ASX ANNOUNCEMENT

Benitec Biopharma Investor Webinar on the Company's Oculopharyngeal Muscular Dystrophy (OPMD) Program Transcript

Sydney Australia, 16 May 2018: Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) today lodged its transcript for the investor webinar on the Company's oculopharyngeal muscular dystrophy (OPMD) Program taking place at 6.30am AEST on 16 May, 2018.

I am Jay Morakis from the M Group in New York and we are the IR advisers for Benitec.

In today's call you will hear from Dr Bernard Brais who will provide an overview of OPMD.

Dr Brais is the Professor of Neurology and Genetics, Co-Director, Rare Neurological Diseases Group at Montreal Neurological Institute, McGill University

We will then hear from the Benitec team of Dr David Suhy and Georgina Kilfoil who will provide a briefing on the unmet medical need of OPMD, Benitec's OPMD therapeutic and planned clinical program. Our speakers will then take questions from Webinar participants.

I will read the disclaimer statement and then hand over to Greg West, the Benitec CEO, who will provide a corporate overview.

[Greg West]

Thank you, Jay**,** and thank you for attending our webinar today relating to our orphan disease program in oculopharyngeal muscular dystrophy, or OPMD.

I will give an overview and then hand over to Dr Bernard Brais.

As some of you may know, Benitec is focused on building a broad scientific pipeline of innovative therapeutics by harnessing the power of our DNA-directed RNA interference technology, known as ddRNAi. This unique platform technology combines gene therapy and gene silencing to change treatment paradigms of human disease.

We are translating our science into measurable clinical outcomes which, if successful in the clinic, will have the potential to provide novel treatment options and hope to patients suffering from disease as well as provide significant shareholder value for Benitec.

We were the first company in clinical studies under a US IND with systemically delivered non-withdrawable RNAi in which we dosed patients intravenously against the hepatitis C virus.

Our pipeline is focused on four therapeutic areas to drive shareholder value. We have transitioned from a platform based company into a business driven by product development with assets in oncology, rare genetic disorders, retinal disorders and infectious disease.

We anticipate that our lead two assets will be in the clinic in quarter 2, 2018 and quarter 1, 2019.

Specifically, our lead oncology asset will be entering a Phase 2 clinical trial this month. In addition, we anticipate having our unique 'silence and replace' therapeutic, designed to treat the orphan disease OPMD, entering the clinic early 2019. And we have other programs targeting retinal disorders and infectious disease.

Benitec is dual listed and trades on both the NASDAQ under the ticker BNTC and the Australian Stock Exchange under BLT. Our fund-raising focus since 2014 has been in the US markets and we have raised over US$50m. We also have a US shelf registration.

We have strong in-house capabilities with operations in both Sydney Australia and Hayward California where we have our laboratories. The Hayward laboratory includes 9 scientific staff who have PhDs with deep gene therapy expertise. In addition, we have a dedicated group of scientists working on process optimization and scalability for manufacturing.

I will now hand over to Dr Bernard Brais who will provide an overview of OPMD

[Bernard Brais]

Thank you. It is a real pleasure to present to you today some information about OPMD, a disease very close to my heart having worked on this condition for close to thirty years now and following hundreds of patients.

What I will discuss with you today is the prevalence of OPMD worldwide, its diagnosis, the progression and treatment of OPMD and discuss the end of life with this condition.

OPMD is a disease that has a world-wide distribution. It is a late-onset muscular dystrophy. The prevalence is variable from one country to another. In other words, some countries have more cases and some less. In France and Europe in general, it is considered that there is about one case per 100,000 people. In some parts of the United States, particularly in the south-west it is estimated it is one in 15,000 people. In Quebec, where I live, it is one in 1,000 so it is a more common disease because it of the founder effect.

OPMD was first described really well in 1915 in French Canadian families in Maine. It was really in 1962 that Victor and Adams out of Harvard described the disease and its mode of transmission. They described that it was a dominant disease and therefore transmits from an affected parent to half of his or her siblings. They described the cardinal manifestations which is the eyelid drooping and the swallowing difficulty which is referred to as dysphagia. They also described the weakness that is present in some patients particularly at the level of the leg muscle although they didn't dwell on this symptom as much as they could have.

In 1980 there was a pathological marker identified for this disease so therefore it was a muscular dystrophy that you could really confirm pathologically.

