INTERSUISSE INVESTMENT RESEARCH

Giaconda Limited GIA Wednesday, 22 August 2007

Interesting Situation…disconnect between market and intrinsic value

Recommendation Speculative Buy.

The Disconnect between the Market and the Intrinsic Value

Myoconda® is an antibiotic combination therapy for the treatment of Crohn's Disease. Previous studies have demonstrated efficacy and it appears more effective than the current therapies including steroid and TNF inhibitors.

The accessible market for Myoconda® was estimated at 204,000 patients globally, which represents a maximum market size for Myoconda® of A$1.53bn per annum.

Myoconda® has two distinct competitive advantages over the current therapy.

- Steroids treat the symptoms, where Myoconda® treats the cause of Crohn's Disease
- Myoconda® is expected to cost US$8,750 per annum, where as TNF inhibitors cost about US$25,000 per annum to manage Crohn's Disease.

For these two key reasons, if Myoconda® is successful in Phase III Clinical Trials and supported in the US and European market by a strong sales force, Myoconda® could experience rapid penetration into the Crohn's Disease market.

Low Liquidity has Held the Share Price Back

With a market capitalisation of only $34m and approval by the FDA to commence Phase II/III clinical trials of Myoconda®, there is clearly a disconnect between the market value and the intrinsic value of the company. We are of the opinion that the issue is due to the company's tight liquidity. In the last week and month, there were 54k and 354k shares traded, valued at $25k and $154k respectively.

309% or 55.7m ordinary shares are currently escrowed and come out of escrow on the 28 September 2007. In addition to this number, there are 17.8m ordinary shares available on the market, plus 1.6m options exercisable at $0.5 for one ordinary share. It is possible that 4.1m (assuming they will be sold) of the escrowed shares would be released onto the market, but most are likely to remain held.

Giaconda is an extreme example of poor liquidity chronically preventing the company from enjoying a price upswing upon the completion of clinical milestones, as experienced by other companies in or nearing Phase III Clinical Trials.

Recommendation

We recommend a Speculative Buy, although we must reiterate that the stock price will remain depressed due to the lack of stock liquidity. The company currently has $1.7m cash, and will have to raise capital in the near future to undertake its Phase III Clinical Trial. Given the company is likely to have to raise capital through equity; the liquidity is likely to increase and allow the market capitalisation to become aligned with the intrinsic value. We estimated the Intrinsic value to be about $238m, but limited liquidity has prevented the market capitalisation from reaching this value.

Nevertheless, with a market capitalisation of $34m there is a clear disconnect between the market capitalisation and the intrinsic value.

Snapshot

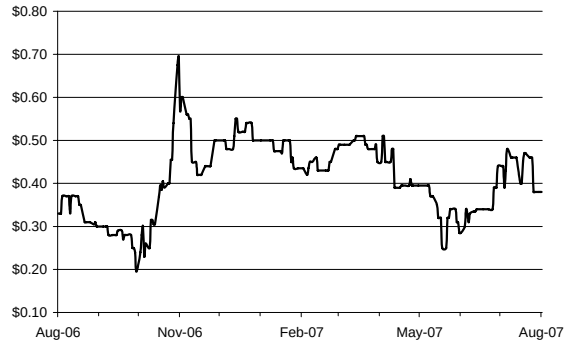
Last Price	$0.38
Market Cap (A$m)	$34m
52 Week High	$0.70
52 Week Low	$0.14
Sector	Pharmaceuticals & Biotechnology

Investment Fundamentals

Year-end June	HY05a	FY05a	HY06a	FY06a
NPAT ($m)	NA	(0.65)	(0.94)	(0.55)
EPS (c)	NA	(0.9)	(1.36)	(0.76)
% Change	NA	NA	NA	NA
DPS (c)	NA	NA	NA	NA
Franking (%)	NA	NA	NA	NA
Yield (%)	NA	NA	NA	NA
PER (x)	NA	NA	NA	NA

Source: Intersuisse Estimates

Price Chart



Business Description

Giaconda (GIA) is focused on the commercialisation of therapies for the treatment of gastrointestinal diseases and disorders.

