

Newsletter: November

Welcome to the first edition of BiotechShares Newsletter. Every month we will feature an area of the biotechnology industry and the major players involved. In addition we will inform you about hot topics and companies in biotech, the top market movers of the month and upcoming biotech floats. We will also have an ongoing educational section., which provides information on common terms and practices in the biotech industry.

This month we will take an in depth look at obesity and the companies and drugs competing for the very lucrative weight management industry. Our educational topic this month will be Clinical trials, what are they and are they important?

In the News



Peptech (ASX:PTD), dispute resolution and imminent product launch

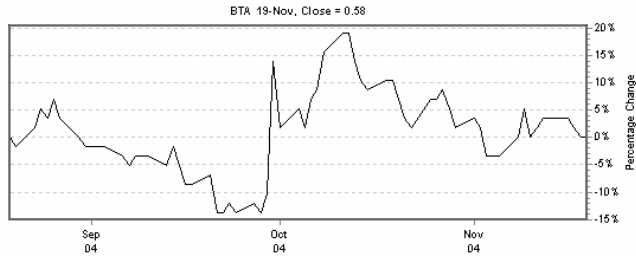
Therapeutic peptide company Peptech saw its share price rocket over 30% in one day this week. The company announced what it refers to as a 'satisfactory' outcome regarding an ongoing licence dispute with Centacor (a division of Johnson & Johnson) in relation to Peptech's patents covering antibodies against tumour necrosis factor alpha (TNF). The company also announced to the market its

expected net profit after tax for the year to be in the range of A\$18m to A\$21m. This guidance includes Peptech's income from its licensing agreements with Centacor Inc and Abbott Laboratories. Hoping to restore further confidence in the market the Peptech board has undertaken to place the issue of dividends, or alternative shareholder returns that increase shareholder value, back on the board agenda.

The company is also in final stages of releasing into the Australian and New Zealand markets *Suprelorin* its slow release implantable technology for veterinary applications. The product is initially being marketed as temporary sterilization of dogs (currently 6 monthly) but is known to work on other animal species and is currently being trialed. The technology has several possible applications and potential benefits in addition to temporary sterilization such as treating incontinence in spayed bitches. The product is protected until 2020 by patents in Australia, New Zealand, the United States and Europe, with patents pending in other countries. Shares in PTD closed down 3% today at \$1.98 after reaching a high earlier in the week of \$2.20.

Chemeq (ASX:CEQ), the worst is over?:

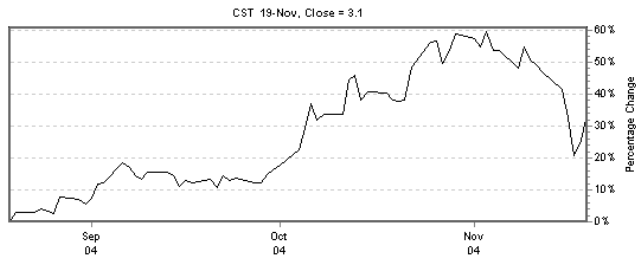
The research-based veterinary bio-pharmaceutical company has seen its share price severely hammered over the past 12 months going from a high of \$6.00 to a 52 week low of \$1.75 with some recent recovery and a current closing price around the \$2.20 level. The company attributes its flagging share price to recent bad press speculating about insolvency and ongoing capital raising. Unexpected delays with the Rockingham production facility of their veterinary antimicrobial drug CHEMYDE have certainly not helped, especially as there is a 1.5 million dollar order from South Africa yet to be filled. Forecasts for EPS are 2.9 cents by next year rising to 8.9 cents by 2006. All going well, this may bring a healthy recovery of the share price.



