BENITEC MID-YEAR SHAREHOLDER UPDATE
JULY 2017

Giving disease the silent treatment ™

BENITEC BIOPHARMA

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The first half of 2017 has seen significant progress made in all of Benitec's pipeline programs covering orphan disease (oculopharyngeal muscular dystrophy), oncology (head and neck cancer), retinal disease (age-related macular degeneration) and infectious disease (hepatitis B). This progress is summarised below.

Program	Delivery	Discovery	Preclinical	IND-Enabling	Phase I/II	Status
Orphan Disease						
OPMD - BB-301	AAV Intramuscular					• *In vivo* proof of concept – 3Q17
Oncology						
HNSCC - BB-401	Plasmid Intratumoral					• Phase 1 clinical POC complete • Phase 2 – 1Q18
HNSCC - BB-501	ddRNAi Intratumoral					• Construct design complete • *In vivo* proof of concept – 4Q17
Retinal Disease						
AMD - BB-201	Novel AAV Intravitreal					• Capsid biodistribution complete • *In vivo* proof of concept – 4Q17
Infectious Disease						
HBV - BB-103	AAV Intravenous					• Pre-IND completed • IND-enabling work ongoing

OCULOPHARYNGEAL MUSCULAR DYSTROPHY
(PIPELINE PROGRAM BB-301)

WHAT IS OCULOPHARYNGEAL MUSCULAR DYSTROPHY (OPMD)?

- OPMD is a rare progressive muscle-wasting disease caused by mutation in the poly(A)-binding protein nuclear 1 (PABPN1) gene
- The disease is characterised by eyelid drooping, swallowing difficulties (dysphagia), and proximal limb weakness.
- OPMD is typically diagnosed when individuals reach their 50's or 60's.
- Dysphagia is a severe, life-threatening complication of OPMD.
- There is currently no effective drug therapy for OPMD. Available intervention is limited to temporary palliative care and do not address underlying progressive muscle weakness.

WHAT IS OUR APPROACH TO TREATING OPMD?

- We believe our ddRNAi approach to 'silence and replace' the mutant PABPN1 protein will result in the correction of the muscular dystrophy and of key clinical features of OPMD including a progressive atrophy and muscle weakness associated with nuclear aggregates of insoluble PABPN1.

WHAT ARE OUR RECENT DEVELOPMENTS IN OPMD?

JANUARY 17: BENITEC RECEIVED EUROPEAN UNION ORPHAN DRUG DESIGNATION FOR BB-301

In January 2017, Benitec announced that the European Commission, based on a favourable recommendation from the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP), has granted Orphan Drug Designation to BB-301 as an orphan medicinal product for the treatment of patients with oculopharyngeal muscular dystrophy (OPMD). Details

APRIL 3: OPMD KEY DATA PUBLISHED IN NATURE

In April 2017, Benitec announced that the initial pre-clinical efficacy results of the OPMD program have been published in Nature Communications, an open access scientific journal published by the Nature Publishing Group. Free access to the paper can be found here. Details

WHY IS THIS IMPORTANT?

Having Orphan Drug Designation from the European Medicines Agency (EMA) 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. The initial pre-clinical efficacy results using a dual vector system that were published in Nature Communications were the outcome of an ongoing collaboration with Professor George Dickson at the Royal Holloway University of London as well as by Dr Capucine Trollet at the Myology Research Center based in Paris. Not only were these published results critical for establishing the proof of concept that a ddRNAi approach may be able to treat this orphan disease, they also highlight one of the unique aspects of the Benitec technology that is not readily attainable by other gene therapy approaches. Specifically, through our unique approach to gene silencing and gene therapy, we are able to knock out the mutated form of the gene and have the ability to express a normal copy to restore function. Over the last year we generated a single therapeutic vector which combines both the silence and replace elements and we look forward to releasing efficacy data in the near future.

HEAD AND NECK SQUAMOUS CELL CARCINOMA
(PIPELINE PROGRAM BB-401 AND BB-501)

WHAT IS HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)?

- Head and neck cancers typically begin in the squamous cells that line the moist mucosal surfaces inside the head and neck, such as the mouth and the throat.
- HNSCC is more than twice as common in men compared to the rate of occurrence in women.
- HNSCC accounts for more than 90% of all head and neck cancers
- More than 50% of HNSCC patients are diagnosed with locally advanced or metastatic disease, which has a higher potential for progression and recurrence.
- In 2016, approximately 64,000 new cases of head and neck cancer were diagnosed in the U.S., resulting in more than 13,000 deaths.
- The relative five-year survival rate for metastatic head and neck cancers is <38%, and can be as low as 4% for recurrent or metastatic forms of the disease.

