

## ASX ANNOUNCEMENT

### Benitec Biopharma Quarterly Report Conference Call Transcript

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**Sydney Australia, 23 March 2017:** Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) today lodged its transcript for the conference call taking place at 8.00am AEDT on 23 March, 2017.

Good morning everyone.

The purpose of today's call is to provide you with a quarterly update.

We have on this call our executive team, Cliff Holloway, Bryan Dulhunty, David Suhy, and Georgina Kilfoil. David Suhy and I will give the briefing which will take about 15 minutes and we will then take questions.

This call is an important opportunity for us to look at momentum in the business.

As noted in previous calls, we have transitioned over the last year to being a product development company with a pipeline focused on areas with a high probability of return on investment and commercial success. We have closed programs that did not fit this brief and established new programs.

Our pipeline is best described today as targeting oncology, ocular diseases, orphan diseases and infectious disease. In addition, we have early stage discovery activities, such as CAR-T and we continue to explore new applications of our ddRNAi technology. David Suhy will provide updates on scientific matters later in this call.

Our strategic focus remains unchanged:

- Firstly, to continue the scientific development on our existing pipeline programs through to commercialisation by Benitec or with pharmaceutical companies.
- Secondly, to prioritise the future development of our ddRNAi technology by identifying those opportunities with a high probability of commercial success and value to shareholders.

By identifying our prioritised future programs and securing the relevant IP, we will have new programs to feed into our scientific development pipeline.

- Lastly, to establish co-development agreements with other companies using our scientific capability and IP platform. That is, we can use our scientific and laboratory capabilities to collaborate with other companies on their targets.

We remain focused on driving our pipeline programs to their appropriate key inflection points and we continue to engage in potential partnership discussions around Hep B and our other programs. In addition, we remain focused on identifying new opportunities to expand our pipeline or leverage off our scientific capability and technology platform.

Over the last year we have communicated what we see as key focus areas to deliver on our strategy and we have stressed the importance of securing collaborations or partnerships to help advance our programs.

The first of these was our strategic engagement with Nant.

The engagement with Nant marks an important milestone for Benitec. Nant sees Benitec as an important long-term strategic investment. The Board expects this engagement to further enhance shareholder value.

Already we have strengthened our Board, improved our financial position, set a course for growth and established support for further funding. Engagement with Nant returns Benitec to a clinical stage company and brings a scientific collaboration with the important extension of our ddRNAi pipeline into oncology.

Signing of the collaboration agreement in January of this year and closing of the second tranche investment with Nant solidifies the strategic relationship between the two companies. In line with our Share Purchase Agreement, the second tranche funding was completed in early March 2017 with Nant investing \$5.5m Australian dollars bringing their holding to 28% of the issued capital.

As a result of the strategic engagement with Nant, we have acquired both a clinical stage oncology asset that we plan to progress to a Phase 2 study in early 2018, and a research collaboration expanding our ddRNAi pipeline into oncology. Further, Nant have provided funding to help advance both of these programs and our other programs.

In referring to the Nant shareholding, I note that Dr Jerel Banks from NantVentures is a medical doctor as are 5 out of our top 10 long term shareholders. I mention this because it indicates the capacity for some of our larger investors to have a deep understanding of the Benitec technology.

With Nant as our cornerstone investor, we will continue to focus on building relationships with long-term strategic partners who share the understanding of our technology as our existing major shareholders do.

I would like to provide you with a snapshot of some of the achievements we have made on our programs and the upcoming milestones that we think will drive shareholder value.

#### **HBV**

In relation to the hepatitis B program, we are delighted with the preclinical data that was presented at the recent APASL conference in Shanghai which demonstrates that ddRNAi constructs, in combination with standard of care therapies, have the potential to become a new treatment paradigm to meet the significant unmet medical need in this indication. We believe these data will generate significant interest from potential partners to allow us to move this program forward. To provide some perspective on the size of the hepatitis B market, there are more than 240 million people chronically infected with hepatitis B worldwide.

#### **OCULAR**

In relation to the ocular program, we have also recently announced very promising results relating to the delivery of viral capsids to the back of the eye. We believe this creates a new opportunity for Benitec to build an ocular franchise. The development of these capsids is complex science and we are particularly pleased about the outcomes. In talking with analysts in the US, some treat this development as a game changing advance in gene therapy. Our capsids allow gene therapy to be delivered to the back of the eye via a simple intravitreal injection as opposed to the more common approach using invasive sub retinal injection. Our focus now is to demonstrate that we can load these capsids with ddRNAi constructs and induce a therapeutic effect, initially targeting Aged Related Macular Degeneration (AMD). Incidentally, AMD is the leading cause of blindness in people aged over 60.

