# biota

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#### 2009 AGM Addresses

Attached are the following documents in relation to the 2009 AGM:

- 1/ Chairman's Address; and
- 2/ CEO Address.

#### **About Biota**

Biota is a leading anti-infective drug development company based in Melbourne Australia, with key expertise in respiratory diseases, particularly influenza. Biota developed the first-in-class neuraminidase inhibitor, zanamivir, subsequently marketed by GlaxoSmithKline as Relenza. Biota research breakthroughs have included novel nucleoside analogues designed to treat hepatitis C virus (HCV) infections, licensed to Boehringer Ingelheim, and a series of candidate drugs aimed at treatment of respiratory syncytial virus (RSV) disease. Biota has clinical trials underway with its lead compound for human rhinovirus (HRV) infection in patients with compromised respiration or immune systems.

In addition, Biota has a key partnership with Daiichi Sankyo for the development of second generation influenza anti-virals.

Relenza<sup>m</sup> is a registered trademark of the GlaxoSmithKline group of companies. \**Further information available at <u>www.biota.com.au</u>* 

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### INTRODUCTION

Good morning, I am Jim Fox, the Chairman of Biota Holdings Limited. Ladies and Gentlemen, the time is now 10.00 am and as there is a quorum of members present I now formally declare the Annual General Meeting of Shareholders open and welcome you to the meeting.

As you have all received a copy of the Notice of Meeting, I propose to take it as read.

May I now introduce the Company's Director and senior executives. From my right/and your left are Directors Professor Ian Gust, Mr Richard Hill, Mr Grant Latta, CFO & Company Secretary Mr Damian Lismore, Managing Director & CEO Mr Peter Cook and Mr Paul Bell.

The other members of the management team, Dr Jane Ryan - Vice President of Product Development, Dr Leigh Farrell - Vice President of Business Development and Dr John Lambert - Principal Director, Product Development Operations are also in attendance. Dr Simon Tucker, Vice President Research is in Oxford settling in our new acquisition.

Also present today are:

- Our Company's Auditors PricewaterhouseCoopers, represented by Ms Nadia Carlin;
- The Company's lawyers (Allens Arthur Robinson), represented by Mr Craig Henderson; and
- The Company's share registry (Link Market Services) represented by Mr Chris Hernandez.

I propose say a few words from my perspective and then have Peter Cook, our Chief Executive Officer, brief you on Biota's operations and plans. I will take comments or questions from shareholders after the end of these presentations as part of the first Agenda Item. We will then move to the order of business as set out in the Notice of Meeting.

Following completion of the meeting we hope that you can join the Board and Management for some light refreshments in the foyer.

### **CHAIRMAN'S ADDRESS**

I would like to say at the outset that I feel privileged to be chairing my first Biota AGM. I joined Biota 10 months ago and with that time under my belt, I am now even more clearly of the view that this an exciting company with a capable and experienced leadership team. We now have strong cashflows due in no small part (but not completely) to our Relenza "flu" product, a stable, reshaped and high capacity board and a pipeline of very interesting products that Peter Cook will touch on shortly. I was keen on my arrival at the company to have the board and the management team review the strategic direction of the company.

In particular, I wanted to make sure that we had the work in motion to deliver a future product stream that could replace the Relenza royalties when they mostly time out in late 2014, but also to ultimately have more than one product in the market at any given time to reduce the volatility and risk profile that being a single product company can produce. That work is complete and Peter Cook will show you a summary of the plan. In my simplified terms, it is all about making sure we have enough "frogs in the pond to kiss to find our princes". Clearly the recent Relenza cashflows are helping to fund this acceleration of our product development and acquisition program. This work was also important because it allowed us to establish an estimate of future cash needs and then in turn test this against our forecast cash position. The result was the decision by the board to return \$20m to shareholders.

I am pleased to advise you that we have just successfully completed two acquisitions that fit our growth plans that Peter will outline and that have the potential to significantly bolster our future product portfolio. Peter will detail these acquisitions shortly.

The 2009 Financial Year has been a transformational one for the Company. The conclusion of the litigation that was draining the Companies resources nearly 18 months ago has allowed the executive and board return to focusing 100% of our efforts on our core business of commercialising new drug products sourced from both our own scientists and from outside the company.

The outbreak of swine flu in late April, and events since, have also focussed the attention of the tier one pharmaceutical companies on the need for new products for the influenza market.

Clearly, we are now finally seeing extra-ordinary global interest in Relenza. Our production and marketing partner, GlaxoSmithKline (GSK), is investing heavily to increase their production capacity to 190 million courses per annum and this should mean that Biota will benefit through a significant increase in royalties in coming years. In addition, the licensing opportunities for our new long acting Flu product "LANI" in the West are being worked on right now and we hope to have some news for you on this by the end of the financial year.

### \$20m return to shareholders

I mentioned earlier that in August, your Board decided that \$20 million will be returned to shareholders in early December, subject to the passing of the resolution on this matter before today's meeting.

We have been in discussion with the Australian Taxation Office since June. Unfortunately we do not yet have a ruling from the Taxation Office in respect of the taxation treatment of this return. Notwithstanding the lack of an ATO ruling, shareholders will still receive their payment in December. When the Tax Office ruling is available, we will publish it on the Biota website to enable shareholders to complete their 2010 Tax Return.

Shareholders should note that the extent to which the ATO decides this payment constitutes a dividend, the non capital return component will be taxable as an unfranked dividend.

We will continue to monitor our cash position against the needs of the plan that Peter will present and make arrangements to return any excess cash to shareholders.

