Benitec Biopharma Overview

September 2021

Safe Harbor Statement

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Gene Silencing: *A Validated Approach to the Treatment of Some Genetic Diseases*

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- Mutation of a single gene can cause a chronic disease via the resulting intracellular production of a disease-causing protein (i.e. an abnormal form of the protein of interest)

- Genetic disorders of this type can often be treated exclusively by "silencing" the intracellular production of the disease-causing protein through well-validated biological approaches like RNA interference ("RNAi")

  – RNAi employs small nucleic acid molecules to activate an intracellular enzyme complex, and this biological pathway temporarily reduces the production of the disease-causing protein

  – In the absence of the disease-causing protein, normal cellular function is restored, and the chronic disease improves or resolves

- However, many genetic disorders are not amenable to gene silencing approaches, as the diseased cells produce a mixture of the normal protein of interest and the disease-causing variant of the protein, and the underlying genetic mutation does not allow for selective targeting of the disease-causing variant

  – Under these conditions, it is impossible to exclusively silence the disease-causing protein without simultaneously silencing the normal intracellular protein of interest whose presence is vital to normal cellular functions

"Silence and Replace": *Permanent Gene Silencing and Tissue-Specific Restoration of Biological Function*

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- Our proprietary DNA-directed RNA interference (ddRNAi) platform combines RNAi with classical AAV-based gene therapy

- Via the ddRNAi platform Benitec creates genetic medicines that, following a single administration, will enable target tissues to perpetually produce siRNA molecules which facilitate the sustained silencing of disease-causing genes

- Importantly, the ddRNAi platform also allows for concomitant delivery of wild type replacement genes, and these distinct genetic elements work in concert to silence the expression of disease-causing mutant genes and to simultaneously replace the mutant genes with normal (wild type) genes to restore the natural underlying physiology of the diseased tissues

- BB-301, the most advanced genetic medicine currently under development by Benitec, employs this "Silence and Replace" approach for the treatment of Oculopharyngeal Muscular Dystrophy (OPMD)

Platform Enables Gene Therapy and Permanent Gene Silencing: *DNA-Directed RNA Interference (ddRNAi)*

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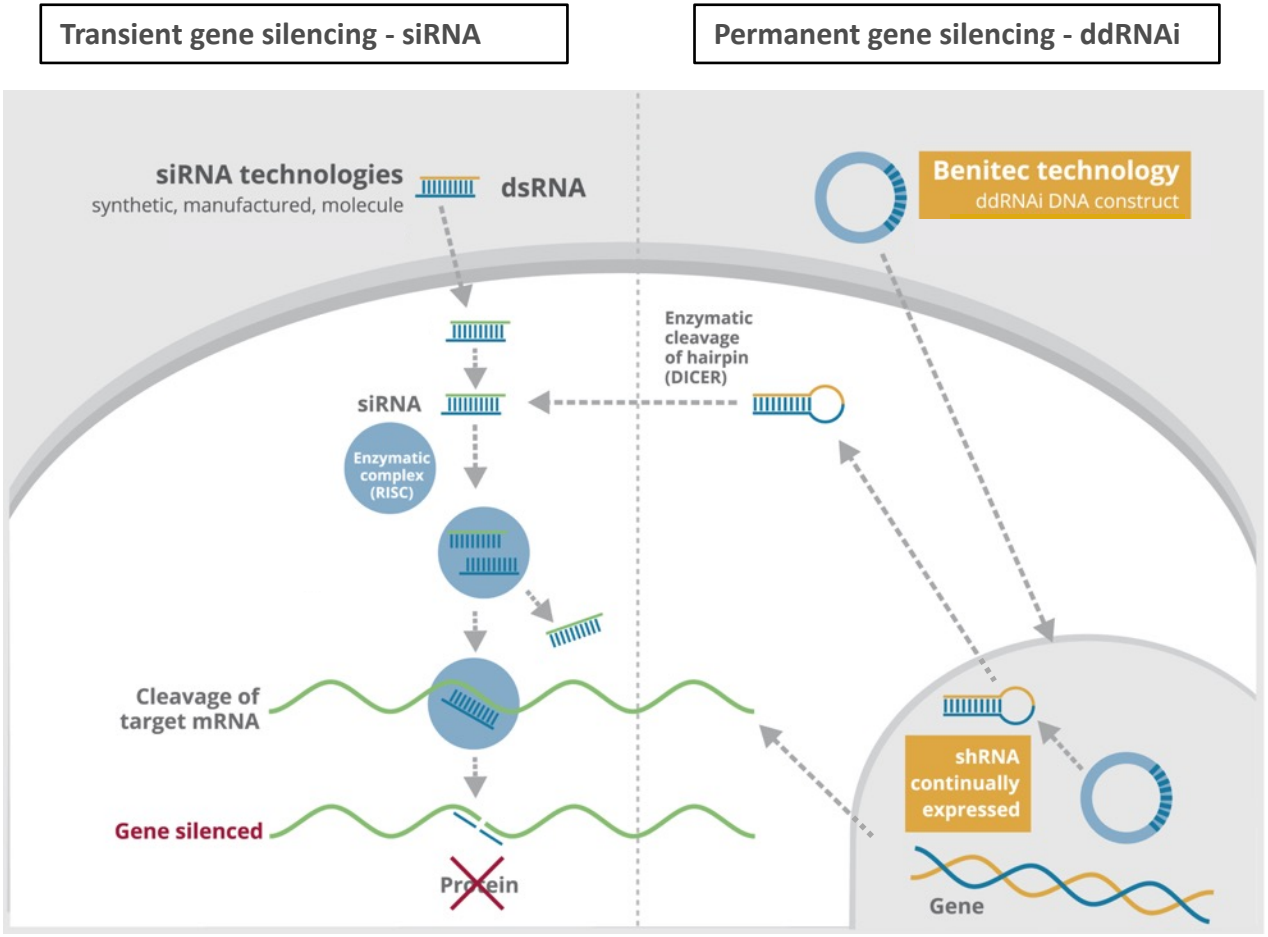
- Combines RNA interference with gene therapy delivery
- Long-term therapeutic potential from a single administration
- Constant, steady-state levels of shRNA expression
- Silence a single gene or target multiple genes simultaneously
- Simultaneous silencing of disease-causing genes and co-expression of normal genes to restore biological function



Executive Team : *Expertise in Gene Therapy Development, Biological Manufacturing and Capital Allocation*

- **Jerel Banks, M.D., Ph.D.**
  - ***CEO and Executive Chairman***
  - Healthcare investment professional with over 15 years of experience
  - Former vice president and co-portfolio manager at Franklin Templeton Investments
  - M.D. and Ph.D. from Brown University, and A.B. in Chemistry from Princeton University
- **Megan Boston**
  - ***Executive Director***
  - CEO and Managing Director of ASX listed entities
  - Chartered Accountant with over 20 years of experience
  - Held senior executive roles at various banking institutions in the area of risk and compliance, as well as PricewaterhouseCoopers
- **Claudia Kloth, Ph.D.**
  - ***SVP of Manufacturing***
  - Over 20 years of cGMP manufacturing and process development experience in therapeutics
  - Led Process Development group at Lonza Viral Therapeutics
  - Developed, optimized and transferred robust viral-based products (Ad5, AAV, lentivirus) to cGMP manufacturing
  - Guided process transfer and process validation activities of Yervoy (Bristol-Myers Squibb)
- **Peter Roelvink, D.Sc.Ag.**
  - ***Senior Director Research***
  - First to demonstrate delivery of a targeted vector from its native receptor to an artificial receptor
  - Co-inventor on 19 issued US patents that cover RNAi vectors, targeted delivery of adenoviruses, and tissue specific expression using AAV

Pipeline: *Oculopharyngeal Muscular Dystrophy (OPMD) and Chronic Hepatitis B Virus Infection*

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Program	Delivery	Discovery	Preclinical	IND-Enabling	Early stage clinical (IND – Phase 2)	Late stage clinical (Phase 2 – Phase 3)	Commercial Rights
Proprietary Pipeline Assets with Peer-Reviewed Proof-of-Concept							
OPMD **BB-301**	ddRNAi Intramuscular	→	→	→			*Global*
HBV **BB-103**	ddRNAi Systemic	→	→				*Global*

Broad Intellectual Property Portfolio

- **OPMD-related intellectual property:**
  - OPMD Family 4 anticipated expiry February 2040
  - OPMD Family 3 anticipated expiry October 2039
  - OPMD Family 2 anticipated expiry December 2037
  - OPMD Family 1 anticipated expiry April 2037

