May 15, 2018

Benitec to present OPMD data at the American Society of Gene and Cell Therapy Meeting

SYDNEY, May 15, 2018 /PRNewswire/ -- Benitec Biopharma Limited (ASX:BLT; NASDAQ:BNTC; NASDAQ:BNTCW) today announced that data from its oculopharyngeal muscular dystrophy (OPMD) program will be presented at the American Society of Gene and Cell Therapy (ASGCT) meeting being held in Chicago on May 16-19.

The presentation provides the new nonclinical efficacy data on BB-301, the single vector system which uses DNA directed RNA interference (ddRNAi) to silence expression of the mutant gene associated with OPMD, while simultaneously adding back a copy of the normal version of the same gene to restore gene function. BB-301 is the clinical candidate that Benitec is progressing towards the clinic.

The 21st Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT) is being held May 16-19 at the Hilton Chicago, Chicago, USA. Details of the oral presentation are noted below:

- Date: Thursday 17 May at 4:15pm CDT (Oral Presentation)
- Title: BB-301: A Single "Silence and Replace" AAV-Based Vector for the Treatment of Oculopharyngeal Muscular Dystrophy (OPMD)
- Presenter: David Suhy, PhD, Chief Scientific Officer

A copy of the full presentation will be posted to thePresentations and Publications section of the Company's website following the talk. The abstract is detailed below.

The Company will also be hosting an OPMD conference call and webcast for investors and analysts on 15 May 2018 at 4:30pm U.S. EDT / 16 May 2018 at 6:30am Australian EST. The presentation will provide a detailed overview of oculopharyngeal muscular dystrophy (OPMD), Benitec's BB-301 gene therapy construct, as well as the associated market opportunity and product pipeline. For more information and to register for the webinar, please contact the persons below or visit https://register.gotowebinar.com/register/8868899774141644803. The event will also be recorded and available for on-demand viewing in the For Investors section at www.benitec.com.

BB-301: A Single "Silence and Replace" AAV-Based Vector for the Treatment of Oculopharyngeal Muscular Dystrophy (OPMD)

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BACKGROUND: OPMD is an autosomal dominant disorder that impacts the muscles of the eyelids and pharynx, leading to ptosis and dysphagia respectively, as well as can lead to proximal limb weakness. Despite the weakness associated with the other muscle groups, it is the complications of dysphagia that most often require serious intervention. The disease is caused by an abnormal expansion of alanine-encoding trinucleotide repeats in the coding region of the poly(A) binding protein nuclear-1 (PABPN1) gene. The A17 mouse model, expressing a bovine PABPN1 with an expanded polyalanine tract, recapitulates most of the features of human OPMD patients including a progressive atrophy and muscle weakness associated with nuclear aggregates of insoluble mutant PABPN1. Previous preclinical studies in A17 mice tested a two-AAV vector system for the treatment of OPMD: one vector produces short hairpin RNA (shRNAs) to silence endogenous (including mutant) PABPN1. The second vector expresses a codon-optimized version of wildtype PABPN1 that takes advantage of amino acid codon degeneracy to produce a wildtype protein that is not cleaved at the RNA level by the anti-PABPN1 shRNAs. Co-administration of both vectors into tibialis anterior (TA) muscles resulted in improvement of many of the disease phenotypes including restoration of muscle strength to wildtype levels.

RESULTS: Here we describe the development of BB-301, a single vector "silence and replace" therapeutic comprised of an AAV9 capsid to deliver a recombinant genome that uses a single muscle specific promoter to produce a bifunctional RNA that expresses shRNA against PABPN1 as well as a codon-optimized shRNA-insensitive wildtype PABPN1. By taking advantage of the existing endogenous RNAi machinery, and the small size of the sequences encoding the shRNAs, leaves sufficient packaging capacity for the co-expression of modestly sized genes resulting in a single vector with 'silence and replace' capabilities. In a 20-week experiment, treatment of TA muscles with BB-301 at a dose of $6e^{10}$ vg/muscle results in robust inhibition of mutant PABPN1 expression by up to 87% and restores wildtype PABPN1 levels up to 91% of endogenous levels. Concomitantly, BB-301 treatment resulted in correction to near wildtype levels of intranuclear inclusions, fibrosis, and muscle strength as assessed by maximal force. A follow-on dose ranging experiment was performed over 14-weeks at administered levels from $4e^{8}$ vg/muscle to $7.5e^{11}$ vg/muscle. Mid-ranged doses of BB-301 that result in 75% inhibition of mutant PABPN1 and 26% restoration of wildtype PABPN1 produces full phenotypic correction of muscle strength and muscle weight, suggesting that BB-301 may provide a broad therapeutic window.

CONCLUSIONS: Cumulatively, these data support the use of a single vector "silence and replace" based approach to treat OPMD. A first-in-man study, in which BB-301 will be injected directly into the cricopharyngeus muscle for treatment of OPMD-related dysphagia, is anticipated in Q1 2019.

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'. Benitec Biopharma is based in Sydney, Australia with laboratories in Hayward, California (USA). The Company is developing ddRNAi-based therapeutics for chronic and life-threatening human conditions including OPMD, head & neck squamous cell carcinoma, retinal based diseases and hepatitis B.

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 late 40s. 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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