Biota (BTA): running strong and entering new markets,

Biota has announced this month that its influenza diagnostic assay, FLU OIA has been approved by the Korean FDA and the company expects it will commence sales of the product in the coming season. According to

Biota the rapid diagnostic kit has important benefits in correctly diagnosing strains of flu and assisting in the appropriate use of antiviral treatments such as the company's product Relenza. After much disappointment regarding the marketing and sales of its flagship antiviral drug and abandonment by GlaxoSmithKline it looks like Biota is hoping to recoup some of the lost profits. It has filed a lawsuit against the GSK in the Victorian Supreme Court for failing to fulfill the agreement to support and adequately market Relenza. We will keep you posted. Biota believes with 'good' recent flu seasons over 2003/4 and increased interest and need for flu antivirals things should start looking up. Shares closed steady at \$0.58.



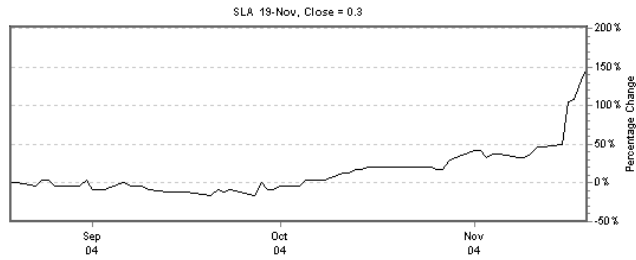
Cellestis (ASX:CST) : close to final FDA approval and recent windfall,

November has seen a return of the company's share price close to record highs. It appears the FDA approval for the company's QuantiFERON-TB Gold detection kit is

progressing well with all queries and recommendations being answered. Cellestis expects further communication from the FDA over the next several weeks. The company also announced on the 8th November that it was awarded a contract by the US Military to Develop a QuantiFERON Leishmaniasis (a parasite infection endemic in many countries in the Middle-east, Africa, and South America) Diagnostic, building on the company's current QuantiFERON kit technology for diagnosis of latent Tuberculosis infection. If agreed milestones are met, Cellestis will receive in excess of US\$1,000,000 in project support payments to develop the new test. The project, which runs over a two year period, covers the development, clinical trials and regulatory approval for the new test. The news was received very favourably by the market with the company's share price steadily heading north over recent months from a 52 week low of \$1.39 to a recent 52 week high of \$3.77. Shares have been quite volatile lately closing this week at about \$2.90 after large volume trading and probable profit taking.

Alchemia (ASX:ACL): Shares in the Brisbane drug-developer rose some 50 per cent to \$0.80, on the back of news that it would be targeting antibiotic-resistant "superbugs" with a novel class of synthetic molecules that disrupt cell-wall synthesis in bacteria. Microbiologists at the University of Leeds' Antimicrobial Research Centre in the UK have shown that the Alchemia compounds inhibit transglycosylase enzymes required for cell-wall synthesis. Describing the compounds as a potential breakthrough for combating hospital-acquired infections, Alchemia CEO Dr Tracie Ramsdale said the UK tests confirmed that the compounds are highly active against multi-drug resistant bacteria. Shares are currently trading at around \$0.90 and a market cap of \$82 million.

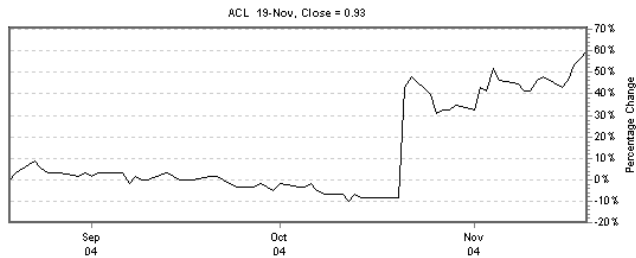
This months top biggest movers



Solagran Ltd (ASX:SLA) more than doubled its share price in the past month from 14 cents, trading 30 cents at the time of writing after reaching a high of 34 cents on Friday. The dramatic rise happened on the back of the news that Phase II clinical trials of BioeffectiveR as a

