Benitec Biopharma Overview

September 2020

Safe Harbor Statement

This presentation 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. Benitec has tried to identify such forward-looking statements by use of such words as "expects," "intends," "hopes," "anticipates," "believes," "could," "may," "evidences" and "estimates," and other similar expressions, but these words are not the exclusive means of identifying such statements. Such statements include, but are not limited to, any statements relating to Benitec's pipeline of ddRNAi-based therapeutics, including the initiation, progress and outcomes of clinical trials and any other statements that are not historical facts. Such forward-looking statements involve risks and uncertainties, including, but not limited to, risks and uncertainties relating to the difficulties or delays in our plans to develop and potentially commercialize our 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 our product candidates, potential future out-licenses and collaborations, our intellectual property position and duration of our patent portfolio, the ability to procure additional sources of financing and other risks detailed from time to time in filings that Benitec makes with US Securities and Exchange Commission, including our most recent annual report on Form 20-F and our reports on Form 6-K. Such statements are based on management's current expectations, but actual results may differ materially due to various factors, including those risks and uncertainties mentioned or referred to in this presentation. Accordingly, you should not rely on those forward-looking statements as a prediction of actual future results.

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

  – In these cases 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 "Silence and Replace" approach to genetic diseases combines RNAi with gene replacement to drive sustained silencing of disease-causing genes and concomitant replacement with functional wildtype genes via a single therapeutic administration

- Benitec employs DNA-directed RNA interference ("ddRNAi") in combination with classical gene therapy (i.e. transgene delivery via viral vectors) to overcome the limitations of RNAi

- "Silence and Replace" employs adeno-associated viral vectors ("AAVs") to deliver genetic constructs which, after a single administration to the target tissues, can:

  – Chronically express RNAi molecules inside of the targeted cells (to silence intracellular production of the disease-causing protein and the related normal protein of interest), and

  – Simultaneously express a normal variant of the protein of interest (to restore native intracellular biological processes)

  – AAV vectors can jointly accommodate engineered transgenes and shRNA/miRNA expression cassettes

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

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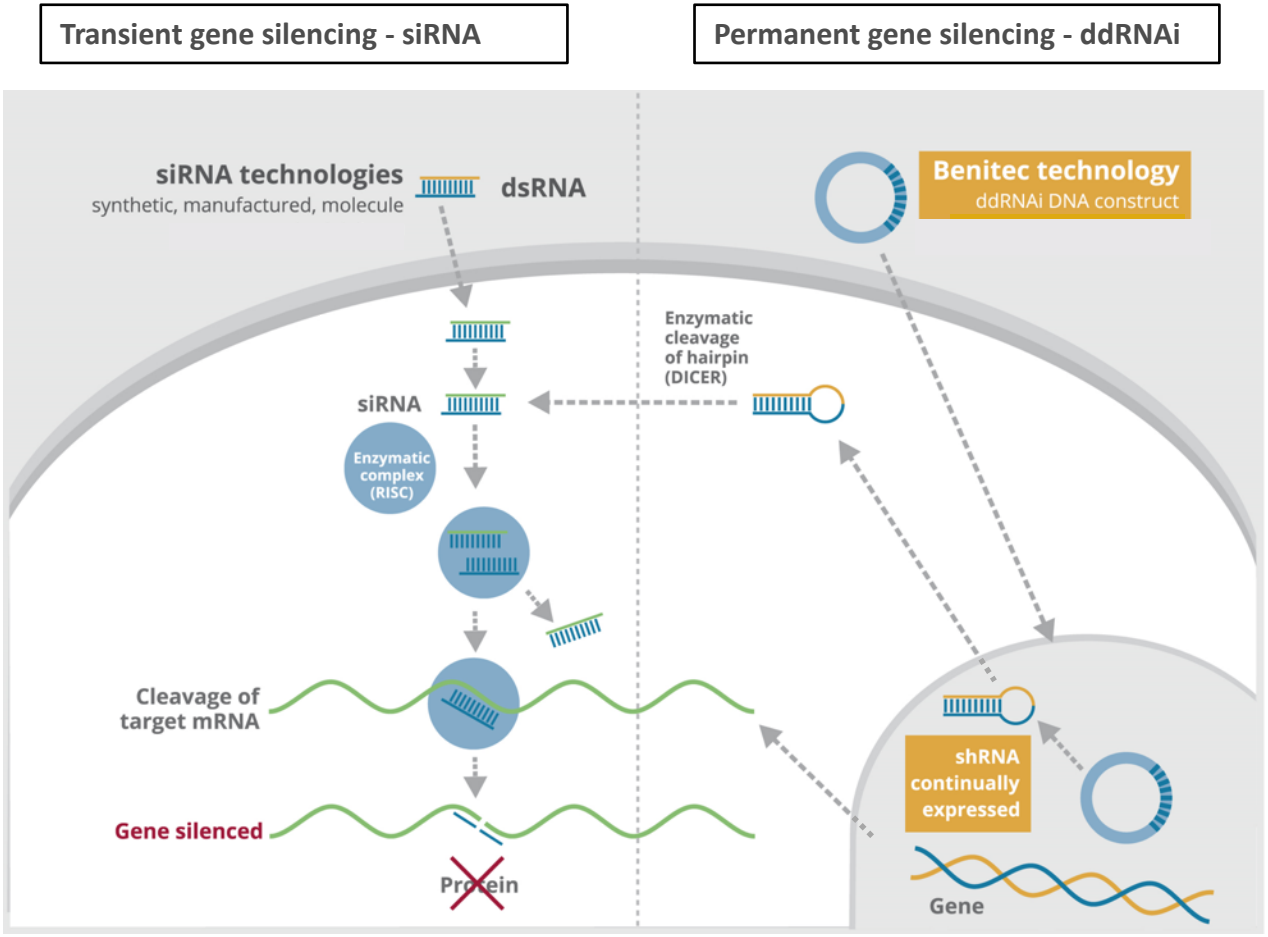
- Combines RNA interference with gene therapy delivery
- Long-term therapeutic potential from a single administration
- Constant, steady-state levels of shRNA expression
- Silence a single gene or target multiple genes simultaneously
- Simultaneous silencing of disease-causing genes and co-expression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



