



NASDAQ: BNTC

ASX: BLT

Path to Value Creation

September 2017

Rodman & Renshaw Global
Investment Conference

Safe Harbor Statement



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Business Overview

A multi-product clinical stage company in 2018



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

PROVEN TECHNOLOGY

Validated technology with two clinical assets by the end of 2018

ROBUST PIPELINE

Assets in oncology, orphan genetic disorders, retinal disease, and infectious disease

VALUABLE PRODUCTS

Human therapeutic products for commercialization, partnering, and collaborations

Programs advancing to the clinic

- Phase II ready EGFR-targeted gene silencing therapeutic achieved POC in **head & neck cancer** entering confirmatory Phase II trial in Q1 2018.
- Unique “silence and replace” therapeutic designed to treat orphan disease **oculopharyngeal muscular dystrophy** by silencing expression of the mutant disease-causing gene (PABPN1) and simultaneously reintroduces a normal copy of the gene. Anticipated to enter clinic at end of 2018.
- Other programs targeting **retinal disorders** and **infectious disease** expected to be clinic-ready late 2018/2019.

Capital markets access

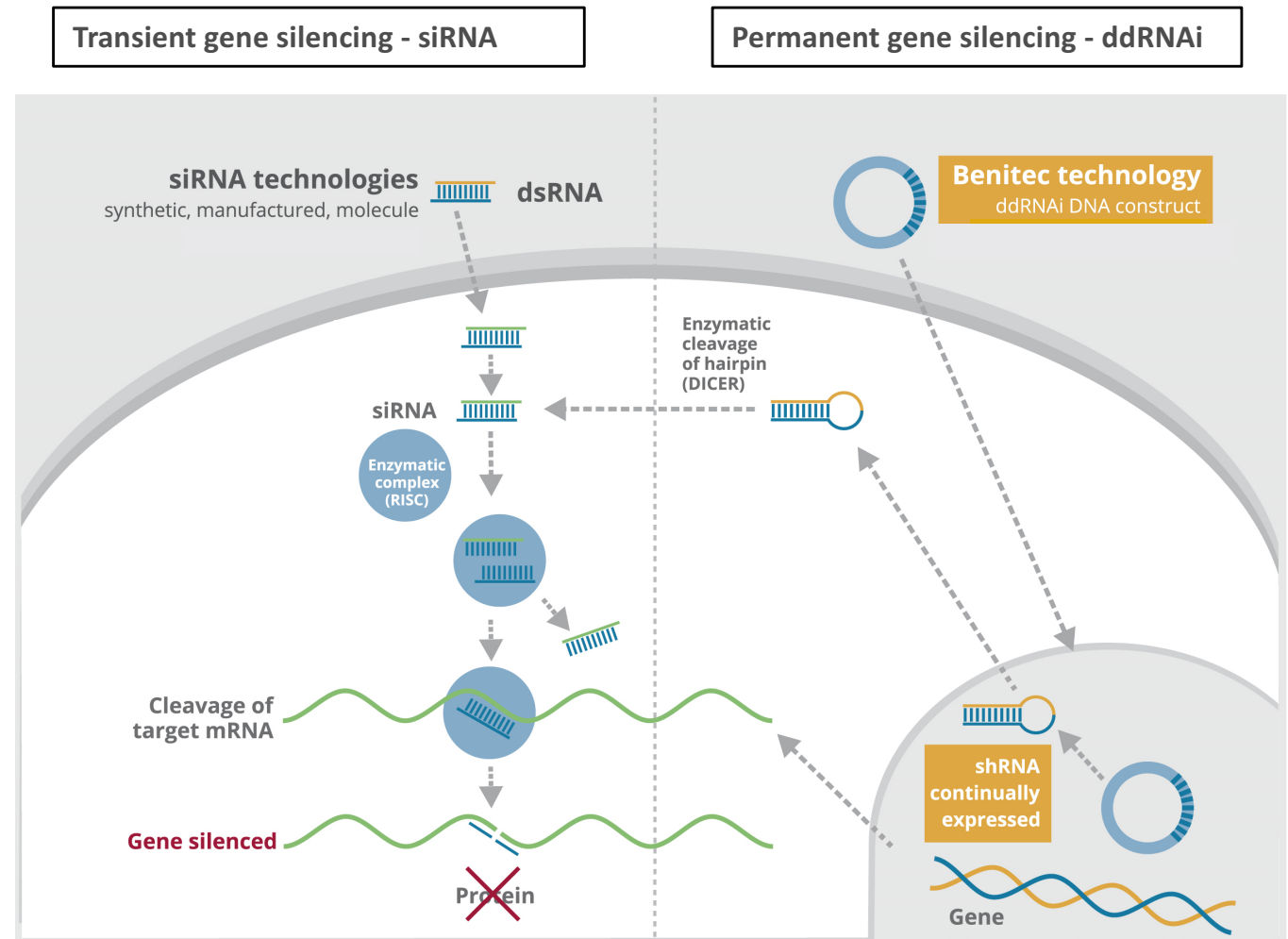
- Listed on ASX (2002) and NASDAQ (2015)
- Has raised US\$40M capital since 2014
- US SEC shelf registration June 2017

Strong in-house capabilities






- 23 staff with scientific operations in Hayward CA, including 13 PhDs with deep expertise in gene therapy
- In-house manufacturing expertise for process optimization and scalability
- Extensive commercial and drug development expertise

Permanent Gene Silencing with DNA-Directed RNA Interference (ddRNAi)

- 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

Program	Delivery	Discovery	Preclinical	IND-Enabling	Early stage clinical (IND – Phase 2)	Late stage clinical (Phase 2 – Phase 3)	Commercial Rights
Oncology – head and neck squamous cell carcinoma (HNSCC)							
HNSCC BB-401	Plasmid Intratumoral						• global
HNSCC BB-501	ddRNAi Intratumoral						• global
Orphan Disease – oculopharyngeal muscular dystrophy (OPMD)							
OPMD BB-301	AAV Intramuscular						• global
Retinal Disease – age-related macular degeneration (AMD)							
AMD BB-201	Novel AAV Intravitreal						• global
Infectious Disease – hepatitis B (HBV)							
HBV BB-103	AAV Intravenous						• global

Recent Achievements and Path to Value Creation



Value Creation

- Near term value inflection points as two programs move into the clinic in 2018
- Multi stage clinical company at the end of 2018
- Flexibility of ddRNAi platform can accelerate clinical and shareholder value with the ability to move proven ddRNAi therapeutics into additional rare diseases

Recent Achievements

- Nant Capital makes strategic investment in Benitec and brings in Phase II oncology clinical asset
- EU orphan drug designation for oculopharyngeal muscular dystrophy (OPMD)
- Nature Communications publication of initial OPMD 'silence and replace' preclinical data
- Proof of concept for ocular delivery of gene therapy
- Pivotal preclinical efficacy data in hepatitis B (HBV)
- Pre-IND meeting with US FDA informed a clear and expeditious path to the clinic for BB-103
- Australian R&D grant income of A\$10.5m for 2016-2017 fiscal year

Experienced Executive Team



Greg West Chief Executive Officer	<ul style="list-style-type: none">• Former CFO of Benitec Biopharma, 10 years biotech experience• Prior roles at PriceWaterhouse, Bankers Trust, Deutsche Bank and NZI
Dr. David Suhy Chief Scientific Officer	<ul style="list-style-type: none">• Former SVP of Research & Development, Benitec Biopharma• Prior roles at Tacere Therapeutics, Antara Biosciences and PPD Discovery
Georgina Kilfoil Chief Clinical and Development Operations Officer	<ul style="list-style-type: none">• Former VP of Clinical Operations, Benitec Biopharma• Prior roles at Anthera Pharmaceuticals, InClin and Peninsula Pharmaceuticals
Dr. Cliff Holloway Chief Business and Operating Officer	<ul style="list-style-type: none">• Former CEO and MD of Sienna Cancer Diagnostics, and Biosceptre International• Prior VP BD role at Arana Therapeutics (now Teva Pharma)
Bryan Dulhunty Chief Financial Officer	<ul style="list-style-type: none">• Former Executive Chairman, Viralytics• Prior roles as NED, MD, CFO and Company Secretary of a number of listed and non-listed biotech companies
Dr. Michael Graham Head of Discovery & Founding Scientist	<ul style="list-style-type: none">• Discoverer of ddRNAi at CSIRO; Former Senior Research Fellow, University of Queensland• Prior roles at QDPI and CSIRO

Company Financial Snapshot



Key Shareholder Details	Australia Listed ASX 2002: BLT	US Listed NASDAQ 2015: BNTC/BNTCW
Share Price as of 30 June 2017: (ADR 25:1)	A\$0.125	US\$1.85 (ADS)
52 week high/low as of 30 June 2017	A\$0.28/A\$0.085	US\$5.48 / US\$1.2 (ADS)
Average daily volume (6 months to 30 June, 2017)	410,067 shares	485,353 shares
Market Capitalization as of 30 June 2017	A\$25.6m	US\$19.7M
Issued ordinary shares as of 30 June 2017	205,140,734	--
Total options and warrants on issue as of 30 June 2017	34,468,203	
Insider holdings – Nant Capital LLC	29%	
Cash balance as of 30 June 2017	A\$17.4m	
Net assets as of 30 June 2017	A\$21.5m	
Net loss as of 30 June 2017	A\$5.6m	
Capital raised	US\$35m since 2014	
US SEC shelf registration	June 2017	
Facilities	Corporate Sydney, Australia	Scientific Operations Hayward, California

Head and Neck Squamous Cell Carcinoma (HNSCC) Program Update



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Head and Neck Squamous Cell Carcinoma (HNSCC)

