



NASDAQ: BNTC | ASX: BLT

# BIOTECH SHOWCASE

8 January 2018

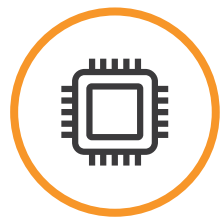
**David Suhy, Chief Scientific  
Officer**

# 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.

# BUSINESS OVERVIEW

A multi-product clinical stage company in 2018



## Proven Technology

First company into human clinical studies under a US IND with systemically delivered non-withdrawable RNAi (TT-034)



## Robust Pipeline

Assets in oncology (Phase 2, 1Q18), orphan genetic disorders (Phase 1/2a 4Q18), retinal disease, and infectious disease.



## Valuable Products

Human therapeutic products for commercialization, partnering, and collaborations

Benitec has created a novel combination of gene therapy and gene silencing to change treatment paradigms of human disease

# HIGHLIGHTS



Programs advancing to clinic

EGFR-targeted gene silencing therapy entering confirmatory Phase II trial in Q1 2018

Unique 'silence and replace' therapeutic designed to treat OPMD anticipated to enter clinic Q4 2018

Other programs targeting retinal disorders and infectious disease could be clinic-ready in 2019



Capital markets access

Listed on ASX (2002) and NASDAQ (2015)

US\$40m capital raised since 2014

US shelf registration June 2017



Strong in-house capabilities

22 staff with scientific operations in Hayward CA, including 12 PhDs with deep gene therapy expertise

In-house manufacturing expertise for process optimization and scalability

Extensive commercial and drug development expertise

# CORPORATE SNAPSHOT

KEY SHAREHOLDER DETAILS	AUSTRALIA Listed ASX 2002: BLT	US Listed NASDAQ 2015: BNTC/BNTCW
Share Price as of 31 <sup>st</sup> December, 2017: (ADR 25:1)	A\$0.20	US\$2.96
52 week high/low as of 31 <sup>st</sup> December, 2017:	A\$0.28/A\$0.105	US\$5.48 / US\$1.39 (ADS)
Average daily volume (6 months to 31 <sup>st</sup> December, 2017)	151,462 shares	49,667
Market Capitalization as of 31 <sup>st</sup> December, 2017:	A\$41m	US\$32M
Issued ordinary shares as of 31 <sup>st</sup> December, 2017:	205,142,734	--
Total options and warrants on issue as of 30 <sup>th</sup> September, 2017:		34,468,203
Insider holdings – Nant Capital LLC		29%
Cash balance as of 30 <sup>th</sup> September, 2017		A\$14.7m
Net assets as of 30 <sup>th</sup> September, 2017		A\$21.5m
Net loss as of 30 <sup>th</sup> September, 2017		A\$5.6m
Capital raised		US\$40m since 2014
US SEC shelf registration		June 2017
Facilities	Corporate Sydney, Australia	Scientific Operations Hayward, California

# EXPERIENCED EXECUTIVE TEAM



**Greg West**

Chief Executive Officer

- Former CFO of Benitec Biopharma, 10 years biotech experience
- Prior roles at PriceWaterhouse, Bankers Trust, Deutsche Bank and NZI



**Georgina Kilfoil**

Chief Clinical and Development Operations Officer

- Former VP of Clinical Operations, Benitec Biopharma
- Prior roles at Anthera Pharmaceuticals, InClin and Peninsula Pharmaceuticals



**Dr. David Suhy**

Chief Scientific Officer

- Former SVP of Research & Development, Benitec Biopharma
- Prior roles at Tacere Therapeutics, Antara Biosciences and PPD Discovery



**Dr. Michael Graham**

Head of Discovery and Founding Scientist

- Discoverer of ddRNAi at CSIRO; Former Senior Research Fellow, University of Queensland
- Prior roles at QDPI and CSIRO



**Bryan Dulhunty**

Chief Financial Officer

- Former Executive Chairman, Viralytics
- Prior roles as NED, MD, CFO and Company Secretary of a number of listed and non-listed biotech companies

# RECENT ACHIEVEMENTS

And path to value creation

## Value Creation

- ✓ Near term value inflection points as two programs move into the clinic in 2018
- ✓ Additional programs which could be clinic-ready by 2019
- ✓ Flexibility of ddRNAi platform can accelerate clinical and shareholder value with the ability to move proven ddRNAi therapeutics into additional rare diseases

# RECENT ACHIEVEMENTS

And path to value creation

## Achievements

- ✓ Nant Capital makes strategic investment in Benitec and brings in Phase II oncology asset
- ✓ EU orphan drug designation for oculopharyngeal muscular dystrophy (OPMD), US application filed
- ✓ Nature Communications publication of initial 'silence and replace' preclinical data (OPMD)
- ✓ Pre-IND meeting with US FDA, Health Canada and several EU informs a clear path to the clinic for OPMD asset
- ✓ Pre-IND meeting with US FDA informed a clear and expeditious path to the clinic for HBV asset
- ✓ Proof of concept for ocular delivery of gene therapy
- ✓ Australian R&D grant income of A\$10.5m for 2016-2017 fiscal year



# PERMANENT GENE SILENCING

## With DNA-Directed RNA Interference (ddRNAi)

**siRNA technologies**  
synthetic, manufactured, molecule  
(non-standard delivery)

dsRNA

**Benitec technology**  
ddRNAi DNA construct  
(standard delivery)

Transient duration

Enzymatic cleavage of hairpin (DICER)

siRNA

Enzymatic complex (RISC)

