



Southern Cross Equities

Biotechnology research

Location: Sydney

Business: Developing adenovirus-based vectors for immunising pigs and chickens, as well as a flea vaccine

Share Price (c): 27

Market Cap. of tradeable shares: \$27m

Twelve Month Range (c): 32 - 9

No. of shares tradeable: 101.1m

Average weekly volume: 2.58m shares

Average weekly value: \$0.57m

% below 12 month high: 15.6%

Main players: Graham Dowland (Executive Chairman), Dr Warwick Lamb (Managing Director), Dr Colin Hort (Commercial Manager), Dr Kevin Fahey (Chairman of the Scientific Advisory Board), Dr Mike Shepherd (Chief Scientific Officer), Dr Wayne Greene and Prof. Andrew Thompson (joint Chief Scientific Officers for Paragen).

Last note: 16 April 2003, Speculative Buy at 11 cents

Analyst disclosure: Stuart Roberts holds 20,334 shares in Imugene as at the date of this report.

A brief update note on **Imugene**

(IMU - \$0.27)

Speculative Buy

(for knowledgeable professional investors)

Tuesday, 2 December 2003

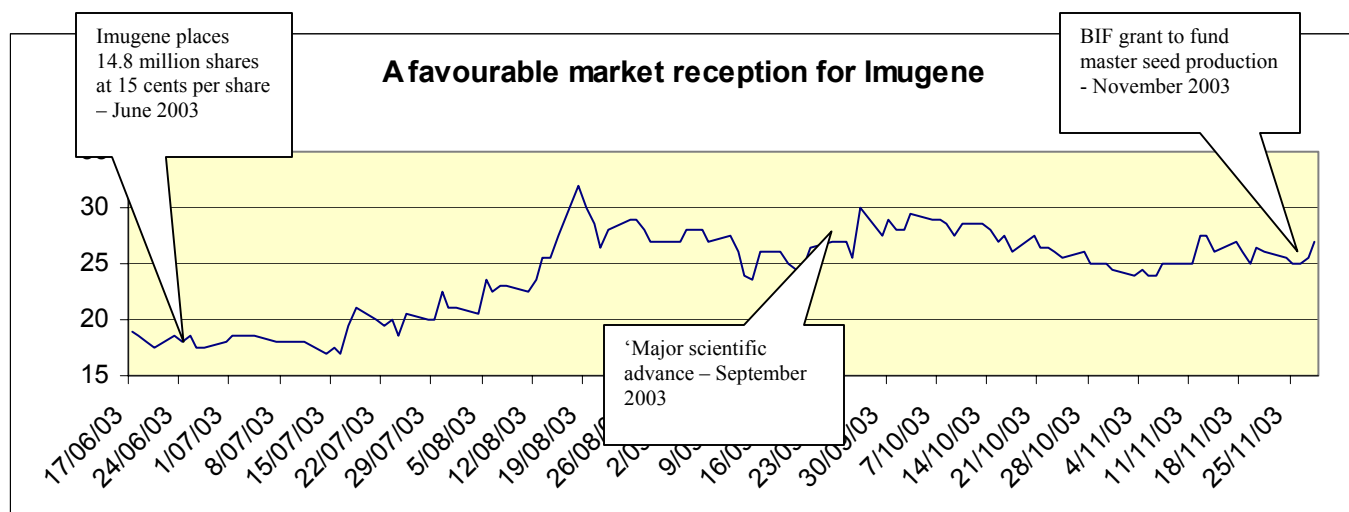
Director: David O'Halloran (doh@sceq.com.au)

Analyst: Stuart Roberts (stuartr@sceq.com.au)

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Imugene delivers on its June 2003 potential

Since its June 2003 placement of 14.8 million shares at 15 cents per share to raise \$2.2m in new capital, Imugene has continued to make progress towards commercialising its CSIRO-developed recombinant adenoviral vector technologies. A deal with the London-based animal health giant Merial is looking increasingly likely for 2004. Imugene's genetically engineered flea vaccine project, now getting close to the animal trial stage, also shows promise. Imugene is a high risk play due to its not yet having commercial products in the marketplace. Nonetheless the deals done so far and the large markets suggest a high potential return. Our optimistic case valuation remains 40 cents per share, a figure still some way above the current share price. However we expect that as Imugene moves closer commercial sales, a significant share price rise is likely to reflect the increased commercial certainty of the company. We'll be revising our Imugene model early in 2004. In the meantime Imugene rates a **Speculative Buy for Knowledgeable Professional Investors**.