#### **Remuneration**

The last matter I wish to cover with shareholders is that of Remuneration. In the opinion of the Board, Biota has one of the most capable and experienced management teams in the biotechnology industry in Australia. Naturally, they each have professionally crafted employment contracts with the Company, which are intended to align the interests of management and shareholders. I believe we have achieved such alignment and that our remuneration program is fair, independently tested and has appropriate reward mechanisms that have the approval of third party advisers. Let me explain.

Our remuneration policy is based on paying for performance and is detailed in the Remuneration Report section of our Annual Report. All staff have the opportunity to be paid at three levels:

- Firstly, a base salary is paid, which is set at the median of survey data;
- Secondly, a cash incentive is offered based on achieving pre-set corporate and individual key performance indicators. This incentive is capped at a percentage of the base salary for all staff, in the range of 10-40%, with the CEO's percentage being 60%; and
- Thirdly, an equity incentive is offered. This incentive is also capped at a percentage of the base salary for all staff, in the range of 0-60%, with the CEO being at 80%. The equity incentive for the executive team is based on Total Shareholder Return measures.

At the start of each financial year, share price targets are set for the next 3 year period. Shares allocated will only vest at the end of this 3 year period <u>if</u> share price targets are met. If share price targets are not met, shares allocated lapse after 5 years. The TSR target to achieve a maximum issue to executive team member effectively means that the share price needs to increase by over 50% over each rolling 3 year period.

The company has a rigorous process of setting and reviewing remuneration of all staff. The Remuneration & Nominations Committee chaired by Paul Bell controls the process that ultimately makes recommendations to the Board. Last year, remuneration survey information was obtained from:

- The Mercer Pharmaceutical & Healthcare Industry Remuneration Review;
- The Hewitt CSI Australia Biotech Industries Salaries & Benefits Survey;
- Monash University; and
- CSIRO.

In July this year, the Board decided to freeze remuneration levels of both the executive and directors given the difficult economic conditions that were prevailing at the time.

Similarly the changes to staff share schemes announced by the Federal Government have unfortunately created a significant level of confusion and uncertainty. All share allocations under the program were frozen given the taxation uncertainty that now exists for the participants. Our plan is that when clarity is restored, our staff will receive their contractually equivalent allocation backdated to 1 July 2009.

One of the key drivers for our reward program is that of share price. Our share price rose from \$0.77 on 1 July 2008 to \$1.19 on 30 June 2009. This performance was in the midst of the very disruptive financial crisis that rolled out around the world. Despite the fact that our share price in fact rose in a period when the ASX 300 fell by 15%, under the rules of the reward program, the six (6) member executive team earned just 44,791 shares collectively for the share price performance component of their reward program. This represents less than 3% of the total shares originally allocated to them, as these allocated shares are subject to testing against the scheme parameters before vesting in the employees favour. So the system works. Management rewards are aligned with shareholder rewards – the share price had not risen sufficiently from the date of the original issue to trigger the receipt by our team. Hopefully this will correct going forward because clearly all stakeholders benefit from this.

I will now ask Peter Cook, our CEO to present to you on the Company and its prospects.

### **CEO PRESENTATION**



Thank you Jim.

### Introduction

Good morning fellow shareholders. May I extend my welcome to our 2009 AGM and thank you for your attendance and your involvement in today's proceedings.

Just before I review our very successful year, there are two announcements that the Chairman has referred to and clearly require some immediate comment and expansion on my part. The ASX was advised of both of these this morning, just before the market opened at 10.00 am.

For some while, Biota has indicated that it has been our intention to complement our development pipeline with additional, strategically suitable, anti-infective programs.

I'm pleased to announce the acquisition of the valuable drug discovery assets of two companies, MaxThera of Boston, Massachusetts and Prolysis of Oxford, UK, in separate transactions.

While I will provide a greater insight and detail on our strategy a little later in this presentation, cleverly expanding our portfolio can deliver a number of fairly obvious advantages including:

- More royalty generating products in markets more quickly;
- Using the available and the foreseeable cash generation to grow shareholder value;
- Continuing to extract value from Biota's experienced scientific team;
- Reloading the portfolio, given our intention to partner laninamivir and HRV in the near future; and
- Investing for growth yet balancing the need for shareholder returns.

#### MaxThera

### MaxThera

- Key staff
  - Dr Ania Knap, President & CEO
  - Dr Roger Frechette, Vice President Chemistry and R&D Operations
- Facilities
  - Cummings Centre Beverly, Boston, USA

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MaxThera is a private company that was established in 2005. Its founders and principle shareholders are Dr Ania Knap and Dr Roger Frechette. Soon after its establishment, MaxThera secured US\$3 million in grants from the US National Institutes of Health to progress its two key programs, known as PPAT and EPT.

Both programs are targeted at drug resistant bacterial infections, including those of the methicillin resistant staphylococcus aureus (MRSA) type, commonly referred to as "super bugs" or "golden staph".

The two programs disrupt different bacterial enzyme systems.

# MaxThera – Key Assets

	PPAT	EPT		
Development	Lead to Pre-clinical	Hit to Lead		
Stage				
Target	PPAT	EPT		
Mechanism	Disrupts the basic	Stops cell wall growth		
	energy pathway of	during replication		
	bacteria's metabolism			

Both programs directed at validated targets
 – inhibiting the target, kills bacteria

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PPAT is an essential enzyme required to synthesise Co-enzyme A, the basic energy producing pathway for bacterial metabolism and EPT is an essential enzyme in one of the steps in cell wall biosynthesis in bacteria.

Successful inhibition of either of these enzymes has been shown to kill bacteria.

