

**Stuart Roberts****From:** Stuart Roberts**Sent:** Tuesday, 16 November 2004 18:09**Subject:** Southern Cross Equities' Australian Biotechnology Buzz for Monday 15 November 2004*Any sufficiently developed technology is indistinguishable from magic. - Arthur C. Clarke*

	<p>Southern Cross Equities'</p> <h2>Australian Biotechnology Buzz</h2> <p><a href="http://www.biotechbuzz.com.au">www.biotechbuzz.com.au</a></p> 
<p>If you've received this email and it isn't your thing even though Australian biotech stocks are yielding some great opportunities at the moment, just send us an <a href="#">email</a> to unsubscribe. If you like it but you're getting it more than once, do please let us know, and if suits you, send us some feedback on our work, which is always welcome.</p>	<p>for the week ended Friday 12 November 2004</p> <p><b>Monday 15 November 2004</b></p> <p>Editor: <a href="#">Stuart Roberts</a>, Biotechnology Analyst, Southern Cross Equities, Telephone 61-2-8224-2871.</p>

*Closing biotechnology stock prices as at Monday 15/11/2004 ... Southern Cross Equities Australia*

[Southern Cross Equities](#), which publishes Australian Biotechnology Buzz on a weekly basis, is a Sydney-based trading participant organisation of the [Australian Stock Exchange](#) with a largely institutional client base. Our firm is one of the Australia's leading equities houses in the area of raising capital and awareness for the nation's biotechnology companies, with a dedicated group of specialists working in the sector. Southern Cross Equities works with Australian biotech companies in three ways: **Raising capital...** Southern Cross Equities has helped fund a number of listed biotechs since 2002. Our firm's track record of success in terms of capital gains for the participating investors in these raisings has, to date, been enviable. **Raising understanding...** The members of the corporate team at Southern Cross Equities between them have decades of experience in the capital markets. The team is therefore well placed to provide biotech companies with strategic corporate advice. **And raising investor awareness...** Our biotech research seeks to cover developments in the Australian sector in a manner that builds investor understanding as well as interest, while pinpointing lucrative investment opportunities in the sector. We are perhaps best known for the iconic publication you are reading now, which has been going out in electronic form since May 2003. We also have a good reputation for doing [in-depth biotech research](#), having published a number of large-scale research notes over the last two years for the benefit of our professional investor clients. This year we have become known for the [Southern Cross Equities Australian Biotechnology Index](#), which was developed in late 2003 to provide a benchmark for tracking biotech share price action in Australia, as well as for our inaugural two-day [Australian Biotechnology Conference](#), which was held in Sydney on 8 and 9 September and attracted around 180 attendees. If you would like to talk about your biotech company to Southern Cross Equities please call, in the first instance, [Stuart Roberts](#), Southern Cross Equities' Biotechnology Analyst, on 61-2-8224-2871. For more on Southern Cross Equities visit [www.sceq.com.au](http://www.sceq.com.au).

**PLEASE NOTE:** The research contained in this document is directed to professional investors and as such is subject to

Good Evening and welcome to Southern Cross Equities' Australian Biotechnology Buzz

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for Monday 15 November 2004

*In this edition of Buzz:*

***[Bionomics is the OPEC of angiogenesis](#)***

***[genes](#)*** if the fruits of its three year gene search is any guide. The Adelaide company and its scientists have now discovered and patented around 600 genes that play a role in angiogenesis, 160 of which had no other known function before Bionomics arrived on the scene. With angiogenesis research so hot at the moment we would suggest that there will be some good partnering opportunities for these genes in the future, and the fact that there are so many genes in Bionomics' portfolio suggests the strong likelihood that at least one will become the good target for an angiogenesis drug candidate in the future. In fact, one such target has already been written up in PNAS. Bionomics may primarily be regarded as an epilepsy play, but it also seems to be on to something special in angiogenesis. Bionomics remains a Speculative Buy for Knowledgeable Professional Investors.

***[Imugene's trial success](#)*** Trial results announced this week for Imugene's FAV-gamma and PAV-PRRS products have given a strong suggestion that Imugene's team is on top of any issues it may have experienced in recent days with regard to the development of its recombinant adenoviral vector technology. Imugene remains a Speculative Buy for Knowledgeable Professional Investors.