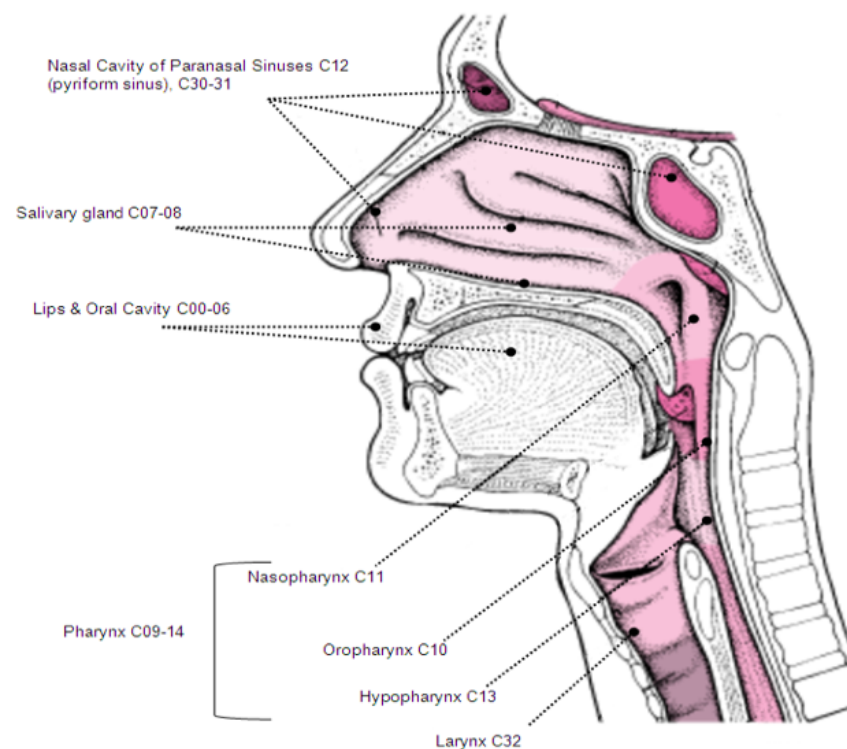
Incidence and Patient Mortality:

- 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



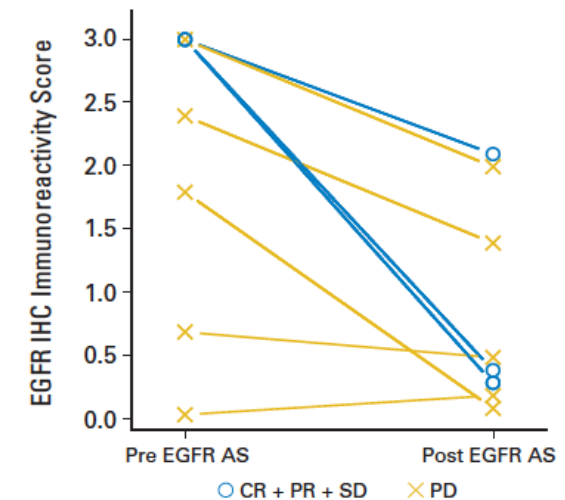
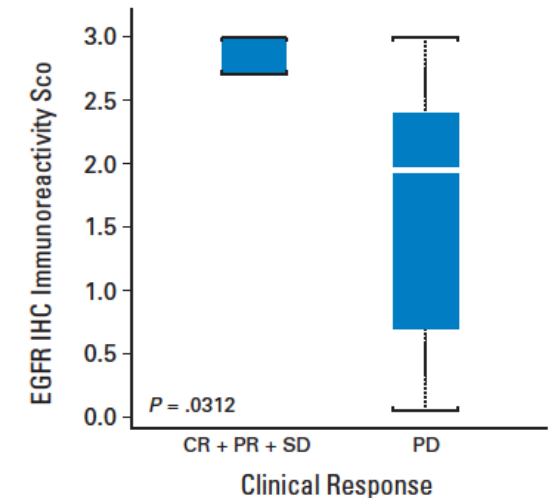
BB-401: Expressed Anti-Sense RNA Against EGFR

Phase 1 Single Agent Clinical Data



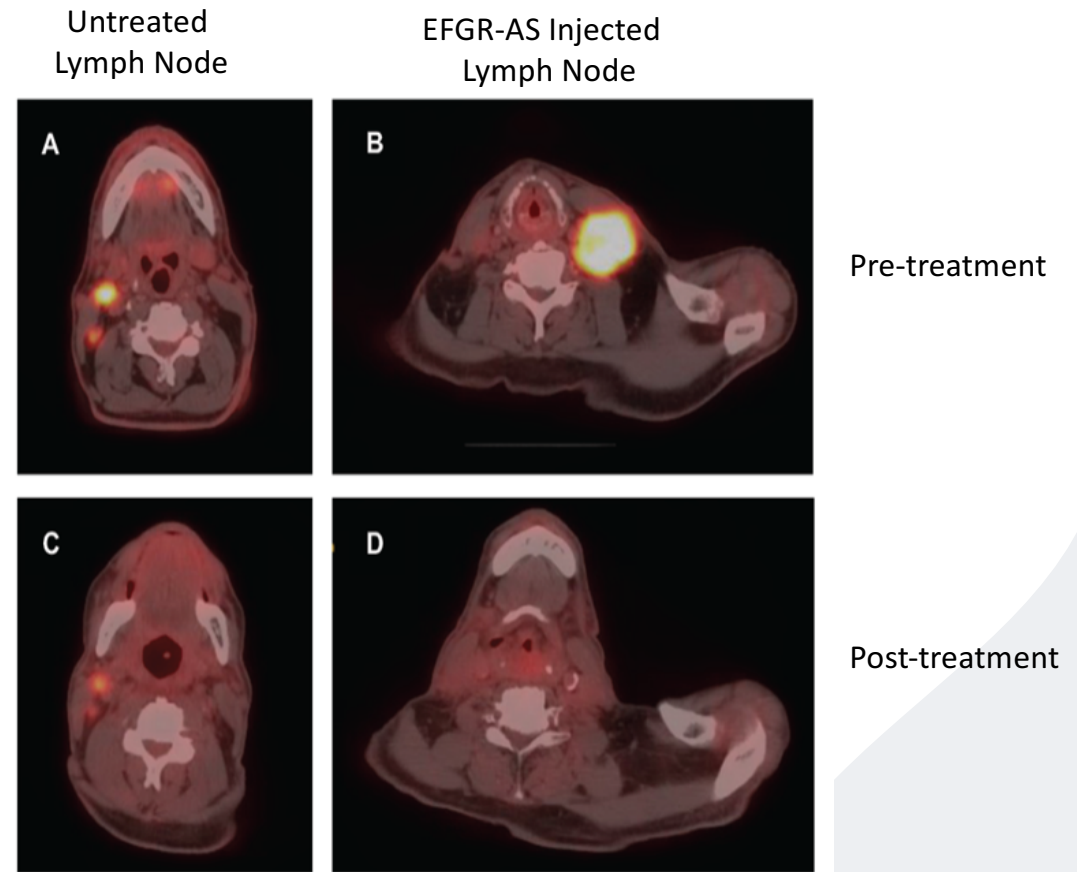
- Phase I study* of 17 patients with advanced, refractory HNSCC
- Safety and efficacy evaluated following direct intra-tumoral injection weekly for 4 weeks:
 - 29 % (5 patients) -Objective Response
 - Of these 2 patients experienced Complete Response (100% reduction in size by RECIST) & 3 patients Partial 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

*Lai *et al.*, Journal of Clinical Oncology, 2009



BB-401: Follow on Phase 1 Study of BB-401 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

- Over 50,000 new cases diagnosed in the US 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 epidermal growth factor receptor (EGFR)

BB-401 Product Profile

- EGFR Targeted via expressed antisense RNA EGFR
- In Phase I, strong correlation of response versus EGFR expression
- Robust response when compared to other monotherapy treatments or when paired with SOC treatments

Value / Commercial Opportunity

- Near-term value inflection point: Phase II study in up to 50 patients planned for initiation in 1Q18
- 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

Oculopharyngeal Muscular Dystrophy (OPMD) Program Update



Program	Delivery	Discovery	Preclinical	IND-Enabling	Early stage clinical (IND – Phase 2)	Late stage clinical (Phase 2 – Phase 3)	Commercial Rights	
Oncology – head and neck squamous cell carcinoma (HNSCC)								
HNSCC BB-401	Plasmid Intratumoral	▶						• global
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Orphan Disease – oculopharyngeal muscular dystrophy (OPMD)								
OPMD BB-301	AAV Intramuscular	▶					• global	
Retinal Disease – age-related macular degeneration (AMD)								
AMD BB-201	Novel AAV Intravitreal	▶					• global	
Infectious Disease – hepatitis B (HBV)								
HBV BB-103	AAV Intravenous	▶					• global	

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:

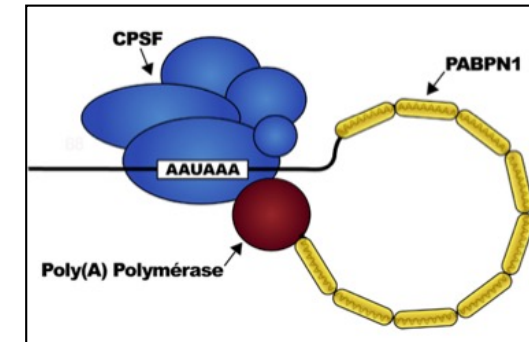
- Decrease of muscle fiber number
- Variation in the size of muscle fibers
- Fibrosis (connective tissue)



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

PABPN1:

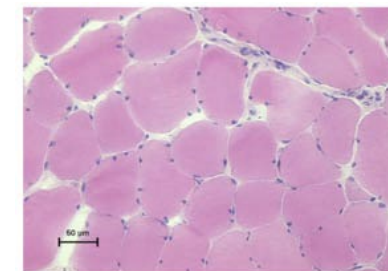
- A ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor) and thus controls the length of mRNA poly(A) tails, mRNA export from the nucleus, and alternative poly(A) site usage.



