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NASDAQ: BNTC
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Biotech Showcase
9th January 2017

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Company overview

Novel application of gene silencing technologies to build a focused product pipeline to address unmet medical needs across numerous indications

NOVEL GENE SILENCING TECHNOLOGY	ddRNAi combines RNA interference (RNAi) with gene therapy delivery to change the way patients are treated and potentially cured
FOCUSED PIPELINE	Programs in indications with high unmet clinical need and/or large patient populations such as hepatitis B, AMD, solid tumors, and rare genetic disorders
COMMERCIAL STRATEGY	Building therapeutic product franchise for commercialization and partnering for diversification of ddRNAi technology

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Gene therapy approach to silence disease-associated genes

Benitec technology platform: DNA-directed RNAi (ddRNAi)

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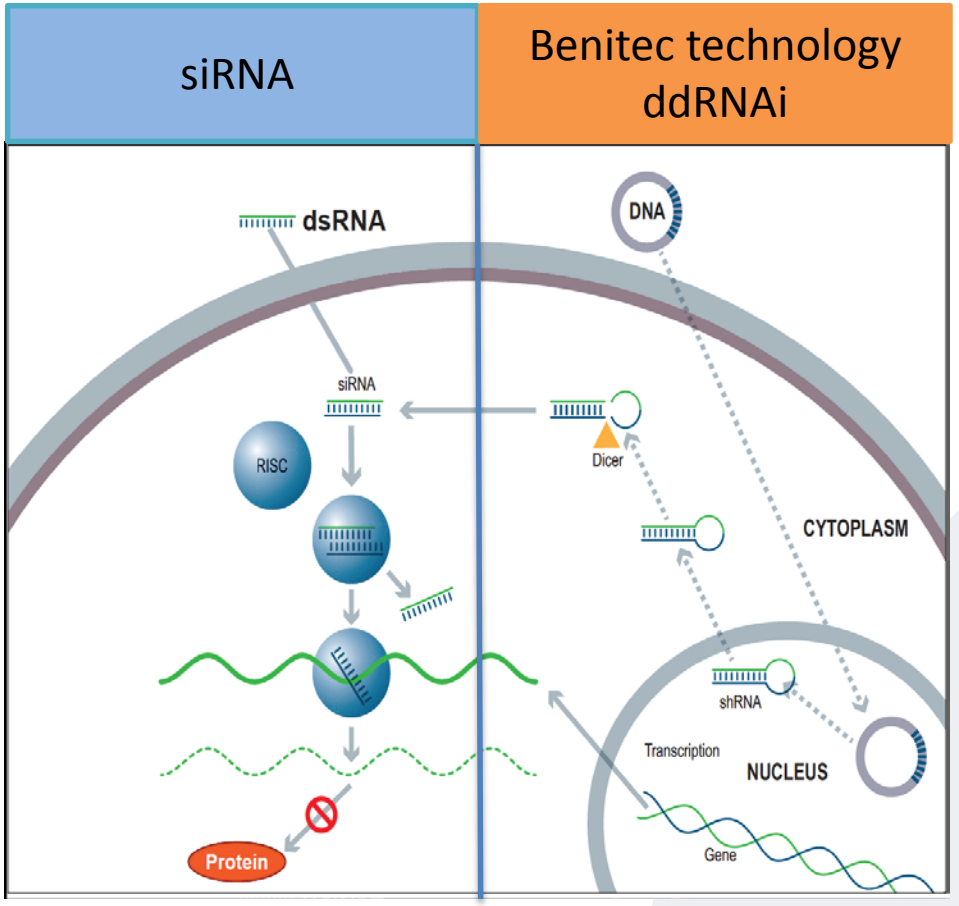
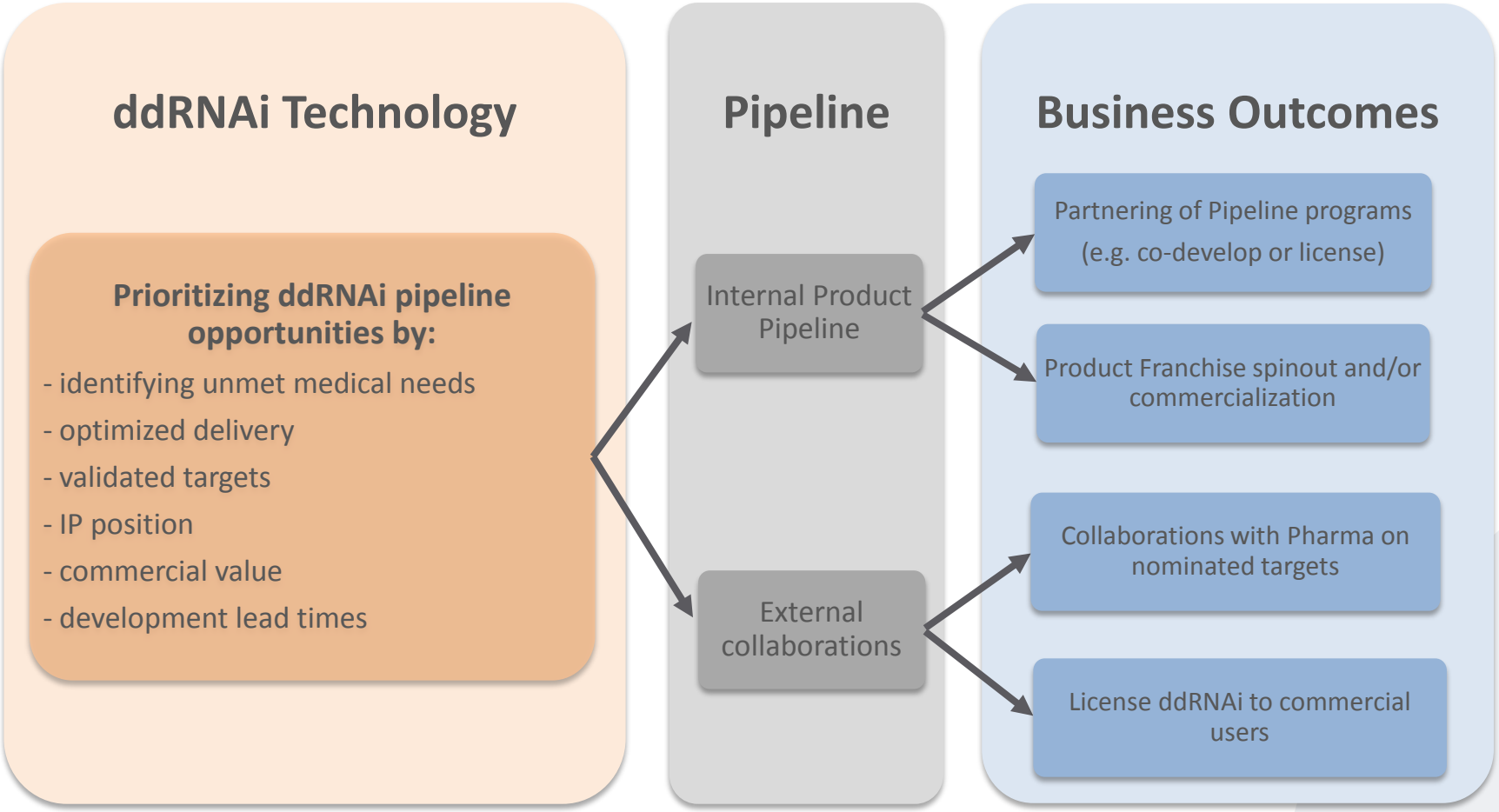
- Combines RNA interference with gene therapy delivery
- Long term therapeutic potential from a single administration
- Steady state levels of shRNA expression
- Silence a single gene or target multiple genes simultaneously
- Silence/replace strategies of mutant proteins