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The Operational Strategy

Giaconda does not develop new drugs so it does not have the massive R&D expense, risk and duration of developing common with developers of novel compounds. Giaconda is a drug reformulation company, in which existing therapeutics are reformulated into combination therapies.

This strategy has advantages and disadvantages, although the overall result is positive as it allows the company to develop new therapeutics more rapidly and more cost effectively.

Advantages

- Illustrating this point, preclinical trials for Giaconda's products were shorter because ADMETox[1] profile of the formulations constitutions are know. Furthermore, manufacturing is not an issue as the synthesis process has been elucidated previously. Given these inherent advantages, Phase II and III trials are not as intensive as those for a novel compound.
- Also certain regulatory routes that are faster to market could be open to the company because the constituents of the reformulations are approved by regulatory bodies such as the FDA, EMEA and the TGA. This is because Giaconda's regulatory approval process could partially rely upon existing data on these drugs. But the company would also have to provide further information demonstrating the safety of the reformulation. However, it remains conjecture that Giaconda's reformulations could follow the faster regulatory route to market as there has been no announcement by the company on this matter.

Disadvantages

- The disadvantage of this strategy revolves around the IP and freedom to operate. Many originator patents teach the use of their compounds in conjunction with an enormous list of compounds, compound families or clinical application. This is a strategy often used by the drug originator to increase patent and branded-product longevity. Nevertheless, we undertook a public IP database search and we could not find any patents that infringe, or are infringed by, Giaconda's technology. However, we are not IP attorneys and search results should be seen as *prima facie* only.
- An additional disadvantage could stem from the individual administration by doctors of drugs in combination to result in the replication of Giaconda's reformulations. Although such practice would breach Giaconda's IP, it would be unenforceable. Although this is a risk, we believe it to be limited because a company could not develop or market a reformulated product without breaching Giaconda's patent position and doctors are more likely to prefer to administer an approved single pill.

Risk Mitigation

Giaconda's board and management are mindful of these facts and have addressed these potential issues accordingly. Firstly, the company has received (or filed for) patent protection over its therapeutics in key markets.

[1] Absorption, Distribution, Metabolism, Excretion and Toxicology

Further patent protection is expected and the patent claims will be based on the class of drug, not so much the individual drug. Secondly, the reformulations will result in one pill, which will be used in further clinical trials.

The Reformulations

Myoconda

Myoconda® is for the treatment of Crohn's Disease and is a combination of the antibiotics clofazimine, rifabutin and clarithromycin in a patented concentration. Evidence is coming to light that suggests that Crohn's disease has a suspected aetiology of Mycobacterium avium sub-species Paratuberculosis (MAP).

Although much of the therapeutic interest for Crohn's Disease is around TNF inhibitors[2,3], there is evidence that Crohn's Disease can be elevated with the use of antibiotics[4,5,6]. However, there is also evidence that they do not[7].

Myoconda® has undergone Phase II and Phase III Clinical Trials. The Phase II study was conducted at the Centre for Digestive Diseases (CDD)[8]. This was followed up with a full retrospective analysis of all CDD Crohn's patients treated for at least six months with anti-MAP therapy. This analysis of 52 patients demonstrated a remission rate of 65% with a clinical response of almost 95%. Company researchers also observed that mucosal healing in some patients after therapy

Pharmacia, who had taken an option for the license to Myoconda® from CDD in 2000, conducted a Phase III clinical trial involving 213 patients. The trial was completed in September 2004. Overall results of the Phase III trial demonstrated a statistically significant improvement in achieving remission at 16 weeks. However, Myoconda® did not achieve statistically significant results in maintaining remission. When Pharmacia and Pfizer merged, Myoconda® was returned to CDD and then on-sold to Giaconda.

On the basis of these trial results Giaconda decided that a revised drug development programme should be pursued. The dosage of clofazimine used in Pharmacia's Phase III trial was lower than that used in previously published studies. In the next trial Giaconda will increase the dosage anticipating that this will improve the efficacy of Myoconda® in achieving and maintaining disease remission.