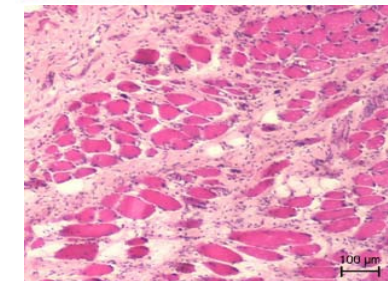
In OPMD:

- 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)₆ -----(GCA)₃ GCG GGG GCT GCG..
MUT ATG (GCG)₆ (GCG)₁₋₇ (GCA)₃ GCG GGG GCT GCG...--

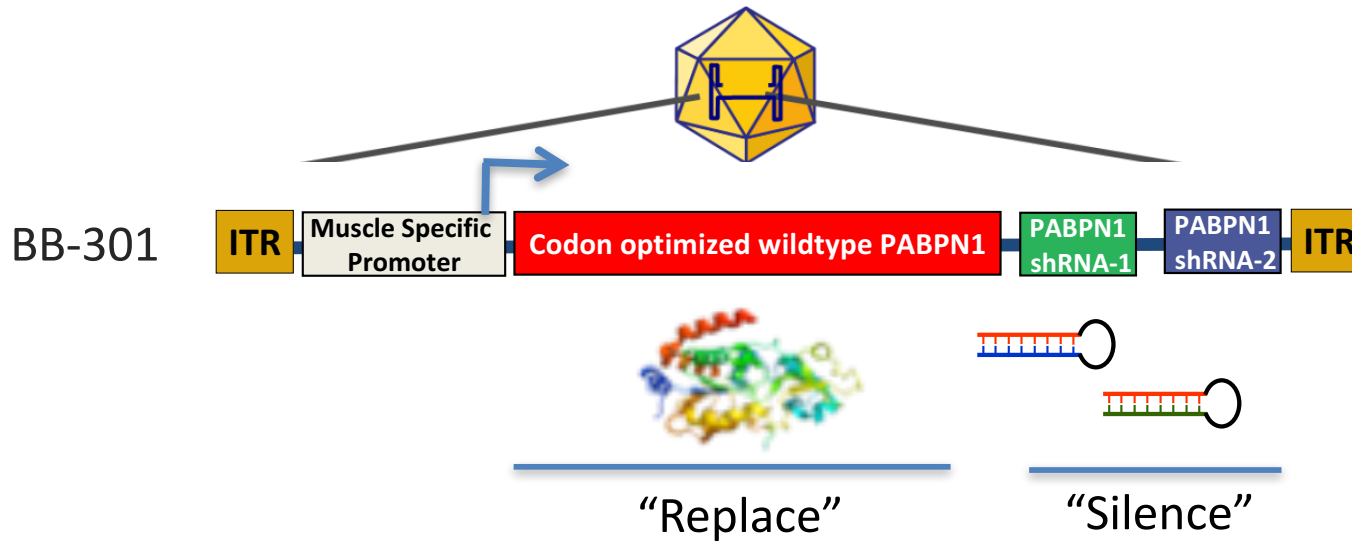


Non-affected



Affected

BB-301: 'Silence and Replace' Approach

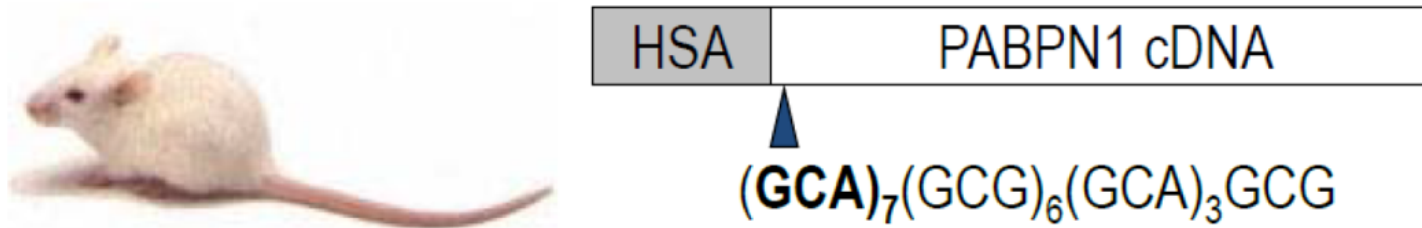


AAV

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

	G	S	G	P	G	R	R	R	H	L	V	P	G	A	G	G	E
Wild type Sequence	ggctccggggccggggcgccggcgccatcttgtgcccggggcccgggtggggag																
Codon Optimized Sequence	ggcAGcggCccTggCAGAcggcgGcatctGgtCccTggCgccggAggggag																
	G	S	G	P	G	R	R	R	H	L	V	P	G	A	G	G	E

← Insensitive to shRNA

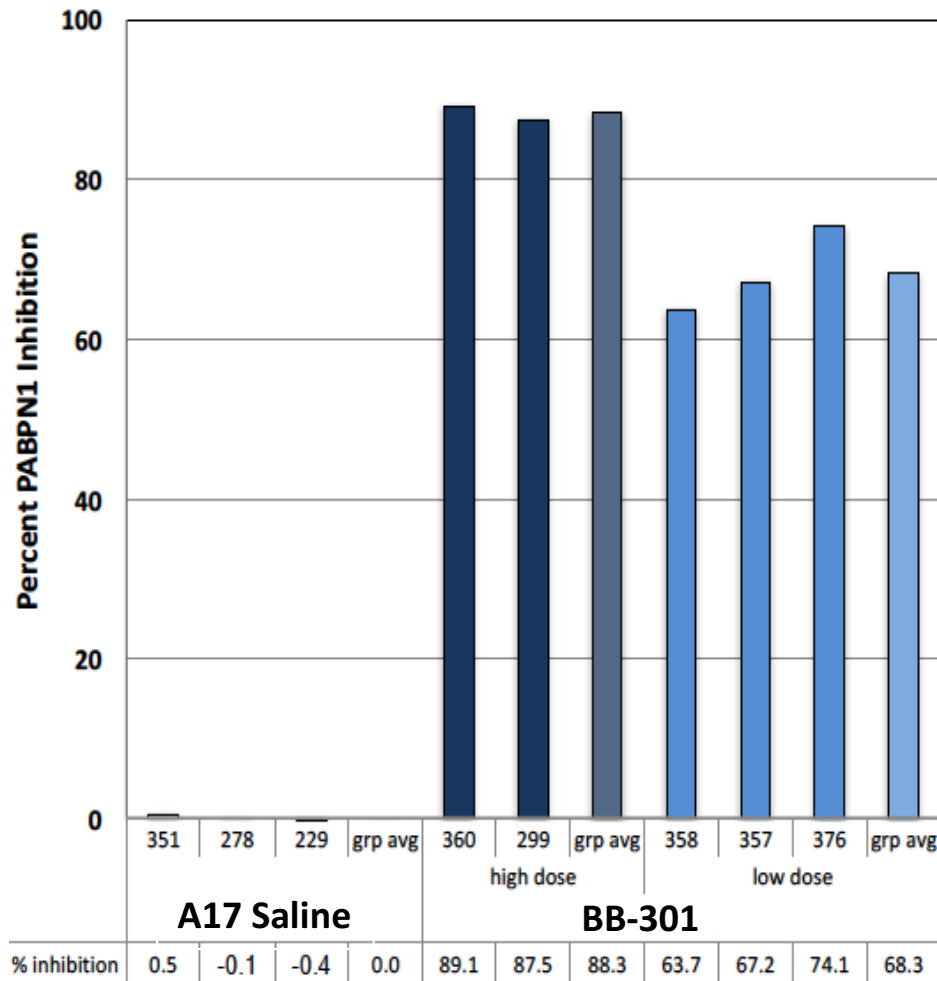


- Transgenic mouse: express a mutated bovine PABPN1 driven by the human skeletal actin promoter in addition to the endogenous PABPN1
- Recapitulates severe muscle atrophy
- Mimics many of the disease pathologies:
 - Progressive muscle weakness/ atrophy
 - Fibrosis
 - Mitochondrial / Ubiquitin-Proteasome defects
 - Muscles contain intranuclear inclusions