Separates siRNA into single strands

Cleavage of target mRNA

Gene silenced

Protein

shRNA continually expressed

Gene



Combines RNA interference with gene therapy delivery



Long term therapeutic potential from a single administration



Constant steady state levels of shRNA expression

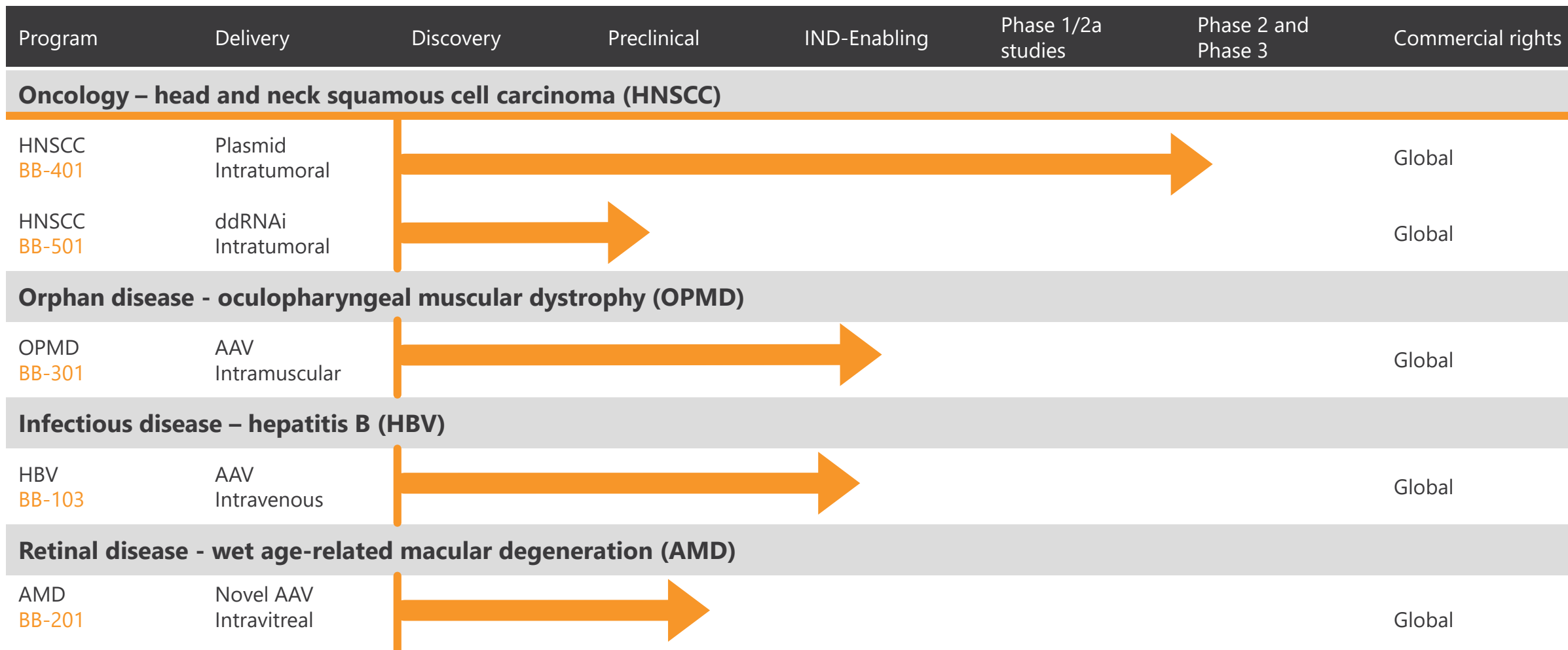


Silence a single gene or target multiple genes simultaneously

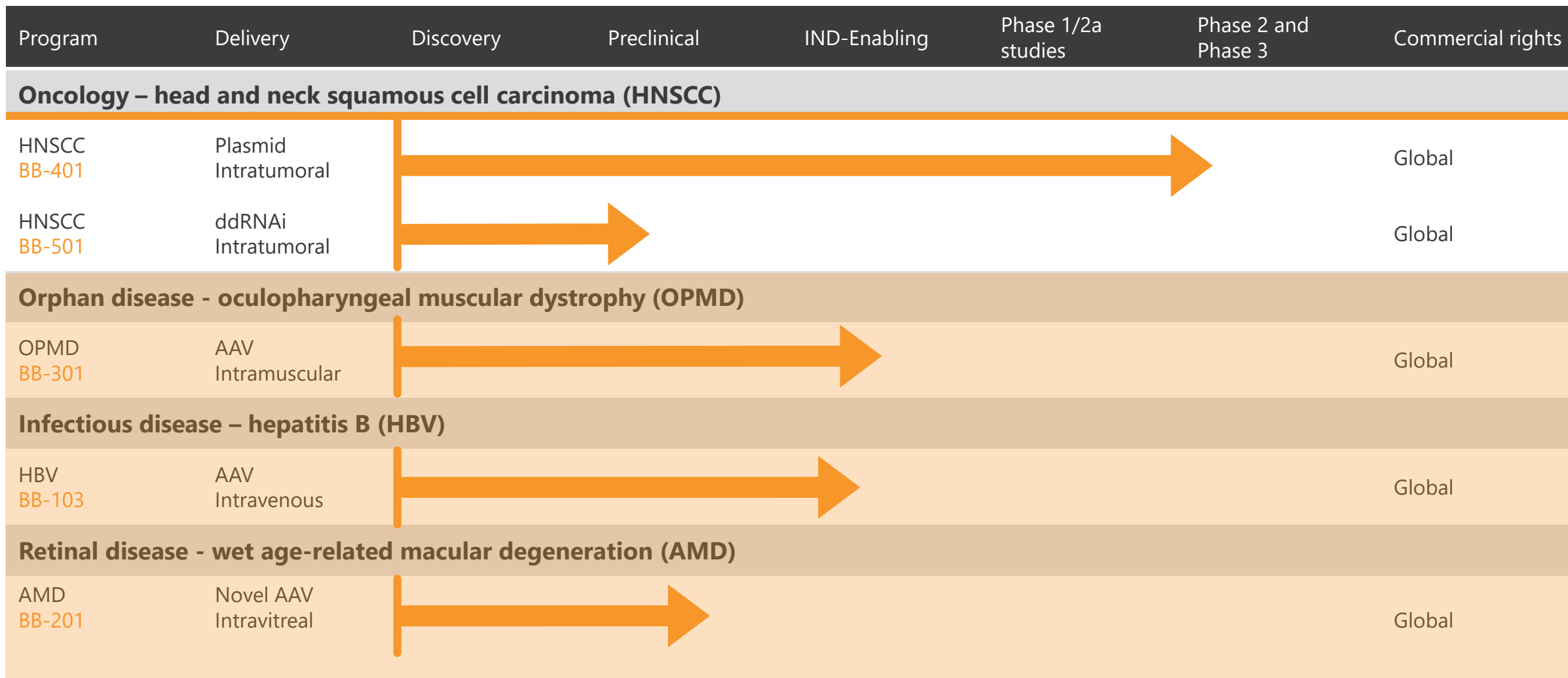


Simultaneous silencing of disease causing genes with co-expression of normal genes to restore function

# DIVERSE PROGRAM PIPELINE



# BENITEC PIPELINE



# HEAD AND NECK SQUAMOUS CELL CARINOMA (HNSCC)

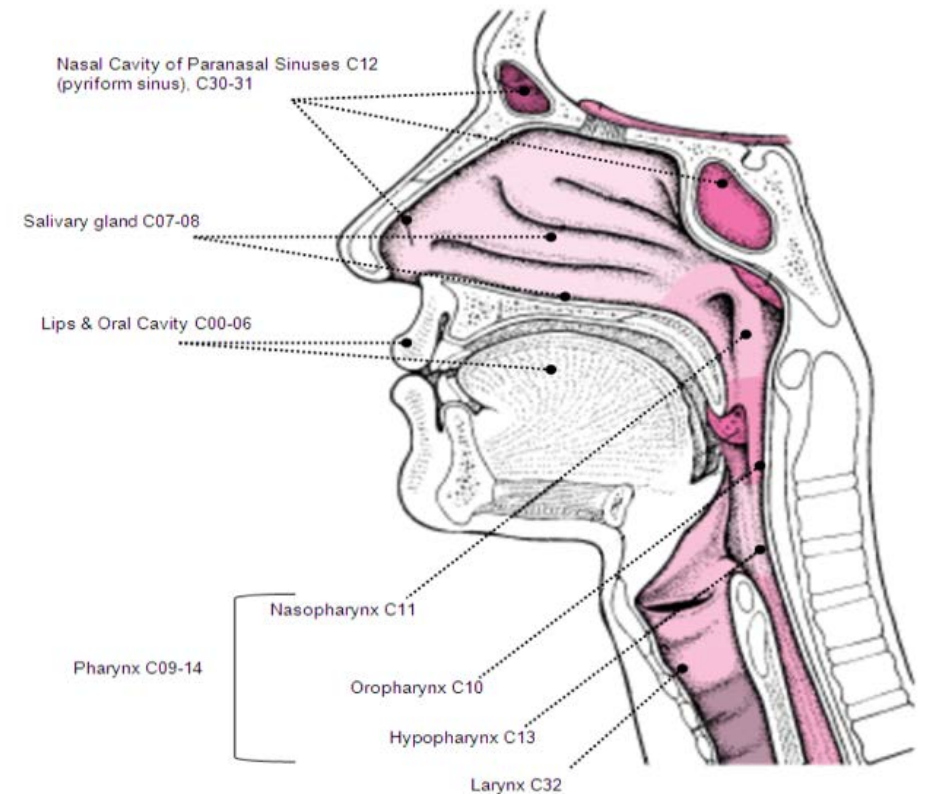
## Incidence and Patient Mortality:

- Circa 64,000 patients diagnosed annually in US
- 50% of patients expected to develop recurrent or metastatic disease
- 13,000 deaths annually in the US
- ***Over 90% of HNSCC lesions overexpress epidermal growth factor receptor (EGFR)***

## Unmet Medical Need:

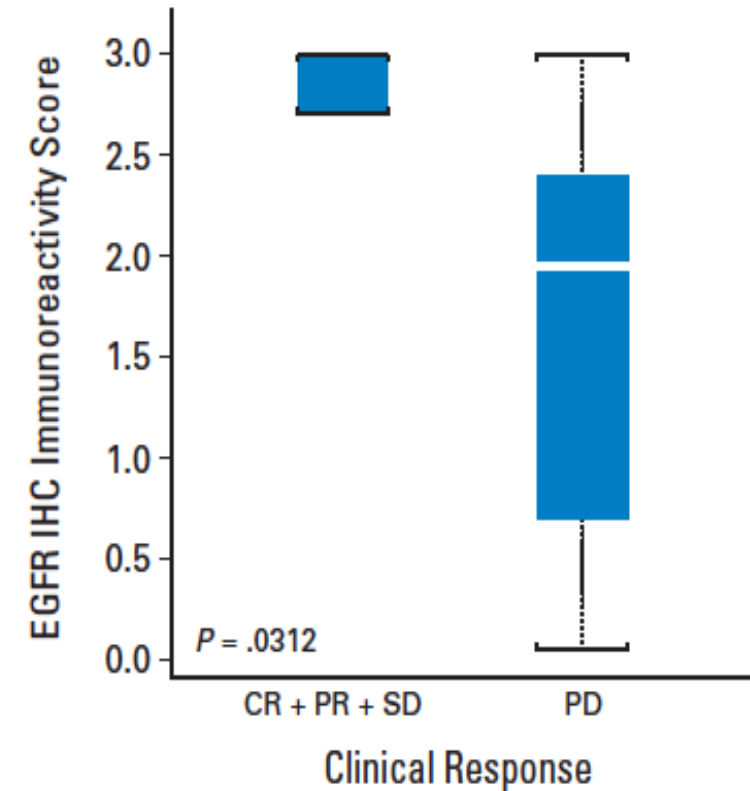
- Significant patient morbidity derived from loco-regional tumor growth and progression in confines of small anatomical space
- Durable tumor reduction or eradication
- Lack of biomarkers to reliably predict response to targeted therapy

## Anatomical sites of HNSCC



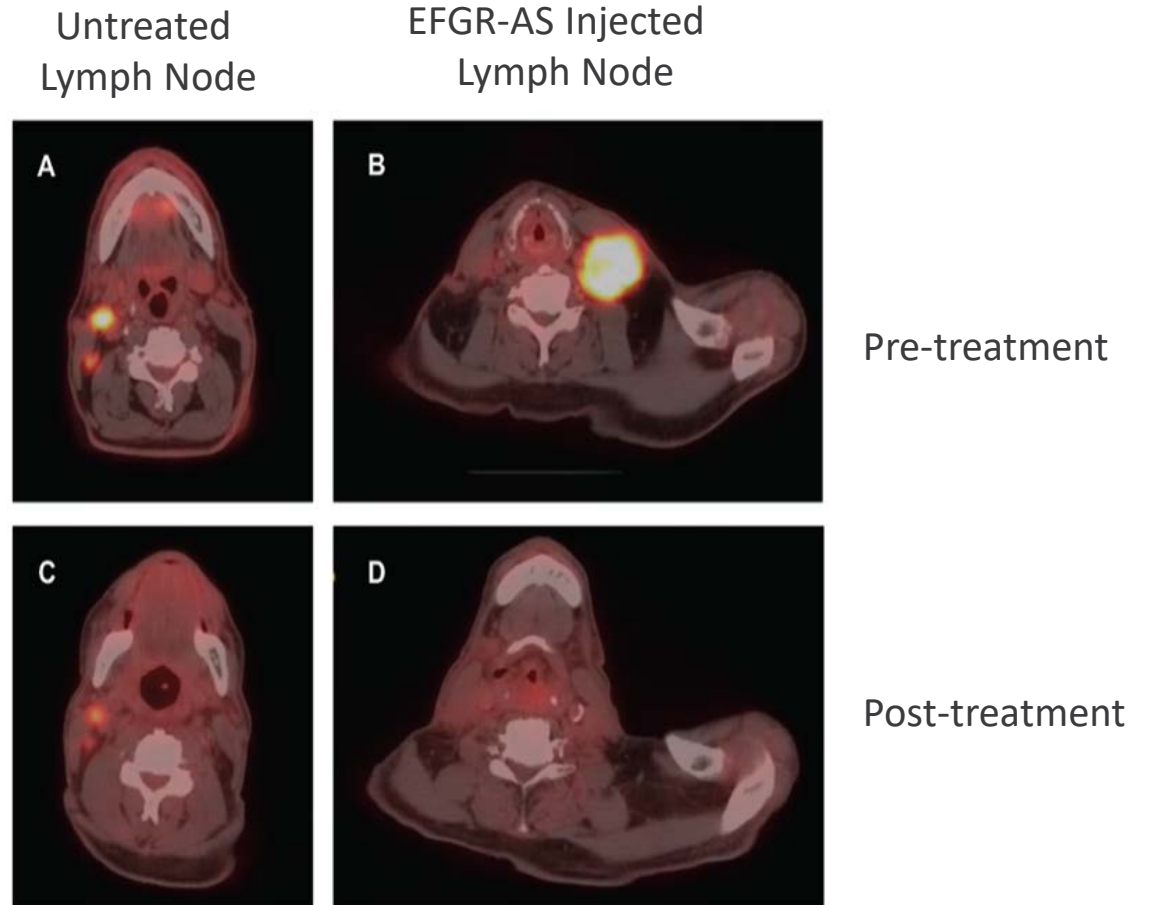
# BB-401: EXPRESSED ANTI-SENSE RNA AGAINST EGFR PHASE 1 SINGLE AGENT CLINICAL DATA