- **HBV-related intellectual property:**
  - HBV Family 3 anticipated expiry May 2037
  - HBV Family 2 anticipated expiry May 2036

- **AAV-related intellectual property:**
  - AAV Family 1 anticipated expiry August 2038

BB-301 for Oculopharyngeal Muscular Dystrophy

- *LATE-STAGE NON-CLINICAL ASSET WITH CATEGORY-LEADING BIOLOGICAL EFFICACY*
- *GLOBAL PREVALENCE OF OPMD EXCEEDS 15,000 PATIENTS AND COMMERCIAL OPPORTUNITY EXCEEDS $1 BILLION OVER THE LIFE OF THE PRODUCT*

Oculopharyngeal Muscular Dystrophy
Lead Candidate BB-301: *Product Overview*

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Oculopharyngeal Muscular Dystrophy

- Rare, autosomal dominant, monogenic disease
- Estimated prevalence of 15,000 patients in Western countries
- Characterized by eyelid drooping, swallowing difficulties, proximal limb weakness, death due to aspiration pneumonia and malnutrition

BB-301 Product Profile/Milestones

- Designed to treat dysphagia associated with OPMD
- 'Silence and Replace' represents a unique gene therapy mechanism
- 'Silence': Inhibits mutant and wildtype PABPN1 gene expression
- 'Replace': Simultaneously reintroduces normal PABPN1 gene to restore function
- Clinical trial to begin enrollment over the next 12 months

Value / Commercial Opportunity

- Orphan Drug Designation received in the US and EU provides commercial exclusivity and expeditious development path
- Large-scale manufacturing process has been optimized and reproducibly executed
- Commercial opportunity in excess of $1 billion over the life of the product

OPMD: *Disease Overview*

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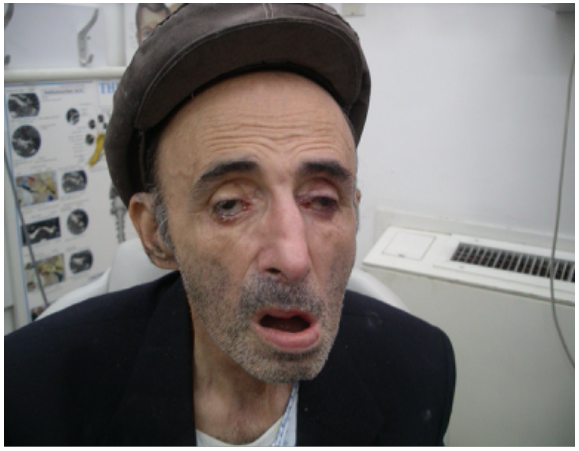
Patterns of Inheritance, Epidemiology, and Age of Onset:

- Rare autosomal dominant inheritance
- Prevalence of 1:100,000 (Europe)
- Prevalence as high as 1:600 in specific populations
- Typical age of onset is 40 years old-to-60 years old

Natural History:

- Progressive eyelid drooping (ptosis)
- Progressive swallowing difficulties (dysphagia)
- Proximal limb weakness
- Chronic choking, regurgitation, aspiration pneumonia
- Death due to aspiration pneumonia and malnutrition



Histopathology:

- Loss of muscle fibers in affected anatomical regions
- Variations in the size of muscle fibers
- Fibrosis (connective tissue)

Genetic Basis of OPMD: *Expansion of the Poly-Alanine Tract Within PABPN1*

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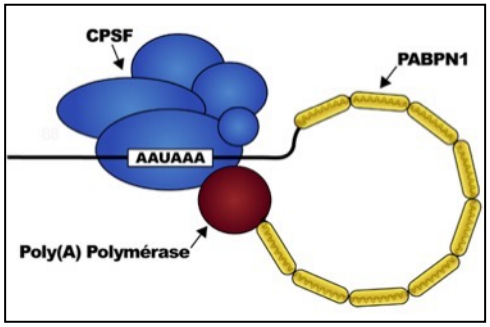
PABPN1:

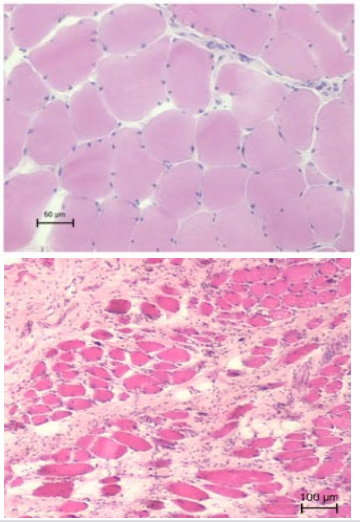
- Ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor) and, thus, controls the length of mRNA poly(A) tails, mRNA export from the nucleus, and alternative poly(A) site usage



In OPMD:

- Genetic mutation results in trinucleotide repeat expansion within exon 1 of PABPN1 and results in an expanded poly-alanine tract at the N-terminal end of PABPN1
- Mutation generates a protein with an N-terminal expanded poly-alanine tract of up to 18 contiguous alanine residues prone to form aggregates called intranuclear inclusions (INIs)
- INIs that also sequester wild type PABPN1 could contribute to the "loss of function" phenotype associated with OPMD

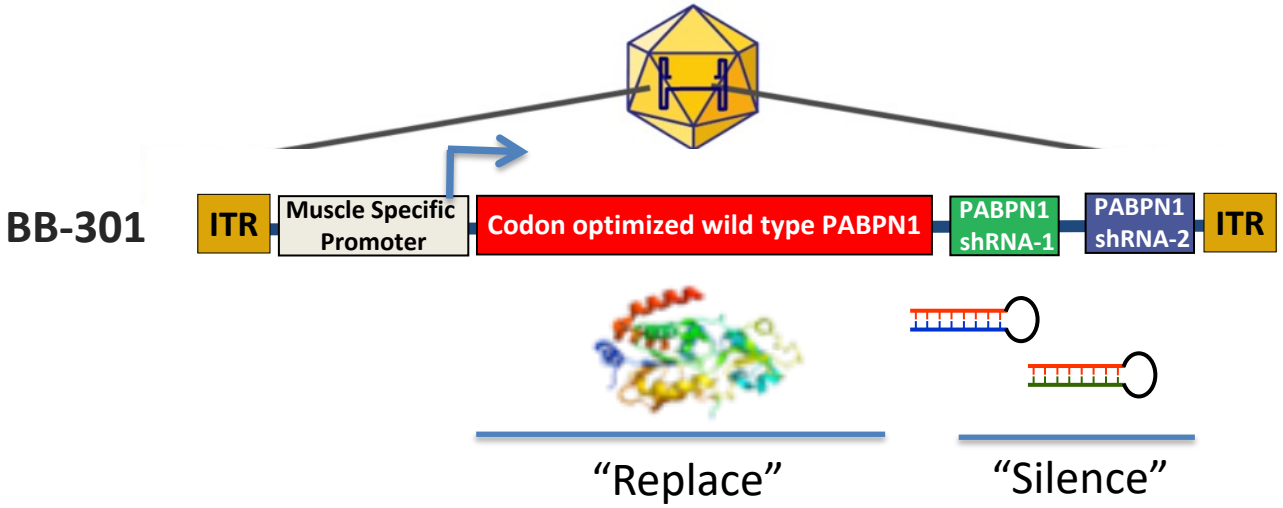
WT ATG $(GCG)_6$ ----------$(GCA)_3$ GCG GGG GCT GCG..
MUT ATG $(GCG)_6$ $(GCG)_{1\text{-}7}$ $(GCA)_3$ GCG GGG GCT GCG…--



Non-affected

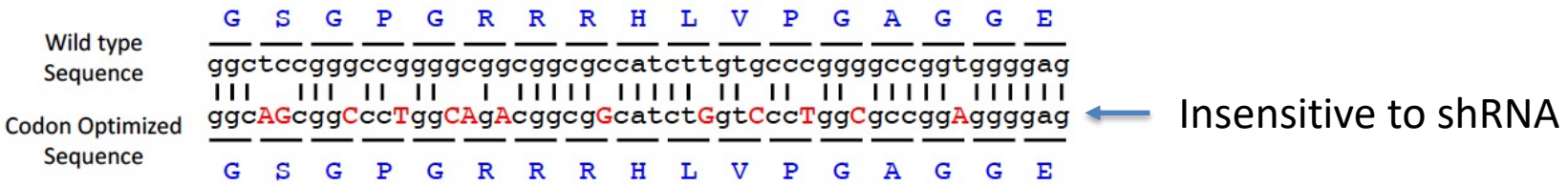
Affected

BB-301: *Single-Vector "Silence and Replace" Approach*

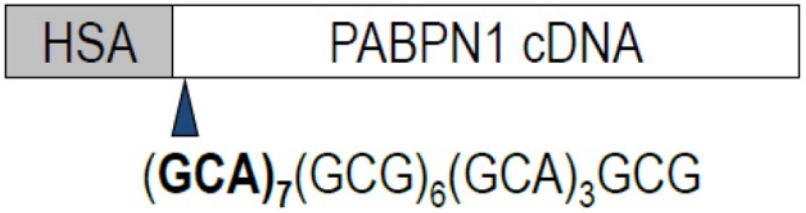


AAV

- Non-integrating, non-pathogenic viral delivery
- To date, AAV has been used in almost 200 clinical trials
- Sustained expression (years) following single injection