Business Model



Pipeline Programs

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Program	Discovery	Preclinical	IND-Enabling	Phase I/II	Status
Oncology					
Head and Neck Cancer (HNSCC) *BB-401 (EGFR-AS)*					• Sublicense signed December 2016 • Phase 1 clinical POC completed in patients with HNSCC • Follow-on PII/III trial design under review
ddRNAi for Head and Neck Cancer *BB-501*					• Scientific collaboration initiated Q1 2017
Infectious Disease					
Hepatitis B *BB-101 / BB-103*					• In vivo efficacy of BB-101 and BB-103 in combination with standard of care agents completed • Pre-IND meeting preparations underway
Ocular Disease					
AMD *BB-201*					• Capsid biodistribution 1Q 2017 • Laser induced CNV mouse models 1Q 2017
Genetic Disease					
OPMD *BB-301*					• *In vivo* POC with clinical candidate ongoing– data in 1H17

New ddRNAi Applications

Program	Discovery	Preclinical	IND-Enabling	Phase I/II	Phase III	Status
Immunotherapy						
CAR-T						• *In vitro* POC completed
New Technologies						
Non-Viral Delivery						• *In vitro* POC underway

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Strategic Collaboration with NantWorks

Strategic Engagement With NantWorks

Highlights:

- Two phased investment by NantVentures with oncology focused R&D collaboration
- Returns Benitec to the clinic through in-licensing of a Phase II ready gene silencing asset for the treatment of head and neck squamous cell carcinoma (HNSCC)
- Follow-on second generation program utilizing ddRNAi for treatment of same indication (HNSCC)

Significance of this Transaction:

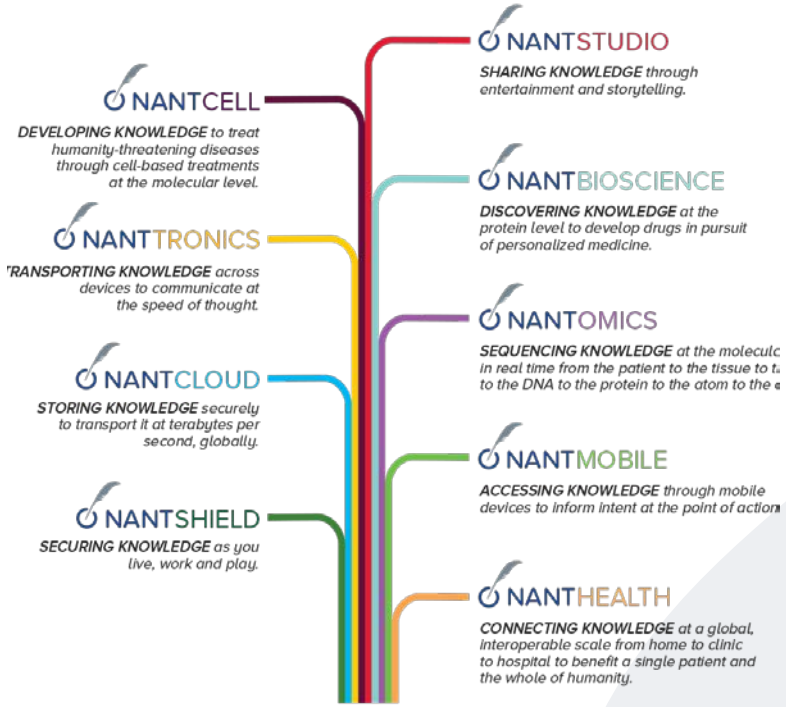
- Demonstrates high regard for Benitec's expertise and capabilities
- Demonstrates Benitec can deliver on previously communicated strategy
- Brings a highly regarded strategic Investor to Benitec with initial 16.67% stock holding
- Returns Benitec to being a clinical stage company
- Extension of ddRNAi platform into oncology
- Enhances funding of programs and provides a platform for additional funding early in 2017
- Strengthens Board through appointment of Dr Jerel Banks, Investment Director NantVentures
- Positions company for growth and enhancement of shareholder value

NantWorks Vision and Focus

‘The Cognitive Age’: Convergence of Science, Technology and Communication

- **Nantworks**: founded by Patrick Soon Shiong in 2011
- Shiong is pioneer of novel therapies for diabetes and cancer (e.g. Abraxane) and prolific innovator
- Ecosystem of companies to create transformative global health information and next gen pharmaceuticals
- Systems-based approach to personalized healthcare integrating novel diagnostics with large-scale, biometric and phenotypic data to track patient outcomes and deliver precision medicine

- **GPS Cancer Platform**:
- Personalized molecular decision support for cancer therapy
- Identify ‘Actionable Targets’



GPS Cancer™

Head and Neck Squamous Cell Carcinoma (HNSCC)

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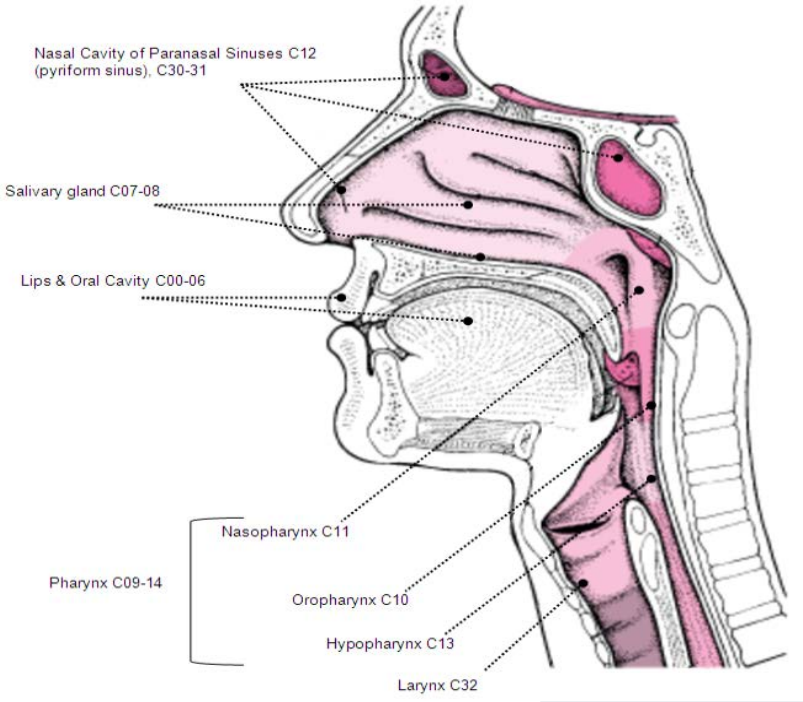
Incidence and patient mortality:

- 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

Unmet need:

- Significant patient morbidity derived form loco-regional tumor growth and progression in confines of small anatomical space
- Need for therapies that facilitate durable tumor reduction or eradication
- Lack of biomarkers to reliably predict response to targeted therapy

Anatomical sites of HNSCC



Over 80% of patients overexpress epidermal growth factor receptor (EGFR)

Framework for Benitec / Nant Research Collaboration

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Gene silencing treatments directed against HNSCC targeting EGFR

RNA antisense program for continued clinical development

- DNA plasmid to produce antisense RNA (***EGFR-AS***)
- Previous clinical proof of concept demonstrating anti-tumor activity and safety
- Clinical development program is under review
- Benitec to be sponsor on record
- Exclusive world-wide sublicensing agreement finalized December 2016

HNSCC ddRNAi Program

- Follow-on program for durable gene silencing of EGFR *via* ddRNAi
- Takes advantage of learnings from BB-401 (EGFR-AS) clinical program
- Benitec and NantWorks to define clinical development plan and regulatory strategy
- Key focus on delivery mechanisms for efficient transfection/transduction in HNSCC lesions
- Approximately 40% of patients express unique variant EGFRvIII targetable by ddRNAi approach