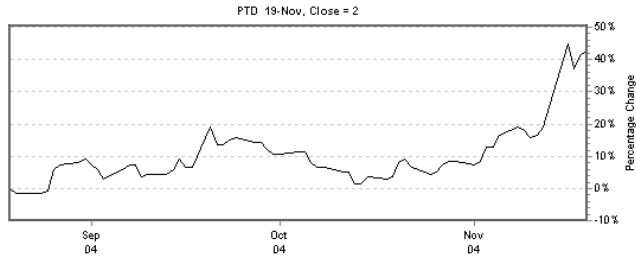
treatment for chronic liver disease have been successfully completed. The company also has recently signed an agreement with Cardinal Health for the sales of their products.

Alchemia (ASX:ACL) rallied from 54 cents to 91 cents at the time of writing. Tests have indicated that compounds developed by the company are highly effective against multi-drug resistant bacteria associated with hospital acquired infections. There is currently no cure for such infections.



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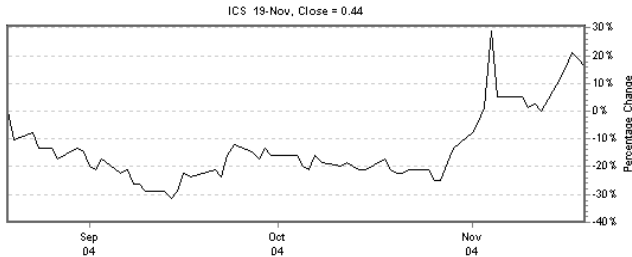
Peptech (ASX:PTD), see above



Metabolic (ASX:MBP) has had a good run earlier this month when it rallied from 88 cents up to \$2.20 in mid November. While there was no announcement, the release of phase 2b clinical trial results for the company's anti-obesity drug AOD9604 is imminent. On Monday



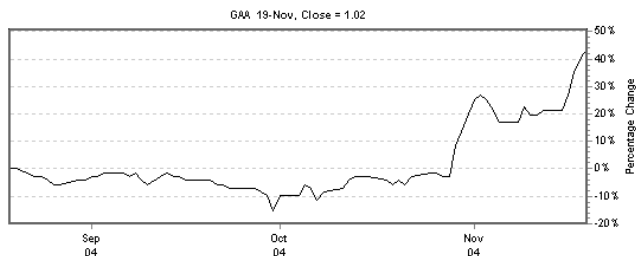
14 November the share price started to take a steep dive, possibly due to overly enthusiastic press about Aventis' competing drug Accomplia (see above).



Other strong performers were **ICS Global (ASX:ICS)** and **Genepharma Australasia (ASX:GAA)** ICS rallied from 28 cents to 49 cents (trading 44 cents at the time of writing) after the company announced a 3 year agreement with Defence Health for their internet based

Health Administration System THELMA as well as a letter of intent from US Health Transaction Network.

GAA is a generic drug manufacturer and announced the intended production and TGA registration of blockbuster drug cholesterol reducing Simvastatin, currently sold under the brand name Zocor. It comes off patent in 2005 and GAA expects to make profits in the first year.



In Focus

This month we are covering a topic close to everybody's heart in more ways than one, obesity. There are many companies worldwide conducting research on obesity trying to tackle this increasing health dilemma. However the market has a lot of room for competitors in this multi-billion dollar industry.

In the field of weight loss and management of obesity there are various therapeutic strategies that have been explored, however no satisfactory solution has reached the market. The numerous herbal weight loss drugs currently available have at best little effect and often produce side effects like high blood pressure, anxiety and insomnia. In addition none of the drugs are suitable for long term use.

The following table gives an overview of weight loss drugs currently on the market. Common problems are either increased blood pressure and high risk for heart patients in the case of drugs affecting catecholamine release, or digestive problems including incontinence in case of fat absorbing drugs like Orlistat or Xenical.