- Phase I study\* of 17 patients with advanced, refractory HNSCC
- Safety and efficacy following direct intra-tumoral injection weekly for 4 weeks:
  - 29 % (5 patients) - Objective Response
  - 2 patients experienced Complete Response
  - 3 patients Partial Responses (reduction >30% by RECIST)
  - 2 additional patients - Stable Disease
  - 41% overall disease control rate
  - 6.5 months observed anti-tumor response
- Strong correlation between baseline level of EGFR expression and clinical response



# BB-401: FOLLOW-ON PHASE I STUDY IN COMBINATION WITH CETUXIMAB AND RADIATION

- 6 patients were treated in a Phase 1 study of BB-401 in combination with radiation and cetuximab
- 5 of 6 patients experiencing Objective Responses (83%)
- 4 patients Complete Response & 1 patient Partial Response



Grandis et al, University of Pittsburgh  
Poster from ASCO 2015

# HEAD & NECK SQUAMOUS CELL CARCINOMA

## Clinical Candidate BB-401: Product Overview



Head & Neck Squamous Cell Carcinoma (HNSCC)

US: Over 50,000 new cases diagnosed in 2017, global market estimated to be US\$1.5 billion in 2024

Morbidity caused by the spatial effects of tumors in the confined anatomical structures of the head and neck

Over 90% of HNSCC overexpress EGFR



BB-401 Product Profile

EGFR targeted via expressed antisense RNA EGFR

In Phase I, strong correlation between BB-401 treatment versus EGFR overexpression

Robust objective response rate versus other monotherapy treatments or when paired with SOC treatments



Value / Commercial Opportunity

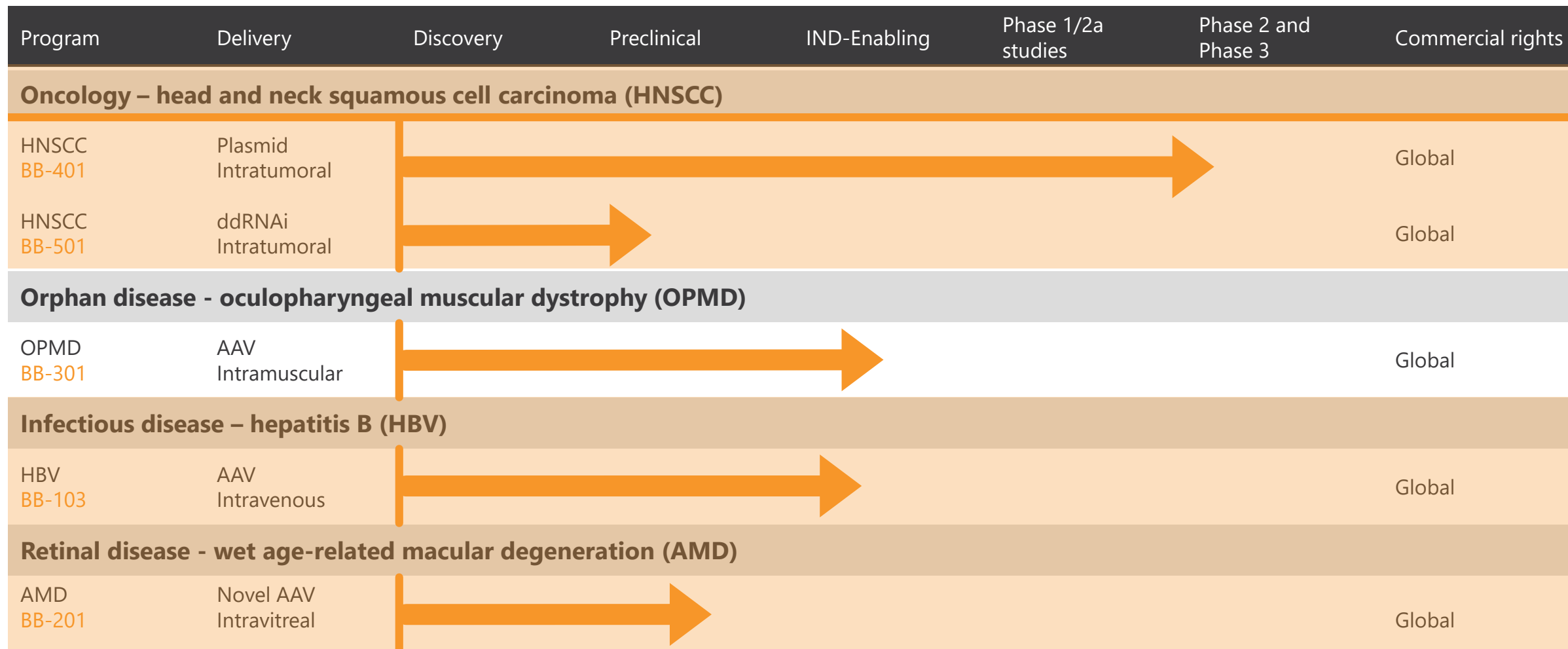
Near term value inflection point:

Phase II open label study in up to 60 patients planned for initiation in Q1 2018

Selective and direct targeting of malignant lesions underlying the core morbidity could uniquely address the unmet medical need in HNSCC

BB-401 is intended to be paired with diagnostic against EGFR

# BENITEC PIPELINE





# OPMD DISEASE OVERVIEW

## Disease:

- Rare autosomal dominant inheritance
- 1:100,000 (Europe)
- As high as 1:600 in specific populations
- Typical age of onset is in 50's or 60's

## Characterized by:

- Eyelid drooping (ptosis)
- Swallowing difficulty (dysphagia)
- Proximal limb weakness
- Death due to aspiration pneumonia & malnutrition

## Histopathology:

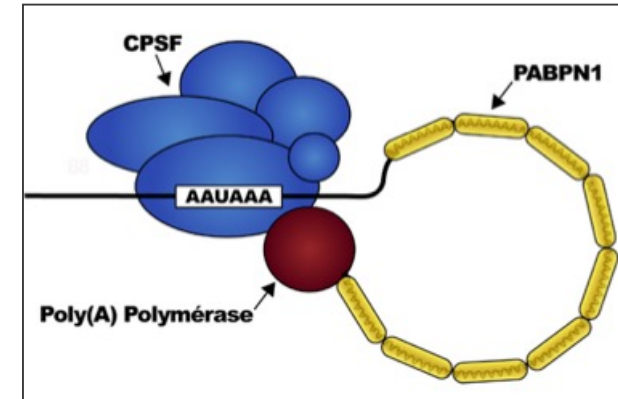
- Decrease of muscle fiber number
- Variation in the size of muscle fibers
- Fibrosis (connective tissue)



# GENETIC BASIS OF OPMD: POLY-ALANINE EXPANSION IN THE PABPN1 GENE

## PABPN1:

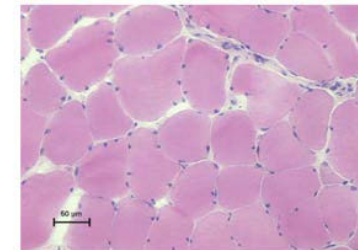
- A ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor) and thus controls the length of mRNA poly(A) tails, mRNA export from the nucleus, and alternative poly(A) site usage.



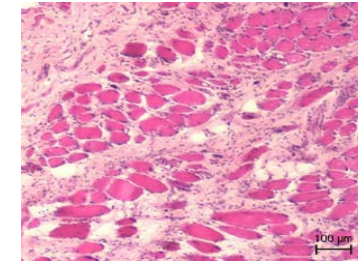
## In OPMD:

- A 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.

WT ATG (GCG)<sub>6</sub> -----(GCA)<sub>3</sub> GCG GGG GCT GCG..  
MUT ATG (GCG)<sub>6</sub> (GCG)<sub>1-7</sub> (GCA)<sub>3</sub> GCG GGG GCT GCG...--

