *Mycobacterium avium spp paratuberculosis* (MAP) to the disease.

**Interviewer:** Can you tell me more about this MAP bacterium?

**Prof. Borody:** In 1895 *Mycobacterium avium spp paratuberculosis*, or MAP for short, was discovered and found to be the cause of Johne’s disease in cattle – a disease of cattle similar to that of Crohn’s disease in humans. In 1913 researchers including Dalziel were proposing that MAP might be the cause of Crohn’s Disease. In fact, if you look at slides of tissue with Johne’s disease and Crohn’s Disease there are some immediately obvious similarities. However, this was largely ignored by the medical community.

In the 1980s and 1990s a number of researchers, such as Chiodini, Hermon-Taylor, Nasser and others, were beginning to isolate the MAP infection in Crohn’s patients. This led to a National Institute of Health/National Institute of Allergy and Infectious Diseases workshop on MAP and its relationship to Crohn’s Disease. However, the outcomes of that workshop were not conclusive. Since then we have been looking at expanding the research to provide an undeniable case for this link between MAP and

Crohn’s Disease. Our proposed paradigm has met with some skepticism from the medical community and this is a major hurdle for us.

**Interviewer:** So this is why Giaconda was founded?

**Prof. Borody:** Giaconda was founded to commercialise the work being done at the Centre for Digestive Diseases. This includes therapies for Crohn’s Disease but also for other conditions such as Irritable Bowel Syndrome, Hepatitis C, and resistant *Helicobacter Pylori* infection.

The Company’s lead product is Myoconda® for the treatment of Crohn’s Disease, a triple antimycobacterial therapy for the treatment of MAP infection. To date the clinical results have been very encouraging and we are finding support for our paradigm with the infectious disease community. Giaconda has approached the European and US regulatory authorities with this novel treatment paradigm and they have demonstrated support and provided advice on establishing the link between MAP and Crohn’s in the next clinical trial. We anticipate commencing the next clinical trial next year.

**Interviewer:** You mentioned some resistance to the idea of Crohn’s being an infectious disease, why is this?

**Prof. Borody:** It is no surprise that our paradigm is meeting resistance. This has often been the case with new discoveries. For example, when Warren and Marshall began their work on *Helicobacter Pylori* (*Hp*) and its relationship with peptic ulcers they met with considerable resistance. Their research was ridiculed and refused for publication a number of times. In fact, after 1984, when I developed a Triple Antibiotic Therapy based on Warren and Marshall’s work for the treatment of *Hp*, the President of the Gastroenterology Society of Australia wrote to me demanding that I justify my use of antibiotics in patients with ulcers. Yet in 2005 Warren and Marshall received the Nobel Prize for their work and it is now accepted that *Helicobacter Pylori* is responsible for 90% of peptic ulcers.

At Giaconda, we hope that through achieving support for our product from the regulatory authorities and patients we will be able to re-educate the medical community about the accepted paradigm for Crohn’s Disease. The most important people remain the patients and we are committed to bringing a new therapy to them which does not have the side-effects of the standard approach.

This newsletter is available via email and on the Giaconda website [www.giacondalimited.com](http://www.giacondalimited.com)

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