EGFR-AS clinical studies compare favorably to other EGFR treatments evaluated in HNSCC

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Phase I study
17 patients with advanced, refractory HNSCC *

- Safety and Efficacy evaluated following direct intra-tumoral injection weekly for 4 weeks:
  - 29 % (5 patients) achieved 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 achieved Stable Disease
  - 41% Overall disease control rate
  - 6.5 months observed anti-tumor response
  - No Grade 3 or 4 toxicity or DLT

Follow on Phase 1 Clinical Study
6 patients with advanced HNSCC
evaluate improvement to multi treatment regimen:

- In combination with radiation and cetuximab the addition of EGFR-AS resulted in 5 of 6 patients experiencing Objective Responses (83%)
- 3 of these patients experienced Complete Response & 2 patients Partial Responses

Biomarker analysis shows strong correlation between baseline level of EGFR expression and clinical response

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

HNSCC Program Highlights

EGFR-AS

- Direct intra-tumoral injection indicates an effective method of administration for a gene-silencing treatment modality
- No concerning adverse events have been reported
- Clinical efficacy observed in combination study point to potential improved clinical outcomes

Biomarker Analysis (patient stratification)

- Opportunity for development of attomolar-level EGFR-sensitivity values determined via GPS-Cancer
- Quantification of intra-tumoral EGFR levels within biopsies and correlation to clinical outcomes

Augmented Gene Silencing via ddRNAi

- Added capacity (e.g. via gene therapy based approaches such as ddRNAi) to drive constant expression of the gene silencing modality to potentially further augment efficacy
- ddRNAi approach can be designed to silence multiple distinct protein targets simultaneously including EGFR wild-type and EGFRvIII

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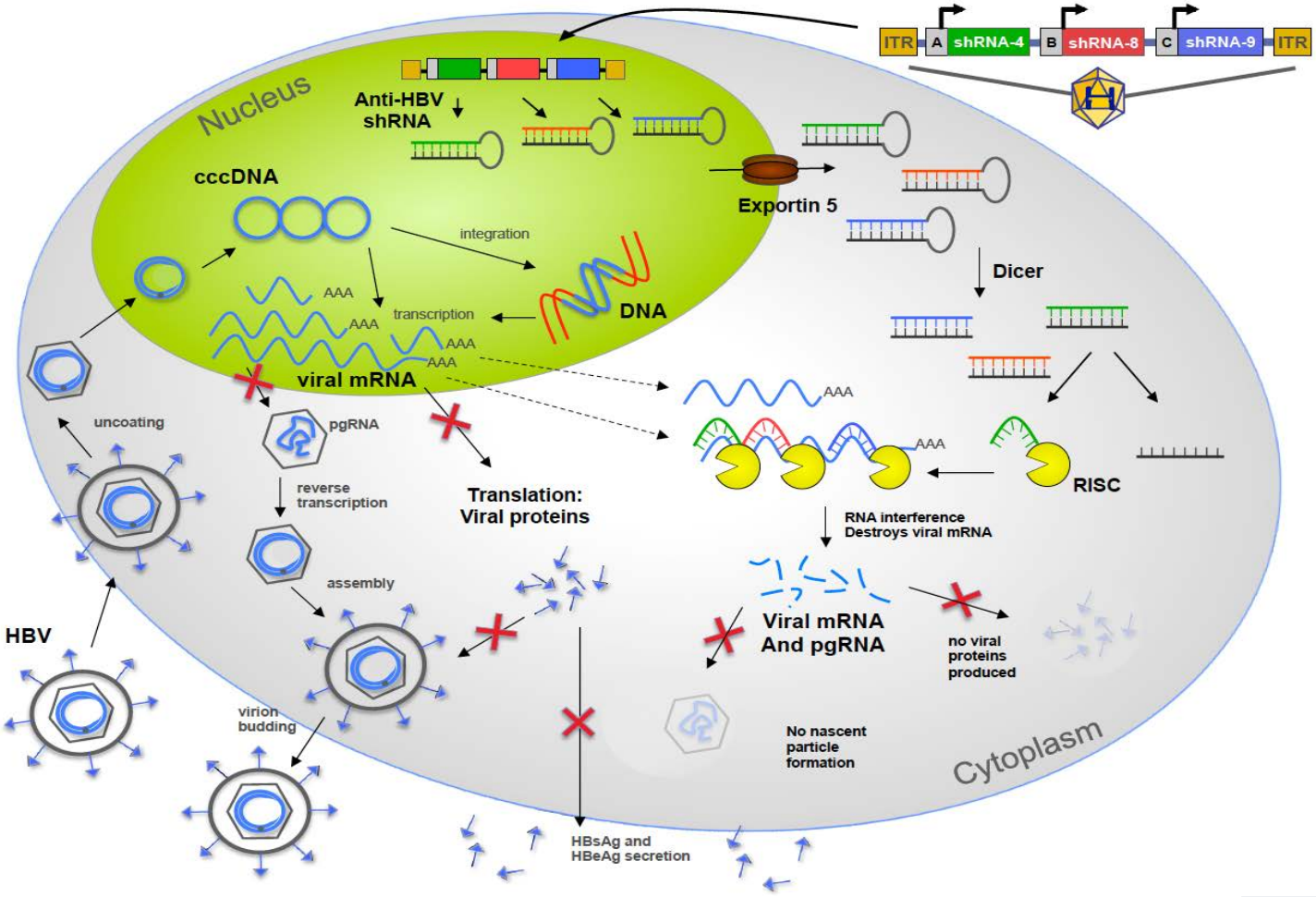
BB-102 and BB-103
Hepatitis B

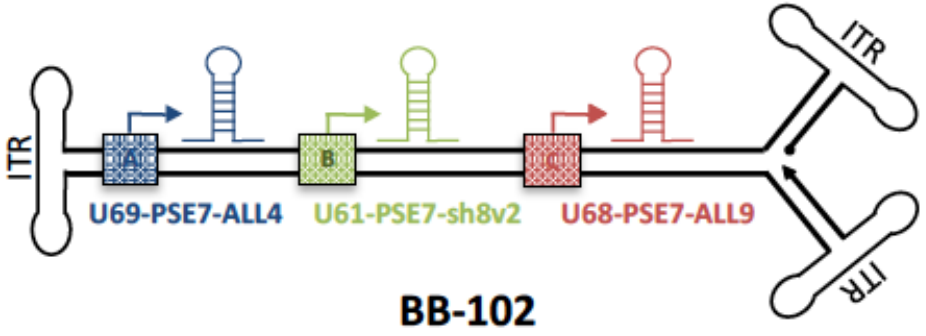
Hepatitis B: Market size

- Hepatitis B is a DNA virus with an unmet medical need
- 240 million infected worldwide, resulting in up to 780,000 deaths per year
- Hepatitis B virus causes 60-80% of the world's primary liver cancers
- Existing therapies have low cure rates
- Current standard of care in non-resolving patients requires lifelong treatment

BB-102/BB-103: Mechanism of Action

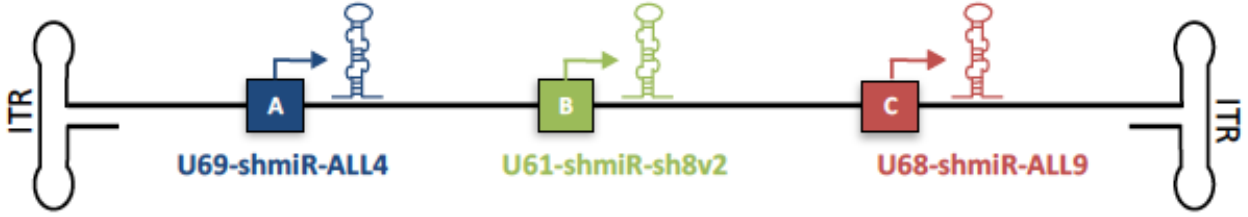


BB-102 vs BB-103:
A Difference in Expression Cassettes



BB-102

- Self complementary AAV8 (double stranded)
- Faster onset of shRNA expression vs ssAAV
- Permuted promoters to reduce shRNA expression (10-100X) vs. wt promoters
- Low Fidelity: heterogeneous pool of siRNAs
- Same configuration as TT-034 (HCV)