Stocks that Southern Cross Equities likes which are covered in some detail in this edition of Buzz:

**[Bionomics \(BNO\)](#)**  
**[Imugene \(IMU\)](#)**



***Week Two of the Official 2004/2005 Biotech Bull Market*** was a period of mild profit-taking. Which was understandable given the previous week's 2.8% leap in the Southern Cross Equities Australian Biotechnology Index. There were 47 biotech stocks that were lower this afternoon when compared to last Monday, with only 29 higher and 12 unchanged. That said, our Index ease back only slightly, finishing this afternoon at 1,674.72, which was 0.15% lower than a week previous. The All Ordinaries Index, by contrast, forged ahead to the tune of 1.5%. It is now sitting at 3,890.9. Average biotech volume over the last five sessions was \$16.6m, down 6%. [Phosphagenics](#) (POH), the Vitamin E people, gained 16% to 32 cents, on no news from the company. [Imugene](#) (IMU) jumped 24% to reach 30.5 cents on a couple of pieces of good news (see [below](#)). And the anti-viral drug discovery company [Biotron](#) (BIT), at 27.5 cents, was 20% better off, thanks to the announcement of a credibility-raising publication in the journal Virology. For a reasonably comprehensive round-up of what has happened each day in the listed Australian biotechnology sector, visit [www.biotechbuzz.com.au/Diary.htm](http://www.biotechbuzz.com.au/Diary.htm). For a summary of what directors have been buying or selling their company's stock and in what quantities, visit [www.biotechbuzz.com.au/DirectorsTransactions.htm](http://www.biotechbuzz.com.au/DirectorsTransactions.htm).

*The healthier a society becomes the more medicine it craves* - [Roy Porter](#) (1946-2002), English historian of medicine.



**Company Name:** Imugene

**ASX Code:** IMU

**Southern Cross Equities' attitude:** We like it

**Disclosure:** Southern Cross Equities has acted as advisor to Imugene, for which Southern Cross Equities has received 4.0 million performance options exercisable at 22.5 cents per share. These options are vested and are exercisable up to 31 October 2007.

**Location:** Sydney

**Business:** Developing vaccines and disease treatments for pigs and

## ***Imugene's viral vector *tour de force*.***

It looks like [Imugene](#) (IMU) has finally shaken off the bad form of recent days. A somewhat indeterminate pilot trial of its Receptor Mimic Technology (7 October) and then a setback in efforts to develop an avian influenza vaccine (18 October) had depressed the stock from 32 cents on 6 October down to 22.5 cents on 27 October. However this week's two market releases, heralding unequivocally good news related to the company's adenoviral vector technology, has helped Imugene stock to almost pick up where it left off.

First came the announcement, last Wednesday, that Imugene had completed another trial of PAV-PRRS, its vaccine for the virus that causes the dreaded Porcine Respiratory and Reproductive Syndrome in pigs. Back

chickens, as well as a flea vaccine for companion animals

**Leadership:** Graham Dowland (Chairman), Warwick Lamb (CEO)

**Share Price (c):** 30.5

**Market Cap. of tradeable shares:** \$33m

**Twelve Month Range (c):** 37 - 21

**No. of shares tradeable:** 108.3m

**Volume this week (Average weekly volume):** 6.75m (2.49m)

**Value this week (Average weekly value):** \$1.94m (\$0.72m)

**% below 12 month high:** 17.6% %

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in April Imugene had announced that it had used its recombinant adenoviral vector technology to develop the world's first effective vaccine for PRRS. The PRRS virus is believed to be responsible for something like US\$600m in annual losses for the US pork industry. Imugene itself is of the view that a PRRS vaccine would sell into a worldwide market of US\$200m p.a., rising to perhaps US\$400m if governments started to sponsor eradication programmes, as they are sometimes wont to do. The fact that Imugene's vector is the only one to date that has been able to stably carry antigens from PRRS and produce a prophylactic response in test animals is probably the best testament yet to the power of the CSIRO-developed technology. The trick to developing an effective PRRS vaccine lay in the choice of which PRRS antigens to use in the