The event of better means to find genes of in the nineties allowed the identification of where the gene was and later publication by a group of the first mutations in the gene in 1998. The gene is now referred to as PABPN1. They consist of an expansion of a triplet of nucleotide coding for an alanine amino acid which is probably responsible for the aggregation of the protein and its dysfunction in the cell. The test is offered worldwide so the confirmation of the diagnosis is quite easy. There are different sizes in the mutation and that may affect the severity. We also discovered that some patients don't have a family history because they receive a small mutation from both the parents and therefore the recessive form of the disease.

So, let us discuss the major symptom of OPMD, which is the dysphagia, the swallowing difficulty. As we show on this slide that represents two large groups of patients, from Quebec and one from Uruguay. It is around the age of fifty-five that 50% of the patients have clear dysphagia or swallowing difficulties. That can be made objective by a simple test of swallowing a cup of cold water. The symptoms tend to start in the late forties and become more and more prevalent. Because of the severity this becomes the most challenging and disturbing symptoms for the patients. Furthermore, as people age, because of this problem of swallowing, some food and liquid may go to the lungs and people develop aspiration

pneumonia which can lead to death if not treated early and certainly lead to a burden of disease that increases with age.

Dysphagia can be treated when patients have moderate to severe dysphagia. The traditional therapy was a surgery that was called a cricopharyngeal dilatation which is now a standard method which is a dilatation at the level of sphincter, though the published evidence is that it is a short-lived effect and therefore a lot of patients have to return to the procedure. The risks are small so it is a valuable procedure, but dysphagia will always return.

The more traditional therapy was cricopharyngeal myotomy. It is a surgery with general anesthesia, complications and is less popular, but it has led to great benefits in some patients so it is still something that should be contemplated. However, it is a surgery that needs to be done using certain protocols to be efficacious because, if poorly made, people can be even worse afterwards. The use of Botox is still controversial and there is no good evidence that it is a proven method of treatment for this condition.

The eyelid ptosis, like dysphagia, affects more than 50% of patients around the age of fifty. The burden of the disease on patients is less important because there is very good surgery now, and therefore it is one of the manifestations of this dystrophy that can be pretty well treated.

Depending on symptoms the timing of the surgery varies. Usually people not operated on until at least 50% of eyelid covers the pupil, or if they have symptoms of difficulty at night, cervical pain which is a common feature of people tilting their head to the back to try to look under the eyelid. There are two surgeries. One is a resection of the tendons, it is not permanent and is losing favor. The surgery which people do now is a permanent surgery which is called frontal suspension, and it consists of using a suture, and bringing a suspender wire to the muscle of the forehead, and using the muscle of the forehead which is not affected by this disease to open the eyes as you see on this picture.

More and more symptomatic preoccupation of patients as they age is the progression of the leg weakness. It appears really early but on average probably ten years later than dysphagia, and in patients with the more standard presentation people start having major complaints related to it mostly in their late sixties. However, some people may have a more severe form and start to complain of their weakness in their fifties. The impact is that stairs become more difficult and then at one point become impossible. Some people will develop weakness in the upper extremities, again proximal muscles, difficulties taking things off high shelves and so forth. But overall it is the leg weakness that is the major problem with very rare loss of walking, though some people will use wheelchairs for longer distances. Driving is usually preserved.

How do people live with this disease as they progress, as the burden increases, as the dysphagia increases? There is social withdrawal. Though the data on life expectancy is not as good as we would like, life expectancy is probably close to normal as long as we treat pneumonia very well and early. But clearly the patients have a harder life post retirement, and the quality of life is moderate to poor, depending on the severity of the disease.

I hope I have summarized what we know on the disease and the impact on the evolution.

Thank you very much.

[Georgina Kilfoil]

Thank you Dr Brais. Good morning everyone, I am Georgina Kilfoil and I am the Chief Development Officer at Benitec.

I would like to take a few minutes to discuss the unmet medical need that exists in OPMD.