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Level 32, 88 Phillip Street, SYDNEY, NSW 2000. Telephone: (612) 9231 0880 • Facsimile (612) 9231 0588

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Imugene makes some gains in the second half of 2003

In June 2003 Southern Cross Equities helped arrange a placement of 14.8 million shares at 15 cents per share to raise \$2.2m in new capital, following on from a note this analyst released a couple of months previous (*Imugene bug-proofs its business – Highly Speculative Buy at 11 cents, 16 April 2003*). In the months since that placement Imugene has continued to make progress towards its twin goals of commercializing CSIRO-developed recombinant adenoviral vector technologies for use in pig and chicken vaccines, and developing a recombinant flea vaccine for companion animals. This note looks at some of those achievements.

Imugene's share price performance has been satisfactory since its June 2003 placement at 15 cents.

The background

In the 1990s scientists at the CSIRO's Australian Animal Health Laboratory in Geelong developed some powerful vaccine technologies based on the adenovirus, a virus particularly good at infecting the mucosal surfaces of its host without greatly harming that host. The CSIRO scientists took the DNA of adenoviruses known to infect pigs and chickens, and spliced in to that DNA some more pieces of DNA, the latter DNA representing part of whatever microbial pathogen it was that had caused the need for a decent vaccine. As the adenovirus replicated itself, it would also replicate the antigen, that is, the spliced-in DNA, and the antigen would in turn persuade the immune system of the animal to respond, thereby creating immunity in the animal against the disease. What the CSIRO scientists thereby created was a number of 'recombinant adenoviral vectors', providing the basis for vaccines against scourges like infectious bronchitis, avian coccidiosis and Newcastle disease (in the case of chickens) and porcine circovirus, classical swine fever and, porcine respiratory reproductive syndrome (in the case of pigs). Imugene is now commercialising this 'platform' technology, which is expected to sell into large and growing markets given the need of pig and chicken farmers to move away from antibiotics as a way of managing animal health. Imugene is also funding a research effort at Murdoch University in Perth to develop the world's first recombinant flea vaccine for companion animals. While this is an earlier stage project than the adenoviral vector effort, the payoff given the market for companion animal health products is significant.

Favourable developments on the technology front

Probably the biggest development to build shareholder value at Imugene over the last six months has been a breakthrough on the technology front that was announced to the market on 25 September. The power of Imugene's vectors depends in part on a number of 'switches' in the genome of the adenovirus that cause the viral DNA to turn into a real live virus. When the adenoviral vector intellectual property was created in the 1990s, the CSIRO scientists relied in no small measure on a gene in the adenoviruses known as the 'major late promoter'. A promoter is a 'gene switch' that starts the process of transcribing DNA into what is called 'messenger RNA', which is what a body's protein making factories need to tell them what to make. In adenoviruses transcription to mRNA happens in two rounds, called 'early' and 'late'. Most of the body of the virus gets created in the late stage of transcription, making the major late promoter notionally the most important promoter in the whole virus-making process. If the promoter doesn't cause viral replication in sufficient quantities to provide an effective vaccine, not enough of the antigen will be created. Imugene's 25 September announcement was that there had been a change in the kind of promoter used in the vectors, and that that change had made for a massive rise in the amount of antigenic material delivered to the immune system of the animal being immunised. Instead of using an adenoviral major late promoter, the CSIRO

Imugene's adenoviral promoter change made for a massive rise in the amount of antigenic material delivered to the immune system of the animal being immunised.

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scientists, working under the direction of Imugene's Chief Scientific Officer, Dr Mike Sheppard, had tried CMVIE, that is, the 'Immediate-Early' promoter (as the name suggests, a gene switch that is the first to turn on) from CMV, or cytomegalovirus (a powerful herpes virus responsible for the disease infectious mononucleosis). CMVIE was, in Sheppard's experience as an engineer of viral vectors, the most powerful promoter available, and the fact that any patent rights over the promoter had ceased to be of commercial consequence suggested the change in promoters was worth a try. The pay-off was remarkable, the best example occurring in a vector designed to deliver an immune system booster called interferon gamma into chickens. Now powered by CMVIE, that vector could now generate as much as 50 times more interferon gamma than before. The promoter change indicates to us that Imugene has harnessed the creativity of its scientists to raise the value of its products. However Imugene is also kicking goals on the commercial front as well.