Mechanism of RNA Interference Through the microRNA (miRNA) Pathway

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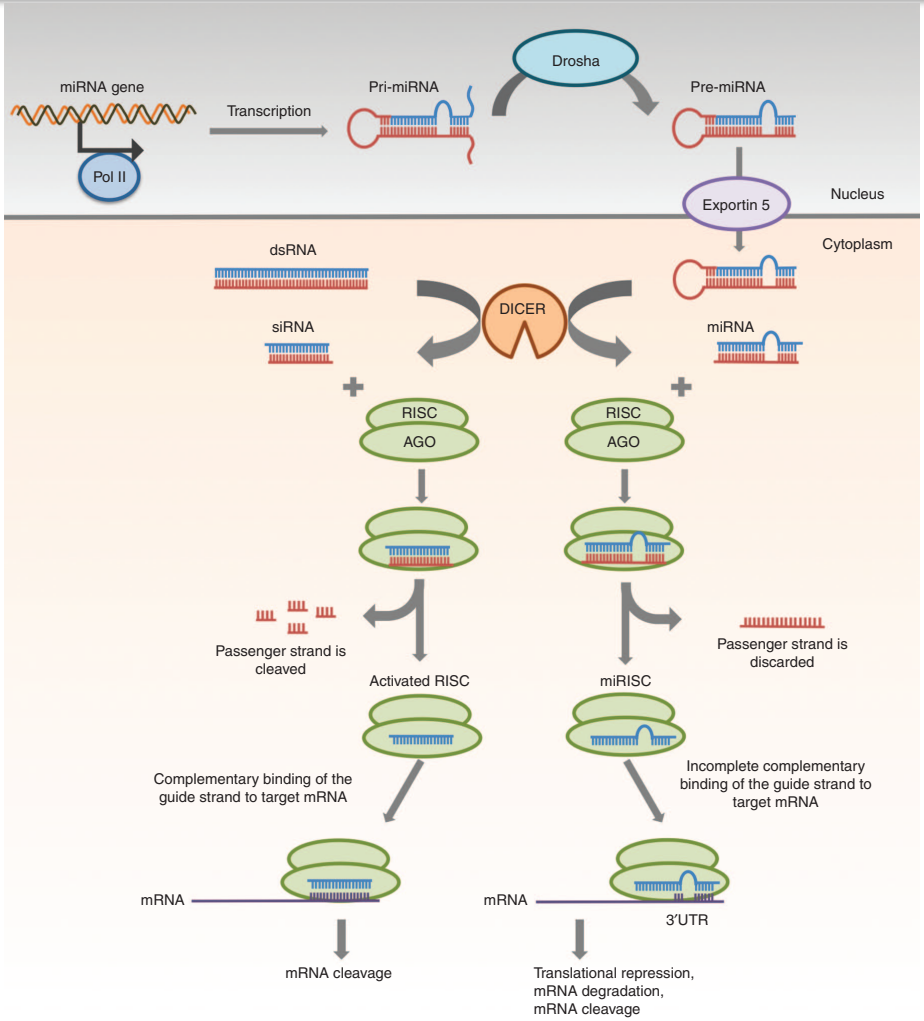
- The use of shRNA/miRNA hybrids confers advantages with respect to expression, safety, and specificity
- Perfectly complementary hairpins are processed by cellular RNAse-III like enzymes at different positions, and a single “perfect” shRNA can be differentially processed into dozens of mature siRNA species
- Due to the intranuclear activity of Drosha, the use of a miRNA backbone allows for efficient processing of the shmiR into functional effector siRNAs with reduced heterogeneity



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 14 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*

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 18-to-24 months

Value / Commercial Opportunity

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

OPMD: *Disease Overview*

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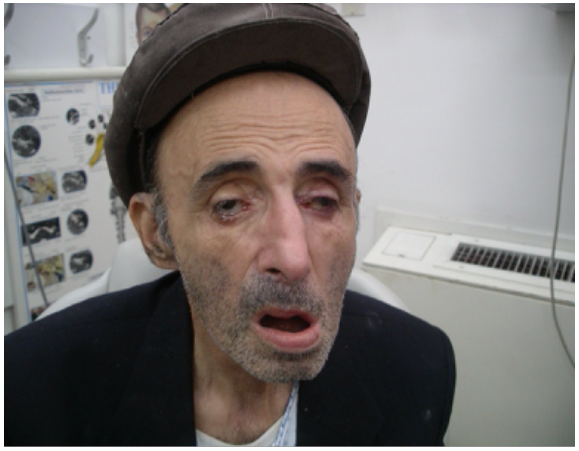
Patterns of Inheritance, Epidemiology, and Age of Onset:

- 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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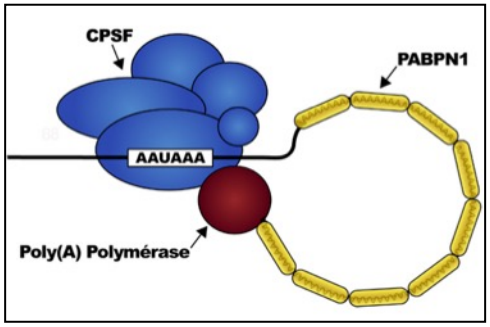
PABPN1:

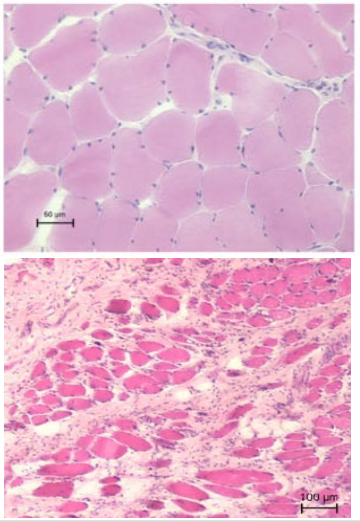
- Ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor) and, thus, controls the length of mRNA poly(A) tails, mRNA export from the nucleus, and alternative poly(A) site usage



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*

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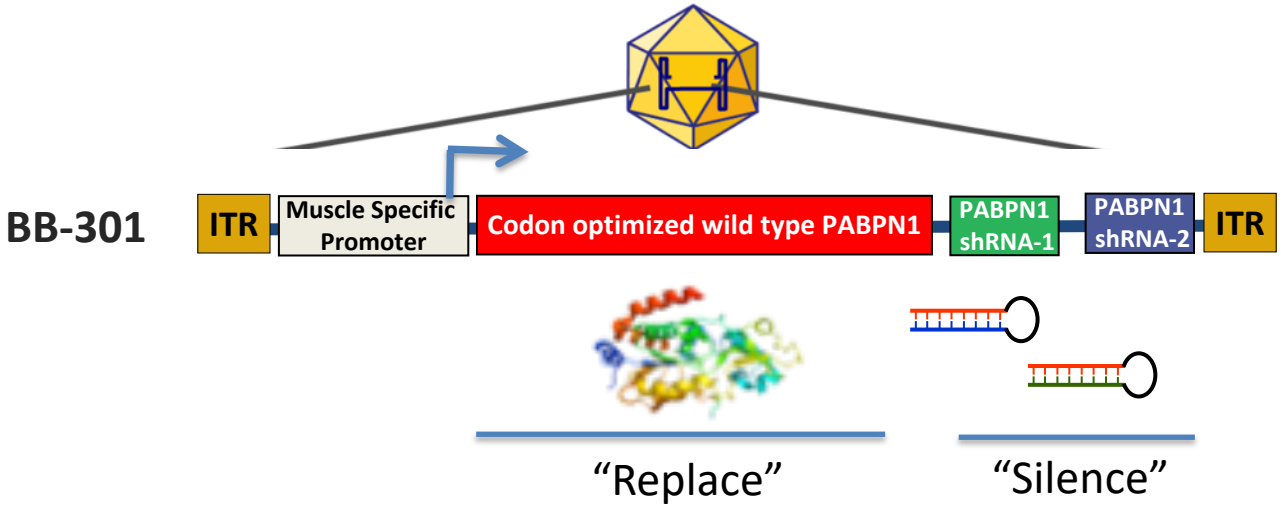
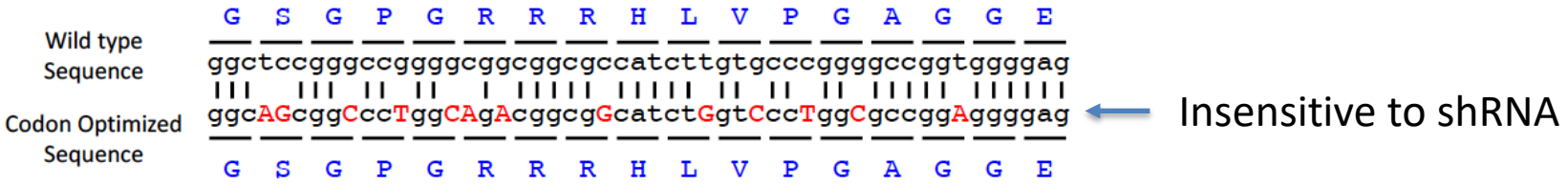
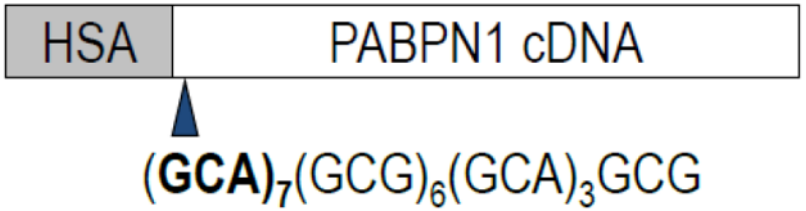