As will be described by David in more detail shortly, OPMD is a slow progressing muscle wasting disease caused by a defect in the PABPN1 gene. Unlike many types of muscular dystrophy, the onset of this disease occurs later in life – typically manifesting initial signs in the patients 40's or 50's and becoming a serious health issue as the disease continues to progress. A critical factor to note is that this type of disease is considered autosomal dominant. This means that the disease can arise in a genetic inheritance pattern in which only one of the two genes that you get from your parents has the mutation. Why this is critical is that these patients do not tend to show symptoms of the disease until they are in their later years, and thus already likely to have had children as a result. Of their children, there is a 50/50 chance that their sons or daughters will also have this disease.

As far as treatment options, the methods used to provide relief do not address underlying progressive muscle weakness and provide only temporary benefits. Patients must therefore rely on adaptive strategies

Benitec is developing BB-301 as a therapeutic to treat the dysphagia associated with OPMD. The data presented here is primary market research data that explores the OPMD patient pathway, treatment trends, factors driving current and future treatment choices and the unmet medical need.

The disease symptoms of OPMD vary depending on severity, rate of progression and pathophysiology but common symptoms include ptosis, dysphagia and leg weakness.

The specialty that patients see at initial presentation depends on the triggering symptom. Most often this may be the ptosis or difficulty swallowing. In a lot of cases the patient will see their primary care physician and be referred from there. It may also be the ophthalmologist because of the ptosis or a gastroenterologist because of swallowing issues.

Patients move through the referral pathway to a specialist. The ultimate diagnosis of OPMD is most often done by a neurologist through clinical history, instrumental assessment and final confirmation through genetic assessment.

Looking briefly at the three most common symptoms associated with OPMD, we can see that dysphagia is the most serious clinical feature of the disease.

Although ptosis is a key symptom that motivates the patient to seek care either through their PCP or an ophthalmologist, this condition can be fixed through corrective surgeries such as a frontal sling

Proximal limb weakness is often not the presenting or first symptom. Although proximal limb weakness is typically not life threatening, it ultimately impact patient's quality of life and their ability to do activities of daily living.

Yet, from an ability of the patient to thrive, the presence and severity of the dysphagia is much more life threatening than the other two. Patients have a daily fear choking to death and it is the inability to swallow and/or restrict food intake into the stomach versus being aspirated into the airways that causes the majority of serious health problems for these patients. As the disease progresses, the incidences of hospitalizations due to aspiration and the seriousness of the resultant lung infections significantly decrease quality of life and can be life threatening. In addition, malnutrition also factors into the equation.

Because of the complexity of the issue, dysphagia associated with OPMD is typically managed by a multidisciplinary team, which is often led by the neurologist and can include gastroenterologists, speech pathologists, dieticians and otolaryngologists.

If we look at the current interventions available we see there is a lot of room for improvement. There is no cure for the dysphagia and current treatment options are all palliative in nature.

At the top of the pyramid, cricopharyngeal myotomy is considered somewhat effective though in most cases full restoration of swallowing does not occur. Even then, scarring from the surgical incision is likely to occur which reducing the efficacy of the treatment over time. In addition, nothing in the procedure has been done to treat the underlying basis of the disease which is caused by genetic changes.

As with the myotomy, the remaining procedures noted here provide only partial restoration of swallowing function and importantly transient symptomatic benefit. In addition, there is nothing on this list that specifically addresses the progressive muscle weakness. As the disease progresses, more invasive treatment options are chosen.

It is also important to note that not only is there no standard of care, there are also local and global variations to treatment approaches that exist. Cricopharyngeal myotomy that is offered as a treatment option in Quebec for example is rarely provided as a treatment option in New Mexico.

I will now pass it over to David Suhy who will provide some background on BB-301

[David Suhy]