BB-103

- Single stranded AAV8
- Wild type Pol III promoters for high expression
- Model into miRNA backbone
- High fidelity: 1-2 predominate species of siRNA
- Reduce potential toxicity

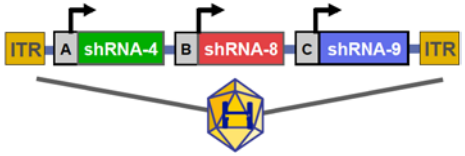
In Vivo Infectious HBV Studies Using PXB Mice

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-102 or BB-103



1. Infect chimeric PXB mice with HBV genotype C

4. Administer Entecavir (Daily) or Pegasys (twice weekly)

5. Follow infected mice for an additional 91 days

RNA (terminal):

HBV viral transcripts
Production of anti-HBV shRNA

Serum (weekly):

Extracellular HBsAg
Extracellular HBeAg
Extracellular HBV DNA
Human Albumin

DNA (terminal):

Total Intracellular DNA (control)
Intracellular HBV DNA
HBV cccDNA

BB-102 and BB-103 Monotherapy vs Entecavir: Reduction of Serum HBV DNA Levels

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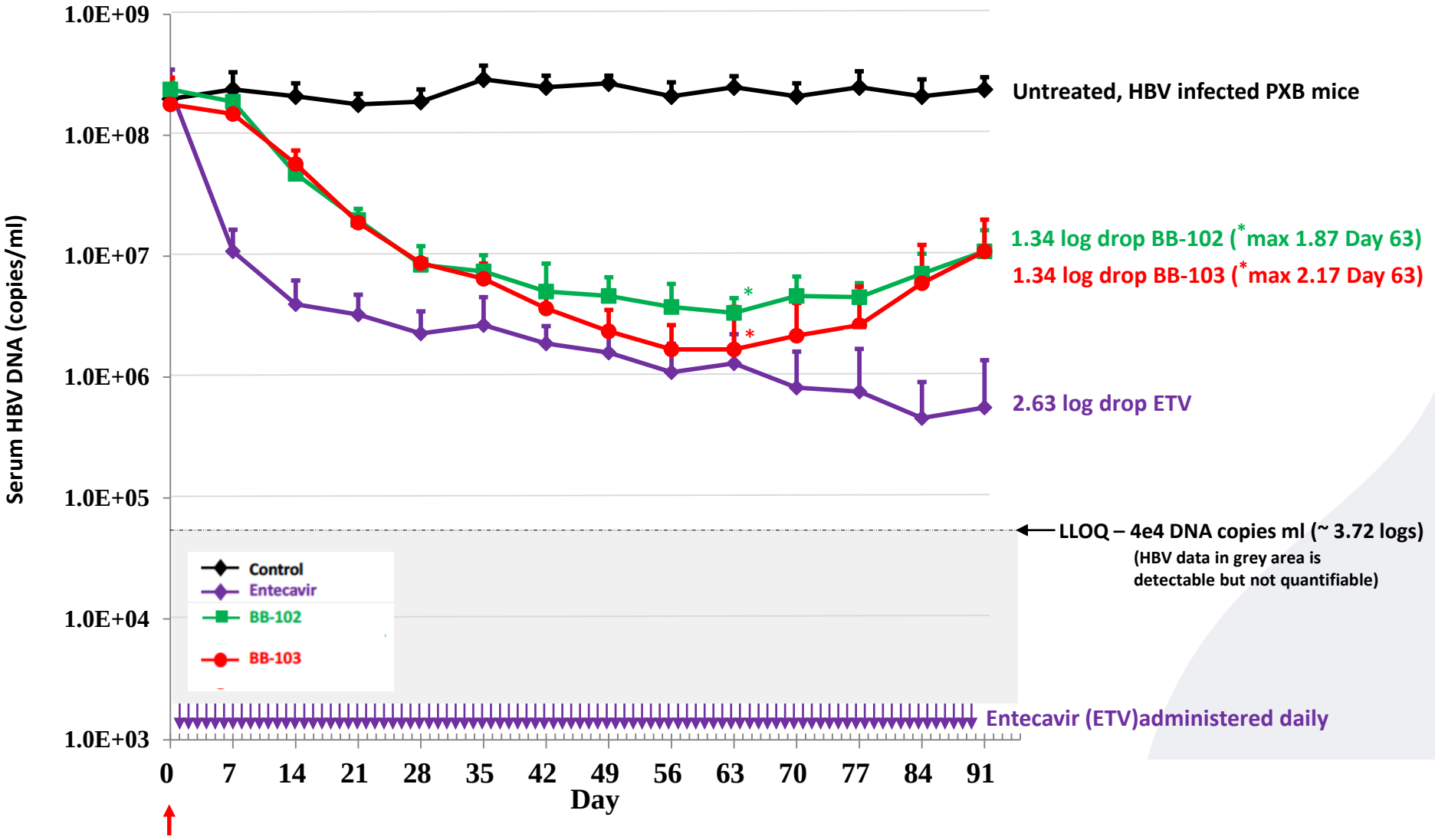

BB-102 and BB-103 Combos with Entecavir: Reduction of Serum HBV DNA Levels

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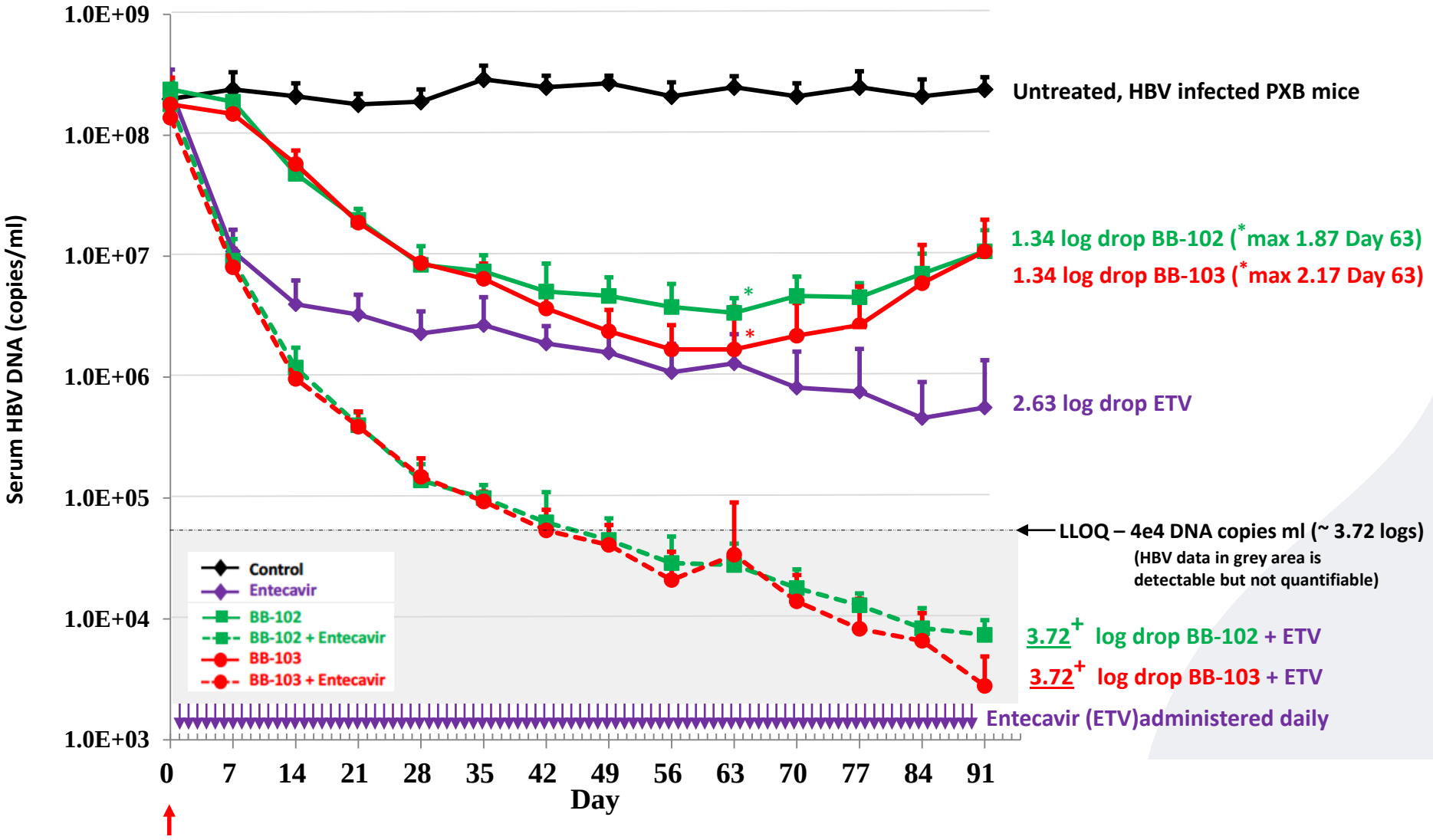