AAV

- 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



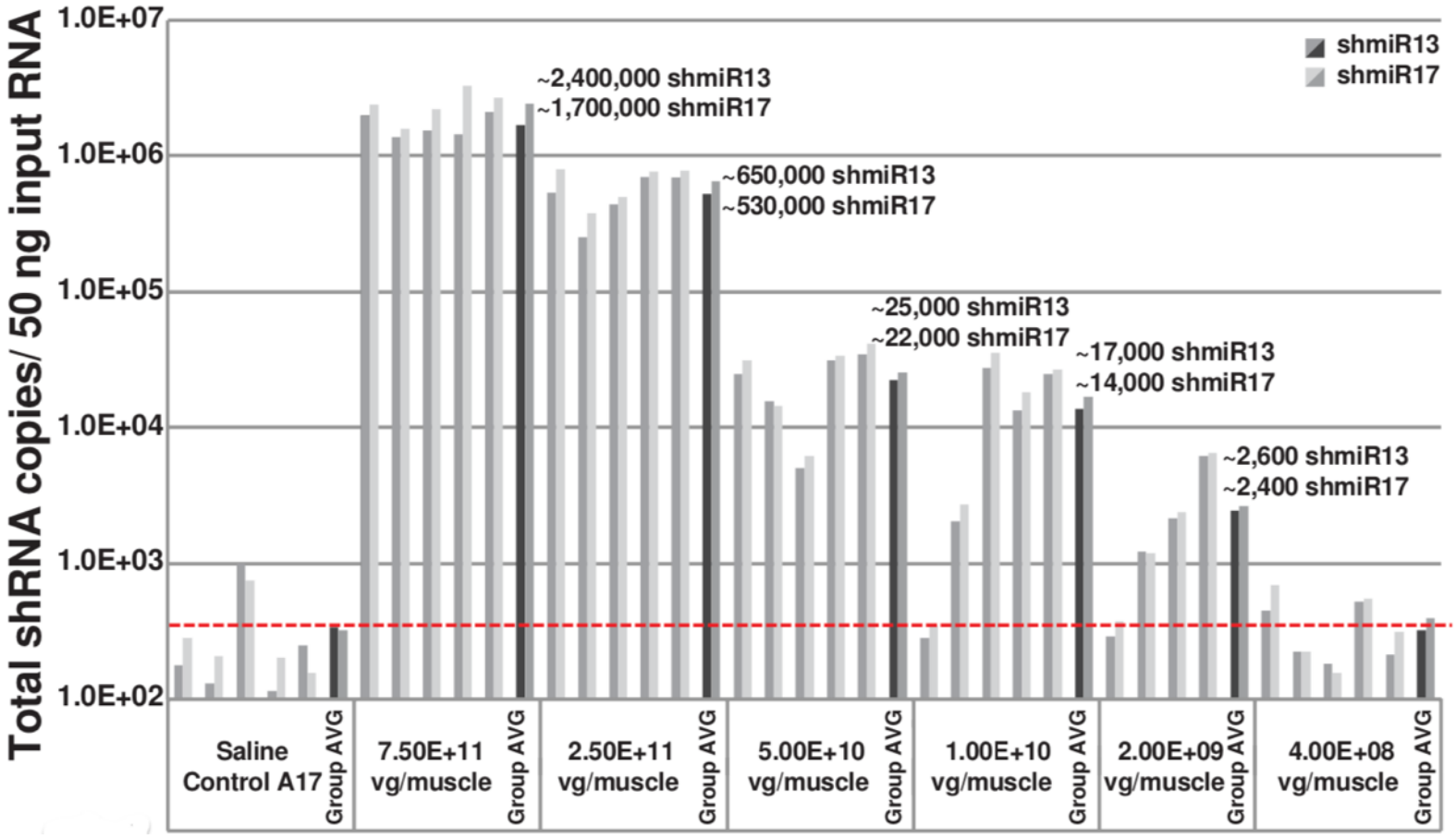
- Multiple A17 animal cohorts received single doses of BB-301 (over a range of doses spanning $4x10^8$ vg/muscle-to-$7.5x10^{11}$ vg/muscle) and, following BB-301 administration, each cohort was observed for 14-weeks