The Pharmacia Phase III trial was not successful for a number of reasons. As mentioned, the clofazimine dosage appeared to have been too low. The synergic effect of clofazimine and rifabutin was not known at the time of the trial and a higher does is required to gain the synergic affect against the Mycobacterium.

Secondly, the role of Mycobacterium was not understood. Therefore the trial probably contained patients who were carriers and who were negative. The anticipated Giaconda

[2] Rev Gastroenterol Disord. 2007;7 Suppl 2:S23-35.
[3] Inflamm Bowel Dis 2004;10:324–326
[4] Gastroenterology, In Press, Online 21 March 2007
[5] Digestive and Liver Disease 34:1:22-28 (2002)
[6] Gut 2006;55(Suppl I):i16–i35. doi: 10.1136/gut.2005.081950b
[7] Inflammatory Bowel Diseases 3:4: 314-317(1997)
[8] Digest Liver Dis 2002:34:29-38

Phase III trial will select candidates who are infected with mycobacteria.

Finally, Remicade was emerging as the dominant new therapeutic and the decision to not continue with Myoconda® appears to have also included market penetration considerations.

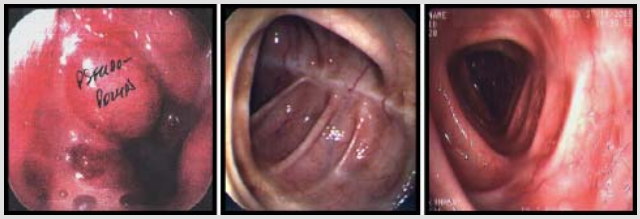
Giaconda has started to establish manufacturing and marketing channels, through smaller distributors. Non binding letter of intent have been signed with;

- Forest Laboratories for the UK market
- Orphan Australia for the Australian, South African, Namibia and Asian markets
- Tramedico for the Benelux market
- IND Swift Laboratories to manufacture Clarithromycin

The Hypothesis

Originally, academics believed that there was a high microbial load in the Crohn's Disease gut due to non-specific tissue damage. Studies showed that a variety of organisms including normal intestinal bacteria and yeasts can be grown from Crohn's disease mesenteric lymph nodes and that the lymphocytes within these lymph nodes are manufacturing antibodies that are directed against a broad range of bacterial antigens so it is a more widely held view that a wide range of micro-organisms invade the mucosa in Crohn's disease[9]. However, some academics are coming to realise that Crohn's Disease is associated with atypical bacterial infections.

It is typified histologically by the presence of granulomata (in over 75% of cases) and closely resembles intestinal tuberculosis, radiologically and histologically. A search for Mycobacteria has produced conflicting results with one centre claiming that Mycobacterium paratuberculosis DNA can be detected in the majority of cases[10] but with others finding Mycobacterial DNA in only about 10%[11].



A *B* *C*

Regression of pseudopolyps in the left descending colon in a patient on anti-MAP therapy. (A), Before anti-MAP therapy – severe inflammation with contact bleeding and pseudopolyps; (B), 1 year on anti-MAP therapy – elevated longitudinal scarring with haustrations pointing to the scar; (C), 2 years on anti-MAP therapy – The scar has now become a faint line lacking distinct elevation from the mucosal wall, suggesting progressive softening of scar tissue.

Source: Dig Liver Dis. 2007 May;39(5):438-44. Epub 2007 Mar 21

The Competition

MAP therapy has not gained medical acceptance and the use of Myconda's constituents are not used to treat Crohn's Disease outside of experimental medicine.

The first line therapies for Crohn's Disease are the anti-inflammatory drugs for the 5-aminosalicylate and corticosteroid families. Also antibiotic therapy with Metronidazole (Flagyl®) and Ciprofoxacine (Cipro®) had proven ability to cure, control and maintain Crohn's Disease.

More severe cases are managed with immunosuppressants of the mercaptopurine family, and if required with the anti-TNF inhibitors Infliximab (Remicade®) or adalimumab (Humira®) or surgery. Antibiotic treatment is not considered due to the lack of a large body of evidence based medicine. Interestingly, there is evidence that Mycobacterium avium Paratuberculosis infestation of the gut correlates with enhanced TNF secretion[12], which could explain the effectiveness of TNF inhibitors and it (if correct) suggests that TNF inhibitors only treat the symptoms and not the cause of Crohn's Disease.