Summary of Non-Clinical Results in The "A17" Mouse



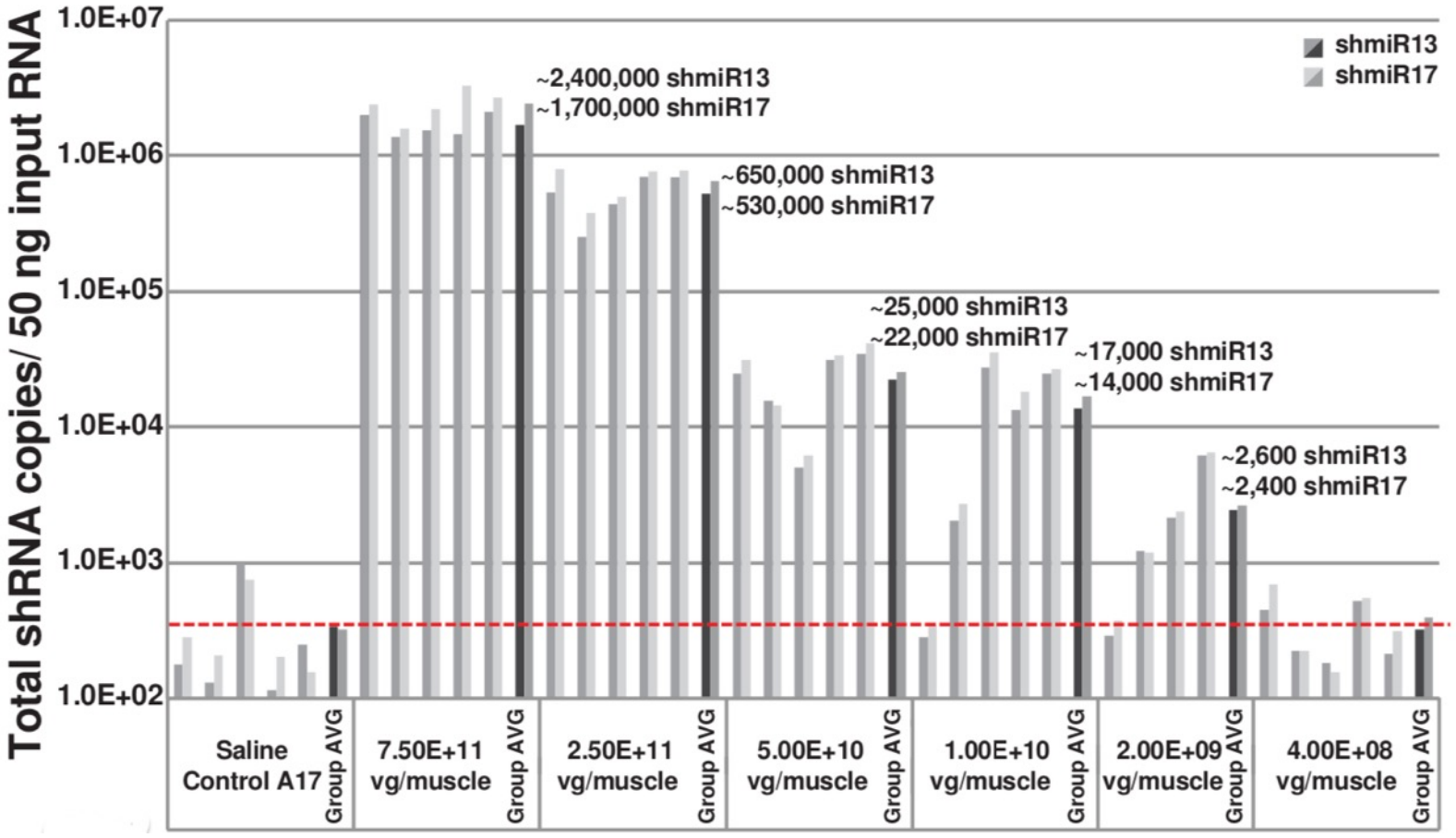
- Multiple A17 animal cohorts received single doses of BB-301 (over a range of doses spanning $4x10^8$ vg/muscle-to-$7.5x10^{11}$ vg/muscle) and, following BB-301 administration, each cohort was observed for 14-weeks

- BB-301 was injected into the Tibialis Anterior (TA) muscle of 10 week old-to-12 week old animals, and 14-weeks post administration each A17 cohort was anesthetized and the contractile properties of the injected TA muscles were analyzed via in-situ muscle electrophysiology

- Intermediate doses of BB-301 resulted in 75% silencing of PABPN1 and 26% replacement of wild type PABPN1 activity, leading to full restoration of muscle strength, clearance of INIs, and a reduction of fibrosis

- An additional experiment conducted over the course of 20-weeks demonstrated that more modest doses of BB-301 (which supported only partial resolution of the disease phenotype at week-14) were able to facilitate significant benefit at 20-weeks, as evidenced by full restoration of all parameters relating to muscle strength, weight and INI formation

BB-301 Drove Dose-Dependent shRNA Expression (Analysis Performed 14-weeks after Administration)



BB-301 Inhibits PABPN1 Expression and Restores Near Wild Type Levels of coPABPN1 (Analysis Performed 14-weeks after Administration)