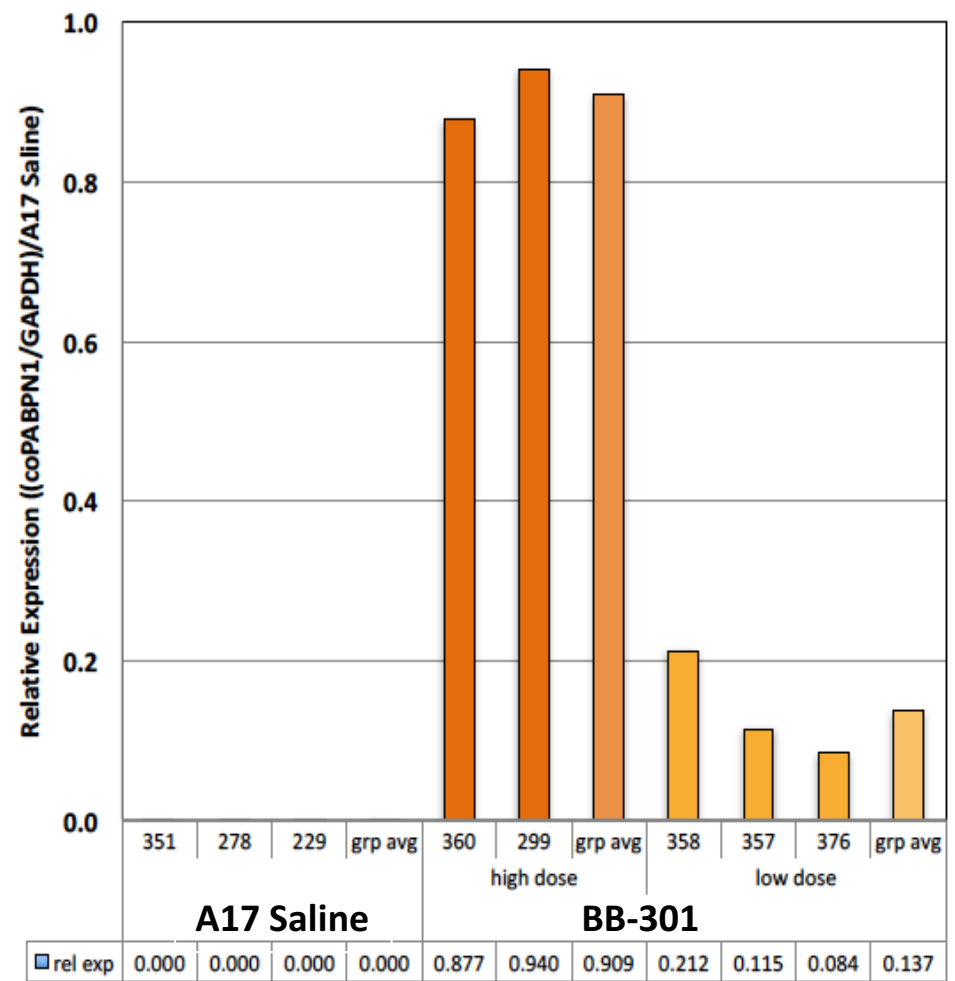
BB-301 Treatment Inhibits Diseased Gene Expression & Restores Wildtype PABPN1 Levels in A17 Mice



SILENCE: Inhibition of PABPN1 Expression

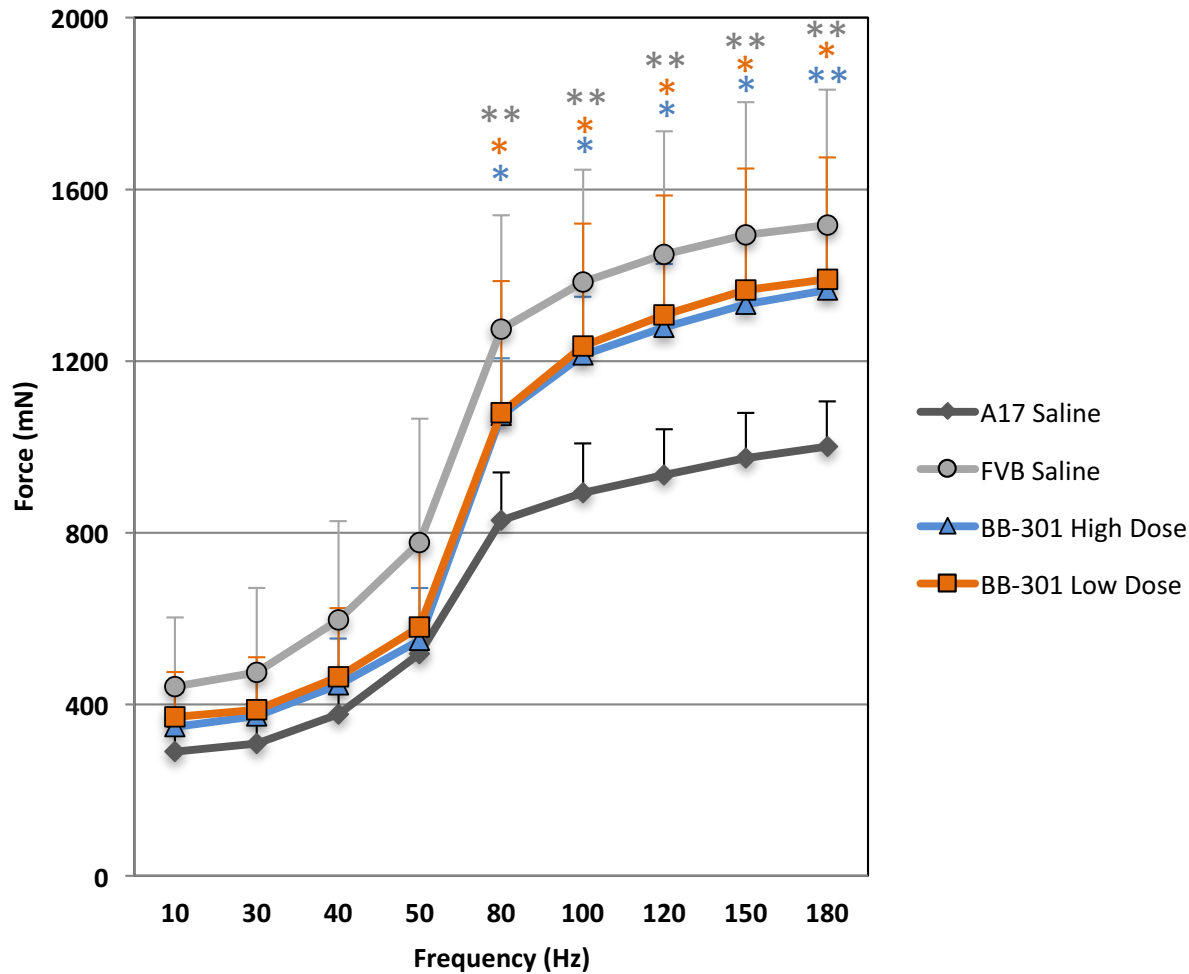


REPLACE: Codon-Optimized PABPN1 Expression

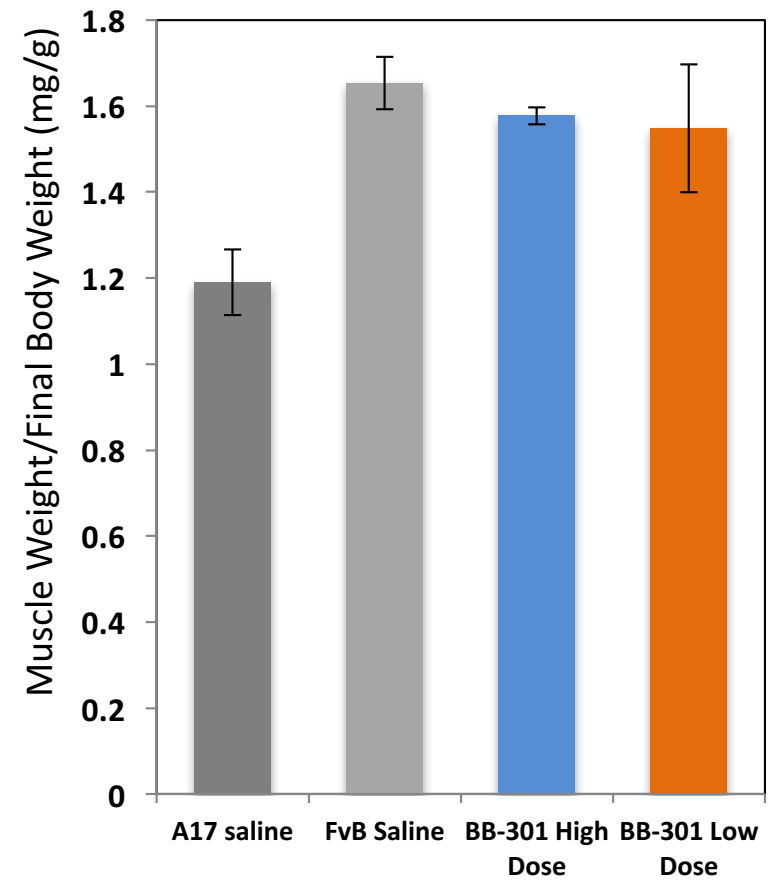


BB-301 Treatment Restores Muscle Force and Muscle Weight in A17 Mice

Restoration of Muscle Force



Restoration of Muscle Weight



Oculopharyngeal Muscular Dystrophy

Clinical Candidate BB-301: Product Overview

Oculopharyngeal Muscular Dystrophy

- Rare, autosomal dominant, monogenic disease
- Estimated 12,000 patients in Western countries
- Characterized by eye lid drooping, swallowing difficulties, proximal limb weakness, death due to aspiration pneumonia and malnutrition

BB-301 Product Profile

- Designed to treat dysphagia associated with OPMD
- ‘Silence and Replace’ – unique gene therapy mechanism
- Silence: Inhibits mutant PABPN1 gene
- Replace: Simultaneously reintroduces normal PABPN1 gene to restore function

Value / Commercial Opportunity

- Near-term value inflection point: 2H18 clinic entry
- Significant unmet medical need with no direct competition
- Orphan status provides expeditious and cost efficient commercialization path
- Commercial opportunity potentially in excess of US\$1 billion
- Potential for silence and replace approach for other monogenic disorders

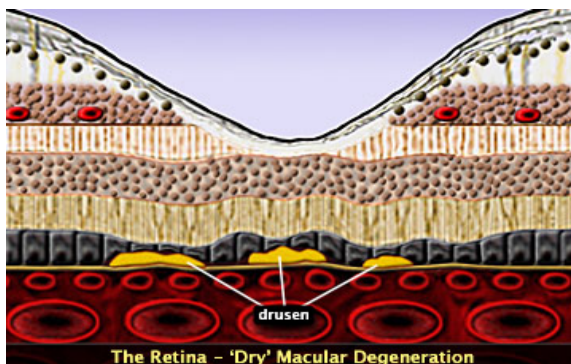
Wet Age-Related Macular Degeneration (AMD) Program Update