Imugene vector. Back in April, Imugene knew it had a workable vaccine based on its choice of antigen or antigens, but it wasn't sure if it had picked the optimal antigenic makeup. It had therefore continued to experiment. The result was last Wednesday's announcement, which was prompted by the completion of a trial of a different PRRS vaccine candidate. Imugene was able to tell the market that the new PAV-PRRS had worked well in terms of protecting pigs against viral challenge. The company is now in the happy position of being able to proceed towards the large scale pig trials that would be necessary for registration of the vaccine. We would suggest that Imugene is on track for a good commercial outcome with regard to PAV-PRRS. The product is not subject to the September 2002 option agreements with Merial, and as a consequence it may attract a favourable deal in terms of milestone payments and royalties from any one of a number of animal health majors. And, as we understand it, Imugene's new vaccine has been attracting multiple licensing interest.

In short, the PAV-PRRS announcement was good. Even better was today's missive from Imugene reporting that the company had successfully completed a second trial of FAV-gamma, which is Imugene's recombinant adenoviral vector for chickens engineered to carry chicken interferon gamma as a growth promotant. This trial result went some way towards realising CSIRO Animal Health's vision from the 1980s of creating 'Superchick', that is, a chicken with a supercharged immune system that could therefore enjoy very strong weight gains vis-a-vis untreated chickens. Back in August Imugene had announced that a 500-bird trial of FAV-gamma had demonstrated a 7% weight gain for the treated birds over the untreated controls, whether or not the chickens that got FAV-gamma were also getting medicated feed. In itself that was great news because 7% extra meat on chickens notionally means a significant bottom-line boost for chicken farmers without the use of antibiotics or hormones. Imugene was, however, somewhat dissatisfied with this first FAV-gamma trial, in large measure because the treated groups didn't experience feed conversion ratios any higher than the other groups. It was thought that the feed that had been used in the trial had been inadequate, in that it was too powdery and therefore not suitable for use in this trial given the shape of the avian beak. In other words, there may not have been enough food inside the stomachs of the treated chickens to be converted into meat in the first place. Secondly, Imugene's people felt that the super-clean buildings in which the chickens were housed at CSIRO's Werribee facility southwest of Melbourne had biased the trial in favour of the untreated chickens. Had there been more chicken-unfriendly bugs lurking in the sheds, then perhaps the growth advantage in favour of the treated chickens would have been much higher. Thirdly, Imugene also wondered if it had been hitting the treated chickens with too strong an initial dose. The avian adenoviral vector is, after all, a chicken virus. Possibly in the first trial the treated chickens had been made a little too feverish by that first exposure to FAV-gamma, and that situation had kept

them from going on to enjoy big growth gains later in their 42 day lives.

Which brings us back to the just-announced second trial results. This time around the investigators were careful in their selection of feed, and also made sure that fresh chicken litter was scattered around the test sheds in order to more closely replicate the pathogen-enhanced environment of a commercial chicken-raising operation. And they also studied 400 more birds than previously so as to be able to compare different dose sizes and dose frequencies, with a view to combating the 'initial dose' problem through a search for the optimal dosing structure. The outcome of all this was the first ever glimpse of Superchook in the flesh. Last time around the weight gain for treated chickens, whether compared to controls on medicated or unmedicated feed, had been in a very narrow range of 7.12% to 7.27%. By comparison, in the just-completed trial, chickens getting both in-feed antibiotics and FAV-gamma were 9.5%-13.75% better off than the controls, while FAV-gamma alone outperformed antibiotics alone to the tune of 7.2%-13.2%. In other words, FAV-gamma was now working more or less as expected, with, among other things, better feed conversion ratios. All of which means that, when the Federal Government's [Office of the Gene Technology Regulator](#) finally gets around to approving a large scale trial of FAV-gamma, Imugene can proceed to work towards registration of the product and getting it into commercial production. To that end, Imugene is currently working on the last of a series of additional laboratory tests of its vectors, the design of which have been worked out by both OGTR and Imugene, in order to satisfy the regulator that its adenoviral vectors are safe for 'intentional release'. If that work leads to approval for intentional release by mid-2005, we believe that Imugene could be making its way towards filing of regulatory dossiers for approval of FAV-gamma before next year is out, meaning that the product would be on track to be in commercial use by 2006.