These are what are called "validated targets" i.e., if you hit them, the bacteria die. We know that a number of big pharma clients have these targets and these types of programs on their shopping lists, to licence. However, they want them further advanced to at least "proof of concept" stage. That is the added value that Biota can bring.

# MaxThera - Investment

- Purchase Price
  - US \$1.2m cash and US \$300k in new Biota shares
  - Deferred consideration
    - Up to 12% of upfronts and milestones
- Future investment
  - Up to A\$15m over 3-5 years

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Our purchase price for these assets on completion will be US\$1.5 million; US\$1.2 million in cash and with US\$300,000 in new issue Biota shares. There may also be an additional payment of 12% of net upfront and milestones received by Biota, if the current lead series and/or the back up series are licensed. The acquisition is subject to several conditions which we expect to be met in the near future.

Dr Knap and Dr Frechette, MaxThera's principle scientists will remain with the Company and continue their involvement with the projects from the Company's facilities in Boston. Biota intends to accelerate the development of the lead compound and invest up to US\$15 million, assuming certain milestones are met, over the next three to five years.

MaxThera's assets have the potential to drive a number of significant clinical breakthroughs and provide a suite of novel antibacterial drugs for the shareholders of Biota.

#### **Prolysis**

The second announcement we made today relates to the acquisition of the assets of Prolysis Limited.

# **Prolysis**

- Facilities
   Begbroke Science Park Oxford, UK
- Staff
  - Approximately 20

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Prolysis is a privately held antibacterial drug discovery company located in Oxford, UK. Its original intellectual property was founded on the work of Professor Jeff Errington, previously of Oxford University and now the Director of the Institute for Cell and Molecular Biosciences at Newcastle University. The aspects of Professor Errington's work have focussed on the molecular process which precede the formation of the septum wall, prior to the division of staphylococci.

Prolysis has two primary projects, also focused on novel antibiotics.

# **Prolysis – Key Assets**

Gyrase (GYR) program

- Lead to pre-clinical stage
- Antibacterial compounds that target bacterial gyrase and topoisomerase enzyme systems
- These enzymes are necessary for bacterial replication
- Inhibiting gyrase kills bacteria
- Inhibiting gyrase and topoisomerase simultaneously makes resistance less likely

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The first called the gyrase or GYR, program targets the bacteria's DNA super-coiling mechanism. In simple terms, gyrase unwinds the bacteria's DNA, an essential step for bacteria to multiply. However, the unwinding needs and a second enzyme, topoisomerase, to un-kink the strands of the disassembled DNA.

Prolysis's GYR program targets both of these two enzymes, simultaneously. For resistance to emerge, the bacteria would need to make two genetic changes simultaneously and this is a much less likely event, than targeting a single enzyme system.

# Prolysis – Key Assets

### **CDI** Program

- Hit to lead stage
- Antibacterial compounds that inhibit staphylococci cell division (CDI)
- Block the assembly of the septum wall, essential for staphylococci to divide & replicate
- Recognised novel target from the research of Prof J Errington

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Prolysis's second program, identified as cell division inhibitor. CDI, is targeted specifically against staphylococci, blocking the assembly of the septum wall components which allows the staph to divide and multiply. I mentioned earlier that the basic bacterial bio-molecular research behind this program has been by Prof. Errington's, at Newcastle University.

The CDI program has attracted earlier interest from big pharma, particularly because of the originality of the basic research I have just referred to. Accordingly, The Wellcome Trust, the UK's largest philanthropic medical trust, has supported this program to the extent of £2.7 million, with approximately £0.8 million still available for the program, subject to the program continuing the deliver the appropriate milestones. The Wellcome Trust has provided the funds in exchange for shares and these arrangements will continue.

# **Prolysis - Investment**

- Purchase Price
  - A\$10.8m in new Biota shares
    - 60% of these shares are escrowed for 12 months
  - Deferred consideration
    - Up to 15% of milestone and royalty payments

#### Investment

- Wellcome Trust to continue to fund CDI program for a further £800k
- Up to A\$25m over the next 3-5 years

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The assets of Prolysis are to be acquired for A\$10.8 million, as new issue Biota shares. This is approximately 4.0 million shares and 2.2% of the capital after the issue. 60% of these shares cannot be traded by Prolysis for the first twelve months. In addition to the shares, Prolysis shareholders could receive up to 15% of the milestone payments and royalties received by Biota, when the products are licensed or sold.

As a result of this transaction, the two principle shareholders of Prolysis, East Hill Management, Providence, Rhode Island, and the Wellcome Trust, London will become shareholders in Biota. We welcome the internationalisation of our share register particularly with such well recognised institutions.

Biota intends to retain all of the staff at Prolysis, approximately 20 predominantly scientific and technical personnel, operating from premises near Oxford in the UK. Prolysis staff's skills are highly complementary to our human resources in Melbourne and will be used on company wide programs, not only the gyrase and CDI programs.

The Board intends to extend an invitation to Professor Jeffery Errington to join the Biota Board at a yet to be determined but mutually convenient time, some stage in the future.

I recognise that both of these assets probably seem to you to be very similar. Both are aimed at providing novel antibiotics which address the limitations of current antibiotics and particularly the issue of resistance and are directed at hospital and community acquired "super bugs". However, that is where the similarity ends.

Each of these programs are quite different and each is a potential product in its own right. They could each be marketed and each meet a viable and useful market segment.

I recognise that I have focused on our scientific interests in these acquisitions. However, they have successfully passed our rigorous internal financial assessments including a risk adjusted success rates and our financial return criteria, very well.