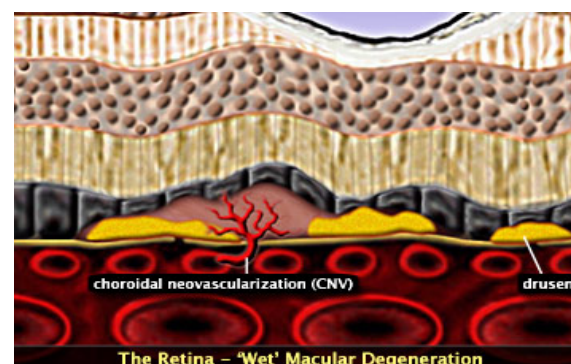
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HBV BB-103	AAV Intravenous	▶					• global	

Wet Age-Related Macular Degeneration (AMD) Disease Overview

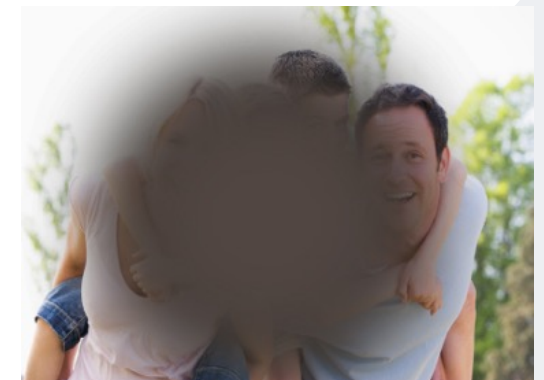
- Leading cause of irreversible vision loss in U.S. with 196M people affected worldwide by 2020
- Lucentis /Eylea act as a molecular sponges to mop up secreted VEGF-a (VEGF-b and PlGF)
- Although drugs stabilize vision in many, most do not see significant improvement in vision
- Ocular half life: ~ 9 days for Lucentis and 5-6 days for Eylea requiring frequent administration (monthly or bi-monthly)



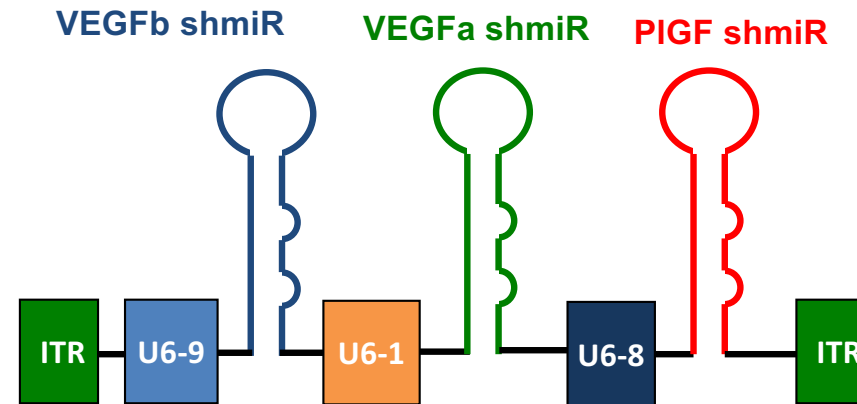
In Dry AMD, drusen deposits start to degrade vision



In Wet AMD, inflammatory cascade further degrades vision through neovascularization

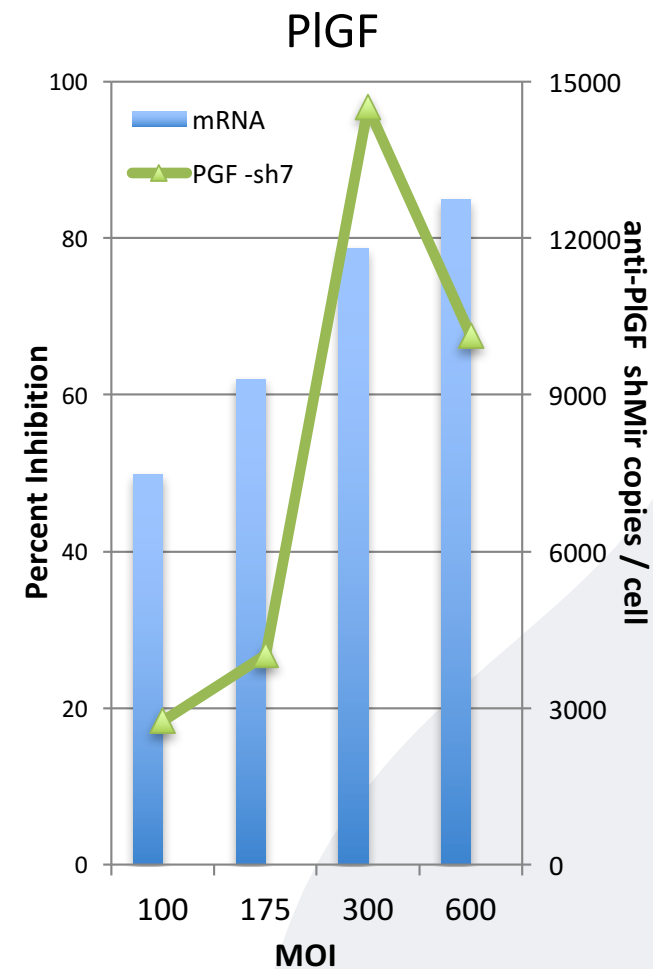
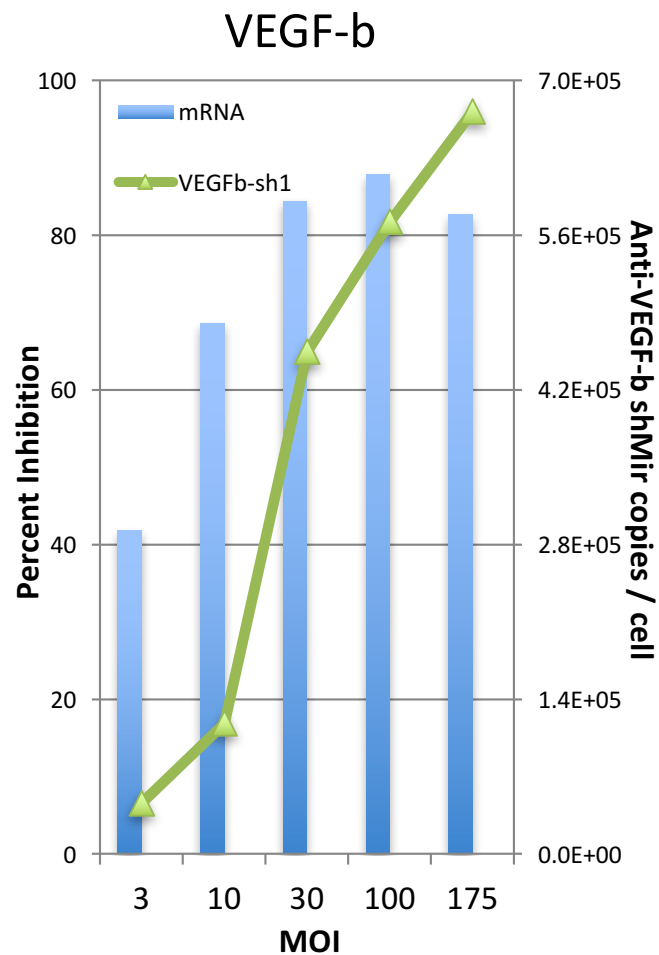
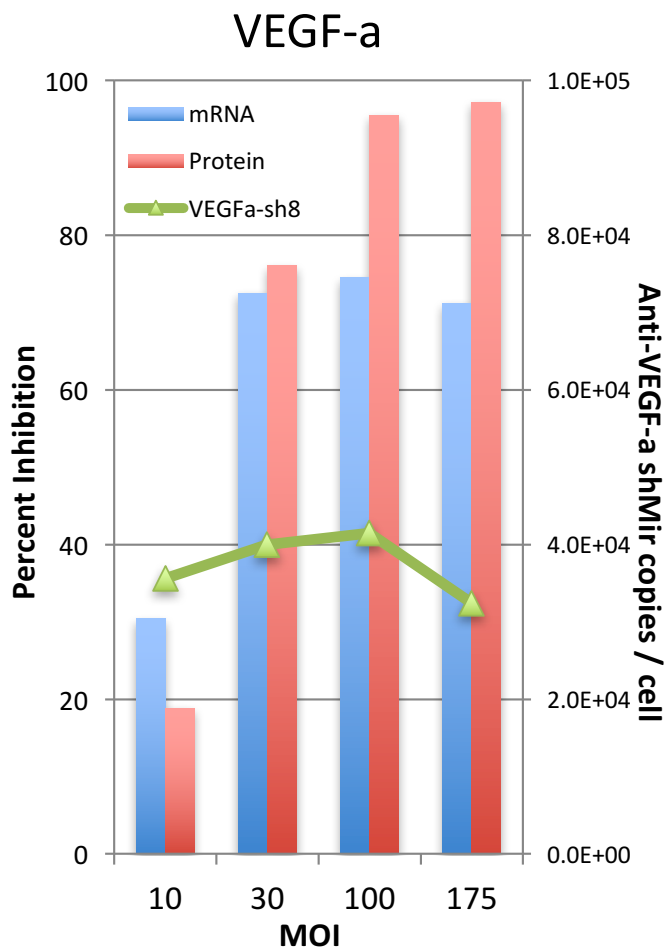


BB-201: Designed to Silence Three Clinically Validated Targets of Ocular Neovascularization