- 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, surprisingly, 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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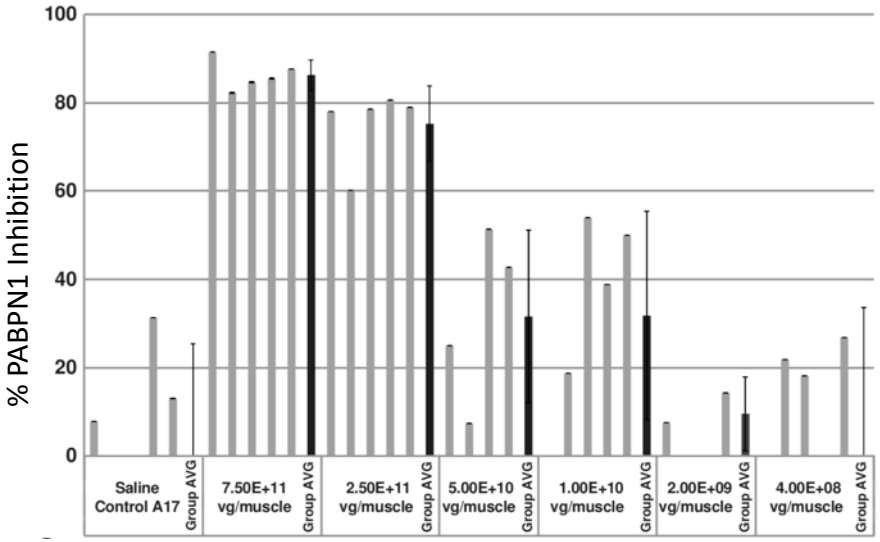
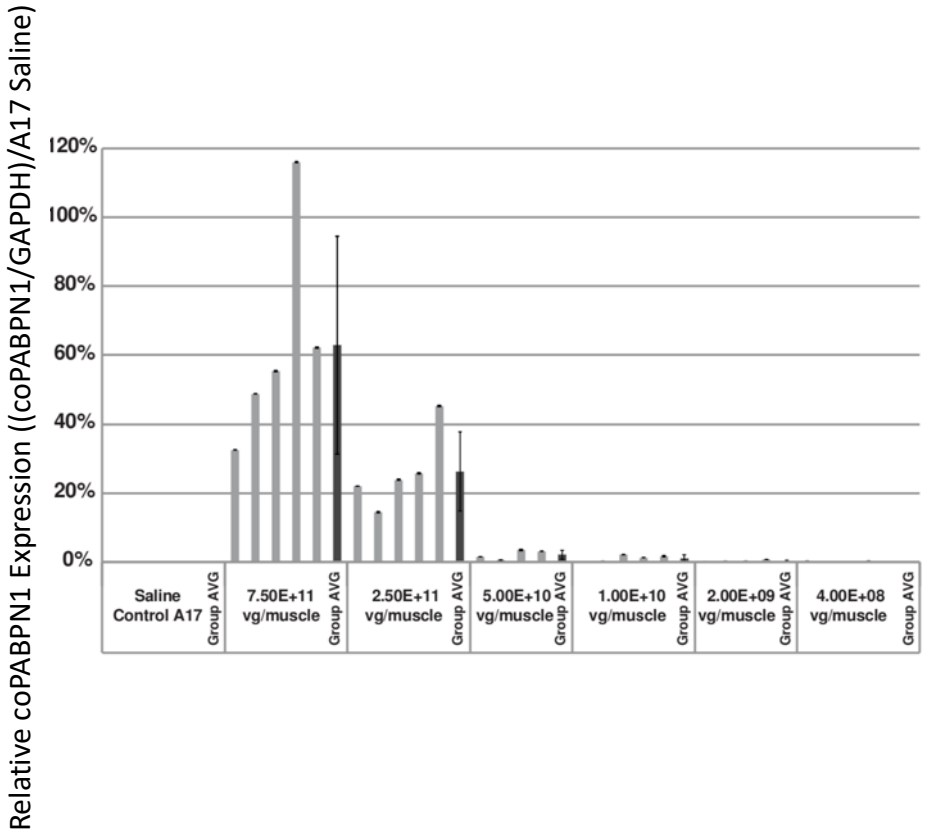
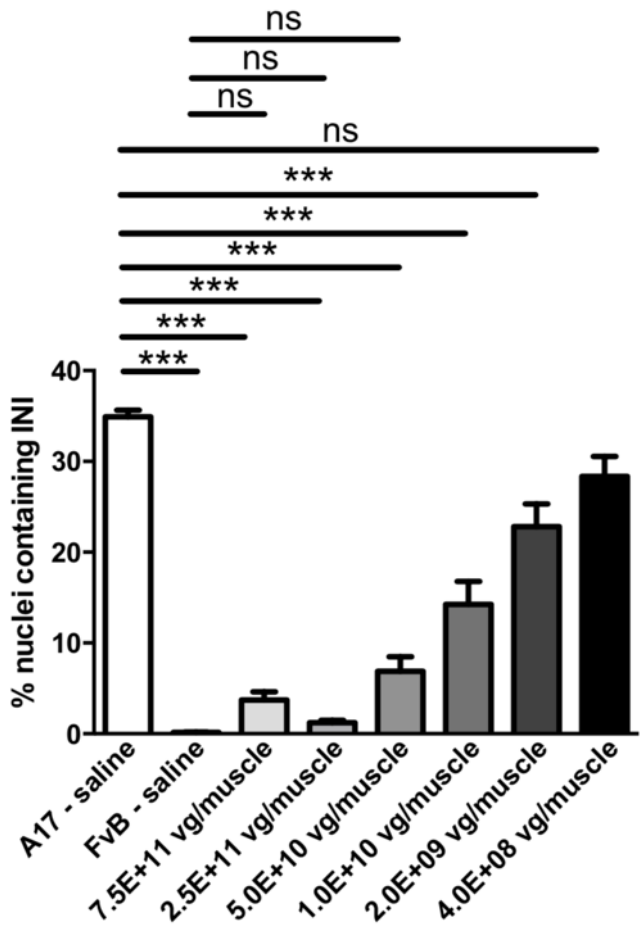




BB-301 Drives Dose-Dependent Resolution of Intranuclear Inclusions in the Injected Muscles



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

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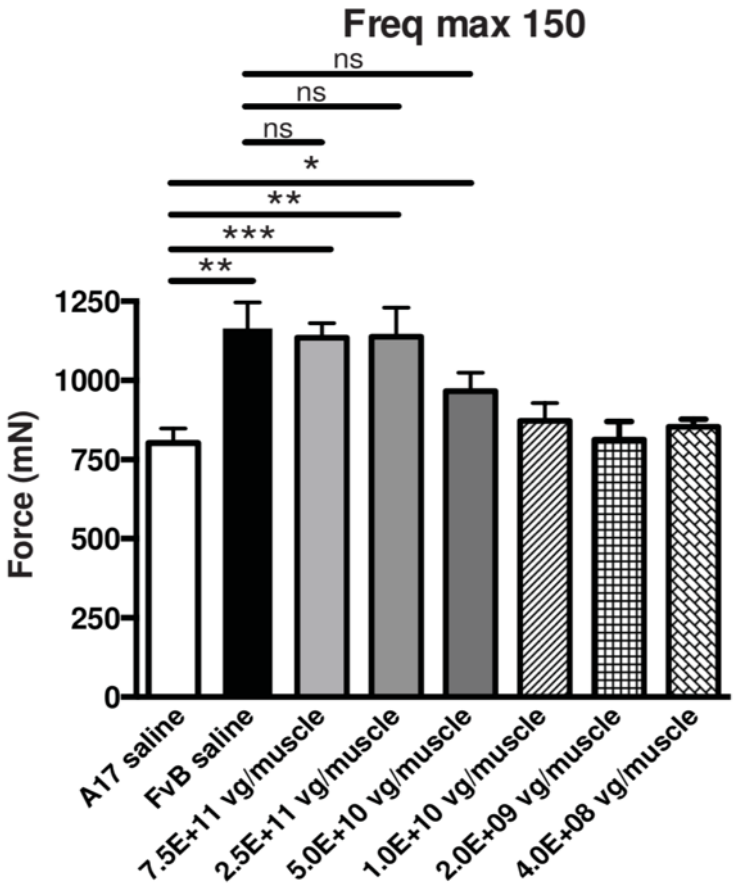