Activity of combinations of BB-102 and BB-103 with SOC on HBV Parameters

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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

HBV Program Highlights

- Development BB-102/BB-103 leverages existing safety and efficacy data in HCV using similar molecular construct and delivery
- Superior Significant and sustained drop of serum HBV levels, HBsAg levels and HBeAg levels with single doses of BB-103 and BB-102 in combination with current standard of care agents
- These data support continued progression of the lead candidates towards the clinic
- Further data (e.g. cccDNA and intracellular DNA) to be disclosed in future presentation at APASL, Shanghai 16th-19th February, 2017

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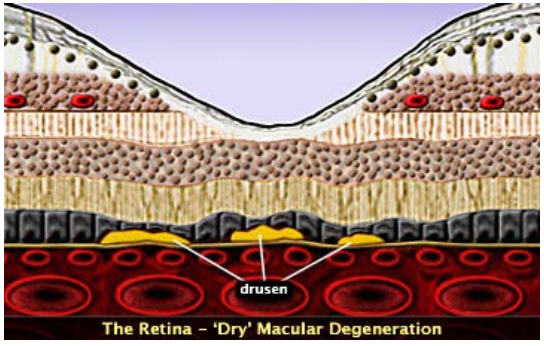
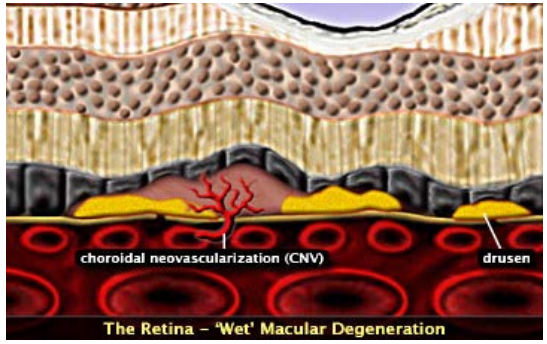
BB-201
Age-related macular degeneration

Dry and Neovascular (Wet) Age-related Macular Degeneration (AMD)

- AMD is the leading cause of irreversible vision loss in the U.S.
- 196M people affected worldwide by 2020
- Ranibizumab (Lucentis) /Aflibercept (Eylea) act as molecular sponges to mop up secreted VEGF-a, (as well as VEGF-b and PlGF) only after they have been secreted from cells
- Although both drugs stabilize vision in a large majority of patients, many do not see significant improvement in vision
- Ocular half life: ~ 9 days for Lucentis and 5-6 days for Eylea. Both require frequent rounds of repeat administration (monthly or bi-monthly)

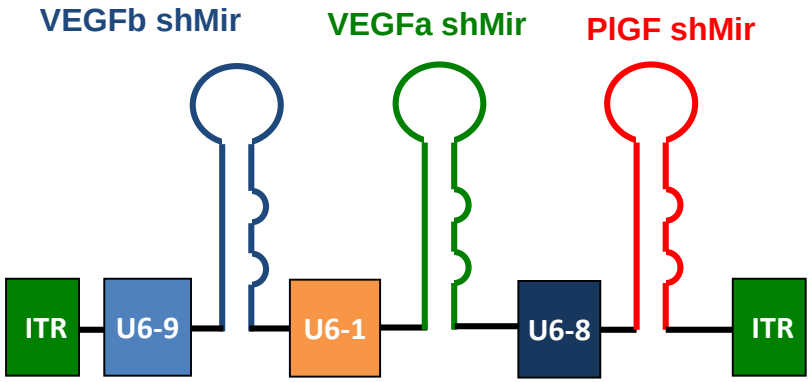


In Dry AMD, drusen deposits start to degrade vision



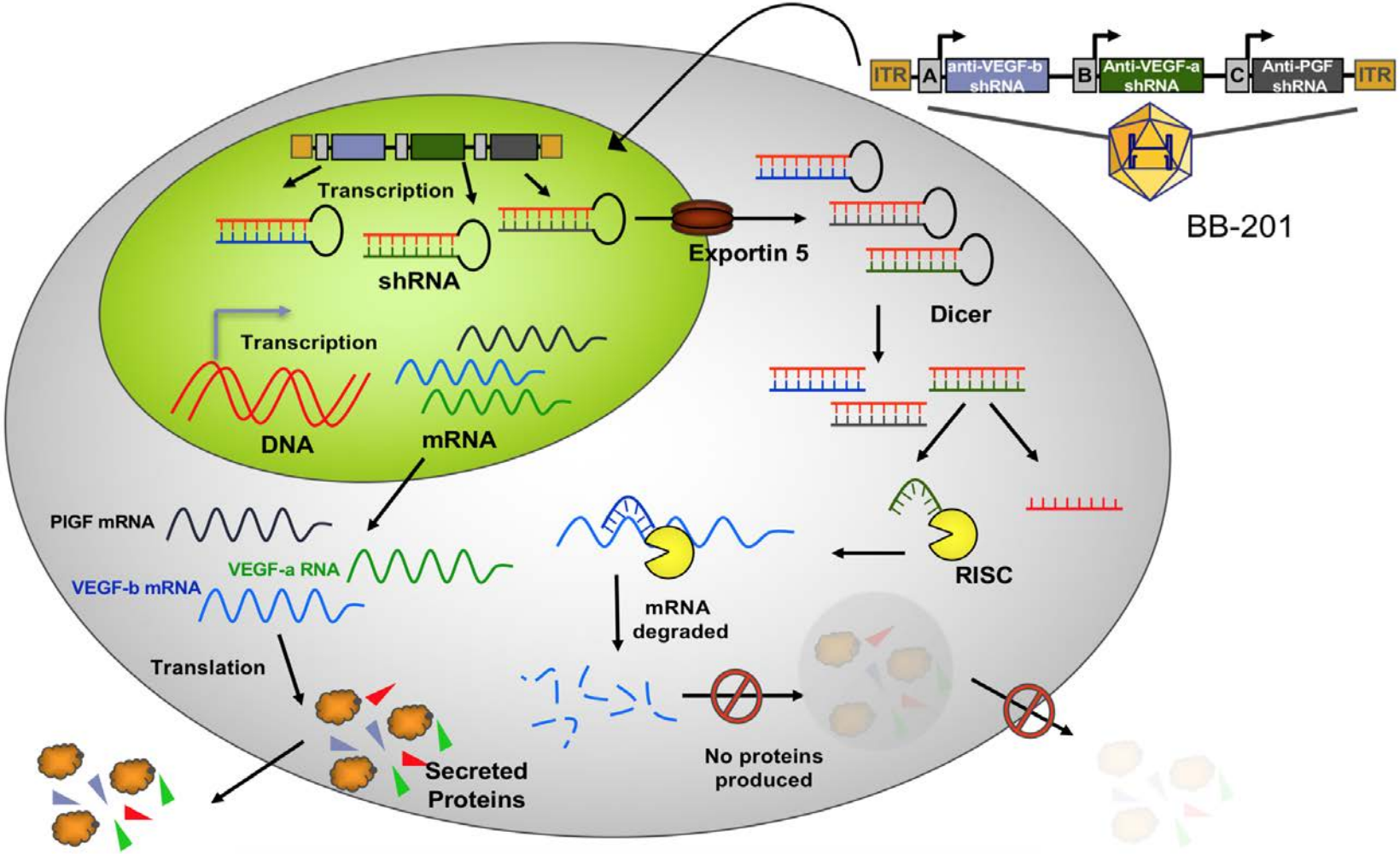
In Wet AMD, inflammatory cascade further degrades vision through neovascularization