At both MaxThera and Prolysis, we have recognised a technical and managerial talent, commitment and culture totally in step with the values and aspirations that we have at Biota.

The programs provide Biota with an immediate impetus in antibacterials in a highly complementary form. We welcome the new shareholders to the register as we welcome those new members of staff and most of all we look forward to delivering value to our shareholders with these attractive acquisitions.

We will continue to be opportunistic and add programs to our portfolio where it makes commercial sense and where we can add value.

With those news-worthy items covered, perhaps I should now resume the main thrust of my presentation to you this morning.

In the Annual Report, I commented that Biota had delivered a number of key milestones for shareholders during 2009. This year, unlike last, I'm happy to report that the achievement of those milestones has been recognised in the market and translated into solid share price growth.

# **Key Milestones**

- The commercial value of Relenza starting to be recognised
- Rapid clinical progress on laninamivir
- HRV proof of concept achieved
- Solid financial performance

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I summarised those milestones as follows:

- The true commercial value of Relenza beginning to be recognised;
- Rapid progress of laninamivir through Phase II and III clinical trials, successfully;
- Proof of concept achieved with the HRV program; and
- Solid financial performance, particularly of cash.

and I will elaborate on each of these areas during the remaining course of my speech.

# **Major results**

- PAT A\$38.2m
- Relenza royalties A\$45.0m
- Cash at 30 June 09 A\$86.7m
- Daiichi Sankyo agreement to market laninamivir in Japan
- Laninamivir successfully completes Phase III in Asia
- RSV license extended for A\$3.5m, BTA 9881 returned
- GSK litigation resolved
- GSK propose to increase Relenza capacity 6 fold
- Proposed A\$20m cash return to shareholders

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### Major Results

Let's start with the major results delivered this year which include:

- Profit after tax of \$38.2 million;
- Relenza royalties of \$45 million;
- Cash generating year with \$86.7 million in cash at 30 June 09;
- Daiichi Sankyo exercised their right to market laninamivir in Japan;
- Laninamivir completed pivotal Phase III studies in Asia;
- RSV licence with AZ extended with the payment of US\$3.5 million, although the program was subsequently returned to Biota;
- GSK litigation resolved at mediation;
- GSK intention to increase Relenza production capacity 6 fold to 190 million courses over 31 March 09 capacity; and
- Proposed \$20 million cash return to share holders.

From this summary, I would like to provide a little more explanation of our financial position during F2009, including comments on revenue and related expenses, as well as profit and cash.

### Financial Report F2009

Profit & loss			
	FY08 \$m	FY09 \$m	
Revenue			
Rovalties	20.8	45.0	
Collaboration income	15.2	12.6	
NIH grant	5.7	2.8	
Settlement	0.0	20.0	
Other	3.2	2.9	
	45.0	83.3	
Expenses			
Medicinal chemistry and research	10.3	13.3	
Product and clinical development	15.3	11.3	
Business development	1.0	1.0	
Sub royalty	1.9	4.2	
Corporate	3.8	4.3	
GSK litigation	21.8	7.2	
Finance costs	0.2	0.1	
	54.3	41.5	
PBT	(9.3)	41.8	
PAT	(6.5)	38.2	
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Revenue was \$83.3 million, up from \$45.0 million in F2008. The two major items that contributed to that increase were Relenza royalties of \$45.0 million, an increase of \$24.5 million over last year and the \$20.0 million settlement payment from GSK in relation to the litigation.

Profit before tax was \$41.8 million and profit after tax of \$38.2 million.

It is worth mentioning that we have been able to recover \$26.7 million of tax losses in this financial year, very good progress by any standard even though the company remains in a net tax loss position. That position should change in F2010 and allow the company to consider the payment of franked dividends.

The increases in research expenses year on year reflect the increased project activity and the \$4.0 million lower expenses in product development year on year, reflect the considerable savings we managed to achieve with the HRV clinical trial, achieving proof of concept with much smaller patient numbers than planned for.

The sub royalty increase is the increased amortisation of the CSIRO and VCP buy-out of their earlier royalty sharing arrangements on Relenza and is in line with the higher Relenza royalty actually received during the year. A further \$8.1 million is to be amortised over the life of the Relenza patent.

The litigation expense of \$7.2 million reflects all expenditure in relation to finalisation of the litigation with GSK.

In summary, the company's financial performance has been particularly good and should be acknowledged as such by all shareholders.

### Q1 F2009 results

I would also like to share with you our financial position at the end of the first quarter of this financial year. I should point out that these results are un-audited, but again are most pleasing.

# Profit & loss – Q1

(unaudited)

	Q1 2009 \$m	Q1 2010 \$m
Revenue	26.3	27.7
Expenses		
Medicinal chemistry and research	3.1	3.7
Product and clinical development	3.4	3.5
Business development	0.2	0.3
Sub royalty	0.4	1.0
Corporate	1	1.1
Litigation	7.5	0.0
	15.6	9.6
PBT	10.7	18.1

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Revenue for the quarter was \$27.7 million, up \$1.4 million on the same period last year, which included the \$20.0 million from the GSK settlement. The \$27.7 million includes the \$24.1 million Relenza royalty on sales reported by GSK for the quarter of GBP 182 million. With expenses at a total of \$9.6 million, the first quarter has generated a profit before tax of \$18.1 million, 69% percent higher that the same period last year.

Cash at 30 September was \$77.4 million.