Weight Loss Drug	Brand Name
Dexfenfluramine	Redux (withdrawn)
Diethylpropion	Tenuate, Dospan, affect catecholamine release
Fenfluramine	Pondimin (withdrawn), affect serotonin reuptake, high frequency of valvular heart disease
Mazindol	Sanorex, Mazanor, affect catecholamine release
Orlistat	Xenical, inhibits fat absorption, steatorroea, problems worse with fatty foods
Phendimetrazine	Bontril, Plegine, Prelu-2, X-Troazine
Phentermine	Adipex-P, Fastin, Ionamin, Oby-trim, affect catecholamine release
Sibutramine	Meridia, acts on both the serotonin and catecholamine systems

The major player in the Australian Market is Metabolic Pharmaceuticals.

Metabolic Pharmaceuticals Limited (ASX: MBP) is an Australian based biotechnology company focused on obesity, obesity-related diseases such as type 2 diabetes, and more recently, pain, and osteoporosis. The company's strategy is to outsource much of its activities to minimise infrastructure and overhead costs whilst maximising access to world-class

expertise. Despite outsourcing these activities they are still closely controlled by the company's management, which has the benefit of substantial skills and experience in the clinical development of drugs, the management of research and a high-level of decision-making experience in the international pharmaceutical industry.



Currently, Metabolic is undertaking a multi-centre Phase 2b study in 300 obese male and female subjects, comparing the weight reduction efficacy of its lead product AOD9604. Dosing for this trial was completed on 17 September 2004 and previous short term trials (up to 1 week) have indicated that the drug is orally active and well tolerated. The current Phase 2b human trial is a definitive test of the efficacy and

safety of the drug over 12 weeks.

With a positive result, Metabolic intends to enter into a partnership with a major pharmaceutical company to assist in financing Phase 3 human clinical trials for worldwide marketing approval as a prescription treatment. AOD9604 is a small orally active peptide variant of human growth hormone (HGH) which when administered to humans causes fat reduction via a process known as lipolysis, this is the breakdown of fat into its basic chemical components.

Growth hormone levels decrease with age and studies have shown that obese people have lower levels of HGH, making it even harder for them to lose weight. Metabolic hopes that because the product acts directly on the metabolism of fat it will not be dependant on modifying an individual's behaviour such as appetite suppression and the associated side effects and thereby increase its acceptance by patients and doctors. The company's share price has taken a healthy hike north recently, going from about 0.90 to \$2.20 by mid November on the back of continuing trial updates.

In Australia there are several other companies looking at ways to tackle obesity. These include ChemGenex/AGT Biosciences and Adipogen.

ChemGenex/AGT Biosciences has a high throughput gene discovery facility for the rapid identification of genes involved in diseases such as diabetes and obesity. In 2001 the company discovered the gene Beacon (AGT-121), which is more active in animals that will develop obesity, even before the illness has set in. According to ChemGenex, Merck will provide expertise and funding for clinical development and pay \$5 million for any target that progresses to phase II clinical trial. With markets worth more than \$8 billion dollars/year Merck agreed to pay royalties in the vicinity of 5-7% on net sales of any product based on a target supplied by ChemGenex, which may be attractive in the distant future.

In the United States there are two main anti-obesity drugs already on the market: Meridia (**Abbott Laboratories**) and Xenical (**Roche Laboratories**). Both have been hampered by some troublesome side effects: high blood pressure in the case of Meridia, and soiling oneself in the case of Xenical (Orlistat) (NY Times 7/9/2004).

Other competing drugs currently in clinical trials or waiting for approval are:

The only anti-obesity drugs in advanced clinical trials are Accomplia and Axokine:

Accompia:

Rimonabant (to be marketed as Accomplia) is the lead anti-obesity drug developed by Sanofi – Aventis. The company says that it could become one of the industry's once-in-a-decade blockbusters. Many doctors and analysts agree. While doubters note that other promising obesity drugs have proved disappointing and that the company has not completed some crucial tests, Sanofi plans to file for regulatory approval early next year in the United States

and Europe. FDA generally requires two years of safety data before approving anti-obesity drugs. Results from the phase III RIO trial programme suggest rimonabant is well tolerated. More safety data, including drop-out rates and weight rebound after treatment, awaits the release of final results from the two-year trial which is anticipated in early 2005.