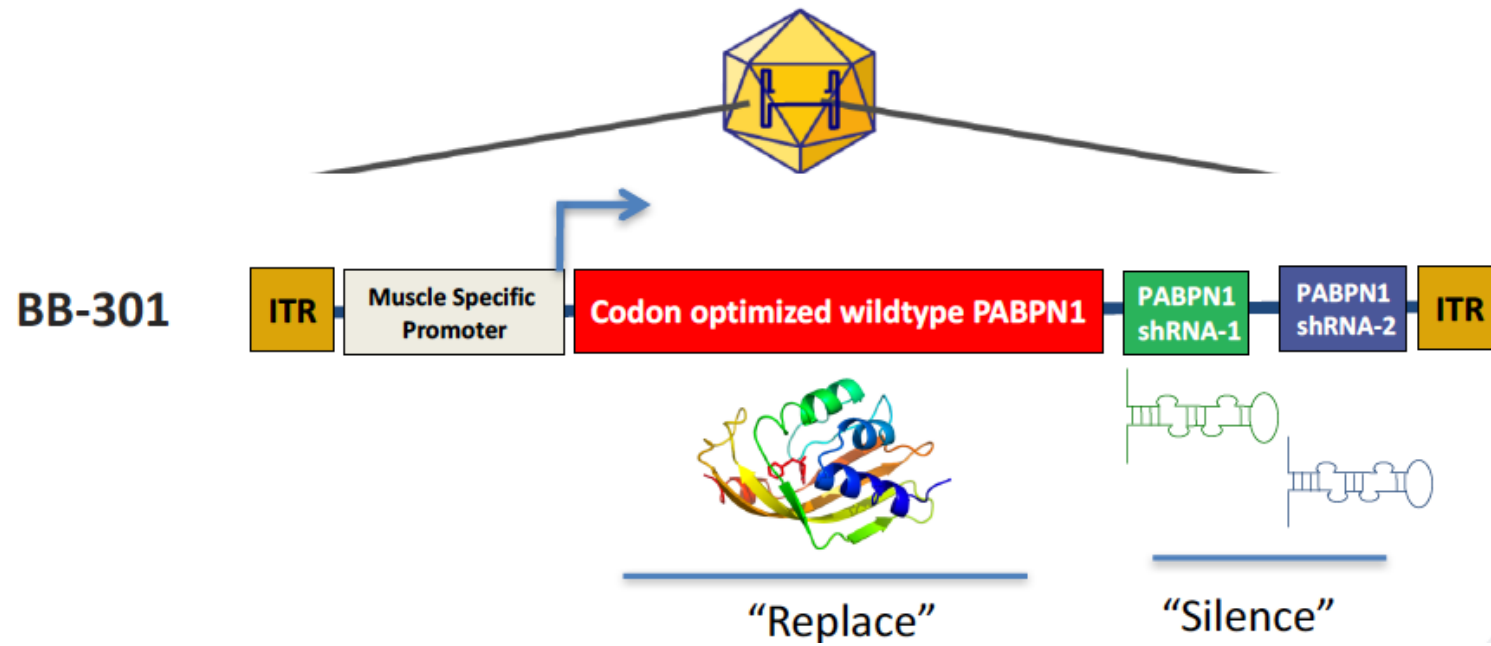


Non-affected



Affected

# BB-301: A 'SILENCE AND REPLACE' BASED APPROACH



## AAV

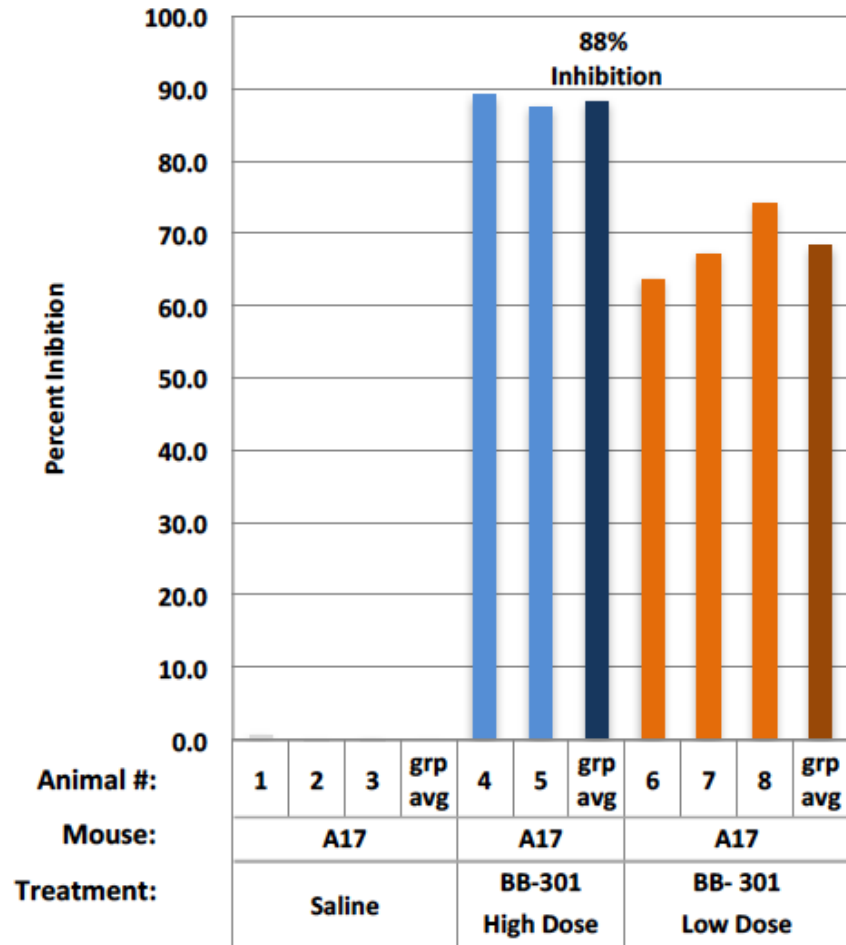
- Non-integrating, non-pathogenic viral delivery
- To date, AAV has been used in almost 200 clinical trials
- Sustained expression (years) following single injection

	G	S	G	P	G	R	R	R	H	L	V	P	G	A	G	G	E													
Wild type Sequence	ggctccggggccggggcggcggcgcctcttgtgcccggggccgggtggggag																													
Codon Optimized Sequence	ggc	AG	cgg	C	cc	T	gg	CA	g	Ac	gg	gc	G	cat	ct	G	gt	C	cc	T	gg	C	g	cc	gg	A	gg	gg	g	ag
	G	S	G	P	G	R	R	R	H	L	V	P	G	A	G	G	E													

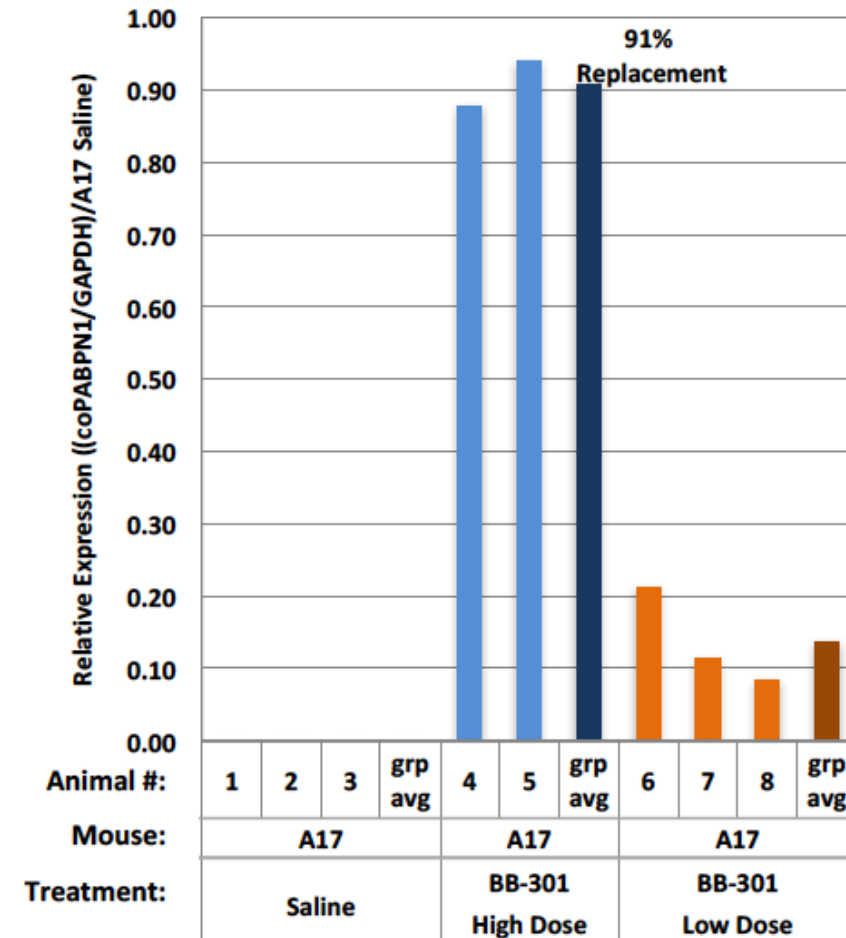
← Insensitive to shRNA

# BB-301 SILENCES MUTANT PABPN1 EXPRESSION AND RESTORES NORMAL PABPN1 IN OPMD MOUSE MODEL

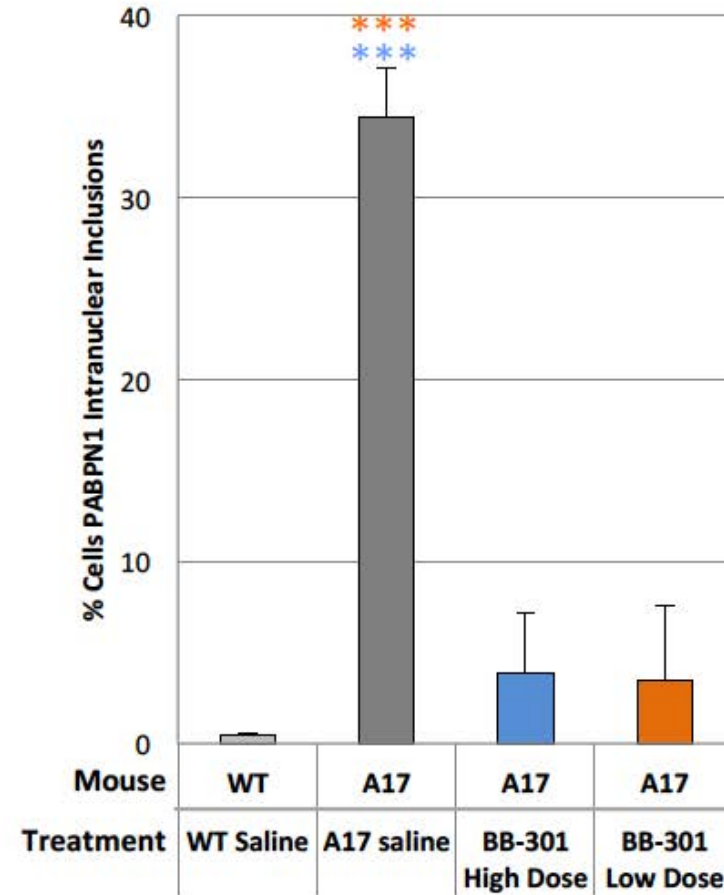
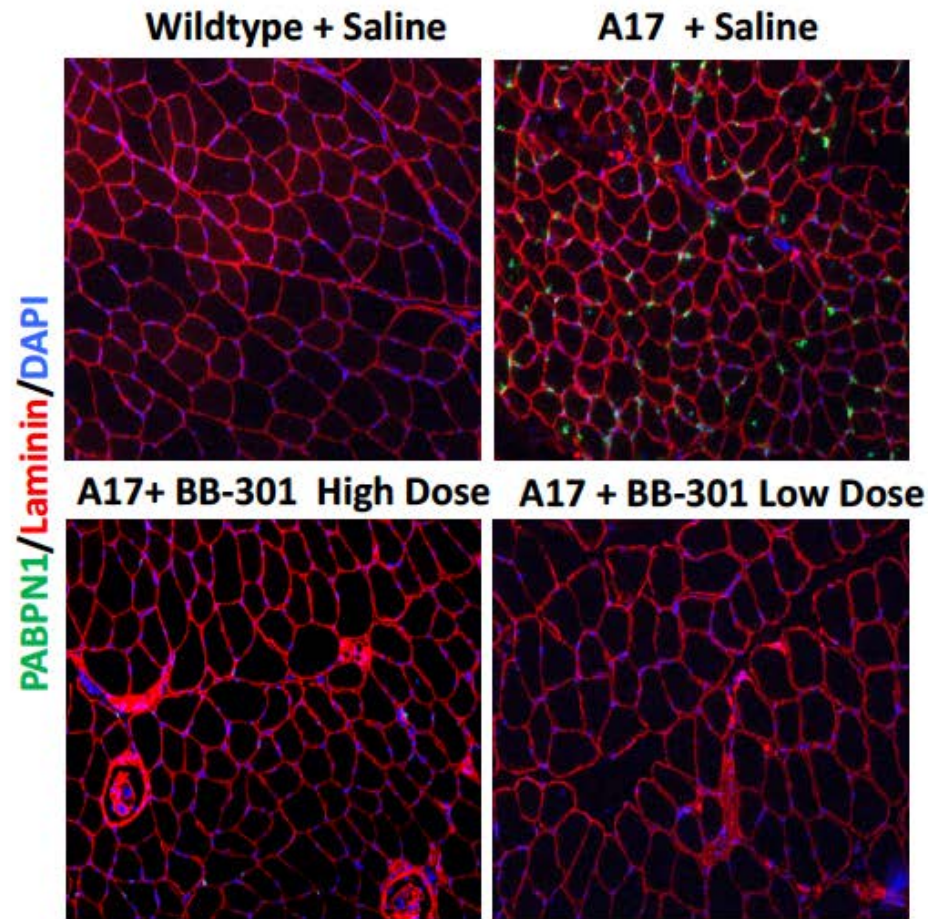
**SILENCE: Inhibition of PABPN1 Expression**