The new financial year has started well, significantly boosted by the Relenza royalty figure, which incidentally, is the first formal reporting of sales that can be attributed to the swine flu pandemic. Shareholders should remember that swine flu was first characterised and officially recognised in late April this year and national health authorities' initial responses were to mobilize existing resources not simply to "order more"; effectively only limited sales for the quarter ended 30 June 09 could be attributed to orders from the swine flu outbreak.

I will talk more about GSK's response to the pandemic when I review our project portfolio.

### Strategy

Before I do that, I want to take the opportunity here to give our shareholders some insight into the extensive re-evaluation of our corporate strategy that has been undertaken by management and the Board, completed in the last quarter of the year. The new members of the Board particularly wanted an in-depth review and all members of the Board recognised that re-assessment was appropriate.

The Chairman has described this year for Biota as "transformational". What he is stating is that our first product, zanamivir, has matured sufficiently to be generating reasonable and sustainable royalties. It has taken approximately 19 years for that achievement. As you will see a little later in my presentation, that is about "on target" with industry expectations. Yes, that is right. Relenza is at or about an average product for the industry in terms of development time, costs and market penetration. In terms of sales, however, it is a "blockbuster", and much better than average.

The year has been transformational to the extent we that have the opportunity to transform the business from a one product success into a sustainable business.

# Strategy: vision

 Create a globally recognised small molecule drug discovery company focused on infectious diseases

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Your company has previously indicated that our intention is to create a globally recognised small molecule drug discovery company focused on infectious diseases. That is our vision; it has not significantly changed over a number of years, but it is reinforced by our successes with Relenza.

Given our business is drug discovery in infectious diseases, it is worth establishing clearly the characteristics of that business and particularly the costs, time lines and risks associated with it.



# Strategy – project cycles

This chart lays out some of those key characteristics. Each of the columns on this chart represents a key step in the discovery process. They provide a continuum of all of the steps that need to be fulfilled for a human therapeutic product to be approved for launch. Across the bottom of the slide, is the typical time frame to complete each of those steps and obviously in aggregate they add up to the time it takes to get a product from the identification of a drug-able target site, to launch. Without becoming alarmist, that is approximately 13 years.

Biota has never held onto a product for the full length of that development period, always licensing or partnering it earlier. Much of the development is simply too expensive to contemplate and/or is better handled by the intending marketing company who will always have a much better knowledge of the specific positioning needs and the corresponding local regulatory requirements to achieve those approvals.

So of those 13 years a product takes in development before marketing, Biota would be investing for somewhere between four and a half to seven years, depending on the licensing point.

On the vertical axis of this slide, we have identified the number of projects that need to be handled at each stage to lead to one product successfully making it to market over the thirteen year cycle. In simple terms, we have to start work on some 21 projects at the target to hit stage, to achieve one product to market thirteen years later.

Each of the blue arrows on that slide are what are called the "value inflection" points i.e., a step at which a significant change in value occurs in the project and one at which the customer, big pharma, is usually increases what they are prepared to pay for the product.

During the period from licence to launch, for a product that has already been licensed to big pharma, at each of these points a milestone is usually paid and sometimes that milestone can be quite large. Royalties are paid as a percentage of sales and therefore do not provide any income to Biota until after the product is launched.



The next slide shows what this looks like for the marketing company. Sales usually start off quite slow and typically do not peak until year 6 after launch. The green line is the cumulative sales picture from launch. It should be noted that there is approximately a 10 year life from launch until patent expiry and therefore defines the royalty life for Biota and usually the valuable period of the product for the marketing company.

It is fairly obvious that only one product in the market generating royalties is not ideal for a company such as Biota. For the first six of the product's ten royalty generating years, there is uncertainty about its likely peak sales and once that is settled, there are only four years of stable and potentially forecast-able royalties.

With these considerations in mind and without taking you into the depths of project costs, the costs of capital debates, discount rates and deal metrics, please accept that these were all considered and challenged at length.

# Statement of strategy

- Two or three royalty generating products in market ASAP
- Increase portfolio, by a combination of original research or M&A
- Use the foreseeable cash generation to fund the portfolio growth
- Continue with early licensing model
   Deeper investment with select opportunities
- Continue to balance business capital needs with shareholder cash returns

The Company's strategy has been restated as follows

- Have 2 or 3 royalty generating products in the market ASAP;
- Increase the portfolio, either from original research or from M&A;
- Use the available and foreseeable cash generation to fund the portfolio growth;
- Continue with the early licensing model but not rule out deeper investment in selected opportunities; and
- Balance the capital needs of the business with shareholder cash returns.

To achieve this strategy, Biota simply needs to do more of what it currently does, increasing its current project expenditure by approximately an additional \$20 million a year. We think this can be funded from future earnings, but by licensing early, some of these costs are carried by our licensee and of course we will continue to source grants where possible.

# **Biota's current projects**



To help you understand where our current portfolio meshes with this plan, this slide overlays all current projects onto the first strategy slide I showed you. The redline towards the bottom of this slide, starting with the blue 1.6 and then progressively dropping to the blue 0.1, shows the level of activity that should be occurring in any one year, toward the target of one product to market every 13 years. The yellow boxes show the actual level of activity. Wherever the yellow box is higher than the red line, we are ahead of target, where it is below and obviously where there is no yellow box, we are behind plan.

The gaps highlight areas where M&A opportunities could neatly complement the portfolio and these are the very areas that we sought to fill over the past twelve months or so and which very neatly, MaxThera and Prolysis's programs do, as are shown here in blue.



In summary, I would like to emphasise some of the important points I have covered here.