The good news from Imugene may have helped the stock recover from the late October nadir, but on Southern Cross Equities' numbers there is still some way to go before the market begins to more appropriately value the power of Imugene's technology, not to mention the quality of its development team. As we noted on 18 October, our target price for the stock is \$1.09 a share. On that basis Imugene remains a good Speculative Buy for Knowledgeable Professional Investors. [Back to top](#)

(Click [here](#) to view a 3-month chart of Imugene. If you encounter a term in this email with which you are unfamiliar, please visit our Southern Cross Equities Australian Biotechnology Glossary at <http://www.biotechbuzz.com.au/Glossary.htm>. We are adding new entries to this easy-to-use lexicon all the time.)



**Company Name:** Bionomics

**ASX Code:** BNO

**Southern Cross Equities' attitude:** We like it

**Location:** Adelaide

**Business:** A company focused on diagnostics and drug discovery in the epilepsy.

**Leadership:** Peter Jonson (Chairman), Dr Deborah Rathjen (CEO)

**Share Price (c):** 29

## Bionomics and its angiogenesis gamble

If success has a lot to do with being in the right place at the right time, then the aspect of [Bionomics](#) (BNO) which we'll look at in this week's email is a good potential indicator of future riches for the shareholders of this under-appreciated Adelaide company. In our previous two emails we've written about Bionomics from the perspective of the company as a contender in the vast US\$5bn-plus market for diagnosing and treating epilepsy. We've taken the view that this part of Bionomics alone is likely, down the track, to be a company-maker if management play their cards right. Today we consider Bionomics as a potential player in the field of angiogenesis, that is, the process underlying 'neovascularisation', or new blood vessel formation. It's an area that is a little more crowded than epilepsy research, but where Bionomics brings to the table considerable advantages, primarily based on its

**Market Cap. of tradeable shares:**

\$18m

**Twelve Month Range (c):** 40.8 - 19**No. of shares tradeable:** 63.7m**Volume this week (Average weekly volume):** 2.15m (0.43m)**Value this week (Average weekly value):** \$0.67m (\$0.13m)**% below 12 month high:** 28.9%[Back to top](#)

understanding of the genes involved.

Angiogenesis is these days considered a 'hot' area of biomedical research because it promises to deal successfully with several problem areas of disease treatment at once. The Harvard researcher Judah Folkman was the first to propose, in 1971, that starving a tumour of the network of blood vessels it recruits to feed itself would make for a new, more effective cancer treatment than traditional 'slash, burn and poison' therapies. Iterations of this bright idea have subsequently absorbed a lot of angiogenesis-related

research interest. However it has also been suggested that an understanding of the causes of neovascularisation in the eye may lie at the core of a future treatment for diabetic retinopathy. And, for scientists focused on cardiovascular disease, there has been much research into the prompting of new blood vessel growth with which to bypass those blood vessels choked up by atherosclerosis. You know an area of biomedical research is really hot when the popular science journalists start to publish books on the subject. For angiogenesis that happened around three years ago when Robert Cooke, the science writer for *Newsday*, published the very readable [Dr Folkman's War - Angiogenesis and the Struggle to Defeat Cancer](#), (New York, Random House, 2001), which as the title suggested was both an overview of the field and a biography of its scientific father. But angiogenesis had been building up a head of steam long before this recognition by the lay public. Back in 1991 researchers had published, in peer-reviewed journals, some 257 papers that had the word 'angiogenesis' in their title or abstract. In 2000, the comparable figure was 1,727, suggesting that, year in and year out for a whole decade, scientific interest in angiogenesis had notionally grown 24% compound in 'mindshare' terms. What had prompted all this new interest was a succession of scientific breakthroughs, beginning in the 1980s, that had explicated certain mechanisms whereby neovascularisation occurs, thereby giving angiogenesis-based disease treatments some hard-earned credibility. For a long time before this few people had believed that Folkman's original idea would go anywhere because there was little hard proof as to substances that were either angiogenic or anti-angiogenic. In fact it was not until 1993 (a year when 298 angiogenesis papers were published) that angiogenesis as a cancer treatment approach gained a critical mass of scientific acceptance. That was the year an Italian-born Genentech scientist named Napoleone Ferrara, following up on his discovery four years previous of a strongly angiogenic substance called VEGF, that is, Vascular Endothelial Growth Factor, demonstrated that antibodies to VEGF could hinder tumour growth in animal models. By the time Genentech took one of those antibodies into the clinic in 1996 angiogenesis as a concept was growing 'warm' (there were 699 angiogenesis papers that year). Then in 1998 the field got positively sizzling (1,084 papers) in the wake of work coming out of the Folkman laboratory which indicated that two anti-angiogenesis substances it had identified over the previous three years worked particularly well in inducing tumour regression in mice.