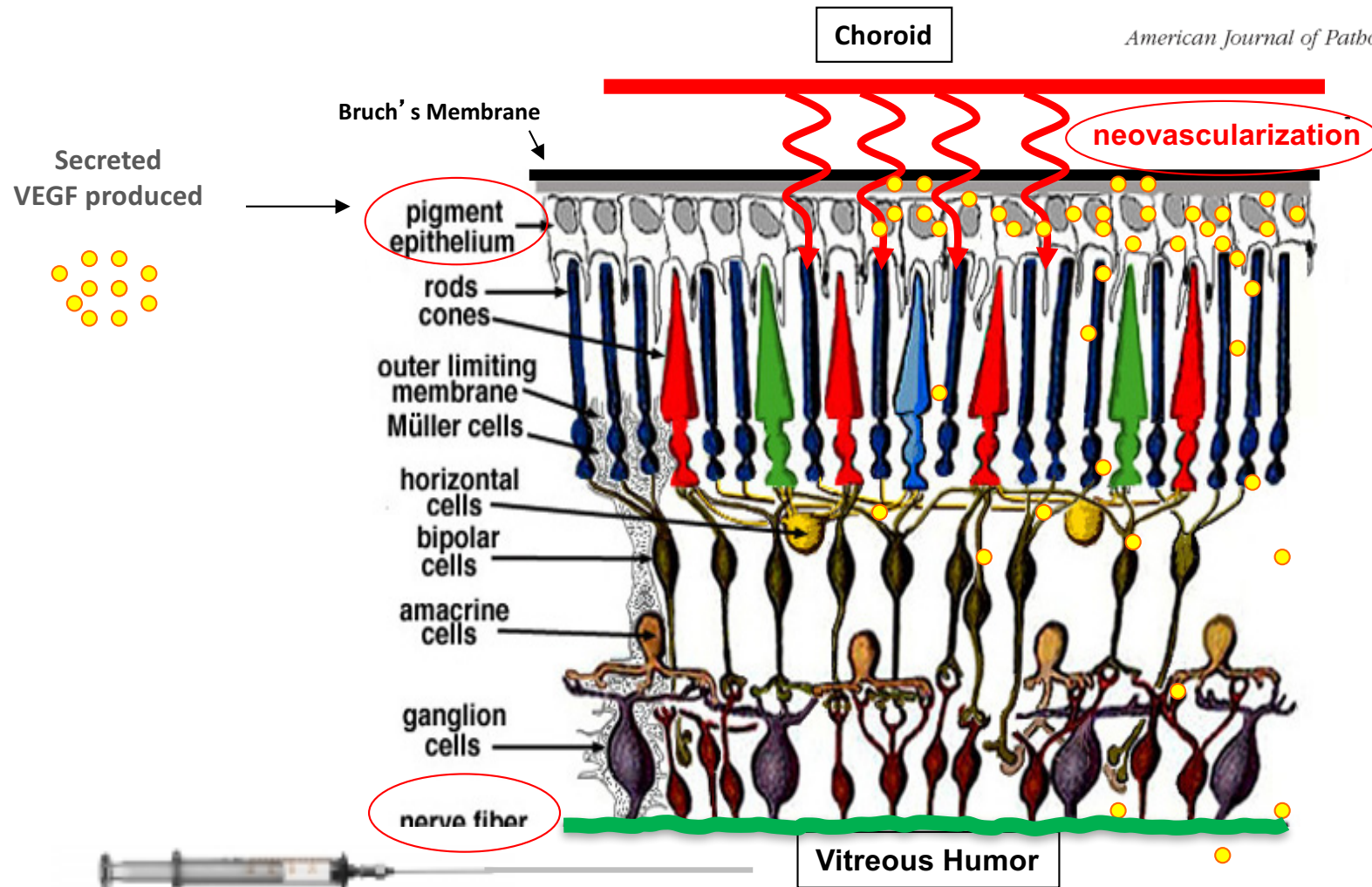
- An AAV-encapsulated construct that produces three independent shRNAs, each modeled into a miRNA backbone, to inhibit the expression of VEGF-a, VEGF-b and PIGF
- Molecular targets are treated with protein-based current SOC that must be administered monthly or bi-monthly

BB-201: *In vitro* Inhibition of VEGF-a, VEGF-b and PlGF



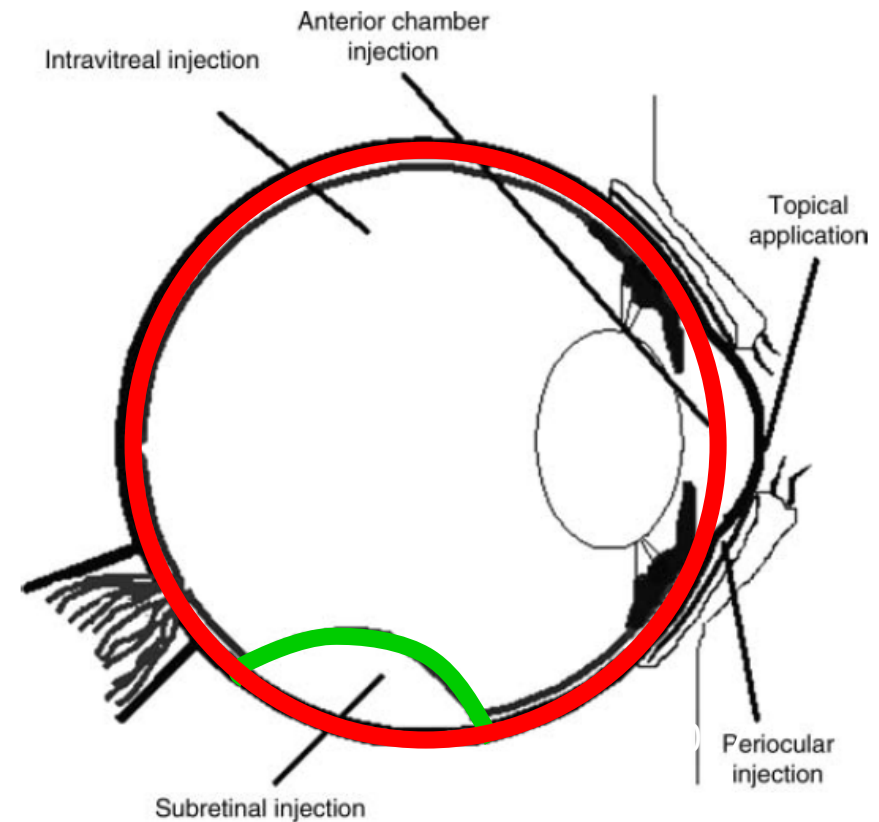
Retina Pigment Epithelia Cells are a Major Source of Secreted VEGF-a in Wet AMD

American Journal of Pathology, Vol. 155, No. 2, August 1999



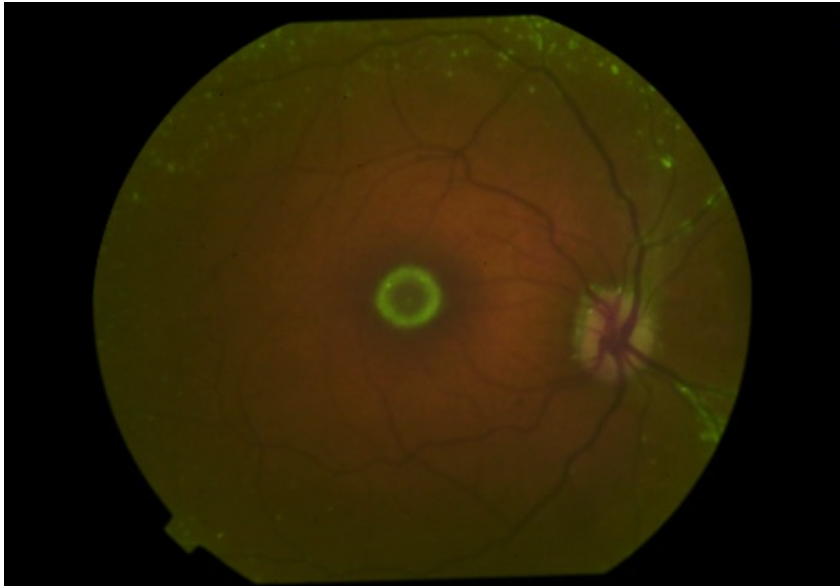
Lucentis , Avastin, Eylea all target the VEGF-a production in the eye

- BB-201 is being developed for intravitreal route of delivery
- Intravitreal is more commercially viable than a subretinal injection (typically used by most gene therapy vectors for ocular diseases)
- Vectors developed through 4DMT's 'therapeutic evolution' process

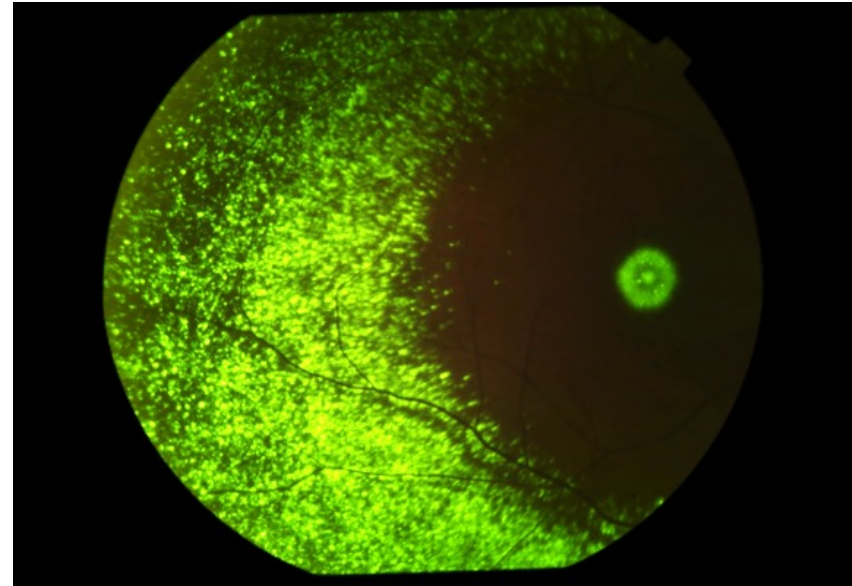


Superior Retinal Transduction Using a Novel AAV Capsid Administered via Intravitreal Injection