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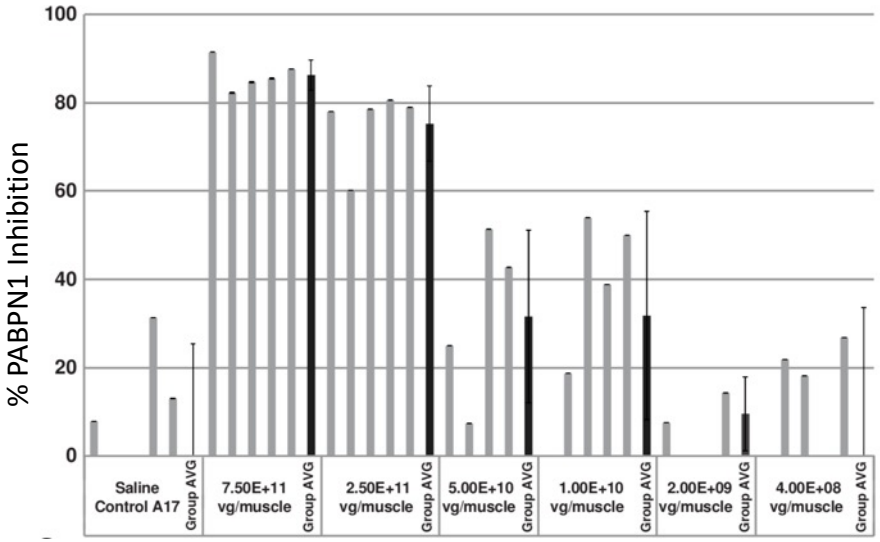
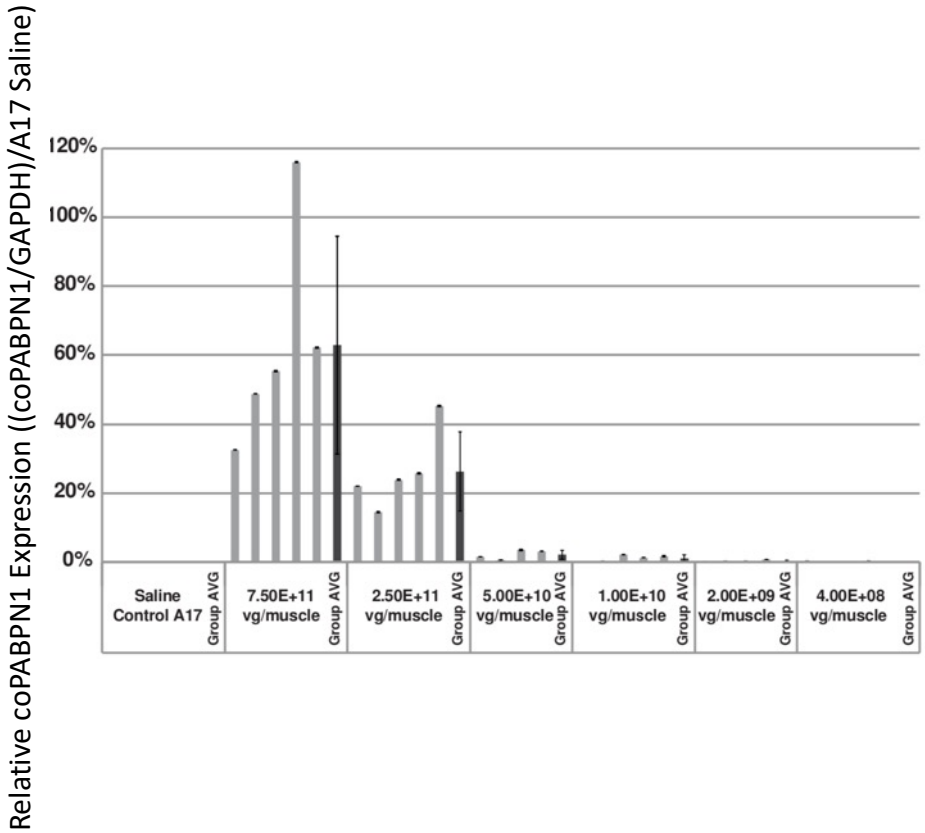
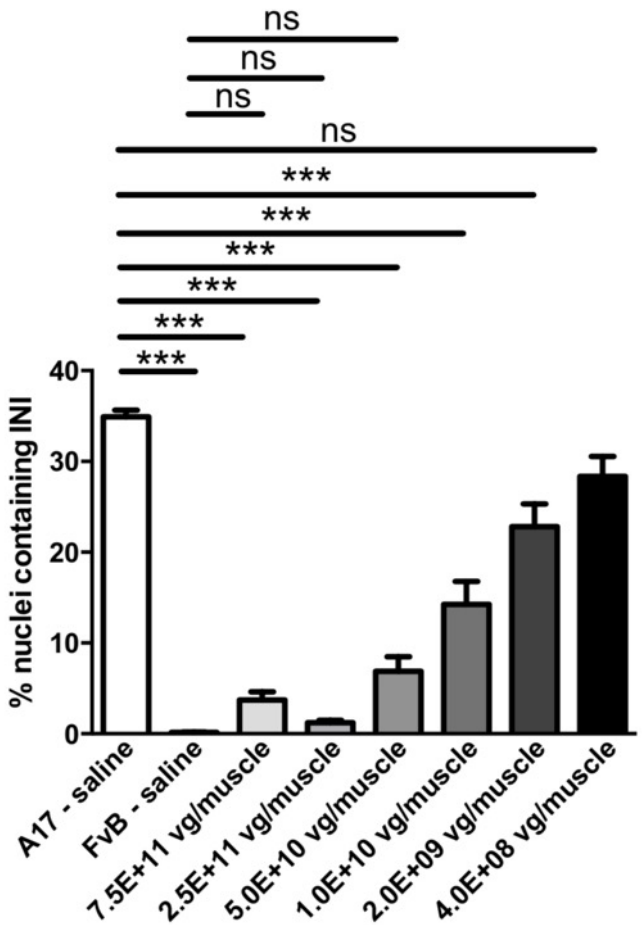




BB-301 Drives Dose-Dependent Resolution of Intranuclear Inclusions in the Injected Muscles



BB-301 Restores Muscle Force to Wild Type Levels (Analysis Performed 14-weeks after Administration)

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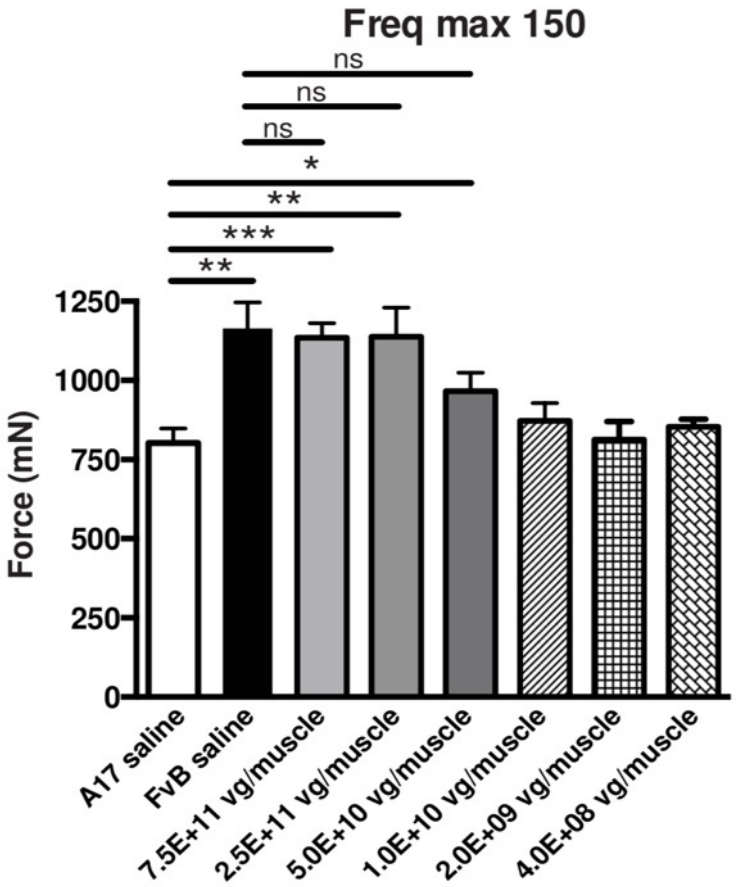

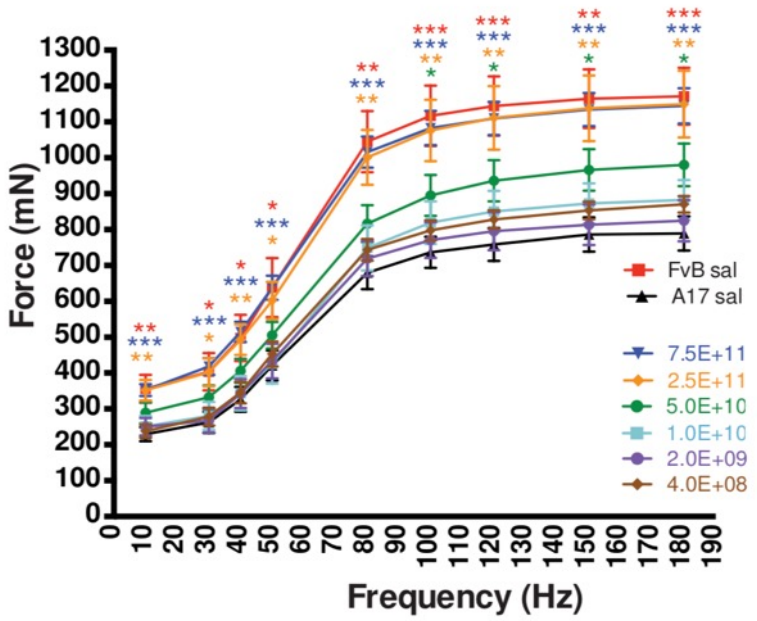

Restoration of muscle strength was assessed by muscle contractility measurements in response to a series of induced impulses that ranged from 10 to 180 Hz

BB-301 Drives Robust Phenotypic Rescue over a Broad Range of Doses

- Early signs of muscle strength restoration were observed at the $5x10^{10}$ vg/muscle dose which reduced PABPN1 expression by 31% and supported replacement of wildtype protein at 2% of normal levels
- Statistically significant improvements in muscle strength (vs. saline-injected animals) and complete phenotypic correction were observed at the $2.5x10^{11}$ vg/muscle dose which reduced PABPN1 expression by 75% and supported replacement of wildtype protein at 26% of normal levels
- These data demonstrate that varying levels of inhibition of PABPN1 expression, when coupled with partial replacement of wildtype PABPN1, are sufficient to significantly reduce INIs, increase muscle function, and correct the disease phenotype (potentially supporting biological efficacy over a broad range of doses)

	"Silence"	"Replace"
BB-301 Dose (vg)	Inhibition PABPN1	coPABPN1 Expression
7.50E+11	86%	63%
2.50E+11	75%	26%
5.00E+10	31%	2%
1.00E+10	32%	1%
2.00E+09	14%	0%
4.00E+08	0%	0%

CTA-Enabling and IND-Enabling Studies for BB-301 to be Completed Over the Next Twelve Months