BB-201: Clinical Construct



- An AAV-encapsidated construct that expresses a single shRNA modeled into a miRNA backbone that inhibits the expression of VEGF-a, VEGF-b and PGF
- Molecular targets are treated with protein-based current SOC that must be administered monthly or bi-monthly
- Molecular variants of expression construct have also targeted VEGFR2, Complement Factor B, and PDGFR-β

BB-201: Mechanism of Action



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

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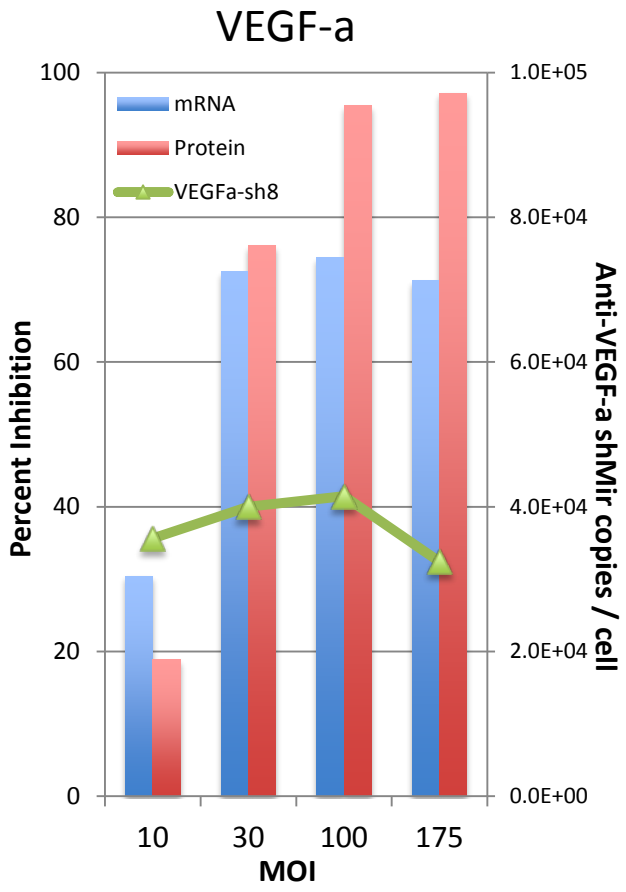
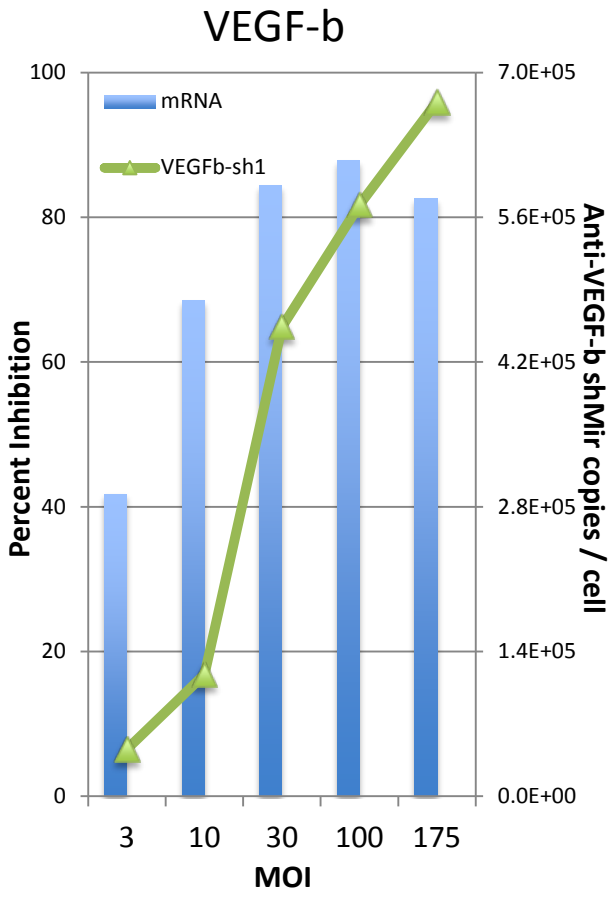
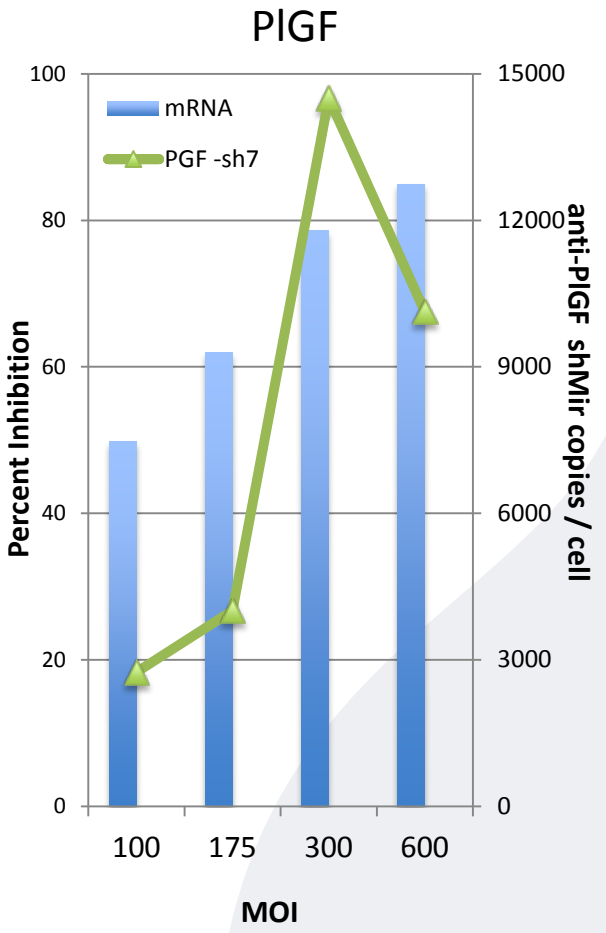
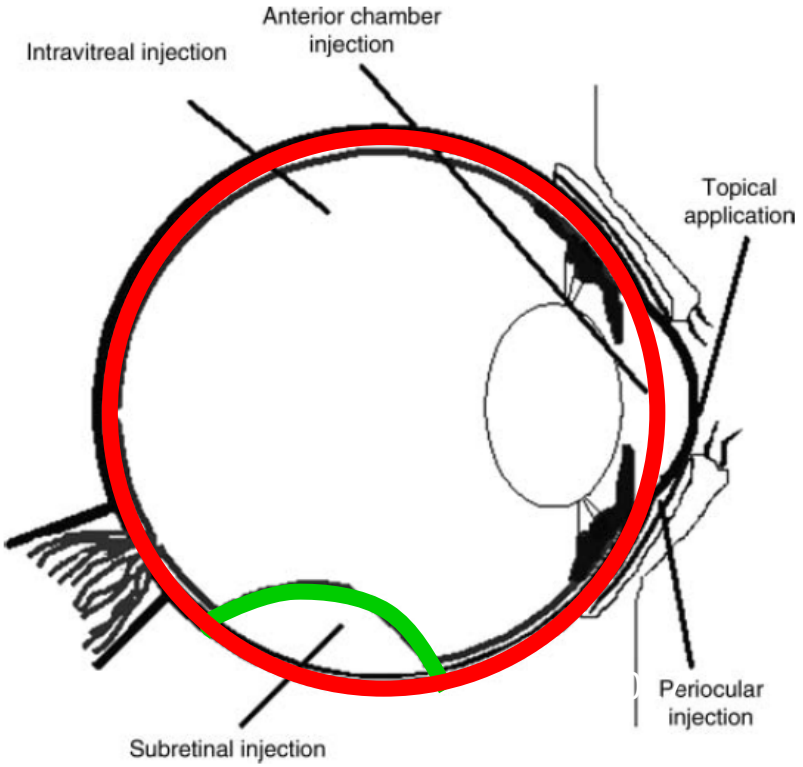