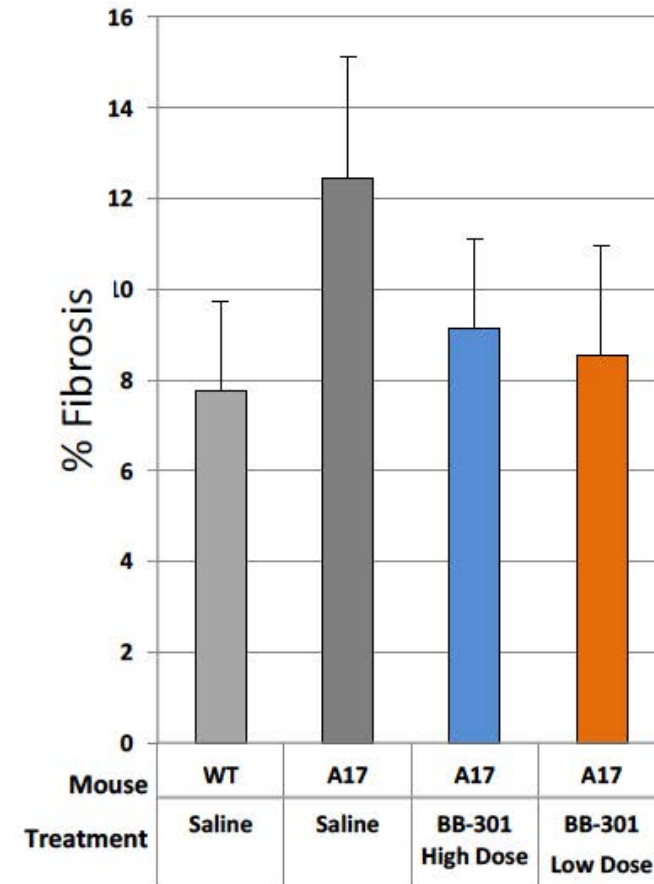
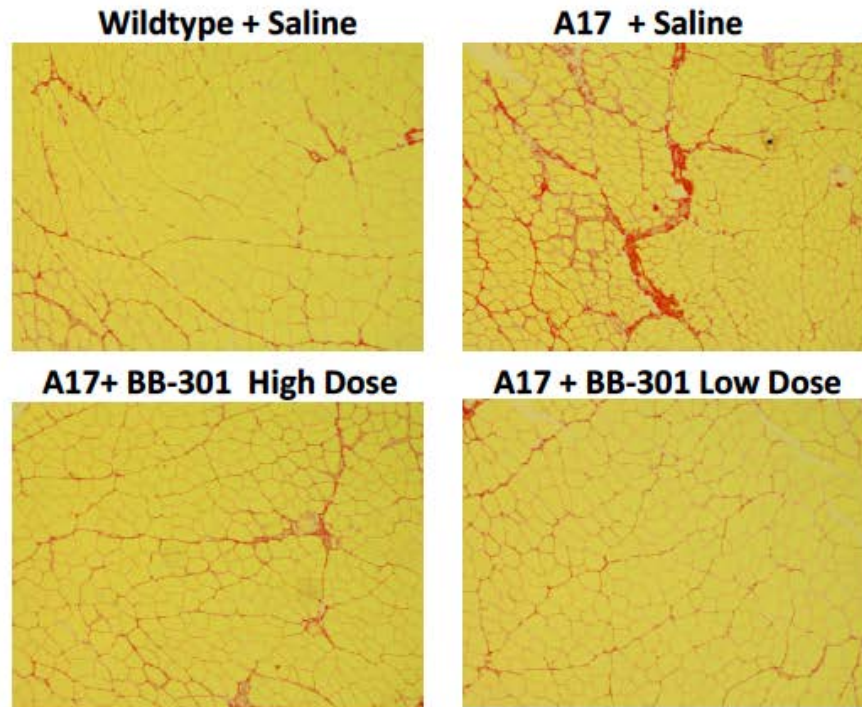
**REPLACE: Codon-Optimized PABPN1 Expression**