This is to be a major issue of Giaconda if its reformulations enter the market. Firstly, an enormous amount of funds are spent on marketing Infliximab by Johnson & Johnson, which includes promotions and Phase IV trials. This marketing strategy has been very effective and the product is familiar among practitioners. Additionally, once a patient is on Infliximab, it is unlikely that they would come off their one dose per eight week treatment if it proves beneficial. The ACCENT 1 trial showed that 39% to 45% patients treated with infliximab who had an initial response to it, maintained remission after 30 weeks, compared to 21% for the placebo. Also a mean maintenance of remission from 38 to 54 weeks was seen compared to 21 weeks for the placebo. It also showed that about 43% patients did not respond within the first 2 weeks of treatment, and of these 59% responded after they were placed on a maintenance dose.

Giaconda (or its marketing partner) will have to undertake a large marketing and education programme, including Phase IV trials that encourage physicians to place patients on MAP maintenance therapy over TNF inhibitor maintenance therapy.

As mentioned above, the Anti-MAP therapy is not generally accepted as a treatment for Crohn's Disease, yet there are several organisations testing Clarithromycin to ameliorate the condition.

- The Royal Liverpool University Hospital and Abbott Laboratories are currently recruiting a Phase III clinical trial. There are only a limited number of studies examining Clarithromycin as a treatment for Crohn's Disease. Slow release clarithromycin (Biaxin) has been used in combination with Prilosec to treat *H.Pylori* infections. Biaxin is manufactured and marketed by Abbott Laboratories.
- An open-label study of a combination of clarithromycin 250 mg bd (or azithromycin in 3 patients) and rifabutin 450 mg per day given for a mean of 18 months to 52 patients by the St George's Hospital group who are the major protagonists of the Mycobacterium

[9] Gastroenterology Clinics of North America. 1995;24:475-507.
[10] Gut 1992;33:890-6
[11] Gut 1994;35:506-10

[12] Dig Liver Dis. 2007 May;39(5):445-51. Epub 2007 Feb 21.

paratuberculosis hypothesis. They report a response in terms of "significant fall in Harvey Bradshaw Index" in 93% but CDAI was not reported and many of the patients seem to have had rather modest elevations of Harvey Bradshaw index on entry[13].

Heliconda®

Heliconda® is designed to address resistant *H.pylori* infection by incorporating the antibiotic rifabutin with another antibiotic amoxicillin and the proton pump inhibitor pantoprazole to reduce acidity in the stomach, which has reported eradication rates of 79-80% in refractory patients. In a registered Phase II study of over 130 patients with resistant *H.pylori* infection, the company demonstrated an eradication of the infection in 90.9% of patients treated with Heliconda®.

Current recommended treatment regimens using a combination of PPI or ranitidine bismuth citrate (RBC), clarithromycin and either amoxicillin or nitroimidazole achieved eradication rates ranging from 81% to 100%. This means up to 20% of patients will fail to eradicate the bacteria and remain *H.pylori*-positive. It is this patient population that Heliconda® will target[14].

The main competition is anticipated to come from PYLERA, also invented by Borody, the inventor of Myoconda®, Heliconda®, Hepaconda® and Ibaconda®. PYLERA is a 3-in-1 capsule triple therapy, for the eradication of *H.pylori*. Each PYLERA capsule contains bismuth biskalcitrate (140 mg), metronidazole (125 mg) and tetracycline hydrochloride (125 mg). The US patent on the PYLERA capsule technology expires in December 2018 and is marketed by Axcan Pharma Inc. The reformulation was approved by the FDA in September 2006 and launched in the first half of 2007.

Hepaconda®

Hepaconda® is for the treatment of Hepatitis C and is based on combination therapy of bezafibrate with chenodeoxycholic acid.

The Hepaconda® programme has been slowed down as the company directs resources to the Myoconda® programme. However a Phase II study has just commenced.