Now, the trouble with 'hot' fields in biomedical science is that even if the mercury remains high at the laboratory level, attitudes towards that field by outsiders, particularly if those outsiders are investors or in-licensing executives at Big Pharma, tend to blow 'hot' and then 'cold'. Every year for the last half decade angiogenesis research output has exploded upwards, from around 1,400 papers in 1999 to what is likely to be around 3,200 this year. In other words, the men and women who live and breathe integrins and CD31s have grown more and more bullish on the concept. But for the outsiders, whereas in 1998 angiogenesis was the in-thing, in 2002 it was very much the out-thing. In May 1998 a little-known Nasdaq-listed company called [Entremed](#), which had licensed Folkman's compounds, could see its stock jump in just a few weeks from US\$12 to US\$32 a share, more or less on the basis of a favourable story in the New York Times (click [here](#) for more

on that). That mania led to something of a global 'angiogenesis bull market'. In this country, over the same period, [Progen](#) (PGL), whose PI-88 anti-cancer compound is, among other things, anti-angiogenic, went from \$4.52 to \$9.30. Now fast forward just three years. In May 2001, when Bionomics got into the angiogenesis gene game, things were cooling a bit, with trials of Folkman's compounds, called angiostatin and endostatin, having proved somewhat disappointing. Consequently you could, at that time, buy Progen for around \$1.30, some 86% below the 1998 peak. In September 2002 came a positive freeze in terms of investor attitudes towards angiogenesis, when Genentech's anti-VEGF antibody, called Avastin, failed in a Phase III trial in breast cancer patients. By that stage Progen was plumbing the depths at around a dollar a share and people, particularly if they worked in Big Pharma, had started to say that angiogenesis as a cancer treatment approach was finished, even if somewhere between 2,000 and 3,000 academic papers were suggesting otherwise. Now, if you're a regular Buzz reader you'll probably know the interest denouement to this story, the moral of which is that it pays not to write off too quickly a field with 30 years of science behind it. Just eight months after the breast cancer debacle, in February 2003, Genentech was jubilantly reporting that a Phase III trial of Avastin in late stage colorectal cancer patients had seen those patients receiving Avastin live for about 20 months post-treatment, which was five months longer than those getting standard treatment. Avastin was back - it gained FDA approval in February of this year. Progen was back - it's now \$5.05 a share. And, most importantly, angiogenesis was back in terms of its credibility with investors. The area has remained in favour with both scientists and businessmen ever since, as evidenced, for example, by the fact that we've used the term in fifteen previous editions of Australian Biotechnology Buzz since August 2003. What all this means for Bionomics is that, having persisted in its angiogenesis programme during the lean times for the concept, the company is now set to reap the benefits of renewed interest in the area.