# BB-301 REVERSES INTRANUCLEAR INCLUSIONS IN OPMD MOUSE MODEL

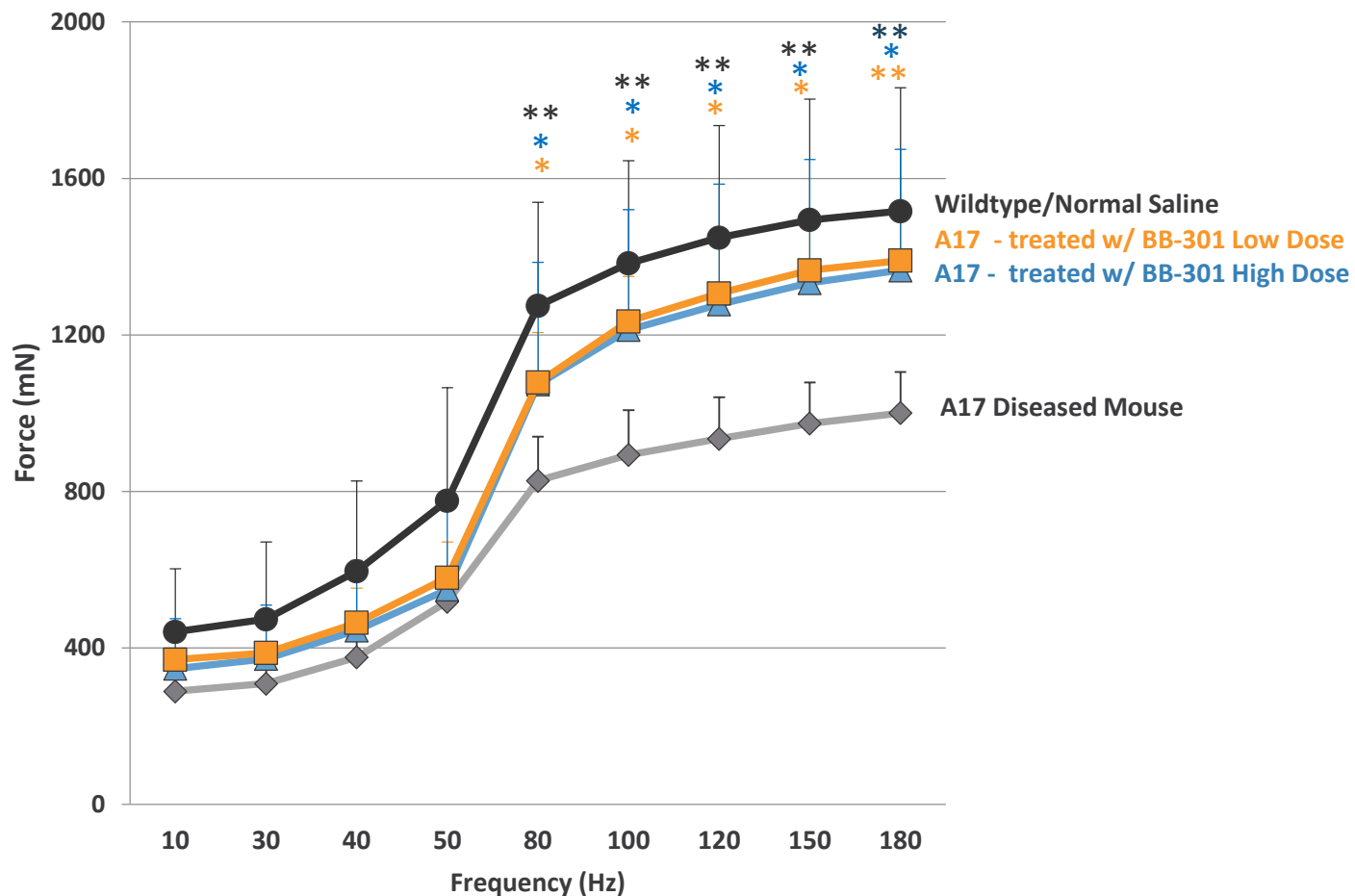


# BB-301 REVERSES FIBROSIS IN TRANSVERSE MUSCLE SECTIONS IN OPMD MOUSE MODEL

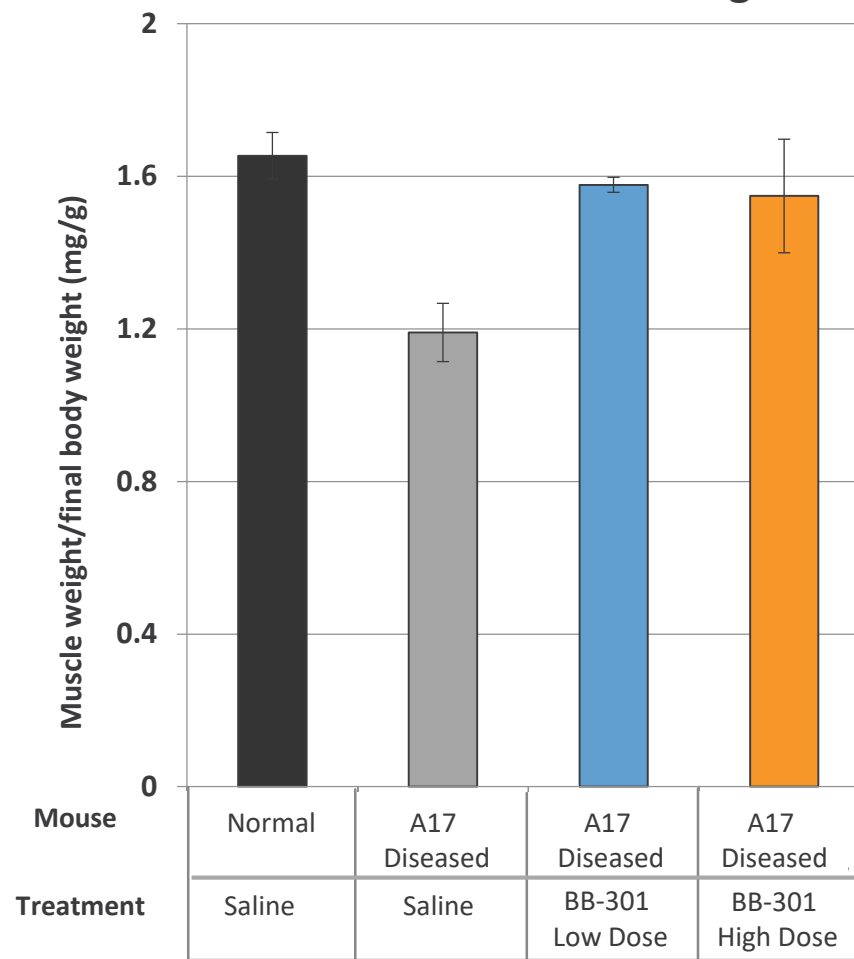


# BB-301 RESTORES MUSCLE FUNCTION IN OPMD MOUSE MODEL

## Restoration of Muscle Force






## Restoration of Muscle Weight



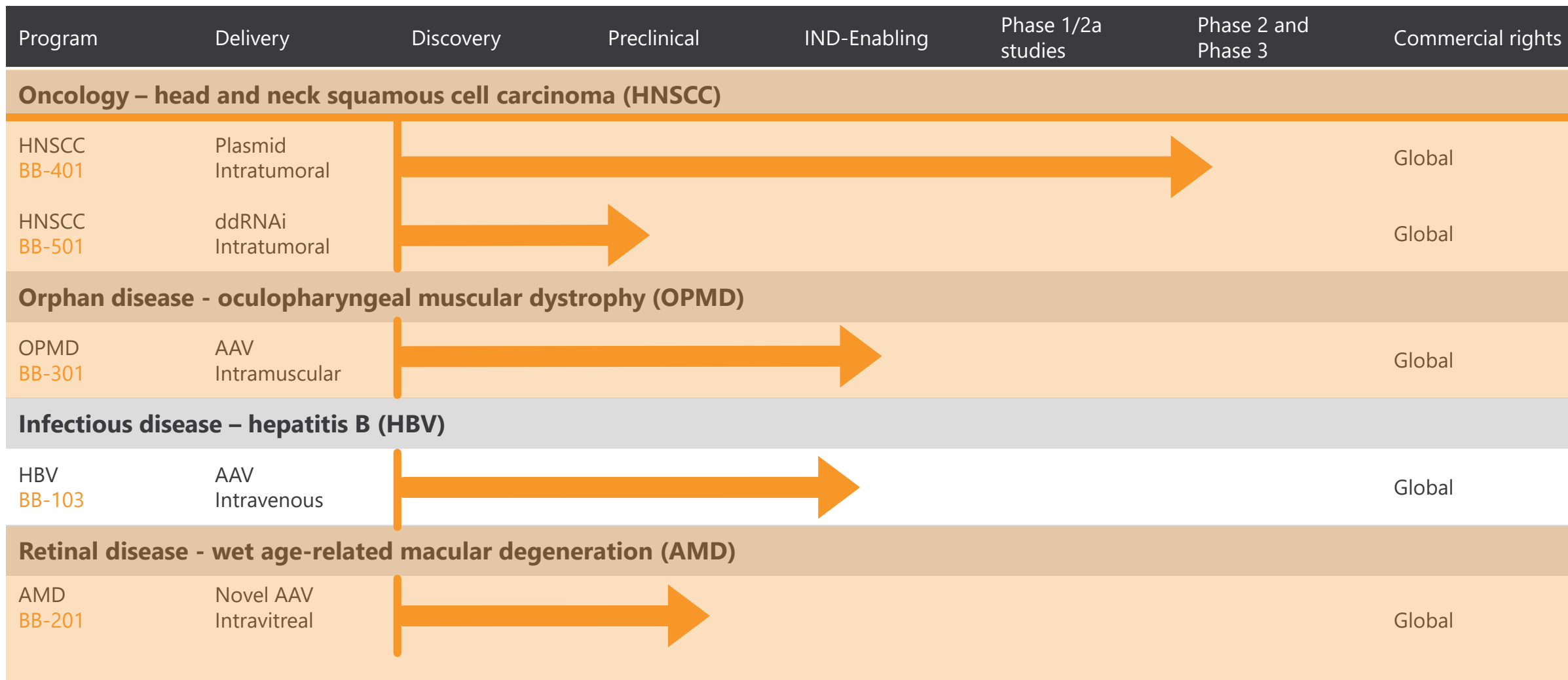
# OCULOPHARYNGEAL MUSCULAR DYSTROPHY

## Clinical Candidate BB-301: Product Overview

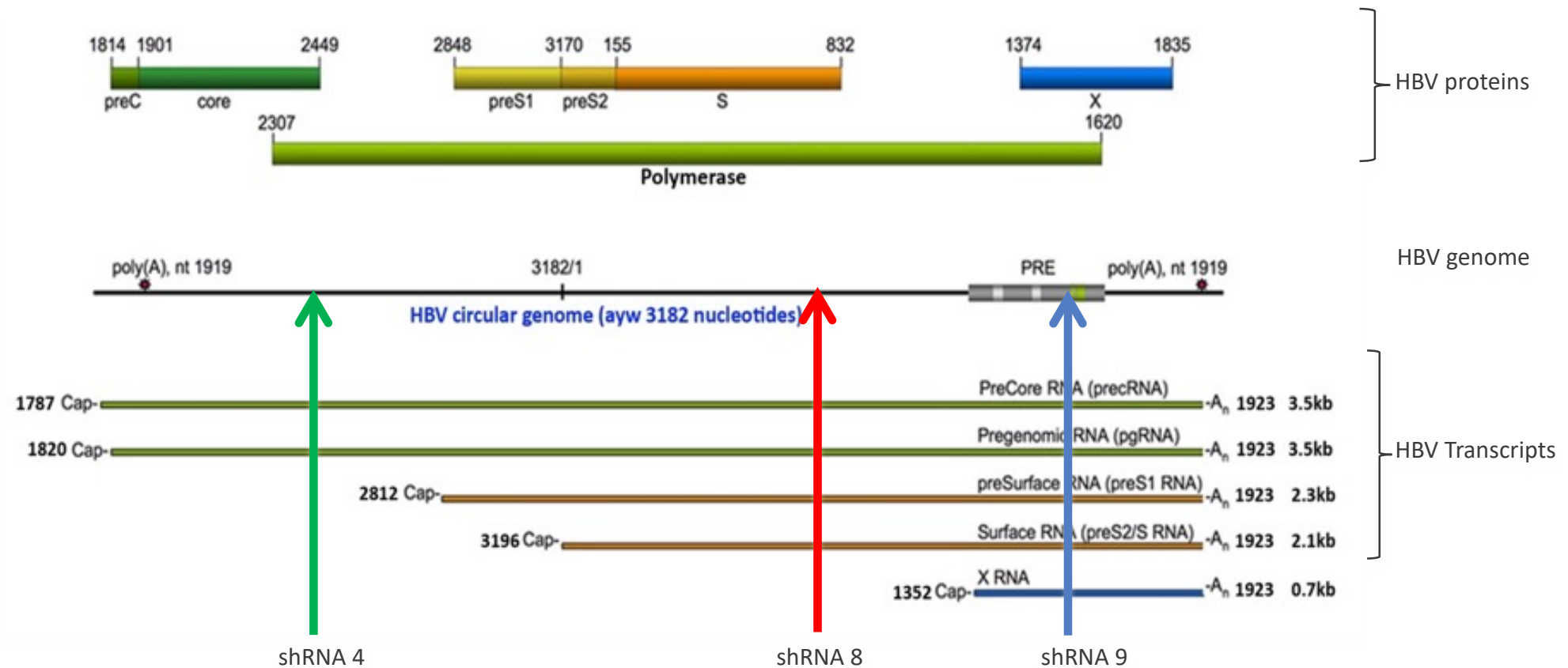
 <p>Oculopharyngeal muscular dystrophy (OPMD)</p>	<p>Rare, autosomal dominant, heritable monogenic disease</p>	<p>Estimated 12,000 effected patients in Western countries.</p>	<p>Eyelid drooping, swallowing difficulties, proximal limb weakness, death due to aspiration pneumonia and malnutrition</p>
 <p>BB-301 Product Profile</p>	<p>Designed to treat dysphagia associated with OPMD</p>	<p>'Silence and Replace' – unique gene therapy mechanism</p>	<p>Silence: mutant PABPN1 gene Replace: Simultaneously introduces normal PABPN1 gene to restore function</p>
 <p>Value / Commercial Opportunity</p>	<p><u>Near term value inflection point:</u> 4Q18 clinic entry Commercial opportunity in excess of US\$1 billion</p>	<p>Significant unmet medical need with no direct competition Orphan status provides expeditious and cost efficient commercialization path</p>	<p>Potential for silence and replace approach for other monogenic diseases</p>