Ibaconda

Ibaconda is designed for the treatment of Constipation-predominant Irritable Bowel Syndrome and a reformulation of two medications, olsalazine and colchicine. Olsalazine is an anti-inflammatory medication currently used to treat ulcerative colitis and produces a laxative effect in some patients. Colchicine is a drug that is used to treat gout. The drug has also demonstrated some efficacy when used to treat the symptoms of constipation. In combination, olsalazine and colchicine could provide more effective relief of constipation.

The Ibaconda programme has been slowed down as the company directs resources to the Myoconda® programme.

Picoconda®

Picoconda® is for use in Gastrointestinal Tract Procedures. Conventional bowel preparations are powders dissolved in large volumes of liquid, which is considered by many patients to be unpalatable. Picoconda® contains a stimulant laxative used to empty the bowel prior to colonoscopy or bowel surgery. Preliminary tests have shown Picoconda® to have an acceptable cleansing capacity and exceptional patient acceptance.

Recommendation

Crohn's disease affects about 400,000 people in North America. Prevalence estimates for Northern Europe have ranged from 27–48 per 100,000[15,16]. However it is clear that Crohn's Disease is caused by a number of different factors. Not unsurprising as Crohn's Disease is the term used to describe the symptoms and not the causation. MAP is one potential factor and MAP DNA has been found in intestinal biopsies from 12 of 31 Crohn's Disease patients, but was only found in 1 of 21 biopsies from healthy patients.

Based on the literature, we estimated the number of patients with Crohn's disease that could be potentially caused by MAP to be about 358,065.

Forecast Pricing and per Myoconda® Treatment Course (in 2007 dollars) and accessible market

Market	Cost per Patient Per Annum	Accessible Population
US	USD 8,750	154,839
Europe	USD 7,350	174,194
Australia	USD 7,350	13,548
Canada	USD 7,350	34,839
Total Market Size‡		358,065
Net Market Size*		204,097
Peak Net Sales per Annum ($A)		AUD 1,531m

‡ Assumes that 38.7% of Crohn's Disease is caused by MAP infestation.

* Adjusted to exclude patients hypothesised to be refractory to Myoconda®, patients who remain on other therapies and patients who otherwise do not respond to the Myoconda®, collectively calculated at 43%.

We would normally place a valuation of a company with product in clinical trials, but on this occasion we cannot because of the low stock liquidity.

Valuation models are based on the premise of that the stock demand/supply does not hinder the ability of the intrinsic value to match the market value. We cannot do this! However, we can estimate the accessible market to be about A$1.5bn per annum. Giaconda's ability to capture this market is dependant upon the outcome of the Phase III clinical trials and its (and any future marketing partners') ability to market and distribute the drug.

Nevertheless, the technology has the potential to revolutionise the treatment of Crohn's Disease if the retrospective human clinical trials are reproducible. Unlike treatment by steroids, MAP therapy treats the cause and

[13] J Antimicrobial Chemotherapy 1997;39:393-400.
[14] Aliment Pharmacol Ther 23, 481–488 (2006)
[15] Alimentary Pharmacology & Therapeutics 16 (1): 51-60 (2002).
[16] The American Journal of Gastroenterology 101 (7): 1559–1568 (2006).

not the symptom. In addition, MAP therapy is more cost effective than TNF-inhibitor therapy.

Moderate to severe Crohn's Disease can be managed with 5 mg/kg TNF-inhibitor administered as a single dose. Severe Crohn's disease is followed with further 2 to 8 week administrations. The cost of Remicade® is about US$1000 for a 100mg dose (average cost per patient US$3,750 per dosage or around US$25k per annum). In comparison, Myoconda® is expected to cost around US$ 8,750 per annum per patient.

Although the cost of Myoconda® is inexpensive, it is administered over a long period of time. Patients treated in the retrospective study were treated for 6 months to 9 years. We expect administration for a similar duration of patients that adopt the therapy once it enters the market. Therefore, once a patient responds to MAP therapy, they become a captive market. This is an important point as once adoption occurs, sales are likely to be compounding.

We recommend a Speculative Buy.

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