

LANI patent granted in Europe

A European patent was granted 11 May 2005, titled: "DIMERIC COMPOUNDS AND THEIR USE AS INHIBITORS OF NEURAMINIDASE". This patent relates to the FLUNET

compounds developed by Biota, which are currently at the preclinical stage of development as potential LANI drugs.

Organisation changes

In May, we announced the resignation of Andrew Macdonald as CFO following his decision to move on to a new company at the end of July. We thank Andrew for his achievements over the last three years and wish him well in the future. We are engaged in a search for a new CFO and in the meantime have appointed an experienced interim CFO, Philip Thomas, to oversee the company secretarial and financial functions until a permanent appointment is made.

With three programs heading towards clinical trials, we have formed a new team and core competency within Biota to oversee clinical development activities. The new team is called the 'Product Development Group' and is led by Dr Jane Ryan, who is currently actively recruiting world class development professionals to augment our existing staff and ensure we have the resources to manage Biota's growing stable of development stage projects. The Product Development Group will be responsible for ensuring that projects, which successfully complete the research phase, progress rapidly and effectively through preclinical testing, manufacturing development and clinical

trials up to the point that they are licensed to a development and commercialization partner. They will work closely with the Research Group and Business Development to ensure that all our projects are conducted to world standards and to meet important medical needs and attractive market opportunities.



Above: Dr Jane Ryan, project leader of the *Product Development Group*, a new team to oversee clinical development activities.

E-communication for shareholders

E-communication enables you to receive Company information promptly and securely in an environmentally friendly format. We encourage all shareholders to register as electronic shareholders by completing the enclosed communication election form or by visiting:

www.asxperpetual.com.au/biota.

Electronic shareholders will receive email alerts on important Company

announcements and notification when future issues of the Biota Bulletin and Annual Reports are available on the website. You will also receive notices of shareholder meetings and advice on how to lodge your proxy electronically.

Each issue of the Biota Bulletin is available for all shareholders to download from Biota's website www.biota.com.au.

Calendar

Biota will be represented and/or presenting at the following upcoming key international meetings:

3-7 July 2005

12th RACI Convention

Sydney, Australia

www.pco.com.au/connect2005

26-27 July 2005

Australian Biotechnology Summit

Sydney, Australia

www.acevents.com.au/bio2005

9-10 August 2005

Best Practice Clinical Trials

Sydney, Australia

www.marcusevansau.com

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Highlights

- **RSV:** program progresses to preclinical stage; another research success from Biota
- **CS8958 (LANI):** formulation deal signed with Aerogen; development progresses under NIH grant
- **HRV (common cold):** preclinical testing continues satisfactorily; Phase I study scheduled for 2006
- **Relenza litigation:** Discovery phase progressing; Biota to file estimate of value of the damages claim by July 22; mediation scheduled for November

Message from the CEO

Biota is internationally regarded by its peers as a leading antiviral research company, focused on new therapies for important viral diseases. While Biota has been successful with a number of research breakthroughs, it is important that the drugs from our research programs progress into human clinical trials and attract valuable commercial partnerships. These clinical milestones and partnerships are the keys to long term share price growth and overall business success in the biotech sector.

Over the last two years, we have seen Biota evolve from a research stage company to one built on a solid clinical stage pipeline. To get there, we needed to make some important decisions, like closing down the US operations to free up cash for clinical development, building a new facility in Melbourne to

cost-effectively house all our R&D, and raising new funds to support our clinical development plans. We achieved all these goals during 2004. On top of that, we succeeded in winning a \$7m NIH grant to bolster funding for our LANI clinical program.

Going forward, the future looks bright for Biota. We now have three respiratory antiviral programs moving towards human trials: LANI (influenza), HRV (common cold) and RSV (bronchiolitis). Not all of these programs may be successful, but with such a buoyant pipeline of clinical programs, Biota is in an excellent position to deliver a string of clinical milestones and valuable licensing opportunities over the next several years.

Peter Molloy, CEO

RSV drug candidate

On 8 June, we announced that Biota scientists had succeeded in discovering a series of novel drug candidates for RSV (respiratory syncytial virus) infection. Although not a disease that is well known in the general community, RSV is the cause of about one-fifth of all lower respiratory tract infections (bronchitis and bronchiolitis) worldwide. In infants, the elderly, and those with underlying respiratory disease, heart disease or damaged immune systems (e.g. cancer patients), RSV

infection can be a serious problem, leading to hospitalisation or even death. There is no vaccine and currently, no treatment.

Biota scientists have developed a series of orally-available drug candidates for treatment and prevention of RSV. The candidate drugs in the series are potent RSV inhibitors and most recently have been shown to be effective against RSV infection in animals.

There are relatively few RSV drugs in development. The one drug currently

available, Synagis™, is an injectable antibody approved in the US for prevention of RSV infection in premature infants. Sales of this drug approached US\$1 billion in 2004. However, the need for RSV antiviral drugs is much greater than just prevention of infection in premature infants, and we believe that an orally available drug could facilitate expansion of the market opportunity to other segments, such as the elderly and other 'at risk' patient groups. It could also expand the market to treatment as well as prevention.