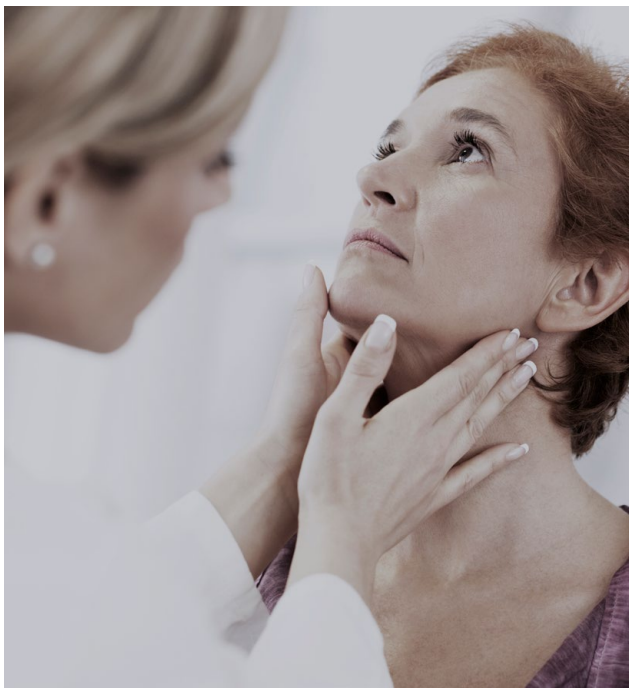
WHAT IS OUR APPROACH TO TREATING HNSCC?

- The Epidermal Growth Factor Receptor (EGFR) is a well validated oncology target and a key driver of the growth of HNSCC lesions. More than 80% of HNSCC lesions exhibit significantly elevated levels of EGFR versus concentrations found in non-malignant tissues.
- BB-401 is a DNA construct that produces an antisense RNA that targets EGFR. We believe that a targeted and rationally-designed approach to treating HNSCC could facilitate durable tumour size reductions or complete eradication of malignant lesions and may lead to an improvement in the quality of life and clinical outcomes for patients suffering from this disorder.
- We are also developing a follow-on compound utilizing our proprietary ddRNAi proprietary technology to silence EGFR. Named, BB-501, early stage iterations of this candidate are currently being tested in preclinical animal testing using xenograft tumour models.

WHAT ARE OUR RECENT DEVELOPMENTS IN HNSCC?

JANUARY 30: ONCOLOGY PROGRAM INITIATED WITH NANT

In January 2017, Benitec announced that it had initiated work on two new oncology pipeline programs after executing a Research Collaboration Agreement with Nant Capital LLC (Nant). This transaction represents a key step in establishing a strategic alliance with Nant around the development of the head and neck cancer squamous cell carcinoma (HNSCC) programs. Benitec plans to initiate a Phase II clinical study with BB-401, an in-licensed antisense-EGFR asset in early 2018 and has initiated a follow-on anti-EGFR ddRNAi program using its own platform technology. Details



MARCH 13: CLOSING OF NANT SECOND TRANCHE PLACEMENT

In March 2017, Benitec announced that in accordance with the Share Subscription Agreement dated 24 October 2016 entered into between Benitec and Nant Capital, LLC (Nant) and as approved at Benitec's Annual General Meeting on 14 December 2016, Benitec issued an additional 29,305,819 fully paid ordinary shares to Nant under the second tranche of the approved placement. Proceeds from the Second Tranche Placement will be used to support both the oncology collaboration between Benitec and NantWorks and the progression of Benitec's existing programs towards the clinic. Details

WHY IS THIS IMPORTANT?

We are working with our Key Opinion Leaders to refine the proposed Phase 2 clinical protocol for BB-401 and have initiated the process to manufacture the clinical grade product for administration into human subjects. We remain on track to initiate our clinical study in the first quarter of 2018.

Selection and optimisation of the short hairpin RNAs has been completed with BB-501, our next generation ddRNAi therapeutic targeting EGFR. Initial in vivo proof of concept xenograft efficacy studies have been initiated. In addition to testing novel delivery mechanisms, BB-501 may also incorporate other therapeutic entities in the same vector. The clinical findings from BB-401 will be used to direct and optimise the development of BB-501.

AGE-RELATED MACULAR DEGENERATION
(PIPELINE PROGRAM BB-201)

WHAT IS AGE-RELATED MACULAR DEGENERATION (AMD)?

- AMD accounts for 8% of blindness worldwide and has been projected to impact up to 196 million patients by 2020 and up to 288 million by 2040.
- The wet form of the disease accounts for about 10% of all AMD patients but accounts for up to 90% of all the blindness.
- Wet AMD is characterised by the growth of new blood vessels into the eye, a phenomenon that has been associated with the expression of abnormally high levels of proteins from the vascular endothelial growth factor (VEGF) family.
- The most commonly used standard of care treatments for AMD require an intravitreal injection into the eye as frequently as monthly or bi-monthly. These frequent injections may be required indefinitely to be able to halt progression of the disease and stabilise vision.

WHAT IS OUR APPROACH TO TREATING AMD?

- Our AMD product candidate, BB-201, is comprised of a novel adeno associated virus capsid (AAV) and a recombinant DNA cassette, engineered to express steady state levels of three short hairpin RNA that inhibit VEGF-a, VEGF-b and PlGF, three clinically validated targets whose expression is shown to lead to the progression of AMD.
- Along with our collaborators, we have identified novel AAV capsids for delivery to key cell layers within the retina using direct intravitreal injection, a commercially attractive route of administration.
- The AMD program is our first program in this space and we anticipate being able to build a ddRNAi franchise for other retinal diseases using the same delivery system.