Which brings us to what exactly Bionomics is up to with regard to angiogenesis. The company has spent the last three years and around \$1m in cash conducting a search for angiogenesis-related genes. The work had started around 2000 in the Vascular Biology Laboratory headed by Dr Jenny Gamble at Adelaide's [Institute of Medical and Veterinary Science](#). Gamble had previously developed, around 1993, an *in vitro* model of angiogenesis that involved adding endothelial cells (that is, the cells to be found lining the surface of various organs including blood vessels) into petrie dishes carrying the protein collagen, which is the main protein of connective tissue. Ordinarily in collagen endothelial cells wouldn't easily form themselves into capillary tubes, but Gamble had found that a chemical called PMA (phorbol myristate acetate), a known inducer of tumours, would provoke just this behaviour, and that the whole vascular formation process was enhanced by the addition of antibodies to certain 'integrins', which are proteins that cells use to attach themselves to other nearby cells or substances in their environment. Thus restricted in what they could attach themselves too, the PMA-stimulated cells proceeded to form what proved to be viable capillary tubes. They weren't *blood* vessels per se, but they were a close analogue of blood vessels. In 2000 the Gamble laboratory started sampling cells at various points in the *in vitro* angiogenesis process, with a view to studying the messenger RNA in those cells and thereby picking out genes that seemed to be activated when vessels were being formed. The programme has, by all accounts, been very successful. When Bionomics started funding the work in May 2001, the Gamble team had come up with the 56 genes involved in angiogenesis, of which 14 were regarded as 'novel', that is, appearing in the human genome but with no known function before Gamble et. al. suggested angiogenesis (the others were genes with known functions but where angiogenesis had not previously been considered one of them). Three years later, by which time the various technologies involved had been given the platform name 'Angene', the Gamble team had managed to garner into Bionomics' patent-pending angiogenesis portfolio something like 600 genes (not gene variants, mind you, but individual genes), of which 160 were in the 'novel' category. The team had also progressed from looking at

angiogenesis *in vitro* to the use of an *in vivo* model of angiogenesis to study the role of its genes. The model, called NeoVascMouse, sees a neovascularisation network being induced in the mice in question through the use of sponges into which has been soaked known angiogenic factors.

All of which sounds formidable. But as far as the market was concerned there was, until Tuesday 10 August 2004, little to indicate to the market that any of those genes was of value in a commercial sense. The event that should have changed the market's perception of Bionomics' angiogenesis work was the publication of a paper by the Gamble team in the prestigious American journal [Proceedings of the National Academy of Sciences](#). We looked at why PNAS is such an important place to get published in our 25 October email, when we considered the paper communicated to the journal by Sir Gus Nossal related to [EQiTX](#)'s peptide vaccine work. The Gamble et. al. paper was communicated to PNAS back in June by the Hall Institute's [Jacques Miller](#) (of T cell fame) under the headline *A vascular cell-restricted RhoGAP, p73RhoGAP, is a key regulator of angiogenesis* (click [here](#) for the abstract to Proc Natl Acad Sci U S A. 2004 Aug 17;101(33):12212-7). The paper is a report on an angiogenesis gene that Bionomics has codenamed BNO69. Let's face it, BNO69 is a lot more euphonious than the name initially given to the protein it codes for, which was 'p73RhoGAP'. What the Gamble team were trying to convey with that moniker was the fact that the gene codes for a 73 kilodalton GAP, that is, 'GTPase activating protein', which regulates the Rho family of small GTPases. Which simply means that it is one of many molecules that cell biologists understand to play a role in regulating the growth and differentiation of cells. What was important from Bionomics' point of view was, firstly, that the gene had been discovered several years previous by a German group but had no known function before the Gamble team did its work. More importantly, when Gamble et. al. tried to find the protein in other cells to see how common it was across the human proteome, they could only find it in endothelial cells (those with the cell surface motif known to biologists as 'CD31'). This meant that a hypothetical anti-angiogenesis drug targeting BNO69 would be more likely to hit the kind of cells it was designed to disrupt - cells in new blood vessels - and less likely to damage tissue that was innocent. When the team either mutated BNO69, or alternately shut down the gene using antisense and gene silencing techniques, the result was that the ability of endothelial cells to make any kind of tube structure was noticeably hampered. Which is to say, without BNO69 endothelial cells wouldn't proliferate as they ordinarily would, nor would they migrate towards fibronectin, a protein best known for its capacity to draw cells towards itself (which is why it is a player whenever the body is seeking to heal a wound). Moreover when one looked under a microscope, the expected pattern of capillaries just wasn't there. And the fact that this phenomenon was observed in NeoVascMice as well as in the test tube also suggested that BNO69 was an anti-angiogenic target of great promise.

