

Biotech Daily

Marc Sinatra's Bioguide

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PHARMAXIS: EYES ON THE BIG TIME

Overview: Pharmaxis occupies a unique position among Australian life science companies. With a market capitalization of \$781 million, it is more than twice as big as its nearest rivals (Biota, Cellestis and Peptech), but it is a long way from joining the Biotech Daily Big Caps - CSL, Cochlear and Resmed, the smallest of which has a market capitalization \$3.5 billion.

For Pharmaxis to join the big guys, its share price would need to move from its current \$4.09 to more than \$18 a share. Does the company have the capacity to grow this rapidly and what will need to happen to do so?

Financials: Market cap: \$781 million; cash: \$126.2 million; last quarter cash burn: \$3.6 million.

Directors & Management: Independent chairman, Denis M Hanley; chief executive officer, Dr Alan Robertson; non-executive directors, Dr Peter Farrell, Charles Kiefel and Dr John Villiger; chief financial officer and company secretary, David McGarvey.

Pharmaxis has an extremely talented board with a wealth of experience in creating successful life science companies.

Products in Development: Pharmaxis has three main products in development. Two based on inhaled mannitol are in the later stages of development, while the other product is in the early stages of development. The products are:

1) Aridol - An indirect bronchial provocation test for airways hyper-responsiveness (a marker of respiratory tract inflammation) with patients inhaling increasing doses of mannitol. The effect of each dose is used to assess the presence and severity of hyper-responsiveness, a hallmark of asthma. Aridol's intended use is for diagnosing and monitoring asthma patients. It may also be useful in chronic obstructive pulmonary disease (COPD) patients as a means of assessing treatment effectiveness. Aridol is the subject of a number of current investigator sponsored trials. It is marketed in the EU and Australia and sales have increased each quarter since its launch. Pharmaxis intends to submit a new drug application to the US Food and Drug Administration next year.

2) Bronchitol - A therapeutic designed to help patients' clear mucus from their lungs. The mannitol inhaled from Bronchitol has an osmotic effect in the lungs, drawing water to the surface and replenishing the airway surface liquid. In doing so, lung mucus is diluted and loosened, making it easier to expel and lung hygiene is restored.

Bronchitol has been granted orphan drug and fast-track status for bronchiectasis and cystic fibrosis in the US, and orphan drug status in the EU. Recent phase III results support the use of Bronchitol for bronchiectasis.

Results from additional phase III trials for both diseases are due in 2008. Bronchitol is also being studied in chronic bronchitis patients in a phase II trial. Pharmaxis intends to submit a new drug application to the FDA in 2008.

3) PXS25 - Identified as a selective inhibitor of T-cell migration. It is being evaluated against several inflammatory diseases. Clinical trials are scheduled to commence in 2008.

Product Markets: Estimated 2007 prevalence for the diseases for which Pharmaxis' products are targeted for the seven major pharmaceutical markets (France, Germany, Italy, Japan, Spain, UK, US) are: asthma, 45 million people; COPD, 30 million; cystic fibrosis, 80,000; bronchiectasis 190,000; and chronic bronchitis, 27 million.

It has proven difficult to find solid market size estimates for pulmonary/asthma diagnostics. A global market size of \$US100 -150 million seems reasonable based on available information. Spirometry is the frontline asthma test. More difficult cases may be given a bronchial provocation test, such as methacholine. There is little product development going on in the asthma and COPD diagnostic area.

The \$US245 million generated in sales of mucoactive drug Pulmozyme in 2006, indicates the level of cash a successful drug for cystic fibrosis can generate. A successful drug for bronchiectasis could bring in that much again. The 2006 sales of anti-bronchospasm drug Spiriva of \$US1.7 billion demonstrates the value of a successful drug for chronic bronchitis. Denufosal, currently in phase III trials and aimed solely at cystic fibrosis, is the only other mucoactive drug in development of note. Nebulised hypertonic saline (HS) is used to treat cystic fibrosis and chronic bronchitis patients. It is cheap and its mode of action and clinical trial results appear similar to that of Bronchitol.

Verdict: Pharmaxis is a company of rare quality. It has an extraordinary board, high calibre management, excellent structure and a track record of moving its projects forward in an appropriate manner at a solid pace. As result, the company is likely to be limited solely by the technology it possesses.

Aridol, like other asthma tests, guides a physician's decision-making. An ideal test would make the decision. Aridol appears superior to other tests, but more for ease-of-use than clinical performance. In a direct comparison Aridol results were indistinguishable from methacholine. Aridol has asthma management utility that methacholine does not. Aridol's COPD trial results indicate more work is needed before a market niche is confirmed.

Bronchitol has a bright future in treating bronchiectasis and cystic fibrosis. This may also be true for chronic bronchitis given that nebulised HS has performed well in chronic bronchitis patients, the similarities between nebulised HS and Bronchitol and that Bronchitol is easier to use. The availability of nebulised HS as a cheap alternative may limit Bronchitol's price and this has been factored into my valuation.

Pharmaxis' chances of joining the Biotech Daily Big Caps are mainly contingent on how well Bronchitol penetrates the chronic bronchitis market. At a maximum market

penetration of 2.5 percent, they will join in eight years. At 15 percent market penetration, they should be there now. A study demonstrating Bronchitol's clear superiority to nebulised HS would help.

The addition of a good clinical stage project to their pipeline wouldn't go astray and this is a possibility given Pharmaxis' recent capital raising. The chronic bronchitis market, however, still remains the key. For now, I have calculated a discounted cash flow share price for Pharmaxis of \$4.69.

Pharmaxis was up cents or percent to \$

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