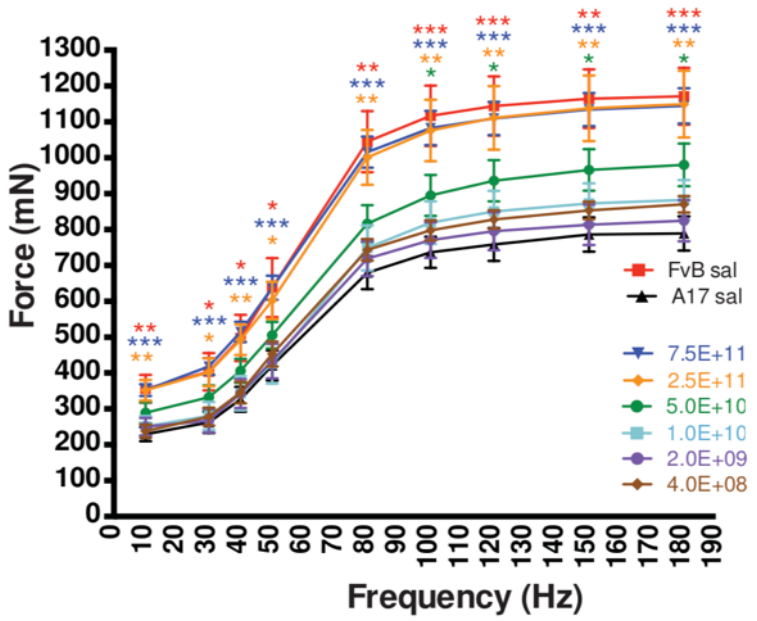

Restoration of muscle strength was assessed by muscle contractility measurements in response to a series of induced impulses that ranged from 10 to 180 Hz

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%

IND-Enabling Non-Clinical Studies Will be Conducted Over the Next 12-to-18 Months

- The IND-enabling non-clinical studies will be carried out under the guidance of the scientific team at Benitec in close collaboration with a team of Thought Leaders in both medicine and surgery that have been deeply engaged in the treatment of OPMD patients for several decades

- 8-week study in Beagle dogs to confirm the transduction efficiency of BB-301 upon administration via direct intramuscular injection into the pharyngeal muscles following an open surgical approach

  – Direct injection of BB-301 into the tibialis anterior muscle of A17 mice achieved robust transduction of the targeted skeletal muscle cells

  – This follow-up study in large animal subjects 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

- 20-week dose-range finding study in Beagle dogs

  – This study will be conducted to further bolster our understanding of the transduction efficiency of BB-301 in addition to providing a more fulsome characterization of the level of shRNA and codon-optimized PABPN1 expression observed across distinct drug doses administered into the targeted pharyngeal muscles (and will facilitate BB-301 dose selection for the Phase I/II clinical trial)

- 12-week regulatory toxicology study in Beagle dogs

BB-103 for Chronic Hepatitis B Virus Infection

- *LATE-STAGE NON-CLINICAL ASSET FOR LICENSURE TO POTENTIAL PARTNERS*
- *CATEGORY-LEADING BIOLOGICAL EFFICACY ACHIEVED IN VALIDATED ANIMAL MODEL*

BB-103 Program Overview: *Biological Activity of BB-102 and BB-103 Combinations with SOC on Key HBV Parameters (Seeking Strategic Partners)*

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	Treatment	Log Reduction of Serum HBV DNA	Log Reduction of HBsAg	Log Reduction of HBeAg
Control groups	entecavir (ETV) 6 mg/kg daily	2.63	0.46	0.37
	pegylated interferon 30 mg/kg twice weekly	2.41	0.96	1.09
Single administration of ddRNAi	BB-102 2e13 vg/kg	1.87 max at Day 63	1.75 max at Day 70	1.17 max at Day 56
	BB-103 2e13 vg/kg	2.17 max at Day 63	1.94 max at Day 70	1.61 max at Day 56
Single administration of ddRNAi with daily entecavir	BB-102 + ETV	* 3.72 +	1.86	1.42
	BB-103 + ETV	* 3.72 +	2.14	1.90

Conclusions

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Bolstered by robust non-clinical proof-of-concept data for BB-301, Benitec will advance BB-301 through IND-enabling studies and subsequent clinical testing in OPMD patients

Continued demonstration of positive non-clinical data and early-stage clinical trial data in an orphan Muscular Dystrophy indication is anticipated to support improved patient outcomes and enhanced shareholder value

Non-clinical data and early-stage clinical trial data supportive of biological and clinical efficacy will serve as validation for the broader research and discovery platform

In infectious disease indications (e.g. Chronic Hepatitis B Virus infection), strategic partnerships for genetic medicine assets have been executed that are valued at more than USD$3 billion with significant up-front cash payments

Benitec Biopharma: *General Financial and Capital Markets Overview*

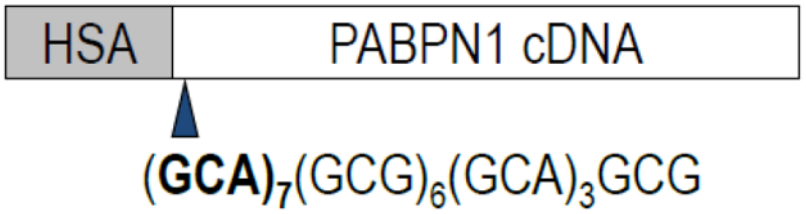
- **Market Capitalization:** $6.3 million
- **Net Cash** (*March 31, 2020*)**:** $11.4 million
- **Public Float:** 1,108,374 shares
- **Public Listing:**
  - **NASDAQ** (*Listed in 2020*)**:** *BNTC*

SUPPLEMENTARY SLIDES

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*

Non-Clinical Model of OPMD: *The "A17" Mouse*



- **Transgenic A17 mouse:** expresses endogenous murine PABPN1 and a mutated bovine PABPN1 driven by the human skeletal actin promoter

- **Reproduces the severe muscle atrophy found in the human phenotype**

- **Mimics other distinct pathological attributes of the human disorder:**
  - Progressive muscle weakness/atrophy
  - Fibrosis
  - Mitochondrial/Ubiquitin-Proteasome defects
  - Muscles contain intranuclear inclusions