# BENITEC PIPELINE

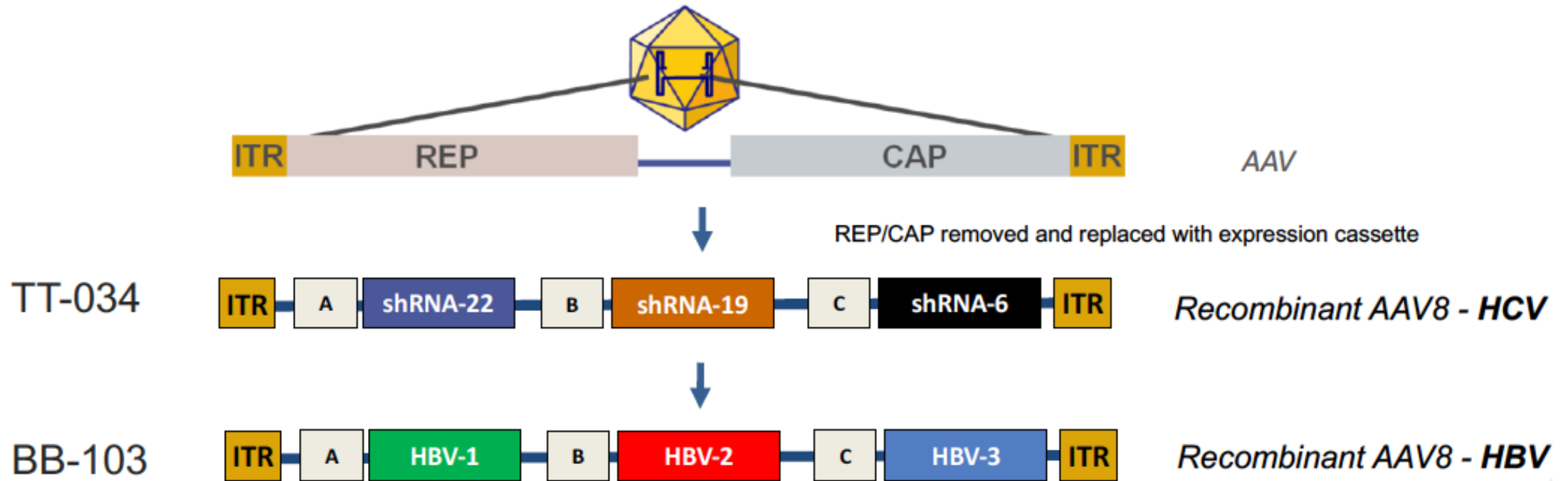


# BB-103 POSITIONS INHIBITORY shRNA ACROSS WELL CONSERVED SEQUENCES IN THE HBV GENOME



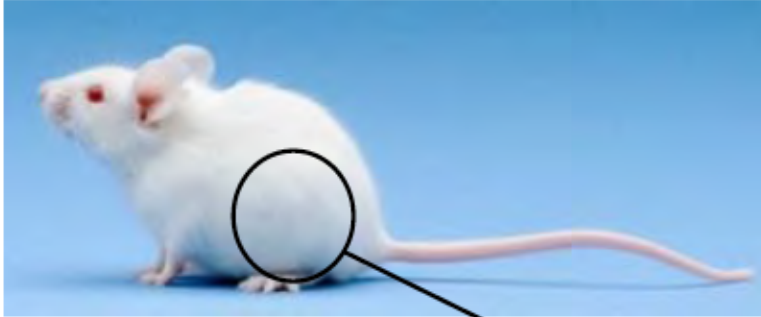
\* Sequences selected for shRNA are well conserved across HBV genotypes A-H

# BB-103 BUILDS UPON THE LEARNINGS FROM BENITEC'S FIRST IN MAN TRIAL WITH TT-034 IN HCV



Safety and Efficacy Study in Single Doses of TT-034 in Patients with Chronic Hepatitis C  
Clinical Trials.gov Identifier: NCT10899092

# PXB MOUSE, A CHIMERIC ANIMAL 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



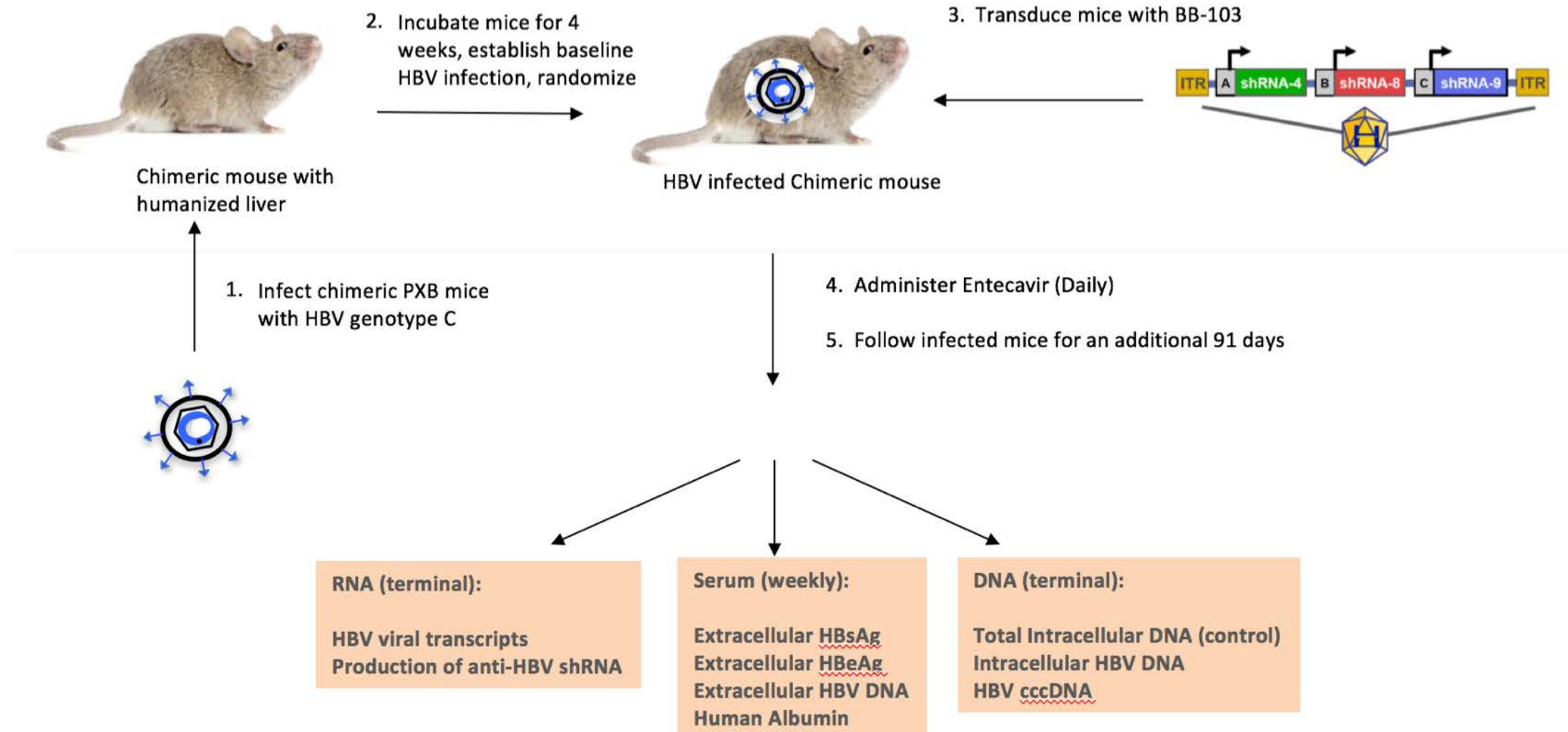
cDNA-uPA/SCID  
Liver weight: 0.7 – 1 g

**Transplantation**



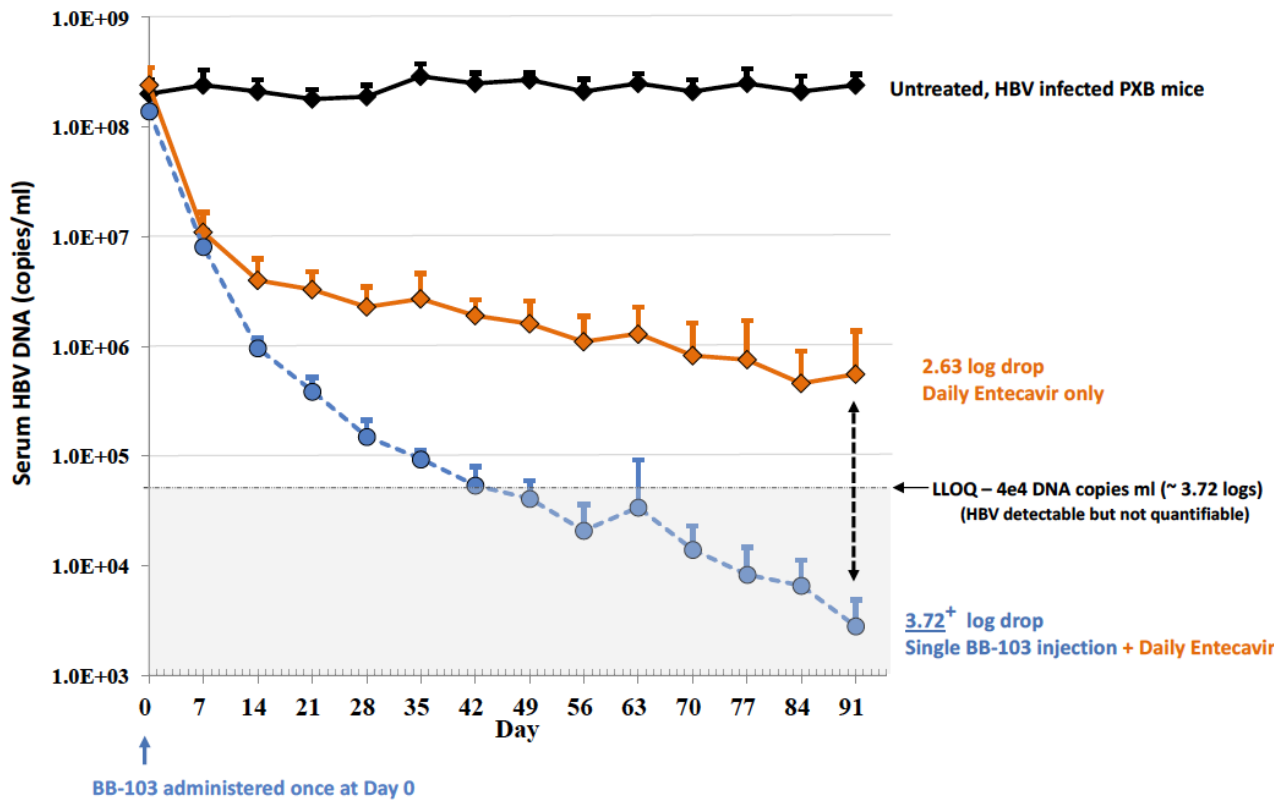
PXB-Mouse®  
Liver weight: 2 – 2.5 g  
(RI: 98 %)