#### **ONCOLOGY**

In relation to our expansion into oncology, as announced in late December, we have completed the in-licensing of the RNA antisense asset from Nant and we anticipate this program being in the clinic by early 2018. Concurrently, we are also developing the ddRNAi program which represents a follow-on product

opportunity with the potential for enhanced efficacy. We have formed our steering committee with Nant and are working with them to advance these programs.

#### **ORPHAN**

The silence and replace strategy we have adopted for our orphan indication, Oculopharyngeal Muscular Dystrophy (OPMD), offers huge potential for the application of ddRNAi in the treatment of this and other orphan diseases. I must say, this approach resonates with potential partners. We were delighted with the European Medicines Agency's decision to grant this program orphan designation and we continue to work with our colleagues at the Royal Holloway University of London and the Institut de Myologie in Paris to further validate this approach.

Lastly, before I hand over to David Suhy, in our last call our Chairman Peter Francis referred to Board renewal and commented on the retirement of one director and the appointment of two directors, Megan Boston as Chair of our Audit Committee and Dr Jerel Banks from NantVentures. From my viewpoint, I am pleased to report that these changes have strengthened our Board and we have a solid working relationship through me with our executive team.

I will now ask David Suhy to provide a more detailed update on selected pipeline programs and scientific matters.

#### Thank you Greg

I'd like to present a bit more additional colour on a few of our major programs. I believe we have had a number of scientific breakthroughs since our last quarterly update.

In our HBV program, we have pre-clinical results demonstrating that a one-time treatment of BB- 103 added on top of a daily dosing regimen of a nucleoside inhibitor (NUC), a drug currently used to treat the HBV in infected individuals, results in a far superior suppression of HBV parameters as compared to that NUC inhibitor alone. Specifically, we demonstrated that the HBV serum DNA levels reaching a greater than 3.72 log drop in serum HBV DNA levels. Perhaps more importantly, we also observe a greater than two log drop in HBV s-antigen levels. Now that the use of chimpanzees for research has been banned, we believe this chimeric mouse model, which has a liver comprised mainly of human hepatocytes, to be one of the most stringent models of HBV currently available to researchers

I'd like to describe why these findings are important.

A "cure" for HBV is often defined as the elimination of HBV serum DNA levels as well as the viral surface antigen (HBsAg). Elimination of the s-antigen is crucial because this high level of viral protein is thought to contribute to long term immunosuppression and chronicity of HBV infection. In effect, it is believed that the s-antigen prevents the body's own immune system from helping control the viral infection. Eliminating the s-antigen may be beneficial in promoting a process known as seroconversion that results in the patient to be able to produce anti-HBsAg (anti-HBs) antibodies.

The appearance of these anti-HBV antibodies typically signals to a physician that there has been clearance of the virus and the patient has immunity against the virus. Although NUC inhibitors often result in significant reductions of HBV DNA serum levels, these drugs have very little impact on s-antigen levels. If this single treatment of BB-103 can suppress the s-antigen levels long term, it may provide clinicians with an important new drug to include in current drug regimen to treat HBV.

To be clear, the treatment of modern day viral diseases will undoubtedly will require a combination approach of many different types of drugs with different mechanisms of action. One only needs to look at the clinical development paradigms currently in use for treatment of HIV and HCV to understand the importance of drug cocktails.

Benitec's goal is to move forward by combining a NUC inhibitor with BB-103 to help the spur the patient's own immune system to produce anti-s-antigen antibodies and eliminate their daily anti-viral treatments to control the disease.

In addition to these efficacy studies, we have also completed the acute toxicity study for BB-103. Our next steps entail meetings with the appropriate regulatory agencies to discuss the clinical development path of this program.

For our Ocular program, we have had the first major data release with regards to our efforts into identifying a novel adeno associated virus (AAV) delivery system that may be used treat retinal diseases using a simple intravitreal injection.

As Greg mentioned a few moments ago, this route of delivery is considered as attractive from a commercial standpoint, particularly when compared to the sub-retinal injection methodologies used by the overwhelmingly large proportion of gene therapy products in development.