Initial Development Approach:
Two-Vector "Silence-and-Replace" Approach

- **Benitec initially employed a two-vector "Silence and Replace" approach composed of:**
  - An AAV8 vector encapsulating an expression cassette encoding three short hairpin RNA ("shRNA") sequences whose expression would drive broad silencing of mutant and wildtype PABPN1 protein production within the target cell
  - An AAV9 vector encapsulating an expression cassette encoding the human "codon-optimized" PABPN1 sequence ("optPABPN1")
  - With codon optimization, the redundancy of the genetic code was exploited to largely modify the nucleic acid sequence of PABPN1 (facilitating 230 out of 921 nucleotide mismatches and a difference of 25% identity) and confer resistance of optPABPN1 to the expressed shRNA sequences
- Critically, *in vivo* evaluation of PABPN1 knockdown alone (i.e. intramuscular injection of AAV8-shRNA) had a detrimental effect in the A17 mouse model, demonstrating that depletion of normal and mutant PABPN1 by shRNAs induced significant muscle degeneration
- By contrast, *in vivo* experiments comprising simultaneous intramuscular injection of AAV8-shRNA and AAV9-optPABPN1 demonstrated increased myofiber cross sectional area of treated muscles (vs. saline-injected muscles), significant reductions in fibrotic tissue (vs. saline-injected muscles), significant increases in absolute maximal tetanic force of treated muscles (vs. saline-injected muscles) and significant reductions in intranuclear inclusions (vs. saline-injected muscles)

Initial Development Approach:
Two-Vector "Silence-and-Replace" Approach

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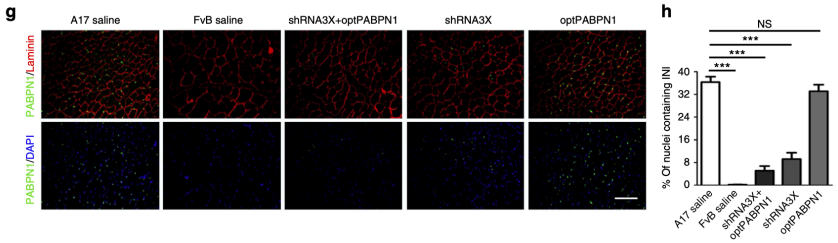
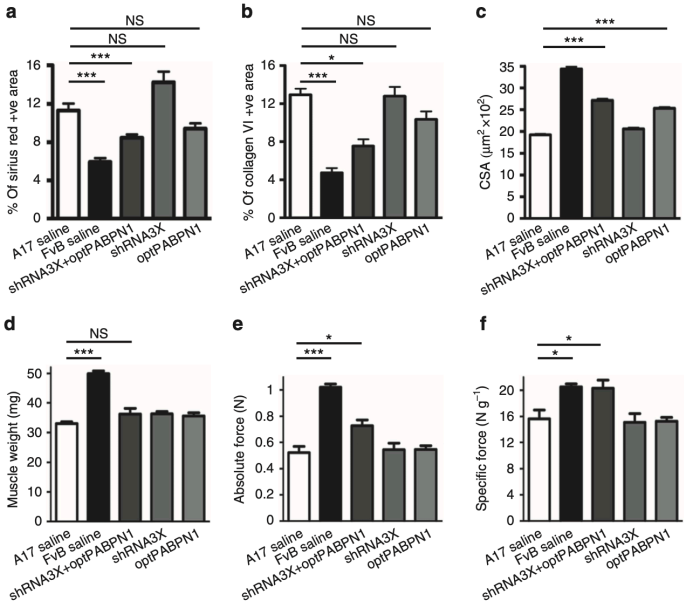
Intranuclear Inclusions



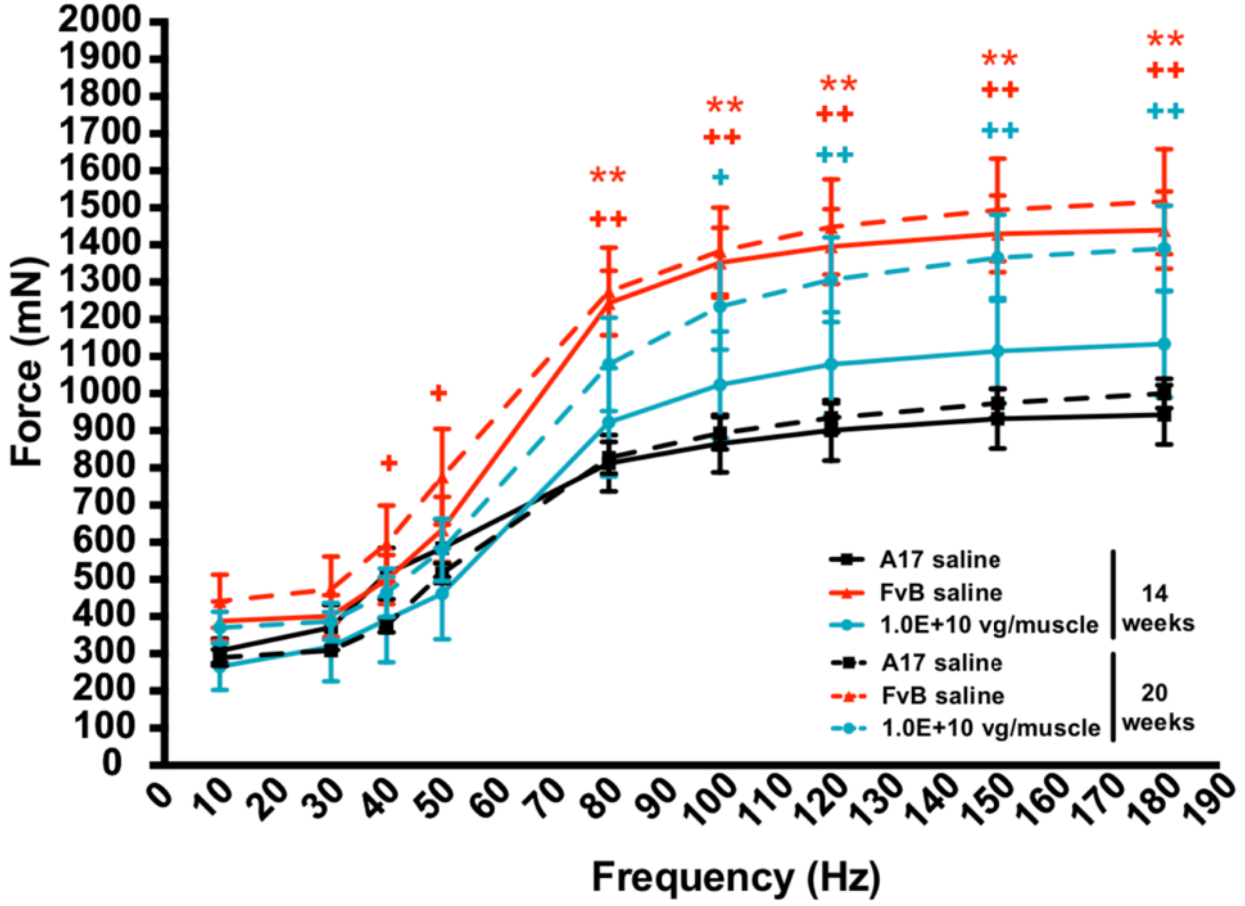
Muscle Force, Fibrosis, CSA



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

- Benitec has engineered a single-vector approach for the treatment of OPMD
  - This proprietary approach combines the essential elements of the initial two-vector system into a single recombinant AAV vector
- The construct (BB-301) is composed of a modified AAV serotype 9 (AAV9) capsid that expresses a bifunctional construct under the control of a single muscle specific Spc5-12 promoter to achieve co-expression of both the codon-optimized PABPN1 protein and two shRNA molecules directed against wild type and mutant PABPN1
- Benitec demonstrated in a key non-clinical model (the A17 mouse model) that a single intramuscular injection of BB-301 results in robust intracellular silencing of PABPN1 protein production and concomitant expression of the normal, biologically functional PABPN1 protein
- In the A17 mouse model, the treatment restores muscle strength and muscle weight to wild type levels and improves other physiological hallmarks of the disease