WHAT ARE OUR RECENT DEVELOPMENTS IN AMD?

FEBRUARY 2: UPDATE ON OCULAR PROGRAM AND PRESENTATION

In February 2017, Benitec announced that it had made significant progress with the Company's ddRNAi technology for the development of therapeutics for the treatment of ocular diseases. Of particular importance is the output from Benitec's collaboration with 4D Molecular Therapeutics to identify novel viral vectors for delivery to the cell layers deep within the retina using direct intravitreal injection, a commercially attractive route of administration. Details

The results of this work were presented by Dr David Suhy, Benitec's Chief Scientific Officer, at the Association for Research in Vision and Ophthalmology (ARVO)-Asia meeting as well as the Translational Vision Summit (TVS). ARVO-Asia is a leading conference dedicated to eye and vision research in the Asia-Pacific region. The TVS meeting highlights "revolutionary approaches to advancing innovation in the diagnosis and treatment of eye disease." Details

WHY IS THIS IMPORTANT?

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. The positive results from these experiments not only validate the AMD program but also provides a platform which will allow us to expand our ddRNAi therapeutics into a broad range of other ocular indications.

We are now moving the most promising AAV capsids forward into non-human primate efficacy studies with our clinical candidates. Termed BB-201, these capsids contain recombinant expression vectors that express short hairpin RNA, or shRNAs, against clinically well validated targets that are the causative agents in wet AMD including VEGF-a, VEGf-b and PlGF. The laser induced model of neovascularization in non-human primates provides one of the most well validated models to test the efficacy of our vectors for the application to retinal diseases.

HEPATITIS B
(PIPELINE PROGRAM BB-103)

WHAT IS HEPATITIS B?

- Worldwide, 2 billion people have been infected with the hepatitis B virus (HBV) and 400 million people have become chronically infected.
- An estimated 1 million people worldwide die each year from HBV and its complications
- Chronic infection with hepatitis causes 80% of all hepatocellular carcinoma and more than 500,000 people die each year from this lethal cancer.
- There is a need for safe and effective therapeutics that can promote the restoration of a host immune response through targeted hepatitis B surface antigen (HBsAg) knockdown offering HBV patients the potential for 'functional cures' by eliminating virus producing cells.

WHAT IS OUR APPROACH TO TREATING HEPATITIS B?

- We believe that a combination of BB-103 and a nucleoside inhibitor (NUC), a type of drug currently used to treat the HBV in infected individuals, may suppress a number of HBV parameters in humans including HBsAg. The HBsAg is a known contributor to immunosuppression and HBV chronicity. The ability to suppress HBsAg may thus help spur the patient's own immune system to produce anti-s-antigen antibodies which is expected to eliminate their need for their daily anti-viral treatments to control the disease.
- Our pre-clinical results demonstrate that a one-time treatment of BB- 103 added on top of a daily dosing regimen of a NUC, results in a far superior suppression of HBV parameters, including a greater than 2 log knockdown of HBsAg, as compared to that NUC inhibitor alone.

WHAT ARE OUR RECENT DEVELOPMENTS IN HEPATITIS B?

FEBRUARY 16: HBV DATA PRESENTATION AT APASL SHANGHAI

In February 2017, Benitec announced presentation of pivotal data from a preclinical in vivo efficacy study at the 26th Conference of the Asian Pacific Association for the Study of the Liver (APASL) meeting, in Shanghai China. During an oral presentation, entitled 'Combinations of a DNA-directed RNA interference Agent with Standard of Care Drugs Results in Superior Suppression of Hepatitis B Virus (HBV) in a Chimeric Mouse Model,' Dr David Suhy, Benitec's Chief Scientific Officer detailed the expanded data set. Details

The data demonstrate that a single administration of one of three DNA-directed RNA interference (ddRNAi) agents, BB-101, BB-102 or BB-103, used in combination with current standard of care agents used to treat HBV, provided significantly robust and sustained suppression of the disease in an in vivo model. These results inform the clinical development path and define the potential of a new treatment paradigm. Details

WHY IS THIS IMPORTANT?

The comprehensive results obtained with the chimeric mouse model have generated a significant and important data set showing the path forward for BB-103 as well as providing important insights into the design of the human clinical study. With this data, we completed a pre-IND submission with the United States Food and Drug Administration (FDA) which provided guidance for a focused and expeditious path towards the clinic. The remaining IND-enabling work has been initiated and we have been working closely with our KOLs to finalise the design of the first clinical trial which is proposed to test the safety and clinical activity of a combination of BB-103 with a NUC inhibitor.

WHAT'S AHEAD FOR BENITEC?
UPCOMING MILESTONES

Program	Milestone	Timing
OPMD	BB-301 in vivo proof of concept efficacy data	3Q 2017
OPMD	BB-301 pre-IND meetings	4Q 2017
HNSCC	BB-501 in vivo efficacy data	4Q 2017
HNSCC	BB-401 Phase 2 clinical supplies	4Q 2017
AMD	BB-201 in vivo proof of concept efficacy data	4Q 2017