On Slide 24 we have a diagram which outlines some of the issues associated with aspiration from dysphagia. Both Dr Brais and Georgina had alluded to dysphagia as being one of the key issues of having patients with OPMD. I thought it was important to further define dysphagia, because an understanding of the symptoms helps define the direction we decided to take in the development program of BB-301.on the left-hand side of this panel gives you an idea of the muscles involved in the swallowing process. Understand that swallowing is a coordinated process that starts at the back of the tongue, utilizes the muscles that go along the back of the throat leading to an area called the cricopharyngeus muscle as outlined by the bottom red box. The cricopharyngeus muscle is really critical as it is the regulator of being able to shuttle food down the esophagus which eventually leads down to the stomach and prevents food from going into the trachea which is an entry point into the lungs. Obviously, food and digested materials going down into the lungs has the capability of leading to aspiration and the types of pneumonia associated with that process. On the right-hand side of the panel we see a video fluoroscopy of the swallowing process and it will illustrate some of the critical issues associated with cricopharyngeal weakness and the muscles in the pharynx in general to be able to swallow. Through the second panel you can see the bolus of food it's starting to be forced its way down the neck where the pharyngeal muscles really act to propel the bolus of food towards the esophagus of the patient. In panel three, what you see is that the bolus of food then starts to gather at a critical point where the cricopharyngeus muscle regulates entry into the esophagus which is noted by a blue oval at the bottom of that slide. However, in patients that have OPMD, most often the muscle strength requires to force that food into the esophagus, past the cricopharyngeus muscle is often too weak to be able to do that efficiently. What happens is you have a build up just above the cricopharyngeus muscle ultimately leading to leakage into the trachea and ultimately into the lungs which can cause the aspiration and ultimately the problems associated with OPMD.

Here we look at the tissue and molecular aspects of OPMD. On the right-hand side, the panel you can see two muscles taken from the same OPMD patient whereas the one on the left comes from an impacted or affected area within the patient versus a non-affected or relatively less affected muscle group from the same patient and the differences are quite obvious. In the affected or OPMD ravaged muscle you can see a significant decrease in the muscle fiber number, a variation in the size of the muscle fibers and ultimately fibrosis surrounding those muscles. The net effective of this, of course, is a decrease in muscle force. As Dr. Brais alluded to earlier, there is a genetic basis for this disease and It is within a protein called poly a binding protein N1. This is a ubiquitous factor or what we would typically call a housekeeping gene that promote interaction between the poly a polymerase and some of that are proteins leading to stabilization

of mRNA poly a tails. As Dr Brais also alluded to, this is an expansion disease. Meaning that in these particular cases there is additional alanine mutations that occur within the PABPN1 genes. Because the protein is unable to fold correctly it typically forms Intranuclear inclusions that are clusters of proteins that ultimately can lead to fibrosis and destruction of muscle strength.

Because there is a genetic basis of this disease and the inappropriate expression of a disease-causing gene leads to this mutant phenotype in this disease-causing phenotype, there is a way to be able to treat, or potentially treat the disease with an RNA interference based approach. On the left-hand side of this panel we see an RNAi based process where typically in siRNA-based strategies you can add pre-synthesized duplex RNA at once it gets inside of the cell, enters the RISC complex, finds the appropriate target mRNA leading to a cleavage event. Because that mRNA is cleaved, no further protein is produced from that particular gene and essentially you have silenced the gene. In a siRNA approach typically needs to be re-administered as often as every 2-3 weeks to maintain therapeutic benefit for extended periods of time. Benitec technology is a little bit different. We don't deliver pre-synthesized RNA duplexes. Instead we typically deliver DNA plasmids or some form of DNA that once it gets inside of the cell it uses the cell's own transcriptional machinery to produce steady-state levels of something called short hairpin RNA that once it's exported from the nucleus and the structure is cleaved at that bulbous end, the two pathways are virtually indistinguishable. A couple of really key differences here, particularly when you use gene therapy vectors. A one-time administration can often last months, years or even potentially for the lifetime of the patient. So as long as those cells are healthy, they will continuously be reprogrammed to produce their own therapeutic RNAs to have it be able to impact on the disease. Second, we use steady state levels of transcription to be able to maintain constant therapeutic RNA activity against the desired target. And lastly, because we are using gene therapy vectors that allows us to have other forms of therapeutic modalities in addition to RNAi. In this case we are using the excess vector capacity of AAV to be able to express a normal form of the same gene. So in this case, essentially what we are talking about is having the ability to use the RNAi component to knockdown the mutant allele of OPMD and in the same vector, the same therapeutic vector, expressing a normal, healthy wildtype copy to essentially restore function.