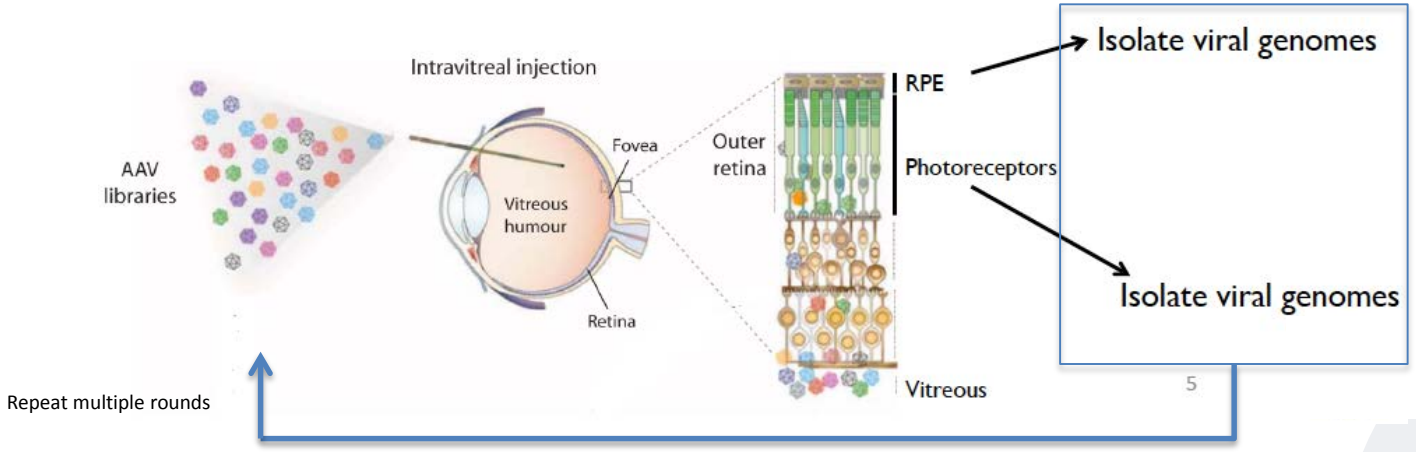
Modified AAV vectors for Intravitreal Delivery

- 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



4DMT Collaboration: NHP Screen for AAV Variants with Pan-Retinal Expression

- Benitec has an exclusive license to ocular vectors from 4D Molecular Therapeutics for use in RNAi applications as well as in 'silence & replace' strategies
- Novel evolution selection in non human primates (complex eye with ILM) to identify vectors with pan-retinal expression following intravitreal injection



Therapeutic Evolution Yields AAV Variants with Optimal Tissue Distribution (Round 6)

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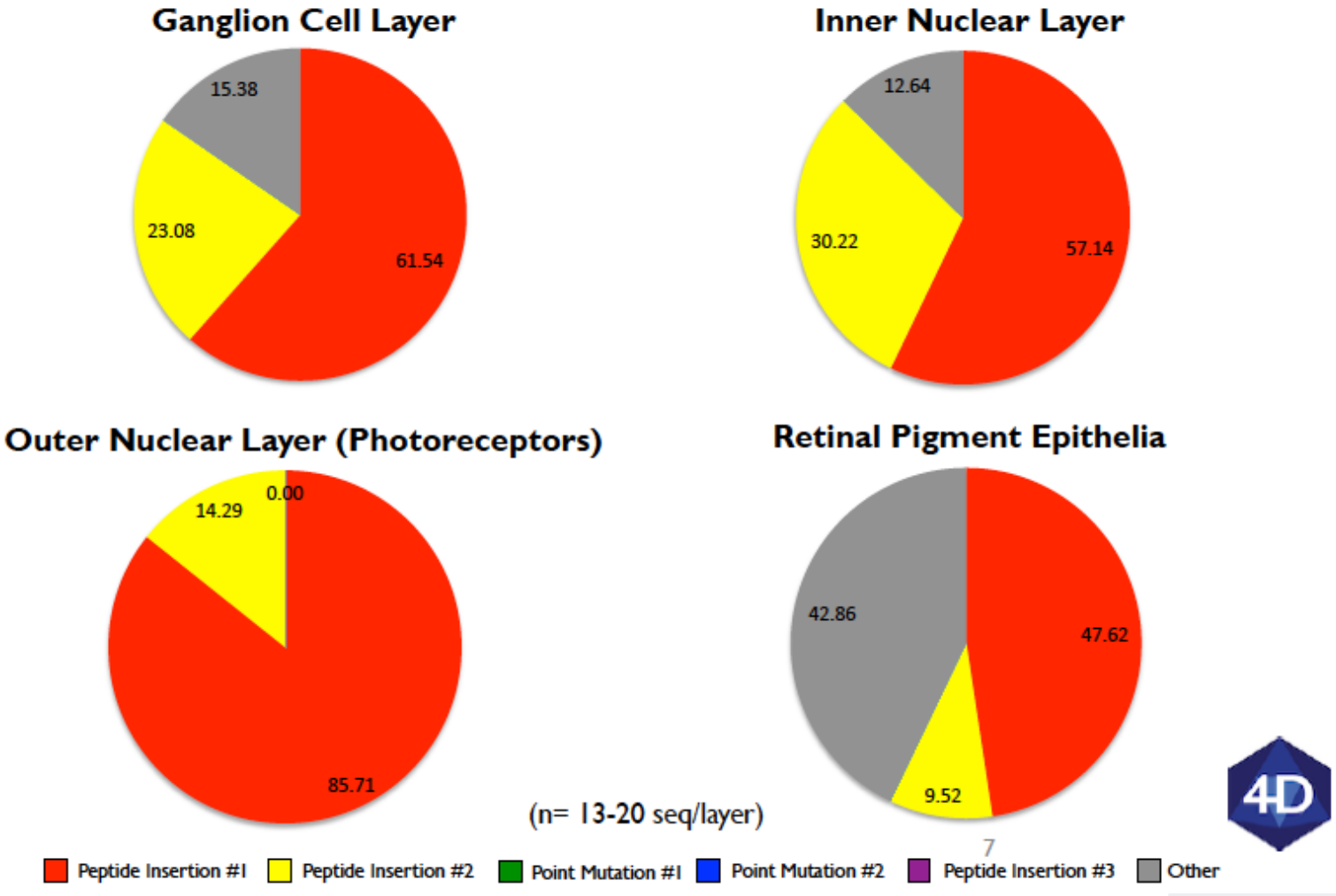