While the company is hopeful of FDA approval and marketing in 2006, the sideeffects (namely depression, mood swings, occasional amnesia) might make this a little optimistic.

Sanofi-Aventis developed Accomplia from the knowledge that cannabis smokers often experience extreme hunger pangs, which cannabis smokers refer to as "the munchies". The company worked on the premise that if cannabinoids stimulate appetite, blocking cannabinoid receptors in the brain might reduce appetite. The central cannabinoid (CB1) receptors are believed to play a role in controlling food consumption and the phenomena of dependence / habituation. Preclinical animal studies subsequently showed that it could reduce consumption of fats and sugars, which contribute to weight gain. There is also speculation that it might help quit smoking.

Regeneron Pharmaceutical's AXOKINE

Axokine (Regeneron Pharmaceuticals Inc (NSDAQ:REGN)) was reported to have efficacy in phase III clinical trials but only 30% of subjects did not develop resistance to the drug. There has not been any news on Axokine since September 2003.

Educational Topic: Clinical Trials



Introduction

Before a pharmaceutical company can initiate testing in humans, it must conduct extensive preclinical or laboratory research. This research typically involves years of experiments in animal and human cells. The compounds are also extensively tested in animals. If this stage of testing is successful, a pharmaceutical company provides this data to the Therapeutic Goods Administration (TGA, the Australian equivalent to the FDA in the US), requesting approval to begin testing the drug in humans.

How are experimental drugs tested in humans?

The clinical testing of experimental drugs is normally done in three phases, each successive phase involving a larger number of people. Once the TGA has granted a New Drug Approval, pharmaceutical companies also conduct post marketing or late phase three/phase four studies.

A Phase One Study:

Phase I studies are primarily concerned with assessing the drug's safety. This initial phase of testing in humans is done in a small number of healthy volunteers (20 to 100), who are usually paid for participating in the study. The study is designed to determine what happens to the drug in the human body--how it is absorbed, metabolized, and excreted. A phase I study will investigate side effects that occur as dosage levels are increased. This initial phase of testing typically takes several months.

Phase Two Study:

Once a drug has been shown to be safe, it must be tested for efficacy. This second phase of testing may last from several months to two years, and involve up to several hundred

patients. Most phase II studies are randomized trials. One group of patients will receive the experimental drug, while a second "control" group will receive a standard treatment or placebo. Often these studies are "blinded"--neither the patients nor the researchers know who is getting the experimental drug. In this manner, the study can provide the pharmaceutical company and the TGA comparative information about the relative safety of the new drug, and its effectiveness. Only about one-third of experimental drugs successfully complete both phase I and phase II studies.

Phase Three Study:

In a phase III study, a drug is tested in several hundred to several thousand patients. This large-scale testing provides the pharmaceutical company and the TGA with a more thorough understanding of the drug's effectiveness, benefits, and the range of possible adverse reactions. Most phase III studies are randomized and blinded trials.

Phase III studies typically last several years. 70 to 90 percent of drugs that enter phase III studies successfully complete this phase of testing. Once a phase III study is successfully completed, a pharmaceutical company can request TGA approval for marketing the drug. Phase III studies are very expensive and are not normally conducted in Australia.

Post-Marketing -- Late Phase Three/Phase Four Studies

In late phase III/phase IV studies, pharmaceutical companies have several objectives: (1) studies often compare a drug with other drugs already in the market; (2) studies are often designed to monitor a drug's long-term effectiveness and impact on a patient's quality of life; and (3) many studies are designed to determine the cost-effectiveness of a drug therapy relative to other traditional and new therapies.



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