- Benitec previously disclosed key data-points related to the non-clinical studies for BB-301 that were anticipated to support the filing of Clinical Trial Applications (CTA) in Europe and in Canada and, similarly, to facilitate the filing of an Investigational New Drug (IND) Application in the United States
  - In addition to the non-clinical proof-of-concept studies carried out in murine models of OPMD (Strings-Ufombah, V., et al., Molecular Therapy: Nucleic Acids, 2021; Malerba, A., et al. Nature Communications, 2017), Benitec recently completed a BB-301 Pilot Dosing Study in large animals (see Beagle dog study description below)
- **8-week Pilot Dosing study in Beagle dogs to confirm the transduction efficiency of BB-301 following direct intramuscular injection into the pharyngeal muscles via the use of an open surgical approach (*Beagle dog dosing has been completed in this study, and tissue analyses are currently ongoing*)**
  - Direct injection of BB-301 into the tibialis anterior muscle of A17 mice achieved robust transduction of the targeted skeletal muscle cells
  - This Pilot Dosing tudy in Beagle dogs is being conducted to optimize the proprietary dosing and surgical administration procedures for BB-301 injection into the pharyngeal muscle tissues that underlie the morbidity and mortality of OPMD and to refine the core analytical methods employed following the completion of dosing
- 12-week GLP Toxicology and Biodistribution study in Beagle dogs (***initiated during the first half of 2021***)

8-Week BB-301 Pilot Dosing Study in Beagle Dogs: *Study Rationale and Background*

- BB-301 is directly injected into the pharyngeal muscles known to underlie the morbidity and mortality characterizing the natural history of OPMD, and large animals (e.g. canine subjects) possess anatomical architecture in the pharyngeal region similar to that of Human subjects with OPMD and were, therefore, identified by global regulatory agencies and our key collaborators as ideal subjects for the IND-enabling studies

- Against this backdrop, the BB-301 Pilot Dosing Study in Beagle dogs was conducted to demonstrate that direct intramuscular injection of BB-301 via the use of a proprietary dosing device in an open surgical procedure could safely achieve the following goals:

  - **Biologically significant, dose-dependent levels of BB-301 tissue transduction (i.e. delivery of the multi-functional genetic construct into the target pharyngeal muscle cells)**

  - **Broad-based, dose-dependent expression within the pharyngeal muscle cells of the three distinct genes comprising the BB-301 gene construct (i.e. siRNA13, siRNA17, and codon optimized PABPN1)**

  - **Biologically significant levels of target gene knock-down (i.e. inhibition of the expression of the gene of interest) within the pharyngeal muscle cells**

8-Week BB-301 Pilot Dosing Study in Beagle Dogs: *Study Design and Background*

- The 8-week Pilot Dosing Study evaluated the safety and biological activity of two concentrations of BB-301 (1.0+E13 vg/mL and 3.0+E13 vg/mL) across three distinct doses (1.0+E13 vg/mL, 3.0+E13 vg/mL with a low injection volume, and 3.0+E13 vg/mL with a high injection volume) following direct intramuscular injection into the Hypopharyngeus (HP) muscles and the Thyropharyngeus (TP) muscles of Beagle dogs via the use of a proprietary dosing procedure
  - **The HP muscle in Beagle dogs corresponds to the Middle Pharyngeal Constrictor muscle in Human subjects, and the TP muscle in Beagle dogs corresponds to the Inferior Pharyngeal Constrictor muscle in Human subjects**
- BB-301 was injected only on Day 1 of the Pilot Dosing Study, and the corresponding canine pharyngeal muscles were harvested for analysis after 8-weeks of study subject follow-up
- BB-301 dosing was carried out by both a veterinary surgeon and a practicing Otolaryngologist who has extensive experience with the provision of palliative surgical care for OPMD patients
- Data analyses are ongoing for the canine subjects treated in the BB-301 Pilot Dosing Study, and the interim data-points highlighted in this presentation are derived from the completed analyses to date for the pharyngeal muscle tissues isolated from 16 Beagle dog subjects (of the 24-subject study population)

Interim Results for the Pilot Dosing Study: *Summary of the Key Observations to Date*

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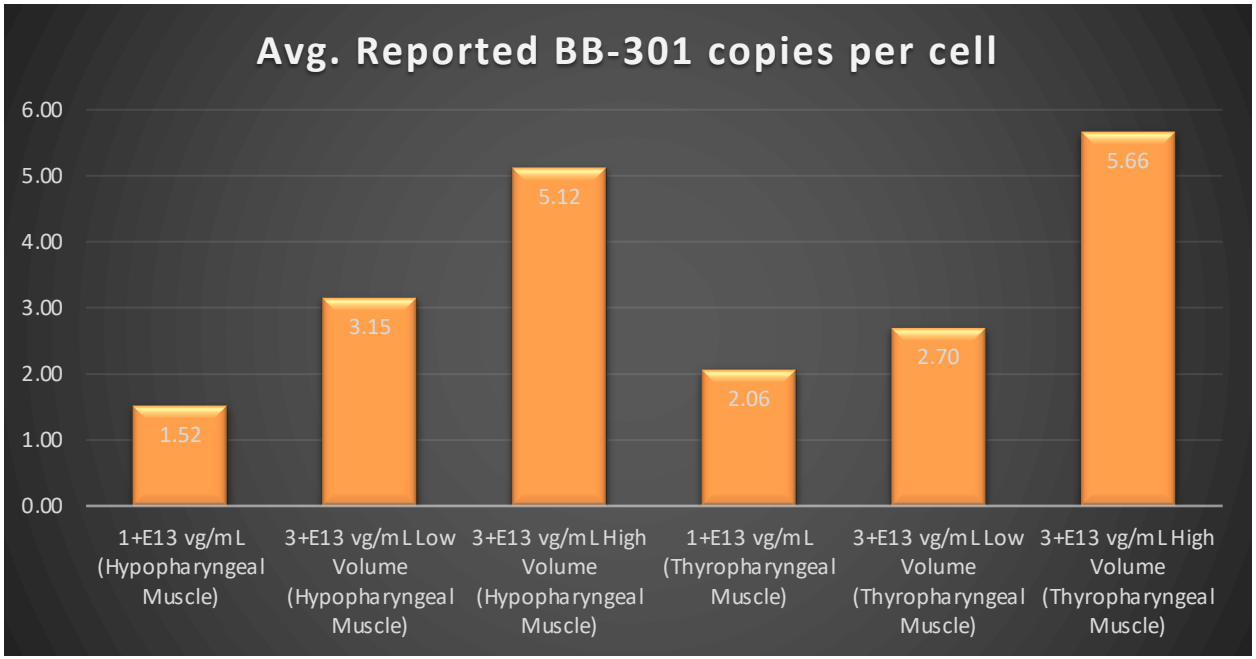
An interim analysis of the BB-301 Pilot Dosing Study in Beagle dogs revealed:

- Biologically significant, dose-dependent levels of BB-301 tissue transduction (i.e. delivery of the multi-functional genetic construct into the target pharyngeal muscle cells)
  - **BB-301 copy numbers ranging from 1.5 copies per cell up to 5.7 copies per cell were achieved in the respective pharyngeal muscles after a single administration of increasing doses of BB-301**
- Broad-based, dose-dependent expression within the pharyngeal muscle cells of the three distinct genes comprising the BB-301 gene construct (i.e. siRNA13, siRNA17, and codon optimized PABPN1)
- Biologically significant levels of target gene knock-down (i.e. inhibition of the expression of the gene of interest) within the pharyngeal muscle cells
  - **Low-Dose, Intermediate-Dose, and High-Dose BB-301 administration achieved similar levels of inhibition, with an average of 72% inhibition of PABPN1 expression observed across all doses**
  - **BB-301 has been evaluated in prior non-clinical studies in A17 mice (i.e. animals that express mutant PABPN1 and manifest the key signs and symptoms of OPMD); and, in this animal model of OPMD, the achievement of PABPN1 inhibition levels of 31% or higher led to complete resolution of OPMD disease symptoms and correction of the histological hallmarks of OPMD**

Interim Results for the Pilot Dosing Study: *Pharyngeal Muscle Tissue Transduction Levels for BB-301*

- The data demonstrate the achievement of biologically significant, dose-dependent levels of BB-301 tissue transduction (i.e. delivery of the multi-functional genetic construct into the target pharyngeal muscle cells)



Interim Results for the Pilot Dosing Study: *Gene Expression Levels for BB-301 within Pharyngeal Muscles*

