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Marc Sinatra's Bioguide

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A DEAL FOR PRANA'S PBT2 WOULD MAKE ALL THE DIFFERENCE

Overview: Prana's trials and tribulations are aptly reflected in a graph of the company's share price since it was listed in mid-2000.

Hype regarding its potential Alzheimer's disease treatment, PBT1, drove the share price to more than $2.40 in late 2001. In 2005 Prana's share price was beaten down to 15 cents when it discontinued development of PBT1 a year after raising $US20 million for development of its successor, PBT2, from US institutions.

The development of PBT1's replacement, PBT2, its positive phase IIa trial results and the hope of a big pharmaceutical partner pushed the share price above 60 cents for the first time in four years. A year on, with little news, the share price is back in the doldrums and PBT2 is yet to be partnered. Where are Prana and PBT2 headed?

Financials: Market cap: $42m; cash: $7.9m; last quarter cash burn: $1.8m.

Directors: Executive chairman and CEO: Geoffrey Kempler; non-executive directors: Dr George Mihaly, Brian Meltzer, Peter Marks. The addition of a couple of new directors with strong drug development and partnering credentials would be desirable.

Products in Development:
1) PBT2: A metal protein attenuating compound (MPAC) that selectively binds metal ions. Amyloid-beta-peptide (Abeta) oligomers are generally thought to play a key role in Alzheimer's disease. Prana believes that through its metal ion binding ability, PBT2 prevents the formation and promotes the dissolution of amyloid-beta-peptide oligomers, particularly the key oligomer Abeta42. A phase IIa study of PBT2 in early Alzheimer's disease patients met its safety endpoint. It also showed significantly reduced cerebrospinal fluid concentrations of Abeta42 and positive changes in two of a battery of cognition tests. A Prana-commissioned independent report from US-based clinical researchers concluded that PBT2 was a suitable candidate for Huntington's disease clinical trials, in addition to Alzheimer's disease. Huntington's disease is another neurodegenerative disease associated with metals.

2) PBT427: Another MPAC in preclinical trials for Parkinson's disease. It has been shown in animal trials to protect the area of the brain affected in Parkinson's disease.

3) Other: Prana also has a further MPAC, an immunotherapy and a metallo-complexing agent, which inhibits the Abeta metal binding site, in late stage research for Alzheimer's disease. In addition, Prana is also developing Alzheimer's disease imaging compounds and possible treatments for cancer.

Development timelines were not available from the company.

Significant Product Markets: Twenty-six million people worldwide, as of 2006, and five million Americans, as of 2007, have Alzheimer's disease.

Decision Resources put 2007 sales of labeled Alzheimer's disease drugs at $US3 billion in the major markets, with forecast sales of $US9 billion in 2017. This fits well Datamonitor's forecast, which has sales at $US1.9 billion to $US12.7 billion for 2017.

Marketed Alzheimer's disease drugs only treat Alzheimer's disease symptoms. Numerous drugs aimed at various targets are in clinical trials that target the underlying cause of Alzheimer's disease. At least five of these drugs are in, or about to start, phase III trials.

Bapineuzumab (Elan & Wyeth) is an anti-Abeta antibody, while IgIV (Baxter) is composed of polyclonal antibodies. Results to date with Bapineuzumab have been disappointing. Semagacestat (Eli Lilly & Elan) is an inhibitor of beta-secretase which cleaves amyloid precursor protein into Abeta. Dimebon (Medivation) is thought to act as a mitochondrial stabilizer. It demonstrated significant improvements in all outcome measures in its initial pivotal trial and is currently undergoing a confirmatory phase III trial. Rember (Taurx), which inhibits tau protein aggregation and may also influence mitochondrial biochemical pathways, is expected to start phase III trials this year.

Opinion: Alzheimer's disease is a difficult indication to tackle. Although the aetiology of the disease is becoming better understood on a daily basis, significant knowledge gaps and alternate hypotheses abound. This is reflected in the large number of targets to which drugs are being developed and the failure of any company to date to develop one which has been approved for treating the underlying disease.

Most experts believe that no single drug will halt Alzheimer's disease and that a combination of drugs will prove the best approach. Although this may reduce the cash flows Prana could expect from PBT2, it also reduces risk.

The scientific rationale behind PBT2 is strong and well supported in the literature, despite the fact that another drug which targets Abeta, Tramiprosate, was discontinued after a phase III trial. Unlike PBT2, however, Tramiprosate did not demonstrate a significant effect on any aspect of cognition in its phase II trial.

Licencing deals often take six to 18 months to negotiate and it is now 12 months since PBT2's phase IIa results were released. If a deal is to be done, it should be done soon, otherwise the share price will continue to slide. Any deal would be important for a number of reasons, not the least of which is the positive signal it would provide regarding PBT2's future in such a difficult area. A deal with PBT2 for Alzheimer's disease is also likely to increase interest in PBT2 for Huntington's disease and PBT427 for Parkinson's disease.

Based on a comparison to five similar companies with Alzheimer's disease therapeutic programs, I have calculated a value for Prana Biotechnology of 35 cents per share. A PBT2 licencing deal on reasonable terms would see the valuation rise considerably.

Prana fell one cent or 5.26 percent to 18 cents.

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