On slide 27, it outlines the design of the molecular construct of BB-301 and this is really where the ingenuity is in this vector. It's a single AAV vector that uses a single muscle specific promoter to drive what we call a bifunctional RNA. A Bifunctional RNA, what that means is that there's two therapeutic modalities coming off of the same piece of genetic material. At the 3', or right-hand side of that RNA we produce the shRNA to be able to silence the mutant diseased allele of PABPN1 that leads to OPMD. However, because its 1) difficult to develop an shRNA that only selectively inhibits the mutant allele but 2) because we need to replace the function of that activity, we utilized a codon optimized form of the PABPN1 gene to be able to essentially restore function. What we like to call a silence, as represented by the shRNA, and replace based approach to be able to do this. In terms of therapeutic vectors, the Benitec technology is one of the few technologies that have the ability to do this within a single vector. That's because the RNAi machinery is already present within the cells ready to understand how to utilize those shRNAs and silence a gene and often times there's packaging capacity leftover to express a protein, in this case the codon optimized PABPN1 to restore function.

So how does gene therapy work in general is shown on the next slide in slide 28 where we have a virus particle which is typical comprised of a protein shell. The protein shell dictates which tissues that construct is delivered to. Typically, viruses have nucleic acids which help reproduce the virus. So, in gene therapy, and particularly how we do it with BB-301, we use methods to produce virus proteins without producing the viral genes inside. Instead we eliminate those virus genes and we design genetic sequences that get inserted into that protein shell that contain that BB-301 cassette that we discussed on the last slide. A manufacturing process is used to insert the BB-301 genes into the protein shell. And once

completed, BB-301 is intended to be injected directly into the muscles impacted in the dysphagia processes. Specifically, we're talking about the cricopharyngeus muscle. Once BB-301 enters into those muscle cells its starts producing the genes and genetic material that may help alleviate some of these symptoms. To utilize the vector, the specific viral vector, we are using a vector called adeno associated virus in which we strip out the virus genes and put in BB-301. Some of the specifics with AAV is that largely it is non-integrating a non-pathogenic virus in terms of delivery. To date it has been used in over 200 clinical trials and we know through several clinical studies, as well as multitudes of preclinical data, that you can have sustained expression for years following a single injection and potentially up to the lifetime of the patient.

So how do we test these types of vectors? How do we ensure that, at least from a preclinical sense, that these vectors will have activity? In slide 29, this really dictates the animal model that we use to test BB-301. It's a mouse model called the A17 mouse. Just as the expanded, or alanine expanded PABPN1 gene causes disease in human beings, we knock in a copy of bovine PABPN1 in which multiple alanines have been expanded into the protein. We set that up in the system with what's called a transgenic mouse. When it does this, and when produce the offspring of these mice they mimic many of the disease pathologies associated with OPMD including severe muscle atrophy. So below I will show a few types of data that i will be looking at as we go through this section. On the far left you see intranuclear inclusions. In normal muscle tissue you typically don't have these clusters of protein that form these clumps. In the A17 model, you can see these green stained punctate bodies which are indicative of these protein clumps. As I told you before, often there's fibrosis associated with OPMD and in the A17 mouse we see a reproduction of the enhanced fibrosis on that bottom panel as compared to the normal animal on top. Because OPMD is a disease of muscle force one of the key parameters for us to look at is the ability, or how much force each of these muscles can exert before and after treatment with BB-301. And what you can see in this panel is that the A17 diseased mouse has significantly less muscle force over the frequencies tested in this stimulation model versus the red line which represents the normal animals. And lastly, because we all know that when you don't use your muscles they tend to shrink, so assessing muscle weight or atrophy is a key parameter as well. You can see that in the last panel on the right that the A17 mouse has significantly reduced muscle weight, relative to overall body weight, versus the normal mouse.

So how are we going to deliver BB-301 in a clinical setting? We're going to do this by direct intramuscular injection. And the question is by whether or not by injecting AAV-based vectors can it transduce, or can it treat the muscles, that we are injecting into? In slide 30 what we've done is we've inserted a gene called the green fluorescent protein into the AAV9-based vector that we are utilizing for BB-301. And as you can see in the bottom of the left-hand panel that when we inject this vector into the leg, or TA muscles, of the mice you have this bright fluorescence glowing indicative that we've been able to treat these muscles. On the right-hand side of the panel is a mouse that has been injected for over a year with this GFP contain protein. You can see that even after a year, the muscles are still quite bright, quite green, and when you look specifically at a cellular level or at muscle level you can see that most, if not all, of those muscle fibers have been treated. So the real question is that how do we know that it is efficacious?