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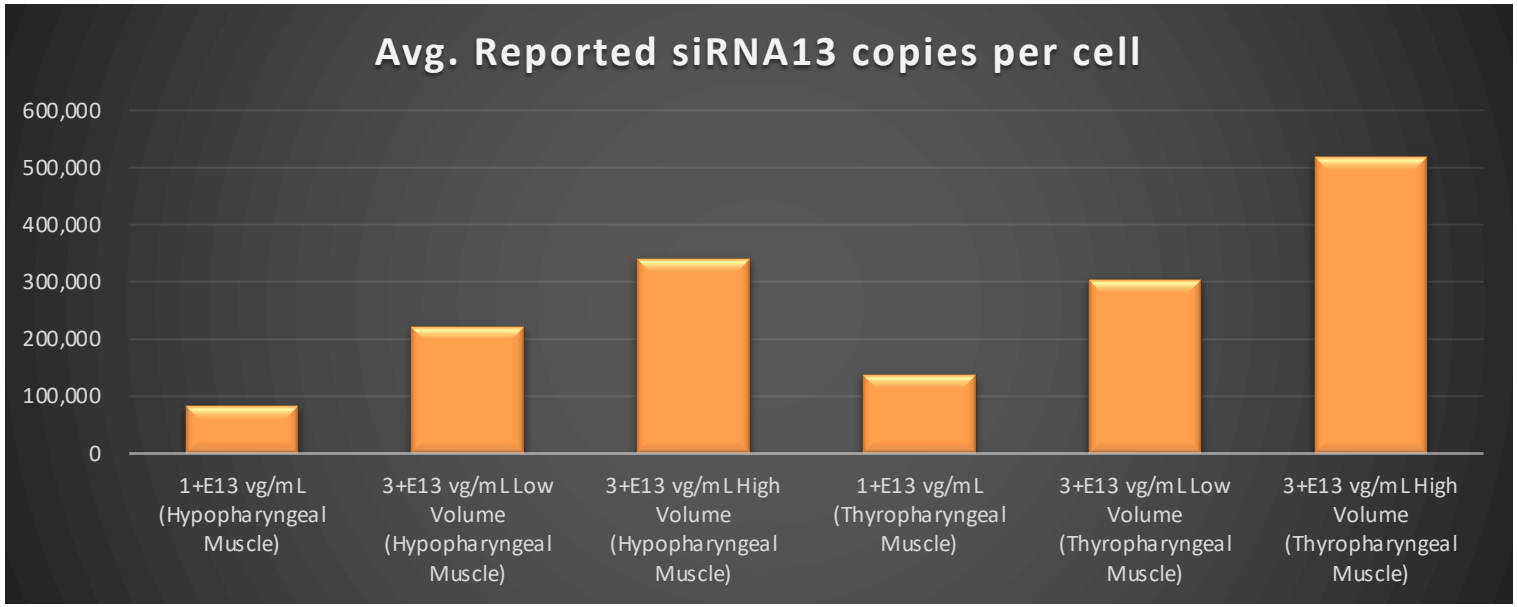
- BB-301 encodes 2 distinct siRNA species (i.e. siRNA13 and siRNA17) which are each, independently, capable of inhibiting (i.e. "silencing") the expression of the mutant form of the PABPN1 protein and the wild type (i.e. endogenous) form of the PABPN1 protein
  - Importantly, the mutant form of the PABPN1 protein underlies the development and progression of OPMD
- BB-301 also encodes a wild type version of the PABPN1 protein whose intracellular expression is unaffected by the inhibitory activities of siRNA13 and siRNA17, and this codon optimized PABPN1 protein (i.e. coPABPN1) serves to replenish the endogenous form of the PABPN1 protein and to replace the mutant form of PABPN1 that underlies the development and progression of OPMD in diseased tissues
  - For comparative purposes, is should be noted that the average level of expression for wild type PABPN1 within the pharyngeal muscle cells of Beagle dogs is 4.5 copies per cell to 7.8 copies per cell

Interim Results for the Pilot Dosing Study: *Gene Expression Levels for BB-301 within Pharyngeal Muscles*

- The data demonstrate the achievement of broad-based, dose-dependent expression of siRNA13 within the pharyngeal muscle cells



Interim Results for the Pilot Dosing Study: *Gene Expression Levels for BB-301 within Pharyngeal Muscles*

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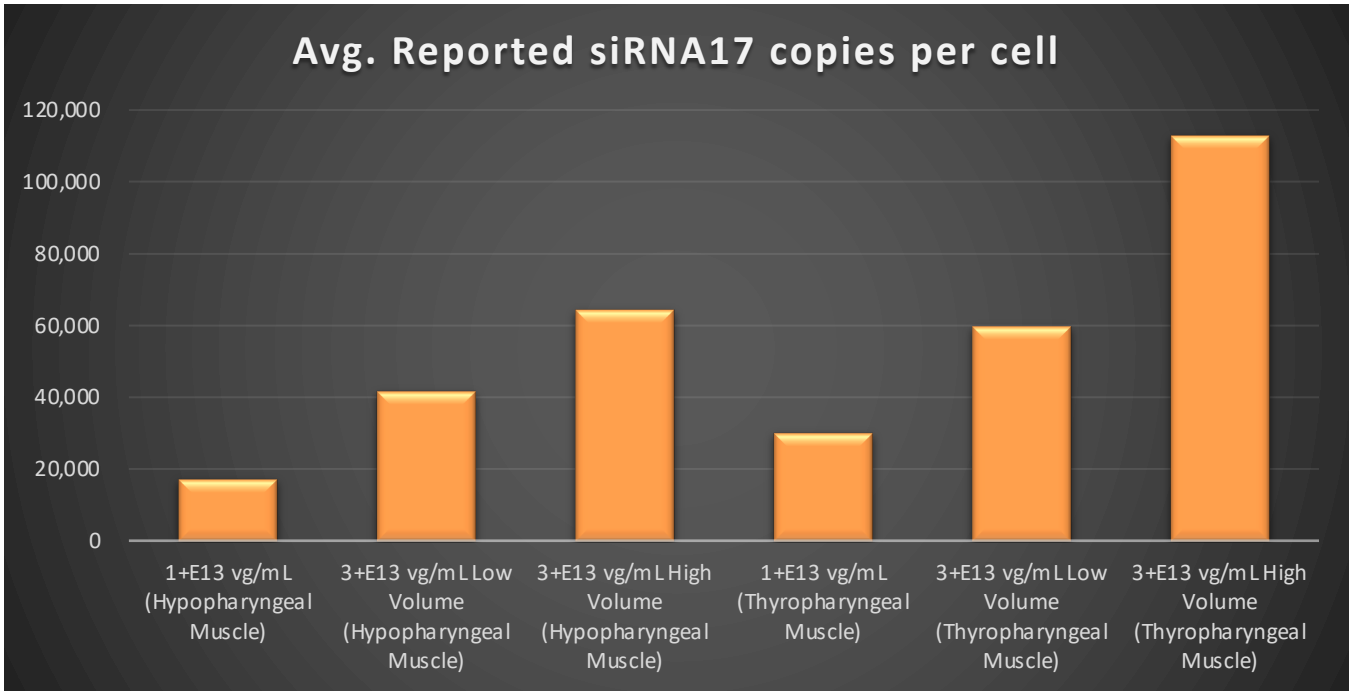
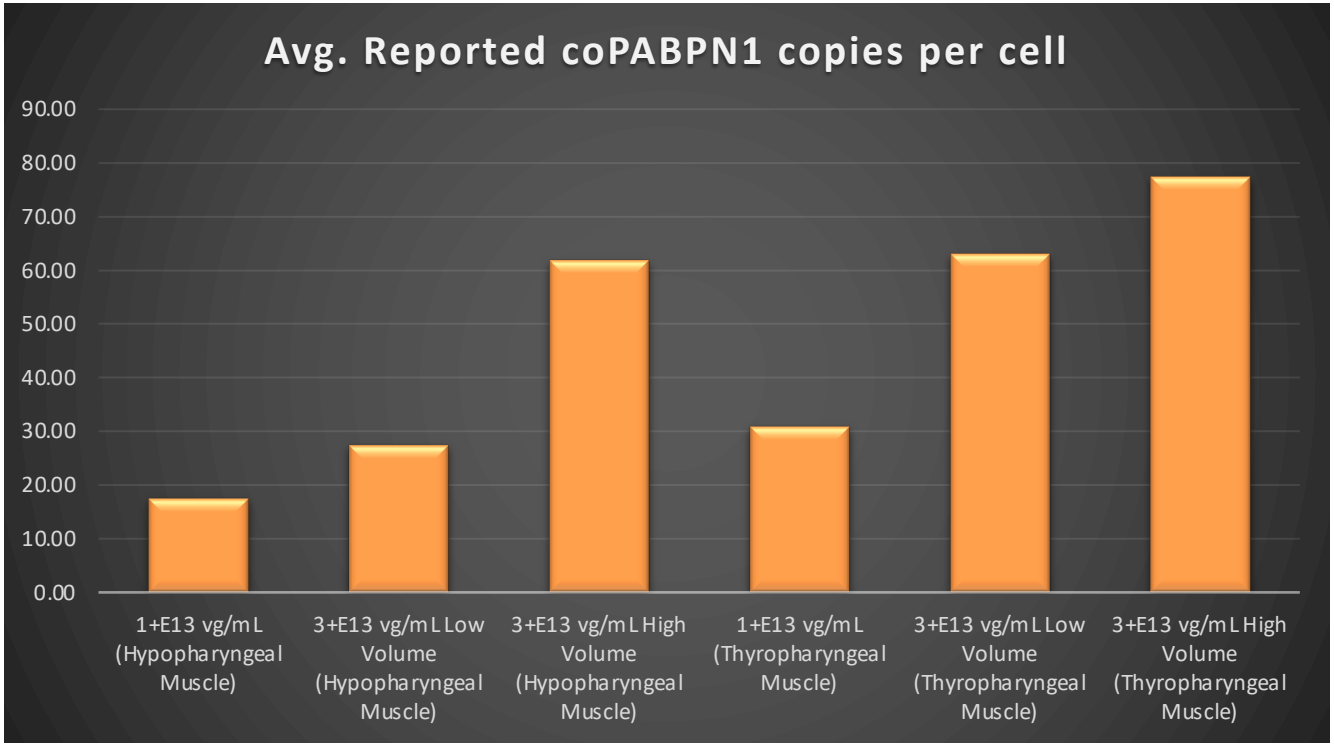
- The data demonstrate the achievement of broad-based, dose-dependent expression of siRNA17 within the pharyngeal muscle cells