The lead drug candidate from the series will now move into preclinical testing, and if it successfully completes the preclinical phase, it will be available to start human clinical trials. The preclinical phase can last a year or more and includes extensive toxicology evaluations and other testing to ensure the safety of any drug before it is made available for human testing. Drug candidates can and do fail during preclinical testing, for example, if they display any safety concerns. If this were to occur, Biota may bring forward a second candidate from the lead series.

Like our HRV (common cold) drug candidate, which is already in advanced preclinical development, the RSV program is the product of original research by Biota scientists, with the most recent phase supported by an R&D Start grant.



Common Cold (HRV) progress

Biota's common cold (HRV) drug candidate, BTA798, has been in preclinical development for around six months and is progressing towards a human Phase I trial. So far, BTA798 is meeting all our expectations and no untoward safety or other concerns have arisen. If the preclinical testing concludes successfully over the next several months, we should file a submission for commencement of human trials and then subject to regulatory clearance should be able to start the Phase I study in the first half of 2006.

Our intention is to commence partnering of the HRV program after successful completion of initial human clinical studies.



LANI progress

LANI (long acting neuraminidase inhibitors) is the name for our pipeline of second generation influenza antivirals, which we are developing in conjunction with Sankyo. The pipeline includes a series of compounds, with the most advanced one, CS-8958, having completed one Phase I human safety study. Several further Phase I studies are planned.

The influenza antivirals market has grown dramatically since the launch of Relenza and Tamiflu five years ago and, based on the latest market data, prescription sales of Tamiflu in 2004/05 grew by more than 40% to approximately US\$400m. In addition, a large government 'stockpiling' market has emerged in response to the threat of an avian (bird) flu pandemic. Based on the available information, we estimate that this market segment represents up to a further US\$500m in future annual sales value.

In line with the two market opportunities, LANI is being developed in two product forms:

- (1) Bulk powder formulation, for use in nebulisers and designed for stockpiling in the event of a flu pandemic ('LANI Nebule'); this project is funded through to the completion of three Phase I studies by a \$7m NIH grant awarded last September.
- (2) Convenient, single dose inhaler product, intended for prescription to patients who come down with influenza ('LANI SDI'). Both products are designed to meet important market opportunities in a market that is expected to reach US\$1 billion in sales.

LANI Nebule/NIH project: An important first step is to develop a formulation of the drug suitable for use in nebulisers, and in March we announced an agreement with Aerogen to conduct this formulation project, which is now underway. If that work is completed on schedule over the next several months, we could file a submission to start a Phase I single dose human study of

the LANI Nebule by early 2006. Then, subject to NIH and regulatory clearance, we could be ready to start the study by mid 2006. In line with the NIH grant timetable, this would be followed by a further two Phase I studies over the following two years.

LANI SDI: In parallel with the NIH-funded project, we are starting formulation studies with two companies that specialise in single dose inhalers. This work should be completed over the next six months.

The longer term goal for the LANI project is to find a pharmaceutical partner that will shoulder the costs of the more advanced clinical studies and ultimately launch the LANI products worldwide. With the growth in the market and the anticipated completion of the formulation development work on both the LANI Nebule and LANI SDI, we believe our prospects for attracting such a partnership will be significantly improved and will be working with Sankyo towards that goal.

GSK litigation

The litigation project has been an important one for the company, yet it has not distracted us from our primary goal of advancing our antivirals portfolio.

GSK was required to deliver their defence to Biota's 'Statement of Claim' by 8 April. They failed to meet this deadline and at a hearing on 29 April, the court admonished GSK and gave them an extension until 11 May. We subsequently received their defence on that date, but it appears to offer no new information that would dampen the merits of Biota's claims, and if anything, it strengthens our resolve and confidence in relation to the suit. Among the noteworthy points in the GSK defence statement were the following admissions:

- 1. GSK acknowledges that Relenza and Tamiflu are equivalent in terms of clinical effectiveness;**

- 2. GSK admits taking the decision to withdraw marketing and promotional support for Relenza as early as September 2001; and**
- 3. GSK admits to not developing Relenza in an improved inhaler, even though other GSK products were converted to an improved inhaler.**



The delay in filing of a defence has not slowed the discovery process, which has been underway since receipt of the first tranche of documents from GSK in April; a second tranche was received in May and a third tranche in June, although likely additional discovery will take place beyond that date. In the normal course of events, after the review of the major body of GSK's discovered documents, Biota will consider whether its statement of claim should be further amended and will prepare for the mediation with GSK, which is to be held by 25 November 2005.

At a hearing on 29 April the judge also required Biota to file details of its loss and damage by 22 July. This means that we will provide the court with our formal assessment of the value of the damages that we are claiming in the suit. We are currently working towards finalising that assessment and intend to file it by the due date.