Apart from the data disclosed in the Gamble et. al. paper, what has Bionomics excited about BNO69 is that it seems to sit upstream from the other usual angiogenesis suspects, including the VEGFs and another important factor called Fibroblast Growth Factor. Hit the BNO69 gene, Bionomics would suggest, and one may just block or at least hinder the production of a whole host of growth factors that are angiogenic in effect. Which makes BNO69 a great target for a company working on angiogenesis-based cancer therapies, a fact also suggested by a July 2004 announcement from Bionomics that researchers at Louisiana State University's Health Sciences Center, which has a gene therapy program in the northern Louisiana city of Shreveport (click [here](#)), will be looking at the gene therapy potential of BNO69. However what this analyst considers to be more significant than BNO69 alone is Bionomics's explanation, in the 2004 Annual Report, that BNO69 had pointed the way towards the discovery of 11 other angiogenesis genes that are also endothelial-specific. Having a whole suite of similar genes will be important to Bionomics because the more clues which the would-be designer of an anti-angiogenesis drug gets as to the kind of protein variants involved, the higher the possibility that that resulting drug will choke off enough angiogenesis pathways for effective tumour regression.

For now, probably the main take-home lesson of the BNO69 discovery is that genomics is a numbers game that Bionomics is setting itself up to win. Here, the more genes one discovers using a particular model-based technique, the more probable it will be that at least one gene will be found to be 'druggable' and therefore of potentially high therapeutic value. The fact that Bionomics now has such a vast angiogenesis treasure chest suggests the high likelihood that other companies will be willing to pony up to gain access to the gene pool. In fact, one company already has. In 2002 the Danish antibody engineering firm [Genmab](#) partnered 50/50 with Bionomics on three of the early genes, with Genmab interested in looking for anti-angiogenesis antibodies. Bionomics and Genmab have now progressed to the point where they have prioritised one target out of the three for use on the generation of lead antibody candidates. Beyond Genmab, there are likely to be other, and more lucrative deals out there for Bionomics to do in angiogenesis. Remember, Big Pharma can be just as sheep-like as the rest of us, so if one company has an anti-angiogenesis cancer drug in its portfolio then eventually they will all likely want one. And as things stand, Avastin's return from the dead has prompted at least one big angiogenesis deal - in September 2003 the Strasbourg-based behemoth [Aventis](#) linked up with that phoenix of American biotech, [Regeneron](#), so as to access the latter company's anti-angiogenesis compound, called VEGF Trap, in a deal with US\$125m upfront (that's right - *upfront*, although US\$45m of that was a placement of Regeneron stock). With more angiogenesis deals still likely to be out there, any company possessing numerous good anti-angiogenesis targets can be considered to be in possession of hot property. Dr Gabriel Kremmiotis, who is Bionomics' Director, Cancer Research, has, as we understand it, fielded many partnering inquiries in recent days, and not just from academic groups like the gene therapy gurus in Shreveport but from commercial biotech people as well. This bodes well for some exciting future news flow. When one considers that Bionomics total investment has only been \$1m, the return on that investment to Bionomics' shareholders given this interest could be considerable.

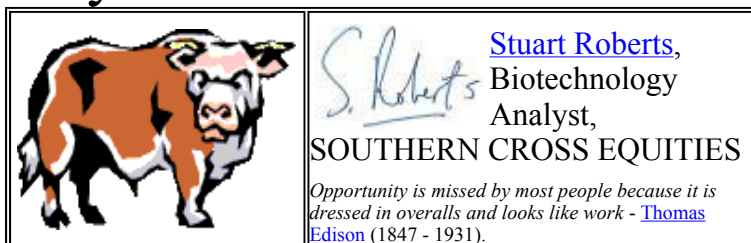
It's fair to say, however, that the potential of Bionomics's 600 angiogenesis genes have yet to be factored into the company's stock price. After all, Bionomics' number one and two priorities at the moment are the forwarding of its epilepsy drug discovery programme and the building of its epilepsy diagnostic business. But as we've lamented for the last couple of weeks, even those programmes have yet to get the investor respect they deserve, given that Bionomics' post-cash market cap is only \$10m. At this ridiculously low price Bionomics remains a good Speculative Buy for Knowledgeable Professional Investors.

