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Benitec Biopharma advances OPMD orphan disease program

- Innovative vector design to 'silence and replace' the disease-causing gene in a single construct

- Single vector performance matches excellent outcomes seen in the dual vector system as reported in Nature Communications in April 2017

- On track to advance into human clinical trials in the second half of calendar year 2018

- New data to be presented at leading Gene Therapy Conference

SYDNEY, Aug. 8, 2017 /PRNewswire/ -- Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) is pleased to announce it has developed a new single vector (gene therapy construct) system which uses DNA directed RNA interference (ddRNAi) to silence expression of the mutant gene associated with oculopharyngeal muscular dystrophy (OPMD), while simultaneously adding back a copy of the normal version of the same gene to restore gene function. This next generation single vector system, termed BB-301, represents the clinical candidate that Benitec intends to advance into human clinical trials in the second half of calendar year 2018.

Simultaneous silence and replace modalities are required for an effective gene therapy for OPMD and other orphan diseases. By combining both 'silence and replace' functions into a single vector, Benitec can focus its manufacturing efforts for the program on a single product, which vastly simplifies the regulatory process and reduces the complexity of the clinical strategy. The innovative Benitec vector design which integrates both 'silence and replace' modalities into a single vector is not readily achievable with other gene therapy and gene editing technologies.

Greg West, Chief Executive Officer, commented on today's news: "This is an important development in our OPMD program. The single vector system shows the same excellent activity as the earlier generation dual vector system where the 'silence and replace' constructs were delivered in separate vectors. Similar application of the single vector technology may allow development of novel therapeutics to treat other orphan diseases. OPMD is a significant commercial opportunity for Benitec and we are working with the regulators and key opinion leaders in this field to advance BB-301 into the clinic as quickly as possible."

Background information
OPMD is a rare progressive, muscle-wasting disease caused by mutation in the poly(A)-

binding protein nuclear 1 (PABPN1) gene, that is characterised by eyelid drooping, swallowing difficulties, and proximal limb weakness.

Since 2014, Benitec has been working on an OPMD collaboration with research groups at Royal Holloway University of London and at the Myology Research Center based in Paris. The previous preclinical studies, conducted as part of this collaboration, used the A17 mouse model of OPMD and used a two vector system, where one vector silenced the production of the disease-causing mutant protein and a second vector produced the wild type (normal) protein to restore muscular function. A17 mice display many of the clinical signs of OPMD including intranuclear inclusions (INIs), fibrosis, and loss of muscle strength. Application of both vectors resulted in improvement of many of these phenotypes including a restoration of muscle strength to wild type levels. These findings were central to Benitec receiving Orphan Drug Designation in the European Union for the OPMD program in January this year and were published in Nature Communications in April 2017.

Latest development

The scientific team at Benitec has now generated a single AAV vector system that uses a ddRNAi approach combined with protein replacement to 'silence and replace' the mutant PABPN1 protein. In a dose-dependent and time-dependent manner, BB-301 treatment produced robust knockdown of PABPN1 levels, including the mutant form of the protein, by up to 88%, while simultaneously restoring wild type PABPN1 to levels of up to 90% of normal. BB-301 treatment results in substantial correction of INIs and fibrosis as well as muscle strength. Importantly, treatment with the new clinical candidate BB-301 restored the ratio of muscle weight to body weight to wild type levels.

Benitec has engaged with a broad group of OPMD clinicians and experts to assist us with defining the clinical development plan that will be considered with the regulatory agencies later this year. Benitec remains on track to be in the clinic by the second half of calendar year 2018, contingent upon favourable discussions with the regulatory agencies.

The OPMD data will be presented on October 4-6, 2017 at the Cell & Gene Meeting on the Mesa conference in California. This is an annual conference which is aimed at the significant progress of the regenerative medicine sector in advancing transformational therapeutics to patients.

For further information regarding Benitec and its activities, please contact the persons below, or visit the Benitec website at 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 OPMD, head & neck squamous cell carcinoma, retinal based

diseases such as wet age-related macular degeneration, and hepatitis B. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain, cancer immunotherapy and retinitis pigmentosa.

About OPMD:

OPMD is a rare inherited myopathy characterized by dysphagia (difficulty in swallowing), the loss of muscle strength, and weakness in multiple parts of the body. Patients typically suffer from severe dysphagia, ptosis (eye lid drooping), tongue atrophy, proximal lower limb weakness, dysphonia (altered and weak voice), limitation in looking upward, as well as facial muscle and proximal upper limb weakness. Progressing throughout that patient's life, OPMD is not typically diagnosed until the individuals reach their 50's or 60's. As the dysphagia becomes more severe, patients become malnourished, lose significant weight, become dehydrated and suffer from repeated incidents of aspiration pneumonia. The last two symptoms are often the cause of death. No cure is currently available for OPMD. The cricopharyngeal myotomy is the only treatment available to improve swallowing in these patients, but because the root cause of the genetic disease has not been addressed, the pharyngeal musculature still undergoes progressive degradation leading to the previously mentioned complications.

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 this ASX/Nasdaq announcement are subject to risks and uncertainties relating to the difficulties in Benitec's plans to develop and commercialise 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.

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