Slide 34 gives you an idea of how we've tested this. Previously we've shown some data in which have had a single vector system of BB-301 introduced at two doses. In the newest experiment, we broadened out significantly the range of doses across the entire group of animals that we were working with. The idea is to get an idea if there is a dose response in relation to how much of the BB-301 compound we introduce. And so the range is significantly broader ranging from 4e8 vector genomes per muscle up to roughly 3 logs higher at 7.5 e11 vector genomes per muscle. Each of the animals were dosed in each leg and so out of a total of five animals, we're looking at roughly 10 muscles, and these were animals that already had the OPMD effect established with in them. We're not necessarily preventing OPMD and its phenotypes,

we're correcting OPMD and its phenotypes. The endpoint parameters were monitored over 14 weeks and we looked at some of the parameters that we mentioned previously.

So in slide 32 we look at levels of shRNA produced from BB-301. Starting at the lowest doses at the far right, we can see that at 4e8, really there's not a significant level of shRNAS that is being produced from that level of dose. Yet when we go to the next highest dose, at 2e9 vector genomes per muscle we're now producing on the order of roughly 2500 copies of each of the shRNAs. By the time we go to the next two doses we're now producing shRNAs in the tens of thousands and by the time we get to the 2.5e11 vector genome muscle group we're now producing hundreds of thousands of copies of these therapeutic RNAs per cell. Finally, at the top level we're producing millions of copies of each of the shRNA. So very clearly as we increase the dose we have the ability to increase the potential therapeutic capacity by simply increasing the number of shRNAs.

On slide 33, we look at the impact of those shRNAs on PABPN1 expression in those muscles. And again, at the lowest doses, you're really not having a significant impact at inhibiting that mutant PABPN1. But certainly as we increase the dose, moving from right to left, by the time that we get to 2.5e11 and 7.5e11 vector genomes per muscle we're now having 75% inhibition and 86% inhibition of mutant PABPN1 respectively. That next question is what happens to the levels of codon optimized protein expression.

In slide 34, we see measurement of codon optimized PABPN1 expression, the replacement protein. Again at the lowest dosing levels we're not seeing significant levels of PABPN1 expression occurring, but certainly the mid-range doses of 1e10 and 5e10 vector genomes per muscle we start producing the protein after 14 weeks. Certainly, at the two highest doses we're now replacing the normal levels of the protein by 26 and 63% respectively. And again, to be clear, this is a single vector silence and replace based system. We silence the bad causing genes and we essentially replace them with healthy normal copies.

On slide 35 we're going to look at intranuclear inclusions, those green spots that we talked about a couple of slides back. On the bottom, you can see again the A17 mouse versus the wildtype saline mouse: in the diseased model you see these punctate bodies. As you now dose the animal, starting at the lowest doses, and as the boxes pop-up, we're going to higher doses. You can see a significant and drastic reduction in the amount of punctate bodies. So the key thing in here is this is not only disease halting, this is reversing the course of the disease. So, the preclinical evidence that we have is that this is a disease modifying type of compound that's being applied in this therapeutic situation. And on the left-hand side of the slide, you can see a graphical representation of the same data from those slides on the right. You can see that as the A17 mice, which have roughly 35% of the cells that have these green punctate bodies that certainly by the time you get to 2.5e11 or 7.5e11 we have all but abrogated the production of these intranuclear inclusions.

On slide 36, we see that measurement of muscle forces associated with the A17 model. Again, just to be clear, OPMD is a disease in which muscle function is negatively impacted, specifically on muscle force. On this first panel to the left you can see that black line, these are the A17 mouse, versus the red line which are the wildtype or FVB mouse. As we have introduced low doses into these animals at 4e8, 2e9 or 1e10 vector genomes per muscle group, we see a slight modification and a slight improvement in muscle force, but nothing really significant as of yet. When we move to a dose of 5e10 vector genomes per muscle, you can now see a restoration of muscle force. Approximately regaining half of the specific muscle force. And now at the two highest doses administered to these animals you can see that we are now near wildtype levels. So we have essentially have restored muscle strength. (CLICK). When you compare this against the indexes for silence and replacing these proteins, you can see that doses of 5e10 or higher have levels that extend anywhere from 31% inhibition up to 86% inhibition. Really minimal levels of codon optimized expression start reversing that phenotype. What this suggests to us, at least in this preclinical setting, is that there is a potential for a broad therapeutic range of BB-301 that when applied to these muscles may have an impact on being able to correct this mutant disease phenotype.