To provide consistent returns to its shareholders, drug discovery companies like Biota need to be sustainable i.e., self supporting. They need to be able to repeatedly replicate the drug development cycle to create new products using a balanced portfolio of programs, with a number of programs at various stages of development. There also needs to be adequate access to sufficient funds – either from shareholders or from retained earnings – to maintain the product development cycle.

The Board is satisfied that all the other pre-requisites needed to achieve this are available; the pool of commercially attractive projects; the management and scientific skills to transform those projects into viable development programs; and, a knowledge of markets and customers to achieve commercial licensing.

As well as can be forecasted, our foreseeable profit and cash generation appears to be sufficient to meet the necessary funding requirements, to meet our goal.

### **Project portfolio review**

### Relenza

Lets move on and undertake a short review of each of our major projects and let me start with perhaps the most obvious, Relenza.

As a reminder, royalties for Relenza in F2009 were \$45 million, up from \$20.5 million in the previous year. That royalty increase was predominantly the result of significant seasonal orders in Japan and for pandemic stockpiling by the UK government. As I indicated earlier, there is almost no volume in those figures from the current H1NI swine flu pandemic demand. Again as a reminder our first quarter royalties, for the period ended 30 September 2009 were \$24.1 million.

# Relenza

Before Swine flu, already a positive outlook

- Stockpiles of only one product was poor practice
- WHO's early advice on percentage coverage of population was too low
- Resistance in circulating seasonal strains, particularly to oseltamivir
- Side effects, particularly to oseltamivir
- Some market segments poorly served by oseltamivir

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Even before the current swine flu concern existed, we had indicated that there was a positive outlook for Relenza sales. There were a number of contributory factors which included:

- The recognition by public health officials that it was not good practice to operate a stockpile of only one neuraminidase inhibitor (or even something that approximated that situation), even if only on logistics grounds;
- The WHO's early advice to governments to build an NI stockpile based on one course of NI for 25% of the population was probably too low and potentially needed to be more like 50% or higher;
- Resistance in the circulating seasonal influenza strains, particularly to Tamiflu, required access to additional products;
- Side effects, particularly CNS effects and nausea, again with Tamiflu, suggested a wider product choice desirable; and
- Certain market segments, notably pregnant mothers, patients on interactive medications and HIV sufferers each had specific problems with access to only a Tamiflu stockpile and they too required access to an alternate product.

These and no doubt some other factors contributed to the useful increase in sales and hence royalties for Relenza in F2009.

I also want to acknowledge here the very visible marketing changes GSK has brought to their influenza franchise since the appointment of Andrew Witty as their CEO, in May 2008. GSK has made major changes to its marketing approach in this sector as well as made considerable investment in both products and capacity to meet the needs of governments trying to manage the threat of a pandemic on top of influenza's significant seasonal presence. That investment amount is well in excess of £50 million. GSK has emerged as the "one stop shop" for public health officials seeking products and solutions for the management of seasonal and pandemic influenza threats. No other company appears to have offered this integrated approach, with the ability to supply vaccines and anti-virals as well as antibiotics for the frequently concurrent bacterial infection associated with influenza, as well as anti-viral masks for those in close contact with patients.



To respond to the emergence of the new influenza A H1N1 pandemic strain, commonly referred to as swine flu, GSK has both in May and again in July, committed to increase Relenza capacity. In May, GSK indicated that it intended to increase its capacity to 60 million courses by the end of 2009. In July GSK indicated that it would more than triple its capacity to 190 million courses by the end of 2009 by increasing its capacity of Relenza Diskhaler to 90 million courses and a further 100 million courses of additional capacity was to be made available as Rotacaps Relenza (this is one of the dry powder inhalers originally used for GSK's asthma product Ventolin). This alternative inhaler format for Relenza has been given temporary approval by Swedish regulators and hence for use in the EU, during a pandemic.

Both in our ASX release on 23 July and again in our Annual Report, I indicated that these notices of GSK are focussed on increased manufacturing capacity for Relenza, not orders or sales. Indeed, GSK has made it clear that additional regulatory approvals will be required for some of the declared capacity increases to be commercially useful and that the capacity will take time to install and commission. They have stated that it is their intention is to have that capacity available from 31 December 2009.



GSK have logically given priority to the stockpile market. Until government demands are met, which are well in excess of capacity, that position will continue. That also removes visibility of their marketing impetus from the popular press and anyone but the specialists in government health. Don't be concerned if Relenza isn't on the front page of the news.

Advice on capacity intentions is however, very useful information for GSK's customers. It allows them to assess peak supply capability under conditions of crisis such as a pandemic or a particularly severe seasonal outbreak and also allows them to determine cost efficiencies that must ultimately have an impact on their frequency and size of order.

However as a result of both the avian flu threat in 2003/4 and the declared swine flu pandemic in April of this year, it is clear that the market for neuraminidase products and for Relenza specifically has altered favourably. Markets have grown, there is an improved understanding at customer level that adequate stockpiles need to be held and maintained current, that more effective distribution systems need to be developed and be in place for patients to benefit from the medication and that above all else, flexibility needs to be a feature of the system, best achieved by control at the prescriber interface and not by metering out product, by formula, from a centralised health bureaucracy.

Notwithstanding the near term unpredictability of the how the current swine flu pandemic plays out in the current northern hemisphere winter season, Relenza should see larger volumes, more stable year on year take-off and improved market share over the medium to long term, compared to what we have seen in the past.



As and when these stockpile needs are met, there is a significant seasonal market available, which I'm sure you will see GSK attack in the Rest of World just as it has now done successfully in Japan. IMS data indicates this market is over  $\frac{3}{4}$  billion annually and I draw your attention to the Japanese growth year on year, principally driven by GSK and Relenza.