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(Click [here](#) to view a 3-month chart of Bionomics. If you encounter a term in this email with which you are unfamiliar, please visit our Southern Cross Equities Australian Biotechnology Glossary at <http://www.biotechbuzz.com.au/Glossary.htm>. We are adding new entries to this easy-to-use lexicon all the time.)

## That's it for another edition of Australian Biotechnology Buzz. Till next time...

### Stay bullish.



**Disclosure of Stuart Roberts' interest:** As at 15 November 2004 Stuart Roberts held shares in [COMPUMEDICS](#), [EQITX](#), [IMUGENE](#), and [PRANA BIOTECHNOLOGY](#), all of which were the

subject of Southern Cross Equities research notes between 2002 and 2004. He also owns shares in [AMRAD](#) and [BENITEC](#) and options over shares in [SOLBEC PHARMACEUTICALS](#). [Back to top](#)



*Stu 'Buzz' Roberts keeping the biotech faith at a Southern Cross Equities morning meeting. His colleagues look suitably unimpressed.*

**About Stuart Roberts:** Stuart has been an analyst at Southern Cross Equities in Sydney since April 2001, focused on biotechnology from February 2002. Before joining the firm he wrote for [The Intelligent Investor](#), probably the most readable investment publication in Australia. Stuart has a Masters Degree in Finance from the [Securities Institute of Australia](#). Stuart is married to Luana and they are expecting their first child in November 2004. His hobbies are jazz, cinema, and reading patent applications filed by biotechnology companies. [Back to top](#)

**About Southern Cross Equities:** Brent Potts and Peter Gray, two men best known for their involvement in the 1980s firm Potts West Trumbull, founded Southern Cross Equities in 1995. Trevor Cain, a Southern Cross

employee from shortly after the firm's inception, joined Potts and Gray as an owner in 2000. Cain is now Director of Corporate, and also takes care of the firm's Compliance program. Also in 2000 Southern Cross added to its dealing desk David O'Halloran and Richard Granger, veterans of County NatWest, where David had been Chief Operating Officer. In mid-2002 Rex Adams, the respected resources analyst, who had been with Southern Cross since 1998, was named Director of Research - he had once held this position at Hambros. And finally in mid-2003 the Southern Cross leadership was bolstered by the addition of Aitken brothers, Charlie and Angus, who were formerly at Salomon Smith Barney, where Charlie had been head of trading. Potts, Granger, Gray and O'Halloran are Southern Cross's four Senior Directors. David O'Halloran, an equities dealer since 1981, has led Southern Cross's biotechnology team since the firm began to build a capability in this space in early 2002. Brent Potts, Southern Cross's Chairman and a renowned name in Australian stockbroking, was inducted into the [Stockbroker's Foundation](#) Hall of Fame in 2003. [Back to top](#)

**About biotechnology at Southern Cross Equities:** The patron saint of biotechnology research at Southern

Cross Equities is [Robert Swanson \(1947-99\)](#), the American venture capitalist whose understanding of the way to get commercial and scientific interests to work in lockstep enabled the founding and building of [Genentech](#). It is aim of the team at Southern Cross Equities to emulate Swanson in getting behind Australian biotechnology companies that are both solidly commercial and solidly scientific. It is our conviction that such companies will be among the nation's leading companies in the 21<sup>st</sup> Century as the biotechnology industry matures the early work that has gone on since the mid-1980s. With over 80 biotechnology companies listed on the Australian Stock Exchange, or 5% of the total, we see the sector as becoming increasingly worthy of investor attention. Through *Southern Cross Equities' Australian Biotechnology Buzz*, the Biotech Team at Southern Cross Equities have sought since 2003 to pinpoint investment opportunities in Australian biotechnology in the most understandable and interesting way possible. For more on the Biotech effort of Southern Cross Equities visit [www.biotechbuzz.com.au](http://www.biotechbuzz.com.au). [Back to top](#)



*Our patron saint (source [The Tech](#)).*

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