On slide 40, we just looked specifically at, on the right-hand side, of this panel whether or not, by restoring muscle function if we also restore muscle weight. Again, if you don't use your muscles they tend to shrink and the overall weight of those muscles goes down. So the left hand side of the panel is the exact same graph from the last panel that we saw. We can see that the brown, purple and light blue groups correlate with minimal increases in muscle function and likewise in muscle weight in the right-hand graph, we see that there's a slight increase over the A17 background. But as we move into doses of 5e10 and higher, you can now see that the corresponding muscle force that we see on the left-hand side of this panel corresponds with the restoration of muscle weight. Again, this is a really great confirmatory set of data that suggests that by restoring muscle function, you're essentially reversing the phenotype and really trying to reset the muscle back to a wildtype condition.

So how quickly does this process occur? So what we see on the left hand side of the panel in slide 37 is that two doses of BB-301 going into these animals. Again, the black line are the diseased animals and the red line represents the wildtype mouse. The green and blue lines show slight improvement by week 14 post a single administration. And we look at week 20, on the right-hand side of the panel, and you can see that those two lines move closer to the wildtype level. So again, it's not an instantaneous effect but it occurs over several weeks as BB-301 has the ability to restore function to these muscles. (CLICK) And ultimately when you look at the levels of inhibition and wildtype expression, you can see at the highest dose we now have essentially silenced 88% of the mutant PABPN1 gene and at the same 20 week timepoint we've restored it by 91%. So we've knocked out 90% of the bad and have replaced it with 90% of good, healthy, normal gene expression. So where are we going with this program and what are the next steps?

As Georgina will discuss shortly, we have had several interactions with regulatory agencies and really the next step in any clinical development pathway is to show safety of these compounds before you initiate a human clinical trial. We have decided to perform our safety studies in sheep. The reason we decided to do this is the animals are approximately the same weight and the muscles being injected into are approximately the same size as human beings. And so on the top left panel is an idea of one of these sheep. On the top right panel is an image of the cricopharyngeus muscle as taken by an endoscopy examination of one of these animals. The white dotted line is now circling specifically the cricopharyngeus muscle. It is a very well-defined structure that we will be able to dose. And finally on the bottom of this slide shows you the endoscopy based instrument that helps guide the surgeon to be able to direct the injection of BB-301 directly into those muscles.

Lastly, to support any human clinical study and through towards any clinical development pathway, you need to have the ability to produce the drug. And on slide 39 we talk about the scalable manufacturing process for BB-301. For BB-301 specifically, we produce this material in a baculovirus based methodology system that allows this process to be very scalable. You can produce materials anywhere from as little as 30 milliliters up to several hundred or a 1,000 liters ultimately. By having a scalable procedure allows you to control the cost of goods ultimately and how much of the material you can produce in a cost-efficient manner. We are using a modified AAV9 based capsid for the generation of highly active BB-301 particles. We already have yields that are in excess of 1e14 vector genomes per liter which is excellent for this type of process. The recovery yields in the final product range from 30 to 40%. We are producing the GMP clinical grade material at a leading contract manufacturing organization. We've actually already produced this material very efficiently at a 50 liter scale and over the summer we'll be producing the specific clinical product at the 250 liter scale. So I hope that gives you a little bit of an overview of the advances that we've made in the science and i will now turn it back over to Georgina Kilfoil to describe the clinical aspects of this compound.

[Georgina Kilfoil]

Thank you, David,

Any drug development process must proceed through several stages in order to produce a product that is safe, efficacious, and has passed all regulatory requirements. Here we look back at where BB-301 has come from and its path moving forward to the clinic.

Once a target has been discovered, in this case the PABPN1 gene, early preclinical work focuses on looking primarily at efficacy, that is whether it works both in vitro and vivo. In the case of BB-301, initial work was done with a dual vector. This is where the 'silence' and 'replace' are given at the same time but as separate components. Based on the results seen, Benitec focused efforts on developing BB-301 which is the current single vector that David described. This single vector greatly simplifies the manufacturing and regulatory process for future development.

Manufacturing process development work is conducted in parallel to these preclinical studies. This is to ensure a process is developed to make BB-301 that is reproducible and scalable.