Most of you are aware that we have been engaged in a collaboration with 4D Molecular Therapeutics to identify novel AAV capsids, the protein shell that helps deliver our ddRNAi constructs into retinal cells. Although it has taken significant time and effort to reach this stage, we are very excited about the results presented at the ARVO conference last month, which clearly demonstrate markedly enhanced transduction of ocular tissues using one of those novel AAV capsids. We are currently testing three additional capsid variants in similar studies before proceeding with efficacy studies in non-human primates.

For any drug development program, the ability to deliver therapeutically relevant concentrations of drugs into the appropriate diseased tissues is a key challenge. Once solved, the delivery technology itself can become a platform to develop a range of products. Indeed, there have been a number of companies in the RNAi space in particular that have built their franchise around application of their proprietary delivery technologies to specific target organs. Although our ddRNAi treatment to target AMD is our first therapeutic program in eye, we anticipate being able to build a ddRNAi franchise for other ocular indications, in particular retinal diseases with high unmet medical need, using these novel viral vectors as a key component in that platform.

Finally, a few words about the OPMD program. Earlier this year, we were fortunate to obtain an Orphan Drug Designation from the European Medicines Agency (EMA). This designation signifies that there is an unmet medical need for OPMD patients and provides a number of incentives to facilitate the clinical development of our innovative gene therapy approach. Along with our collaborators, we have presented our results at several scientific meetings over the past year that demonstrate the utility of a 'silence and replace' based approach which allows us to carve out a unique space within the field of gene therapy.

The work from our collaborators used two different viral vectors. The first vector expresses short hairpin RNAs to knock out the mutant gene that causes OPMD, while the second viral vector expresses a normal copy of that gene to restore function. Our recent work has combined the critical elements from both constructs into a single therapeutic vector. Additional safety features have also been built into the construct in anticipation of progressing the construct into the clinic. The efficacy experiments with these single vectors are ongoing and we look forward to reporting those results later in the year.

Collectively, I hope you'd all agree that the scientific team has made a significant amount of progress over the last few months and we look forward to continuing to build upon that momentum.

[Back to you Greg](#)

[Thank you David](#)



Let me now provide you with an overview of key deliverables.

Coming into 2018 will see us initiating our Phase 2 trial in head and neck cancer in addition to having in vivo proof of concept with our next generation ddRNAi therapeutic for head and neck cancer. Further we will have initiated the IND-enabling work necessary to progress our key internal pipeline programs towards the clinic toward the end of 2018 or early 2019.

I am confident that as you look over the next 18-24 months you will see a very different Benitec with multiple programs in the clinic.

A year ago we had no clinical programs and no deals in place.

Today we have an engagement with Nant which represents a turning point for the Company. This valuable strategic engagement with a highly respected partner has provided funding, returns us to the clinic and enables us to further our ddRNAi platform technology. In addition, all of our other programs are progressing towards the clinic by the end of 2018 or early 2019.

As a management team, we believe in the potential for our technology to address unmet needs in human therapeutics. As a company, we continue to focus on executing on our strategy. Over the past year, we have communicated what we are going to do and we have demonstrated that we can deliver on our promises.

We will continue to develop a unique combination of gene therapy and gene silencing technology, in-house, in collaboration with partners and out-licensing to companies developing ddRNAi for their own targets.

At this time, I will ask the operator for questions.

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Thank you to all our participants today, and especially those shareholders and analysts who provided questions. I would like to thank all our investors for their continued support.

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For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at [www.benitec.com](http://www.benitec.com)

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***About Benitec Biopharma Limited:***

Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) is a biotechnology company developing innovative therapeutics based on its patented gene-silencing technology called ddRNAi or 'expressed RNAi'. Based in Sydney, Australia with laboratories in Hayward, California (USA), and collaborators and licensees around the world, the company is developing ddRNAi-based therapeutics for chronic and life-threatening human conditions including hepatitis B, wet age-related macular degeneration and OPMD. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain and retinitis pigmentosa.

***Safe Harbor Statement:***

This press release contains "forward-looking statements" within the meaning of section 27A of the US Securities Act of 1933 and section 21E of the US Securities Exchange Act of 1934. Any forward-looking statements that may be in the press release are subject to risks and uncertainties relating to the difficulties in Benitec's plans to develop and commercialize its product candidates, the timing of the initiation and completion of preclinical and clinical trials, the timing of patient enrolment and dosing in clinical trials, the timing of expected regulatory filings, the clinical utility and potential attributes and benefits of ddRNAi and Benitec's product candidates, potential future out-licenses and collaborations, the intellectual property position and the ability to procure additional sources of financing. Accordingly, you should not rely on those forward-looking statements as a prediction of actual future results.