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ASX ANNOUNCEMENT

Significant Gene Silencing Demonstrated in Benitec's Muscular Dystrophy Program

- Encouraging early *in vitro* results from the Benitec-Royal Holloway program treating a form of Muscular Dystrophy
- Unique gene silencing ddRNAi construct targeting multiple regions on the mutant gene
- Highly efficient silencing of the target gene (90% knock down) demonstrated
- Encouraging efficacy of replacement healthy gene

Benitec Biopharma Limited (ASX:BLT) and researchers at the Royal Holloway, University London and the Institut de Myologie, Paris, are pleased to announce significant data from their oculopharyngeal muscular dystrophy program (OPMD), which is targeting the silencing of a gene (PABPN1), the mutant form of which causes this muscle disease. On the basis of these data, Benitec and the research team has decided to proceed to development of a vector for combined silenciong of the mutant gene by ddRNAi and replacement with the normal gene.

The data confirm that delivery of a unique multi-shRNA cassette, Pabparna™, to cells expressing the target gene is highly effective at silencing the target gene in those cells, reducing the expression levels to around 10%. If achieved *in vivo*, this level of silencing by the clinical candidate is likely to result in significant improvement of the muscle disease which is currently untreatable.

Furthermore, it is anticipated by the research team that the optimal therapeutic will be based on both suppression of the target mutant gene with ddRNAi and replacement with the normal (healthy) gene. In order to achieve this, a normal gene has been successfully engineered to be expressed in the ddRNAi-treated cells *in vitro*.

The Chief Investigator on the program, Professor George Dickson from the Royal Holloway, University of London, commented: "These results are very encouraging. OPMD is a currently untreatable disease, which is particularly amenable to Benitec's unique gene silencing approach. These *in vitro* results indicate that the program has the potential to be able to deliver a combined therapeutic that both suppresses the causative gene and replaces it with a healthy gene. This is an ambitious program but these data give us confidence that an effective therapeutic is achievable."

"Once again we are seeing positive data from one of Benitec's portfolio of programs[1]," Dr Peter French, Benitec's CEO commented. "This data, whilst early, gives the Board and me confidence to commit to the next step of developing a therapeutic for this currently untreatable disease for *in vivo* testing. Successful results at that stage will be pivotal for committing to advance the program into the clinic. The advantage with working with Professor Dickson in London, and with Dr Capucine Trollet and the team at the Institut de

[1] **Benitec** announced significant *in vivo* data from their non-small cell lung cancer program on November 13.

Myologie (IdM) in Paris is that the IdM is the French National Reference Centre for muscle diseases and as such is readily able to recruit patients with OPMD into a clinical trial. As an orphan disease, OPMD has a number of regulatory advantages, and we anticipate fast track clinical entry following confirmed pre-clinical *in vivo* data. Whilst there is much more work to be done, at this stage the program is on track and is meeting or exceeding anticipated milestones."

About OPMD

Oculopharyngeal Muscular Dystrophy (OPMD) is a genetic (autosomal dominant) orphan disease that appears in middle age. Symptoms include drooping of the eyelids, limb weakness, severe swallowing difficulties, eventually leading to choking and death. OPMD is a rare disease, affecting around 1 in 100,000. This means that there are over 6,000 cases in the EU and US. In addition there are population clusters with higher prevalence. These include French Canadians (1:1,000 = 5,000 cases), Bukhara Jews (1:600) and Hispanics in New Mexico. No effective treatment exists for OPMD. The most common treatment is surgery to improve swallowing. The treatment does not correct progressive degradation of the pharyngeal musculature and has a long-term effect in only a limited fraction of the patients. Eventually many patients die from suffocation. There is therefore a very high medical need for effective therapeutics.

The target and molecular mechanism behind OPMD is well known. The cause is a mutation in the gene for the Poly(A) Binding Protein Nuclear 1 (PABPN1). The mutation affects only a defined group of small muscles (eyelids, throat and parts of limbs).

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About Benitec Biopharma Limited:

Benitec Biopharma Limited is an ASX-listed biotechnology company (ASX:BLT) based in Sydney, Australia. The company has a pipeline of in-house and partnered therapeutic programs based on its patented gene-silencing technology, ddRNAi, also called expressed RNAi. Benitec Biopharma is developing treatments for chronic and life-threatening human conditions such as cancer-associated pain, Hepatitis B, Hepatitis C, drug resistant lung cancer and oculopharyngeal muscular dystrophy based on this technology. In addition, Benitec Biopharma has licensed ddRNAi technology to other biopharmaceutical companies for applications including HIV/AIDS and retinitis pigmentosa. For more information on Benitec Biopharma refer to the Company's website at www.benitec.com.