Once we have a product that is efficacious in an animal model and we have the basis of a manufacturing process, we then move into what we call IND-enabling work.

It is important, especially for gene therapy products and for a novel silence and replace approach, that these IND-enabling studies are discussed and agreed with the regulatory agencies. This improves the likelihood that BB-301 will pass all the regulatory requirements to enter the clinic. With this in mind we met and discussed our plans for BB-301 with the regulatory agencies in key OPMD countries such as the US, Canada and France.

There are three main parts to the IND-enabling work

- Firstly, the definitive toxicology studies that establish the safety characteristics of BB-301. Here the FDA or other regulatory agencies want to understand the safety signals seen from doses that are higher than the expected clinical dose. The first of these studies is underway for BB-301.
- Secondly, the scale up of manufacturing to provide material to support the toxicology studies (GLP manufacturing) and material that will be used in the clinic (GMP manufacturing). GLP manufacturing for BB-301 has been completed at a 50L scale and we are now moving into the GMP manufacturing at a 250L which will produce enough high-quality material to support the first clinical study.
- Lastly, is the development of the clinical protocol. For BB-301 we have spent much of the last 6-9 months working closely with Key Opinion Leaders to design the first clinical study. These are individuals that either treat patients with OPMD or are experts in understanding swallowing function.

We feel we are well positioned now to progress BB-301 into the clinic. The pathway has been set and it is now just the time it takes to complete the required toxicology and manufacturing work to support a high quality regulatory filing.

I would like to provide you with a brief overview of the planned Phase 1/2A study with BB-301. Because BB-301 is a gene therapy, the first clinical study is in patients which means that, while the primary goal of the study is safety and tolerability, we can also look for signs of clinical activity.

Keep in mind that as you view this, it reflects our current thinking and it is possible that the design may change. We are meeting with our KOLs in person this week to discuss and further define the study design. In addition, the study design parameters are subject to change based on nonclinical toxicology results and regulatory feedback.

As currently written, the study will be in patients clinically and genetically diagnosed with OPMD who have an impairment in swallowing function. Patients will receive a single intramuscular dose of BB-301 into the cricopharyngeal muscle in the throat.

This clinical protocol is designed as a dose escalation study so we enroll patients at increasing doses with a time period between each cohort to ensure it is safe before we proceed to the next dose. Once we reach the top dose or define a dose that is the maximally effective dose we will enroll an additional number of patients.

All patients will be followed for a year on this study. The primary endpoint is safety and tolerability. However, because these are patients, we will also be looking at quantitative clinical improvement in swallowing as well as patient reported improvements in swallowing and quality of life.

Slide 42 – Potential for Early Adoption

So as described in the slides above, we have a clear unmet medical need and a therapeutic in BB-301 which has the potential from a single intramuscular administration to restore muscle strength and improve the symptoms of dysphagia.

This would support the potential for early adoption and high market penetration of BB-301 if it is approved.

Additional factors that may well contribute to the potential market are:

- Possible orphan drug exclusivity under the orphan drug designation we have in both the US and EU
- An increasing diagnosis of OPMD due to the aging population and an increased awareness of OPMD – this includes education of patients with confirmed genetic diagnosis to communicate the risks associated with children also being at risk for this heritable disease.
- Life cycle expansion opportunities for BB-301 that we can consider once we have initial signs of clinical proof of concept. These include expansion of the IM administration into the earlier stages of dysphagia before tissue damage has been detected, the potential for developing a formulation of BB-301 that can be given systemically so it treats the proximal muscle weakness and ptosis as well as the dysphagia and finally the use of BB-301 as a prophylactic for preventing the symptoms of OPMD.

I will now pass back to Greg

[Greg West]

Thank you, Georgina,

As you can see today, we are well advanced from a scientific and clinical perspective to achieve our plan to be in the clinic early 2019 in our OPMD program

Benitec's long-term objective is to become the leader in discovering, developing, clinically validating and commercialising ddRNAi-based therapeutics for a range of human diseases with high unmet clinical need and, as a result, provide a better life for patients with these diseases.

We believe that the initiation of our clinical studies will be the major catalyst for value creation in 2018 and 2019. These milestones speak to our strategy of becoming a multi-product, clinical-stage company and represent an opportunity for significant shareholder value.

Thank you

I will now hand over to Jay for questions

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.