Interim Results for the Pilot Dosing Study: *Gene Expression Levels for BB-301 within Pharyngeal Muscles*

- The data demonstrate the achievement of broad-based, dose-dependent expression of codon optimized PABPN1 within the pharyngeal muscle cells



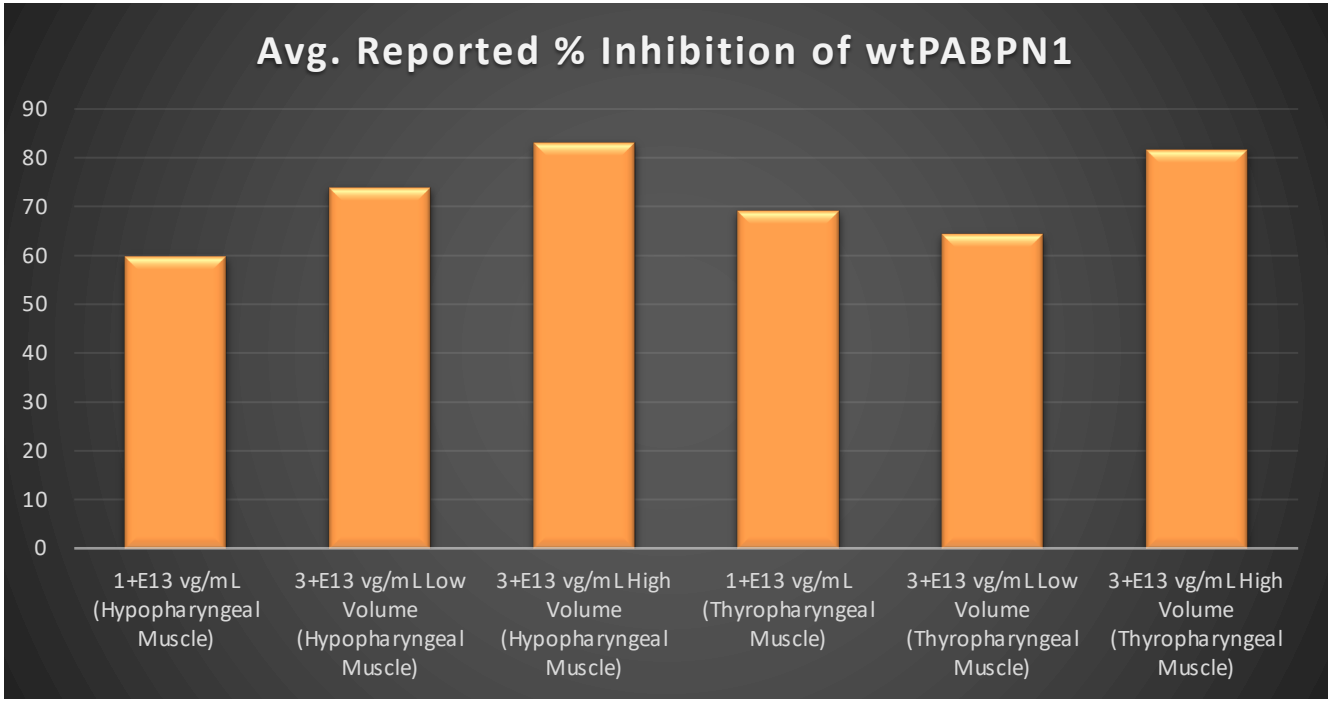
Interim Results for the Pilot Dosing Study: *PABPN1 Silencing (i.e. target "knock-down") within Pharyngeal Muscles*

- As noted above, BB-301 encodes 2 distinct siRNA species (i.e. siRNA13 and siRNA17) which are each, independently, capable of inhibiting (i.e. "silencing") the expression of all forms of the PABPN1 protein
  - **siRNA13 and siRNA17 silence the expression of both wild type PABPN1 (wtPABPN1) and mutant PABPN1**
- While the Beagle dog subjects treated in the current BB-301 Pilot Dosing Study do not express mutant PABPN1, the level of BB-301-driven gene silencing for the PABPN1 target can be assessed due to the equivalent inhibitory effects of siRNA13 and siRNA17 on both wtPABPN1 and mutant PABPN1
  - **Thus, the wtPABPN1 silencing activity observed in the current BB-301 Pilot Dosing Study serves as a surrogate for the activity that would be anticipated in the presence of mutant PABPN1**
- **BB-301 has been evaluated in prior non-clinical studies in A17 mice (i.e. animals that express mutant PABPN1 and manifest the key signs and symptoms of OPMD); and, in this animal model of OPMD, the achievement of PABPN1 inhibition levels of 31% or higher led to complete resolution of OPMD disease symptoms and correction of the histological hallmarks of OPMD**

Interim Results for the Pilot Dosing Study: *PABPN1 Silencing (i.e. target "knock-down") within Pharyngeal Muscles*

- An interim analysis of the level of PABPN1 silencing achieved at 8-weeks revealed durable and biologically significant levels of target gene knock-down (i.e. inhibition of the expression of the gene of interest) within the pharyngeal muscle cells

  – **The average level of inhibition observed across all study subjects was 72%**



BB-301 Pilot Dosing Study: *Key Methodological Improvements to the Study Design and Analytical Procedures*

- It is critical to highlight the key methodological distinctions between the current BB-301 Pilot Dosing Study in Beagle dogs conducted by Benitec as compared to the prior BB-301 Beagle dog dosing study carried out independently by the previous BB-301 licensee

- The BB-301 dosing study conducted by the prior BB-301 licensee employed:

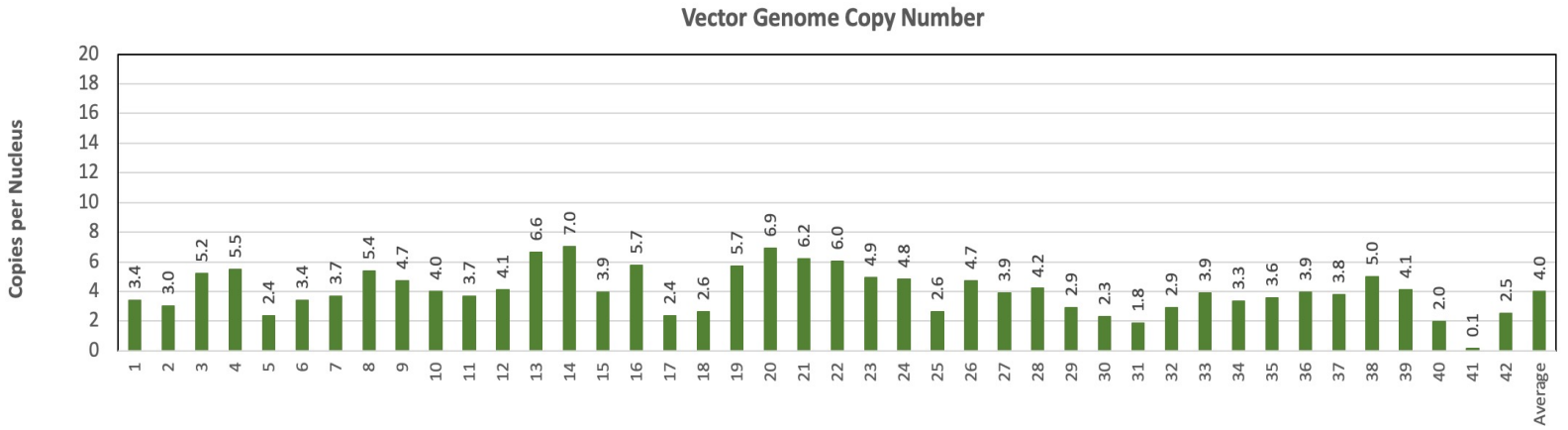
  - **Non-ideal routes and methods of BB-301 administration to the target pharyngeal muscle tissues, and**