BB-301 Injected at More Modest Doses Restores Muscle Force to Wild Type Levels (Analysis Performed at 14-weeks and 20-weeks after Administration)



BB-301 Program Review

- Over the preceding 12-months an unsatisfactory series of BB-301-focused non-clinical experiments were conducted in large animal subjects and, due to the inherent inadequacies of the experiments, the results were inconclusive
  - These core non-clinical studies, therefore, require repetition
- Benitec will complete three non-clinical studies for BB-301 that will facilitate the filing of an Investigational New Drug (IND) application and the formal initiation of a Phase I clinical trial in patients suffering from OPMD
  - The three non-clinical BB-301 studies will be conducted in canine subjects and will support the optimization of the methods of administration, confirm the efficiency of vector transduction in the key tissue compartments underlying the disease phenotype, confirm the optimal drug doses in advance of initiation of human clinical studies, and facilitate observation of key toxicological data-points

Large Animal Experiments Conducted in the Past Employed Substandard Dosing Methods and Tissue-Processing Techniques

- **Regarding the Prior Method of Drug Administration:** An endoscopic injection procedure was employed to deliver BB-301, however, this protocol was executed without the aid of fluoroscopy or electromyography to aid in the direct identification the target muscles of interest
  - This flawed method of BB-301 injection led to serial under-dosing and significant variability with respect to the vector copy numbers achieved for BB-301 within the targeted anatomical sites (e.g. contralateral sides of the same target muscle contained vector copy numbers that were observed to vary by up to 8-fold)
- **Regarding the Prior Method of Tissue Processing:** Inadequate practices for in-situ tissue labeling, DNA and RNA isolation and vector copy number analyses were employed, and these methods did not support accurate characterization of the level of tissue transduction achieved following BB-301 administration

BB-103 for Chronic Hepatitis B Virus Infection

- *LATE-STAGE NON-CLINICAL ASSET FOR LICENSURE TO POTENTIAL PARTNERS*
- *CATEGORY-LEADING BIOLOGICAL EFFICACY ACHIEVED IN VALIDATED ANIMAL MODEL*

Chronic Hepatitis B Virus Infection

Clinical Candidate BB-103: *Product Overview*

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Chronic Hepatitis B Virus Infection	• Global prevalence estimated at 257 million people • Need for safe and effective therapies that promote the restoration of a host immune response through targeted HBsAg knockdown
BB-103 Product Profile/Milestones	• Designed as a single-dose treatment to be paired with existing standard of care • Combined with a daily NUC, a single dose of BB-103 results in a > 4 log drop in HBV DNA and > 2 log drop in HBsAg in human chimeric liver mouse model • Clinical trial could begin enrollment over the next 18-to-24 months • Pre-IND FDA meeting informed a clear and expeditious path to the clinic
Value / Commercial Opportunity	• BB-103 is the only gene silencing agent that guarantees perfect compliance, providing the opportunity to reduce the development of drug resistance • Commercial opportunity in excess of $1 billion

shRNAs Employed in BB-301 Construct Ensure Cleavage of Multiple HBV Transcripts

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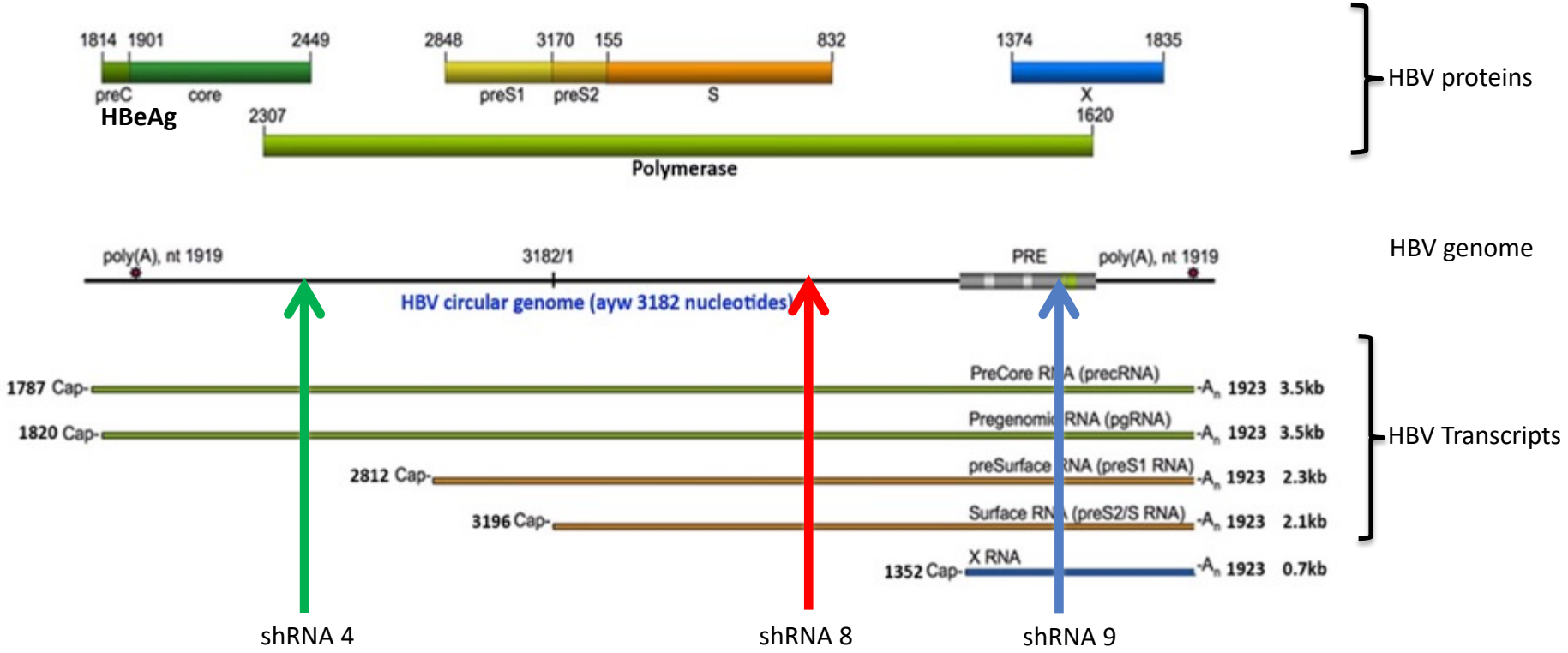
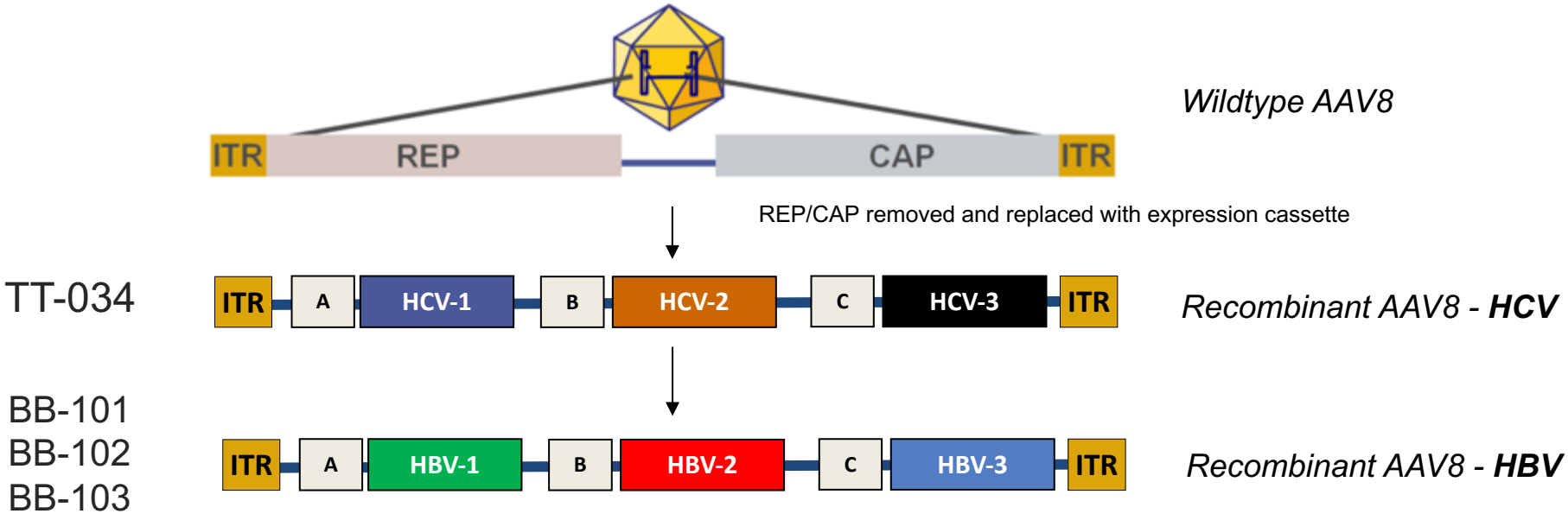