GFP in retina after intravitreal injection of standard AAV2 capsid



GFP in retina after intravitreal injection of novel AAV capsid



In non human primates

Wet Age-Related Macular Degeneration

Clinical Candidate BB-201: Product Overview

Wet Age-related Macular Degeneration

- 196m people impacted worldwide by 2020
- Characterized by growth of new blood vessels into the retina as a result of abnormally high levels of proteins from the VEGF family
- SOC typically requires monthly or bimonthly subretinal injections and may be required to be given indefinitely to halt disease progression






BB-201 Product Profile

- Designed as a single shot treatment
- Intravitreal delivery is a commercially attractive route of administration
- Novel AAV capsid delivers ddRNAi against VEGF-a, VEGF-b and PIGF, three clinically validated targets

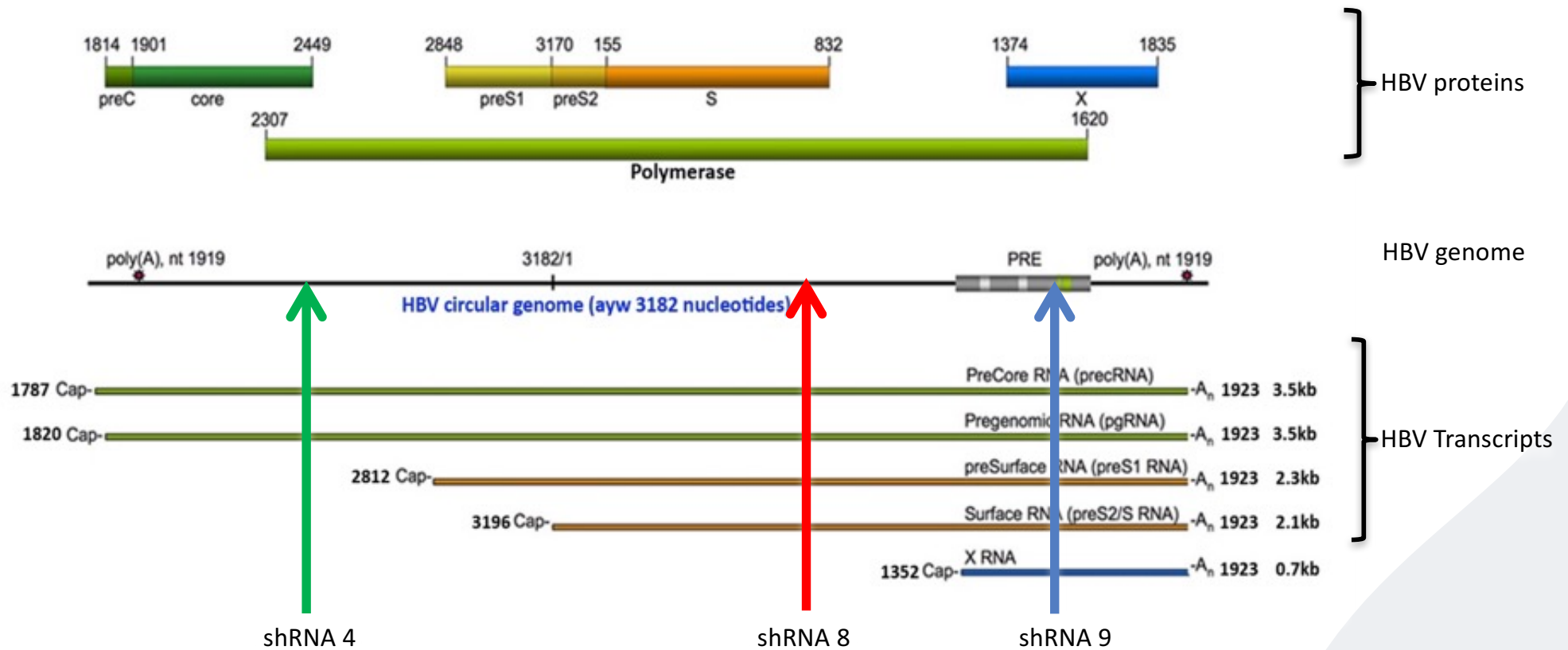
Value / Commercial Opportunity

- Near-term value inflection point: 4Q17 nonclinical proof of concept data
- Expected to be clinic ready towards the end of 2018
- Novel AAV vector provides a delivery platform for any ddRNAi based therapeutic for a broad set of retinal disorders

Hepatitis B (HBV) Program Update

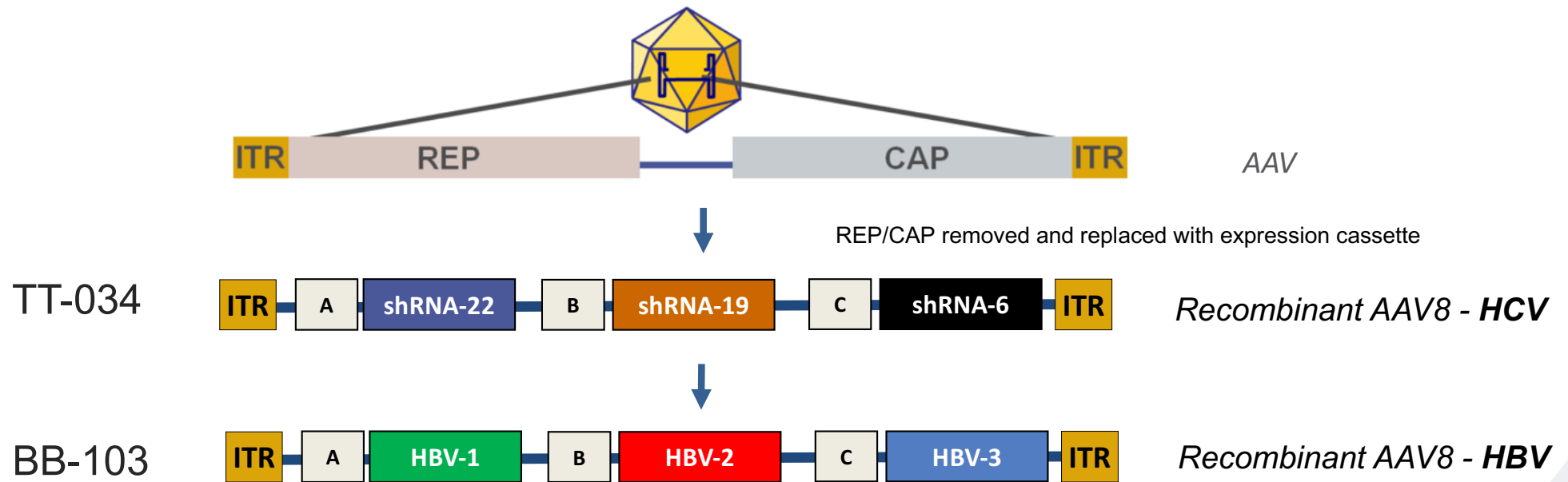
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Positioning of shRNA Used in Clinical Construct Ensure Cleavage of Multiple HBV Transcripts



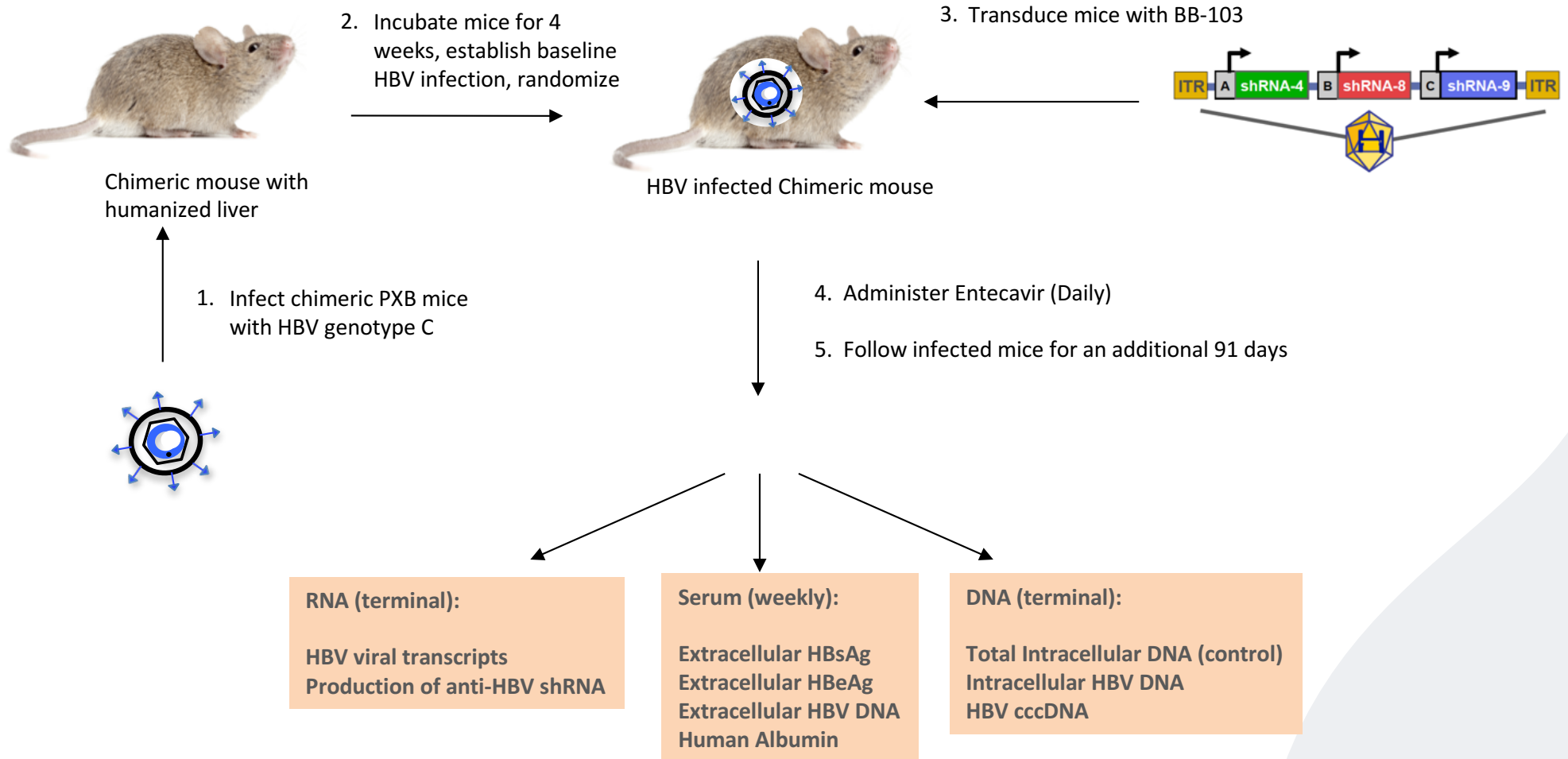
* Sequences selected for shRNA are well conserved across HBV genotypes A-H