# IN VIVO INFECTIOUS STUDIES USING PXB MICE

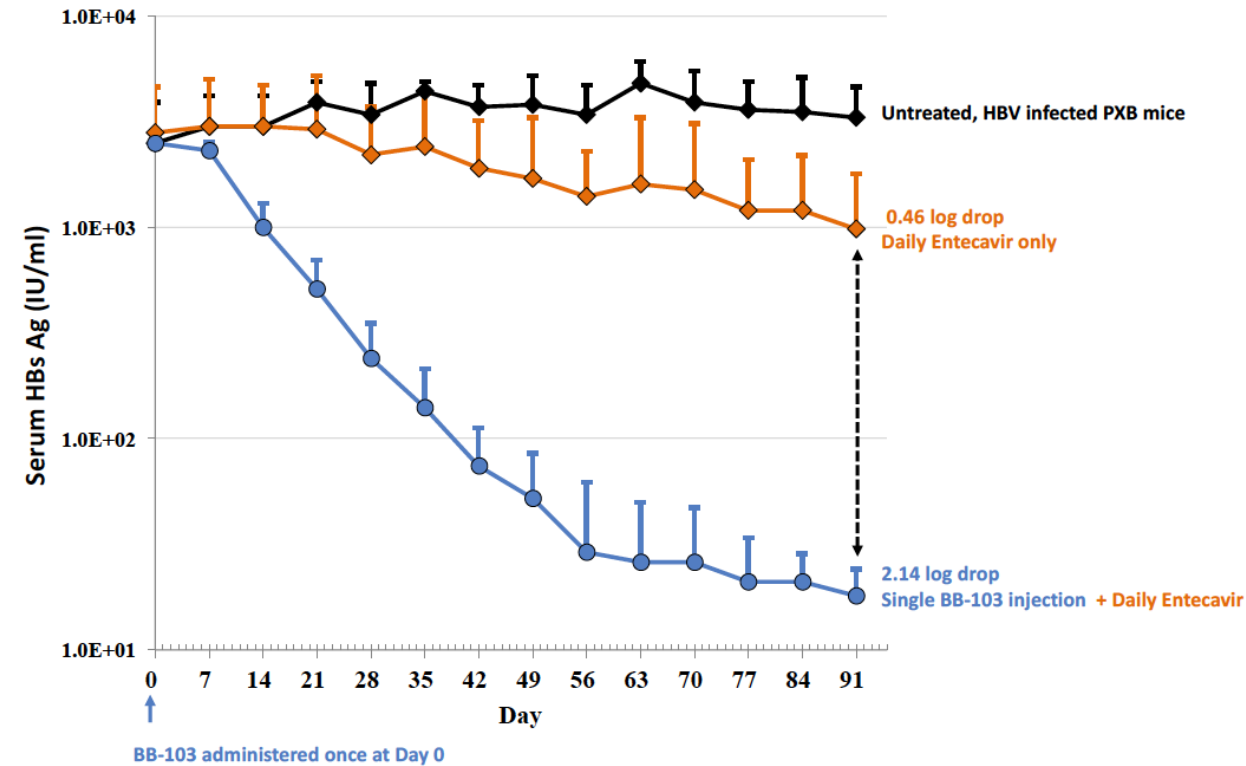


# A SINGLE DOSE OF BB-103 + DAILY ENTECAVIR RESULTS IN >4 LOG SUPPRESSION OF HBV DNA AND >2 LOG HBsAg

## Reduction in HBV serum DNA

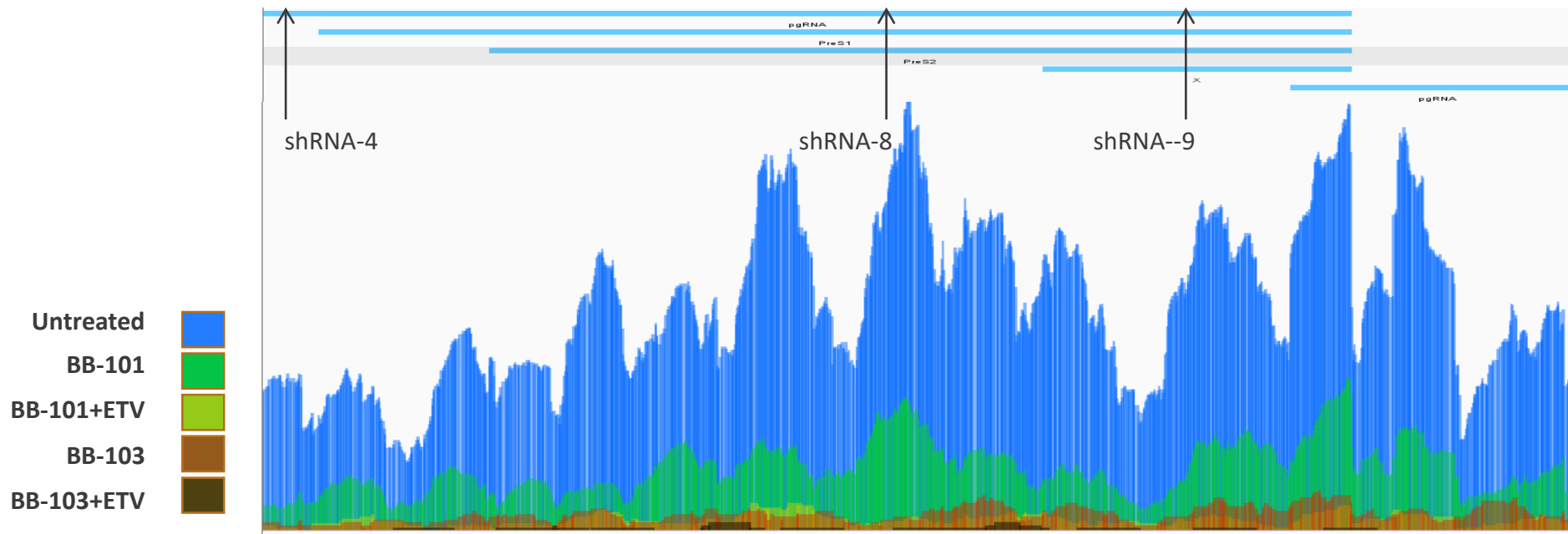


## Reduction in HBsAg (s-antigen)



# BB-103 + ENTECAVIR REDUCES HBV VIRAL RNA BY > 99%

	Total HBV Reads (per 1M reads)	Reads Normalized to RNA Length (per 1kb)		
		pgRNA (3.5Kb)	PreS1/S2 mRNA (2.4/2.1 Kb)	X RNA (0.7kb)
Untreated	1674	435	171	112
BB-101	457	119	45	31
BB-101+ETV	72	19	8	5
BB-103	122	30	12	9
BB-103+ETV	13	3	2	1



Max Read Depth: 136

# HEPATITIS B

## Clinical Candidate BB-103: Product Overview



### Hepatitis B (HBV)

WHO estimates HBV infects 257 million people resulting in up to 780,000 deaths per year

HBV viral proteins, especially HBsAg causes hepatic inflammation, liver dysfunction, acute hepatic failure, cirrhosis, or HCC

Need for effective therapies that promote the restoration of a host immune response through targeted HBsAg knockdown



### BB-103 Product Profile

Designed as a single dose treatment to be added on top of existing SOC

Designed against well conserved sequences in all major HBV genotypes

Superior efficacy: Combined with ETV, a single dose of BB-103 in chimeric mouse model:  
> 4 log drop in HBV DNA  
> 2 log drop in HBsAg



### Value / Commercial Opportunity

Near term value inflection point: With partnership could be clinical ready 2019

Pre-IND FDA meeting informed a clear and expeditious path to the clinic

Leverages use of TT-034 clinical data, Benitec's first in man HCV study



# PROGRAM SUMMARY



## **BB-401:** Oncology (HNSCC)

- EGFR antisense asset BB-401 into clinic in open label study in 1Q18
- Clinical studies planned in recurrent or metastatic head and neck squamous cell carcinoma



## **BB-301:** Orphan disease (OPMD)

- Unique single vector 'silence and replace' mechanism
- Pre-IND regulatory meetings completed with FDA, Health Canada and several European Agencies
- Clinic entry planned for 4Q 2018



## **BB-103:** Infectious disease (HBV)

- Preclinical POC showed significant reduction in viral load (>4 log) and HbsAg (>2 log) combined with SOC
- Pre-IND April 2017 informed direct path to clinic entry
- Seeking partnerships to move the program into the clinic



## **BB-201:** Retinal disease (AMD)

- Identified novel viral capsids for delivery to retinal cells via intravitreal injection
- Ongoing PoC in non human primates using laser induced model of neovascularization – final data 1Q18
- Delivery platform may be used to treat other retinal diseases



# INVESTMENT HIGHLIGHTS



## **Novel combination of gene therapy and gene silencing**

- **Validated ddRNAi technology**
- **Robust pipeline in oncology, orphan genetic disorders, retinal disease and infectious disease**
- **Two programs in clinic by the end of 2018**



## **Capital market access**

- **Listed on ASX and NASDAQ**
- **US shelf registration**
- **US\$40m capital raised**



## **Strong in-house capabilities**

- **Scientific operations**
- **Deep gene therapy expertise**
- **In-house manufacturing expertise for process optimization and scalability**



**BENITEC**  
B I O P H A R M A

NASDAQ: BNTC | ASX: BLT

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