  - **Limited analytical methods**

- The Benitec team worked to optimize the route and method of administration of BB-301 and to refine the core analytical methods employed following the completion of Beagle dog dosing

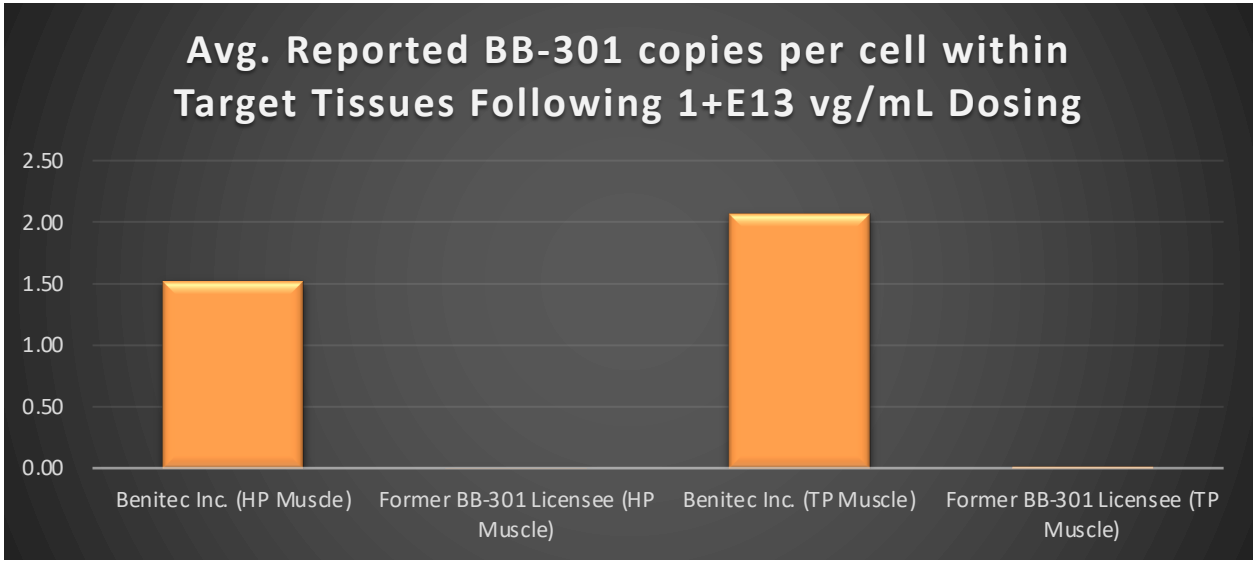
BB-301 Pilot Dosing Study: *Key Methodological Improvements to the Study Design and Analytical Procedures*

- These newly developed proprietary methods of BB-301 delivery, as well as the analytical methods developed to evaluate the key target tissues of the Beagle dog subjects, led to broad-based transduction of the pharyngeal muscle tissues
  - **see figure below with individual sections of the TP muscle following BB-301 dosing**



BB-301 Pilot Dosing Study: *Key Methodological Improvements to the Study Design and Analytical Procedures*

- These newly developed proprietary methods of BB-301 delivery, as well as the analytical methods developed to evaluate the key target tissues of the Beagle dog subjects, demonstrated a 228-fold improvement (+22,647%) in BB-301 transduction of the HP muscle and a 113-fold improvement (+11,163%) in BB-301 transduction of the TP muscle relative to the levels of BB-301 transduction observed by the previous BB-301 licensee



BB-301 Development Program: *Key Regulatory Updates*

- Benitec completed a Scientific Advice Meeting in France in the first half of 2021

- **The Scientific Advice Meeting was conducted to review and confirm the adequacy of:**

  - The non-clinical data derived from the evaluation of BB-301 in both the murine proof-of concept studies and the Pilot Dosing study in Beagle dogs

  - The experimental, analytical, and statistical methods comprising the 12-week BB-301 GLP Biodistribution and Toxicology study in Beagle dogs

  - The large-scale manufacturing plan for clinical grade BB-301 drug product for use in the Phase 1b/2a clinical study in OPMD patients

  - The design of the Phase 1b/2a clinical study slated for initiation in 2022

BB-301 Development Program: *Key Regulatory Updates*

BENITEC BIOPHARMA silencing genes for life™

- **Regarding European Regulatory Interactions:**
  - The BB-301 Pilot Dosing Study was viewed as an appropriate dose range finding study
  - The design of the ongoing GLP Biodistribution and Toxicology study was viewed as appropriate to support Phase 1b/2a testing of BB-301
  - BB-301 drug product has been reproducibly manufactured at large-scale in the past, and the manufacturing plan for clinical grade BB-301 drug product can be conducted under GMP conditions with a production process analogous to that that employed in prior large-scale production runs
  - The design of the Phase 1b/2a clinical trial can support the evaluation of BB-301 safety and clinical efficacy in key populations of OPMD patients

BB-301 Development Program: *Key Regulatory Updates*

- **Regarding U.S. Regulatory Interactions:**
  - Benitec has been granted a Type C meeting with the U.S. Food and Drug Administration ("FDA") in the fourth quarter of 2021

- **BB-301 Phase 1b/2a Clinical Study Design for 2022**
  - *Study Rationale:*
    - Evaluate the safety, tolerability, and clinical activity of ascending doses of BB-301 administered to subjects with OPMD via local intramuscular (IM) injection into the middle pharyngeal constrictor (MPC) muscles and the inferior pharyngeal constrictor (IPC) muscles following open surgical dissection of the pharyngeal region under general anesthesia
  - *Study Design:*
    - This Phase 1b/2a, first-in-human (FIH) study is a single arm, open-label, sequential, dose escalation cohort study with a six-month pre-treatment observation period and a 52-week post injection follow-up period in up to 24 subjects diagnosed with OPMD
    - BB-301 will be administered in three sequential escalating dose cohorts
    - After the initial three cohorts have been dosed, additional subjects may be added at the Maximally Effective Dose (MED), or at an alternate dose as determined by review of cumulative safety and efficacy data
    - At 76 weeks all subjects will be enrolled into a long-term safety follow-up study

BB-301 Development Program: *Key Development Updates*

- **Primary Endpoint (assessed at screening and through end of treatment):**
  - To assess the safety and tolerability of ascending IM doses of BB-301
- **Secondary Endpoints (assessed at Day -180, Day -90, Day -2, Day 90, Day 180, Day 270, Day 360):**
  - ***To evaluate the impact of ascending IM doses of BB-301 on key functional elements of the pharyngeal phase of swallowing as measured by the following videofluoroscopic assessments:***
  - Global swallowing function as measured by the Dynamic Imaging Swallowing Toxicity (DIGEST) scale
  - Pharyngeal constrictor muscle force generation as measured by the Pharyngeal Area at Maximum Constriction (PAMC)
  - Pharyngeal constrictor muscle force generation as measured by the Pharyngeal Constriction Ratio (PCR)
  - ***To evaluate the impact of ascending IM doses of BB-301 on dysphagia severity as measured by the cold-water timed drinking test***
  - ***To evaluate the impact of ascending IM doses of BB-301 on patient reported dysphagia (Sydney Swallow Questionnaire)***
  - ***To evaluate the impact of ascending IM doses of BB-301 on functional oral intake (International Dysphagia Diet Standardization Initiative Functional Diet Scale)***

Benitec Pipeline Updates: *Key Upcoming Milestones*

- Initiation of the Phase 1b/2a clinical study of BB-301 in OPMD patients in 2022
- Benitec plans to provide additional pipeline updates in the second half of 2021