With that concluding comment on Relenza, it is probably worth staying with the topic of influenza and moving onto laninamivir and FLUNET, Biota's second and third generation influenza products, respectively.

### LANI

In 2003, Biota and Daiichi Sankyo merged their respective long acting neuraminidase programs, the lead compound of which was CS-8958, whose active metabolite has now been assigned the generic name of laninamivir. Under this co-ownership agreement, Daiichi Sankyo held an option to manufacture and market CS-8958/laninamivir in Japan, in return for funding the Japanese clinical trials.

It is worth confirming, because I have had queries from a number of shareholders who seem to have misunderstood this point, that CS-8958 and laninamivir are novel chemical entities. They are of Daiichi Sankyo origin. CS-8958 is what is called a pro-drug i.e., a material that is converted into its active species, laninamivir, by the body's own chemical processes. While the active compound is very closely related to zanamivir and is likely to have a therapeutic and prophylactic profile very similar to zanamivir, it is not zanamivir. There is an independent suite of patents around the pro-drug and the active entity that provides the protection for a new set of royalties, independent of those with any association with zanamivir.

The co-ownership has been established at minimal cost to Biota's shareholders and all of the product development costs and Japanese clinical studies have been met by Daiichi Sankyo. Those western studies that have been undertaken have been funded by grants from the US National Institutes of Health. In short, very few Biota funds have been used to advance this program, yet considerable value has been created.

# LANI summary timetable

- Jul 2008 Phase II completed
- Mar 2009 Daiichi Sankyo formally commit to manufacture and market CS-8958 in Japan
- Aug 2009 Completion of Phase III in Asia
- Nov 2009 Phase III prophylaxis study commences

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During the year the program has rapidly advanced as the following timetable shows:

- July 2008, the initial Phase II was successfully completed, showing favourable outcomes against all measured endpoints;
- March 2009, Daiichi Sankyo formally exercised their option to manufacture and market the product in Japan;
- August 2009, successful completion of the Phase III trials in Asia in which a single inhaled dose of laninamivir was shown to be as effective as 75 milligrams of oseltamivir (Tamiflu) administered orally, twice daily for five days; and
- This month, a Phase III prophylaxis study has commenced.

Laninamivir has a number of potential advantages and benefits over the current neuraminidase inhibitors.

# LANI

#### Advantages & Benefits

- Stockpiles are more economically stored and deployed
- Improved patient compliance
- Effective against all actual and threatened pandemic strains over the last decade but with a potentially modified resistance profile



These include:

- Any stockpile of a weekly dosed drug is likely to be more economically or conveniently stored and deployed, both significant cost factors for governments operating stockpiles;
- Improved compliance i.e., the patient is more likely to take the drug as intended; and
- A different resistance profile. However, it is known to be effective against the A4H5N1 avian flu, the A9H1N1 swine flu strains as well as being effective against the broad classes of influenza, identified as causes of the disease in man, the influenza A & B viruses.

# LANI program

Other key points

- Daiichi Sankyo seeking a JNDA for therapy in March 2010 with approval March 2011
- Daiichi Sankyo indicated they will seek a prophylaxis claim in March 2011, with approval March 2012
- Biota receives a royalty on sales and fixed sum payments on specified sales milestones in Japan
- Westernisation of the clinical program will continue
- Actively seeking a licensing partner for ROW

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Some other points that are worthy of note in relation to this program are:

- Daiichi Sankyo is seeking approval of a Japanese New Drug Application (JNDA), which is planned to be submitted in March 2010. On approval, the JNDA would allow for the marketing of the product in Japan;
- Biota receives a royalty on sales in Japan and receives fixed sum payments on the achievement of sales milestones in Japan;
- Biota will continue to advance the clinical development program in the West, including where-ever possible, additional clinical trials and funding for those clinical trails; and
- A licensing partner is actively being sought for all markets outside of Japan. Some promising discussions have been initiated.

### FLUNET

FLUNET is emerging as the third generation of neuraminidase inhibitors. While FLUNET maintains the primary mechanism of action as other neuraminidase inhibitors, the higher potency (up to 4000x that of Relenza) suggests a potentially additional complimentary mechanism of action.

This group of compounds are also being partially funded by the US NIH and are completing pre-clinical stages of development.

# Influenza antiviral landscape

Trade name	Generic/ Code name	Company name	Formul'n	H5N1 Avian	2008/09 Seasonal A H1N1	2009 Pandemic A H1N1	Status
Not recomme	nded for seaso	nal flu:					
Symmetrel®	amantadine		Oral	×	~	×	Marketed
Flumadine®	rimantidine		Oral	×	~	×	Marketed
Marketed neu	raminidase inhi	bitors:					
Relenza®	zanamivir	Biota/GSK	Inhaled	×	✓	✓	Marketed
Tamiflu <sup>®</sup>	oseltamivir	Gilead/Roche	Oral	✓	×	~	Marketed
Development pipeline:							
	laninamivir	Biota/ Daiichi Sankyo	Inhaled	1	1	1	Japan Phase III complete
	FLUNET	Biota/ Daiichi Sankyo	Inhaled	~	Untested	Untested	Preclinical
	peramivir	BioCryst	IV	~	×	~	Phase III
	favipiravir (T-705)	Toyama	Oral	~	Unknown	~	Phase III initiated
	A-315675	Abbott	Unknown	Unknown	Unknown	✓	Preclinical
Biota hold significant portion of the current treatment options biota and development pipeline				options			

Of all of the influenza anti-virals that are either in the market or in development your company owns a significant proportion of the total landscape, and importantly one of the more advanced product candidates.