Other developments since June 2003

In September 2002 the London-based Merial, a significant manufacturer of animal pharmaceuticals and vaccines that is jointly owned by two pharmaceutical majors, America's Merck and France's Aventis, took out an evaluation and sublicense option on the Imugene viral vectors. The deal was significant because Merial has been a pioneer in the use of viruses as animal vaccine vectors, as evidenced by products such as Purevax, a canarypox vector rabies

Imugene has affirmed that it enjoys Merial's strong commitment and support.

vaccine. We understand that Merial has evaluated Imugene's adenoviruses in a trial conducted in Europe, with favourable results, and has only delayed formally exercising its option until the CMVIE-powered adenovirus can be trialled as well. Should Merial choose to exercise any of its options, that company can then proceed to a 'global registration process', that is, register the products with the various Departments of Agriculture in order to bring it to market worldwide, with Imugene then receiving license fees based on milestones and royalty payments on commercial product sales. At its 27 November 2003 Annual General Meeting Imugene affirmed its view that it enjoyed Merial's 'strong commitment and support'. We believe that Merial will move to exercise some of its options in 2004.

Imugene has done some further work on what it understands to be the markets into which its viral vectors would be sold by Merial. The current market for pig health has now been estimated at US\$3.4bn, of which US\$285m represents the amount currently spent by pig farmers on 'biological' products like those Imugene is seeking to commercialise, and US\$1.04bn represents the current market for 'medicinal feed additives', that is, the antibiotics now being phased out of animal health worldwide due to the increasing capacity of microbes to not be killed by the drugs. With the biologicals market likely to subsume the antibiotics market over the next few years there's a fairly attractive market opportunity for the likes of Imugene's porcine adenoviral vector. For chickens, Imugene estimates that the entire health products market is something like US\$3.14bn, of which US\$550m is spent on biologicals and US\$650m on antibiotics. With pigs the larger market of the two, Imugene is putting more effort into porcine applications, working in particular on vaccines for the abovementioned Porcine Reproductive and Respiratory Syndrome (a disease for which there is currently a vaccine in the market but which Imugene reckons it can beat), and adding an effort to go after porcine foot and mouth disease. Imugene's current figures on market size are a little more conservative than those we were working with a few months ago, where Imugene estimated the pig and chicken markets to be perhaps US\$4.8bn and US\$4.3bn respectively. On the other hand our assumptions on market size, product launches and royalty rates were fairly conservative at that time, so we don't feel the need to change our valuation of Imugene's adenoviral vectors at this stage.

Imugene's adenoviral vectors will sell into markets worth US\$3-3.5bn for both pigs and chickens

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Southern Cross Equities

Research on *Imugene*

PAGE 4

Tuesday, December 02, 2003
Speculative Buy at 27 cents

We expect next year will be a good one for Imugene on the adenoviral vector front. Regulatory dossiers are now being prepared to submit to the various departments of agriculture worldwide, and as part of this filing Imugene has applied to the Australian Federal Government's Office of the Gene Technology Regulator for permission to conduct a large-scale trial of its vectors in Australia. The company is also getting set to produce 'Masterseed', that is, an initial batch of virus from which all commercial product will be made, and to this end the company was able to announce on 21 November that a Biotechnology Innovation Fund grant of \$250,000 had been made available by the Australian Federal Government.

Imugene has kept its recombinant flea vaccine work, now ongoing at Murdoch University in Perth, fairly quiet due to its being early stage and not yet covered by patent applications. That venture, however, is now expected to be trialling a vaccine in dogs from around mid 2004. Broadly speaking, what the Murdoch scientists have in mind is challenging the dog's immune system with key antigens extracted from the flea genome in the hope that the animal's immune system will produce antibodies to those fragments which, when ingested by a flea from its host's bloodstream, will kill the flea. The key antigens have now been identified and are in the process of being cloned into the appropriate bacterial vectors.

A good 2004 coming up

With Imugene gaining ground on both the commercial and scientific front at the moment, and a licensing deal from Merial on the cards for the not-too-distance future, the Imugene story remains one to stay close to, particularly since the stock is still discounting our 40 cents per share near-term price target from our mid April 2003 note. The stock is a **Speculative Buy for Knowledgeable Professional Investors**.

Director: David O'Halloran

Analyst: Stuart Roberts

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Disclosure of interest

Southern Cross Equities Ltd and its associates hold 26,739,800 shares in Imugene as at the date of this report. This position is subject to change without notice. Southern Cross Equities was named Imugene's stockmarket advisor in March 2003, at which time it received 4.0 million performance options exercisable at 22.5 cents per share. These options vest on 31 December 2003 subject to the performance terms and, once vested, are exercisable up to 31 October 2007.

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Below: Imugene has lagged the Southern Cross Equities Australian Biotechnology Index since August but not by much



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