BB-103: An Anti-HBV Agent that Builds in Learning From Benitec's First in Man TT-034 Trial in HCV

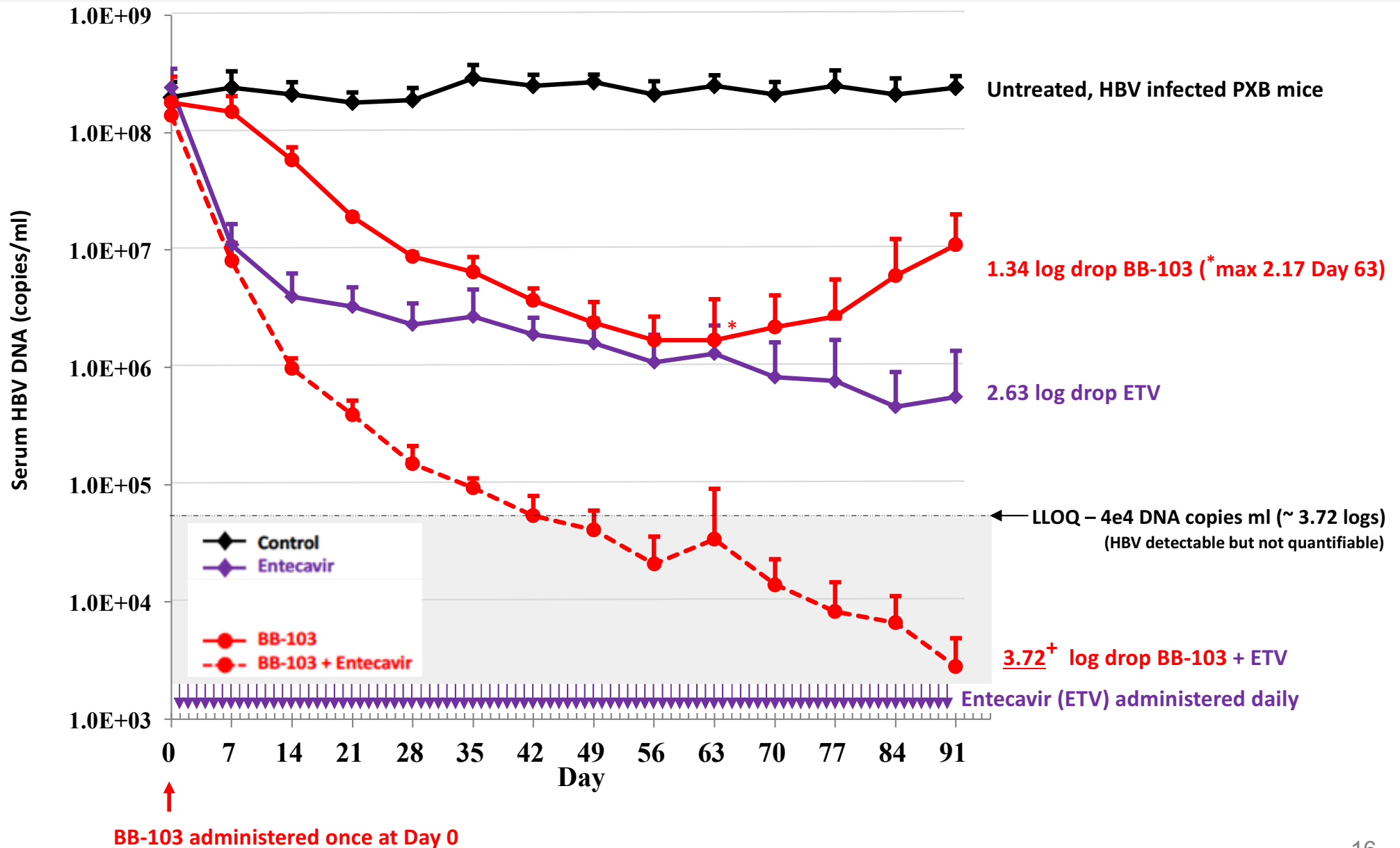


Safety and Efficacy Study in Single Doses of TT-034 in Patients with Chronic Hepatitis C
Clinical Trials.gov Identifier: NCT10899092

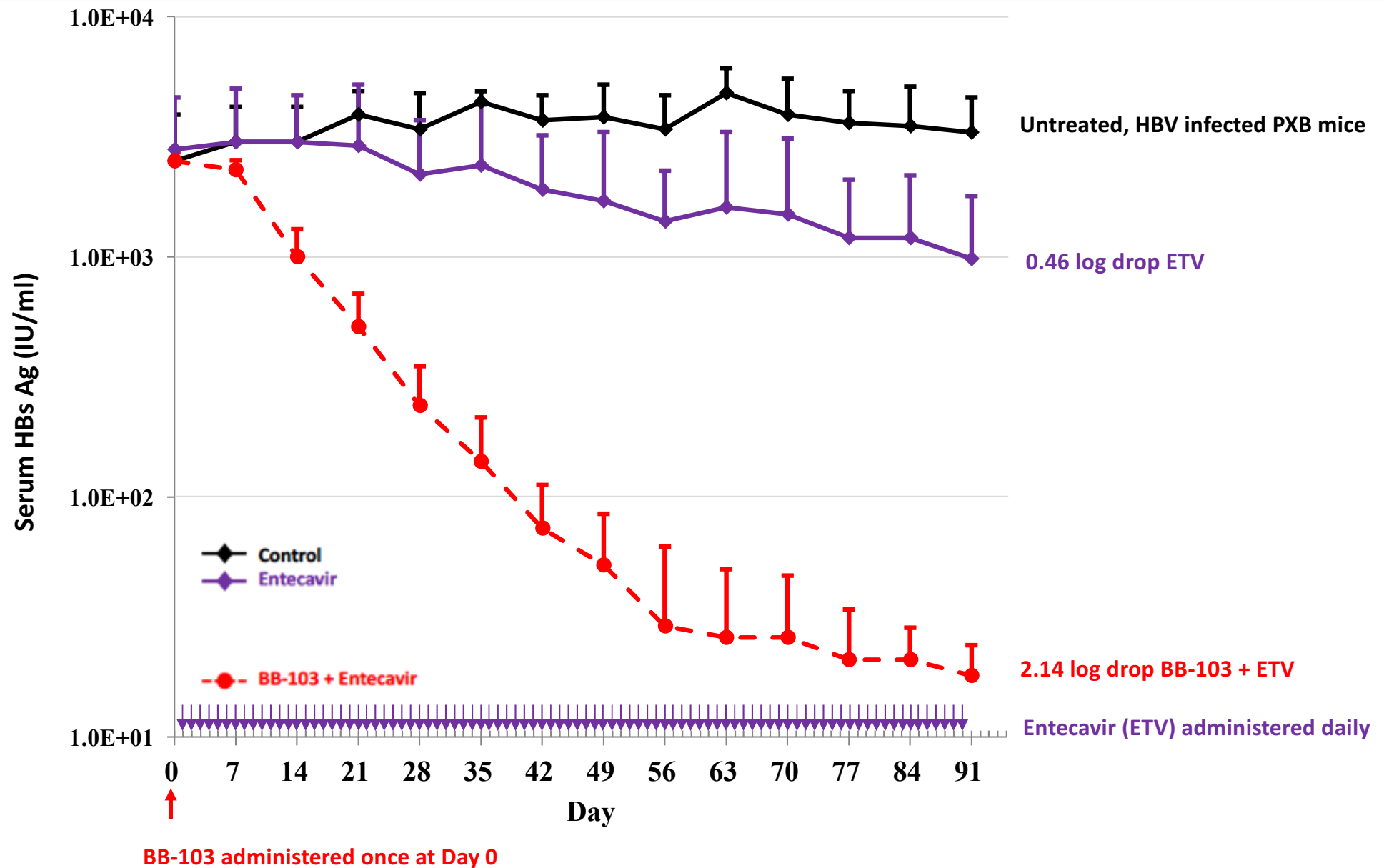
In Vivo Infectious HBV Studies Using PXB Mice



BB-103 as a Monotherapy and in Combination with Entecavir: Reduction of Serum HBV DNA Levels



BB-103 in Combination with Entecavir: Reduction of Serum HBsAg (S-Antigen) Levels



A Summary of Anti-viral Activity of BB-103 as a Monotherapy or in Combination with Entecavir

	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
Single administration of ddRNAi	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-103 + ETV	* 3.72 +	2.14	1.90

Hepatitis B

- An estimated 257 million people with HBV infection
- Need for safe and 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
- 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

Value / Commercial Opportunity

- Near-term value inflection point: 2H18 clinic ready
- 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



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