* Sequences selected for shRNA are well conserved across HBV genotypes A-H

BB-103: *Anti-HBV Agent Builds on Key Lessons from First-in-Man TT-034 Trial in HCV*



- Replacement of three anti-HBV shRNA into anti-HCV shRNA positions
- Maintains AAV8 capsid – biodistribution identical to TT-034 (can use other capsids)
- Employs optimal aspects of the recombinant expression cassette
- TT-034 clinical data guides HBV Protocol development and provides simpler regulatory path

BB-103 vs. TT-034: *Key Lessons Learned*

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TT-034 for HCV

- Mutant promoters led to suboptimal expression of shRNA hairpins and modest suppression of HCV replication
  - Drove expression of 3-to-191 shRNA copies per cell
- Wild type shRNA constructs drove variable expression of biologically active hairpins
  - Led to expression of a mosaic of RNA molecules and diluted biological activity

BB-103 for HBV

- Wild type Pol III promoters increased expression of shRNA hairpins by several orders of magnitude
  - Drove expression of 903-to-129,670 shRNA copies per cell
- shRNA constructs were embedded into an artificial miRNA backbone
  - Significant reduction of unprocessed precursor shRNA species and improved production of core biologically active species

Humanized Animal Model: *PhoenixBio*
PXB Human Liver Chimeric Mouse

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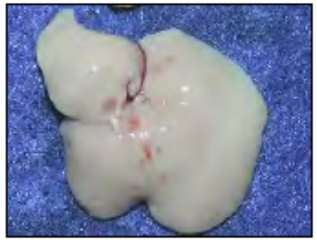
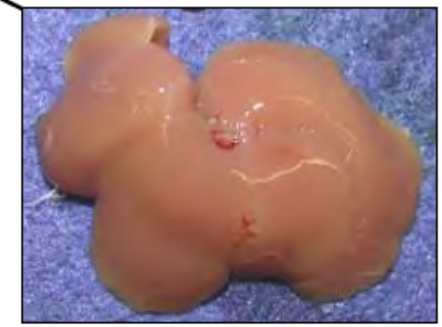
A chimeric mouse with a liver highly replaced by human hepatocytes

1. Human hepatocytes proliferating under physiologically relevant conditions
2. Histologically normal liver constitution
3. Human specific metabolism and excretion pathways
4. Infectable with HBV and HCV



cDNA-uPA/SCID
Liver weight: 0.7 – 1 g

Transplantation
3-week old mice



PXB-Mouse®
Liver weight: 2 – 2.5 g
(RI: 98 %)

10-week old mice

PhoenixBio

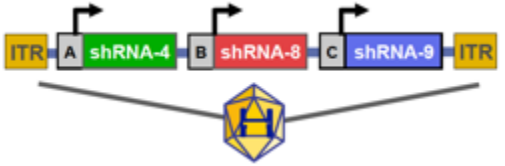
In Vivo HBV Studies Using PXB Mice

Chimeric mouse with humanized liver

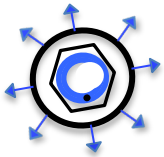
2. Incubate mice for 4 weeks, establish baseline HBV infection, randomize

HBV infected Chimeric mouse

3. Transduce mice with BB-101 BB-102 or BB-103 at **2e13 vg/kg**



1. Infect chimeric PXB mice with HBV genotype C



4. Administer Entecavir (Daily at 6 ug/kg) or Pegylated Interferon (twice weekly at 30 ug/kg)
5. Follow infected mice for an additional 91 days

RNA (terminal): Day 91

HBV viral transcripts
Production of anti-HBV shRNA

Serum (weekly):

Extracellular HBsAg
Extracellular HBeAg
Extracellular HBV DNA
Human Albumin

DNA (terminal): Day 91

Intracellular HBV DNA
HBV cccDNA

Biological Activity of BB-102 and BB-103 Combinations with SOC on Key HBV Parameters

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	Treatment	Log Reduction of Serum HBV DNA	Log Reduction of HBsAg	Log Reduction of HBeAg
Control groups	entecavir (ETV) 6 mg/kg daily	2.63	0.46	0.37
	pegylated interferon 30 mg/kg twice weekly	2.41	0.96	1.09
Single administration of ddRNAi	BB-102 2e13 vg/kg	1.87 max at Day 63	1.75 max at Day 70	1.17 max at Day 56
	BB-103 2e13 vg/kg	2.17 max at Day 63	1.94 max at Day 70	1.61 max at Day 56
Single administration of ddRNAi with daily entecavir	BB-102 + ETV	* 3.72 +	1.86	1.42
	BB-103 + ETV	* 3.72 +	2.14	1.90