Our influenza franchise is of considerable value and our intention is to maximise its value for all shareholders, particularly as we license LANI.

#### RSV



Biota's RSV program was licensed to MedImmune Inc in December 2005 at the pre-lead stage. In 2007 MedImmune was acquired by AstraZeneca. In August 2008 the License and Collaboration Agreement with MedImmune was formally transferred to AstraZeneca with an additional US\$3.5 million payment to Biota for rights to Asian territories not held by MedImmune under the original agreement. In all, Biota has received in up front and milestone payments a total of US\$11.5 million in relation to this program and has been paid an additional US\$18.7 million in research income, from the collaboration.

In August 2009, we announced the completion of the Phase Ia clinical trial and that AstraZeneca had terminated the Licence and Collaboration Agreement and that further development of the lead compound BTA9881, had been halted. The Phase Ia clinical trial had not produced any safety concerns about the compound but after extensive consideration by ourselves and AZ, it was felt that the desired safety margin did not exist in the compound to warrant ongoing development and particularly in a paediatric product.

All rights in the program have reverted to Biota.

The company has at least three series of compounds from which we expect to identify a new lead compound with attributes superior to those of BTA9881. We intend to invest approximately \$3.0 million in F2010 in their development and believe that the prospects for licensing the program in the future are quite favourable.

Despite the lack of a more positive outcome with BTA9881, the company has been able to generate over US\$30.0 million in revenue and achieve a reasonable profit from this program. It gives weight to the "license early" business model that we outlined in the strategy section of this report and demonstrates that managing risk and cash are the keys to success in drug discovery.

### **HCV** – Boehringer Ingelheim

Hepatitis C virus
<ul> <li>Boehringer Ingelheim Licence – Nov 2006</li> <li>Technology Access Fee of US\$3m</li> <li>Joint Research Committee</li> <li>To US\$102m in milestones &amp; research support</li> <li>BI to fund development costs</li> <li>Future royalties</li> </ul>
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In November 2006, the company entered into a research and collaboration agreement with Boehringer Ingelheim to develop and commercialise Biota's nucleoside analogues intended to treat Hepatitis C infections and potentially other diseases.

Under the terms of the agreement Biota may receive payments of up to US\$102 million.

While very good progress has been made, no financial milestone has yet been delivered.

HRV

### Human rhinovirus: BTA798

- Description: HRV is the most frequent cause of the common cold
- MOA: capsid inhibitor
- Oral delivery
- Target market
  - Serious complications in patients with other underlying respiratory issues (COPD, Asthma, Cystic Fibrosis)
  - Patients with compromised immune systems (chemotherapy, transplants)
  - No antiviral treatment available
- Phase IIa completed in June 2009
  - Phase IIa successfully demonstrated proof-of-concept in humans
  - Phase Ia proved safe and well-tolerated in healthy volunteers at all single and multiple doses
- Next Step: Actively seeking global pharmaceutical partner

#### biota

The last of the programs I specifically wanted to review with you today was our Human rhinovirus program.

In August 2008 we commenced dosing in the first Phase IIa challenge study of BTA798. The drug is an orally active capsid binder of human rhinovirus. It works by stopping the virus's access into the cells lining the upper respiratory tract, the site of the initial infection. The purpose of the study was to establish "proof-of-concept" in humans which was successfully achieved in June 2009. The drug reduced both the incidence and severity of an induced HRV infection in healthy subjects.

The application of this product will be in patients with pre-existing or compromised lung function, such as in asthma, chronic obstructive pulmonary disease, cystic fibrosis or where there is a compromised immune function, such as transplant patients. In these patients rhinovirus infection becomes difficult to control through the bodies normal defence mechanisms and/or the infection becomes chronic and debilitating.

There are no available anti-virals for HRV infection.

The successful "proof of concept" study was the critical value inflection point for interest from licensees. We have previously indicated that we are actively seeking commercial partners.

### Outlook

# Outlook

Solid F2010 from

- Increasing Relenza royalties due to Swine Flu and increasing GSK production capacity
- Strengthening interest in laninamivir, NDA in Japan and licensing opportunities
- Licensing opportunities with HRV
- Starting to unlock the value in our new antibacterial programs from Boston and Oxford

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I'm excited about our prospects for both F2010 and the near term. The Board and management are confident of a solid F2010.

That sound performance is based on our expectations from:

- Increasing Relenza royalties due to the A9H1N1 swine flu pandemic. Although this is yet to run its full course and is still evolving, increased activity by governments, including and expansion of up to 60 countries that have or intend to have stockpiles of Relenza, the concerns over emerging resistance to other neuraminidase inhibitors and anti-virals in the circulating strains of influenza and the recognition that stockpiles need to be better balanced, larger and more accessible, all suggest growth in sales. That GSK has seen to plan to increase its capacity by a six fold over its estimated capacity this time last year by December 2009, confirms that assessment;
- The successful completion of the Phase III studies on laninamivir and its product profile. In a world continuing to be concerned with the A9H1N1 swine flu pandemic, there is increasing commercial interest in a second generation neuraminidase inhibitor by potential licensees and the progress of our partner Daiichi Sankyo towards NDA approval in Japan brings the date of new royalties from that market closer;
- Licensing opportunities with the HRV program following its successful proof of concept studies; and
- Our reasonable expectations about the performance of our now newly expanded anti-infective pipeline.

As I said this all adds up to a very exciting F2010 and beyond, for Biota.

I thank you all for your continuing support.

Mr Chairman.