AMD Program Highlights

- Demonstrated knockdown of of clinically validated targets in an *in vitro* model
- Completed 'Therapeutic evolution' selection of AAV variants validating biodistribution in the back of the eye
- Next steps: efficacy model utilizing laser induced choroidal neovascularization in NHP
- Oral presentations at ARVO (Asia) and Translational Vision Summit, Brisbane February 4-8th 2017

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BB-301 Oculopharyngeal muscular dystrophy (OPMD)

Clinical Features of OPMD

Rare autosomal dominant inheritance

- 1:100,000 (Europe)
- As high as 1:600 in specific populations
- Founder effect in Quebec, Canada

Typically age onset occurs in subjects 50's or 60's

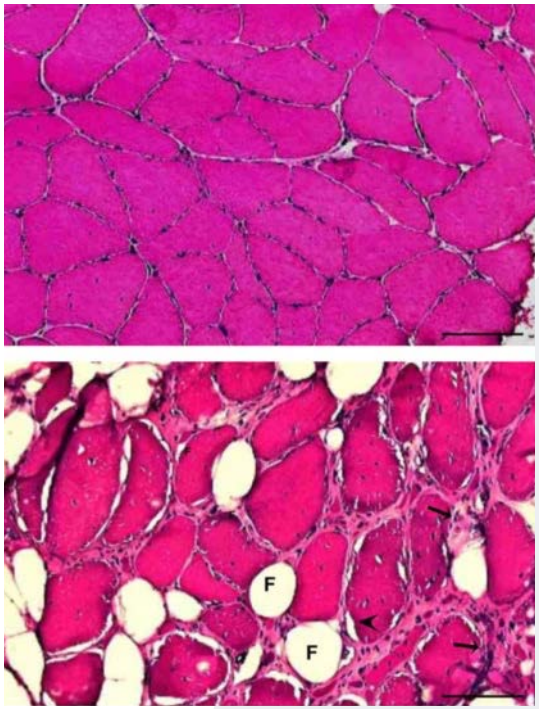
Characterised by:

- 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)

Raz et al., *BMC Neurology* 2013, **13**:70



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

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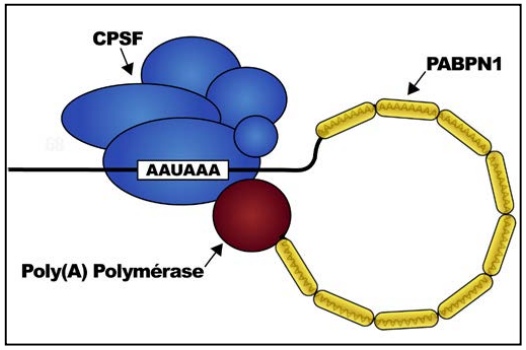
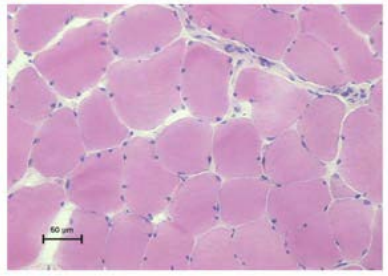
PABPN1:

- Ubiquitous factor that promotes interaction between the poly(A) polymerase and CPSF (cleavage and polyadenylation specificity factor)

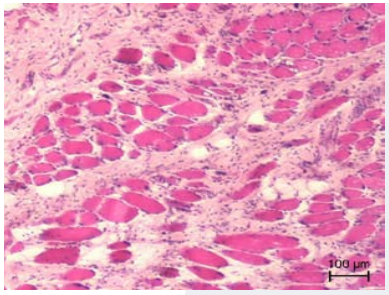


In OPMD:

- Genetic mutation results in trinucleotide repeat expansion results in an expanded poly-alanine tract resulting in protein misfolding



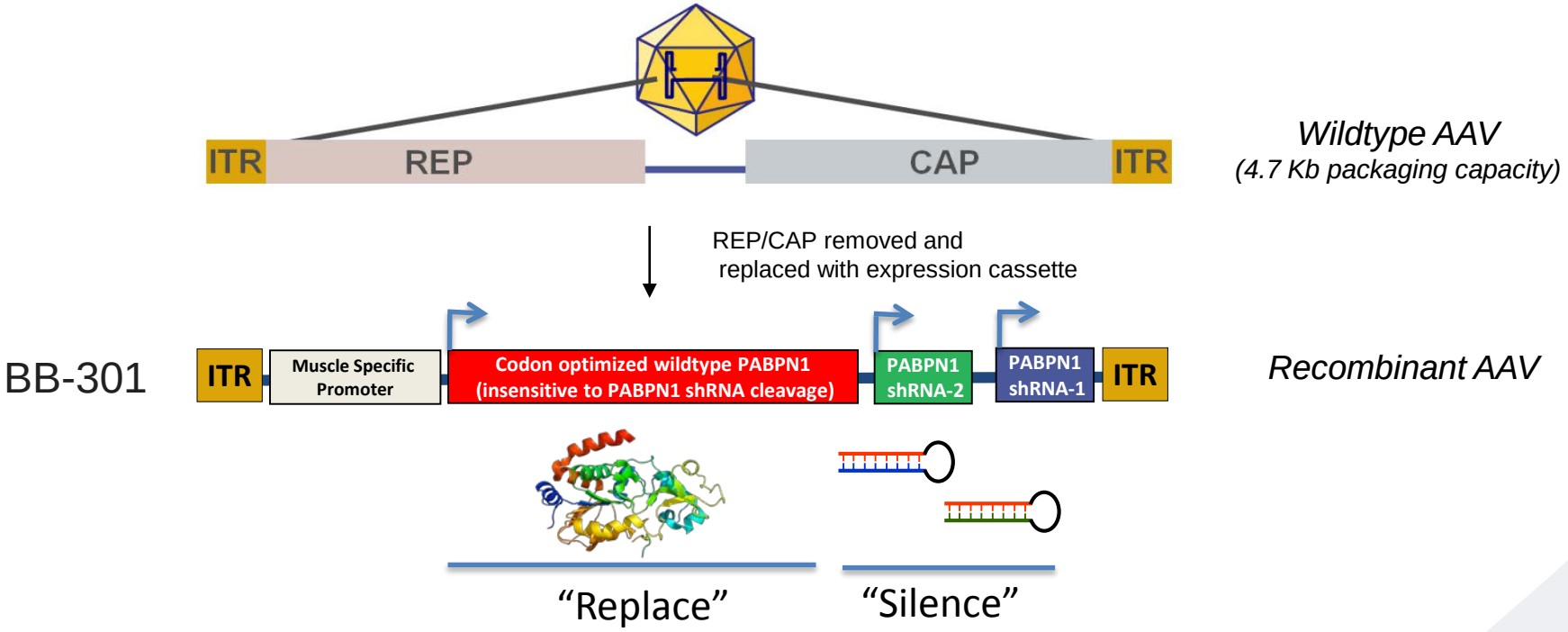
Non-affected



Affected

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

BB-301: 'Silence and Replace' Approach



- Non-integrating, non-pathogenic viral delivery system
- To date, AAV has been used in over 162 clinical trials with excellent safety record
- Sustained expression (years) following single injection

BB-301: Mechanism of Action

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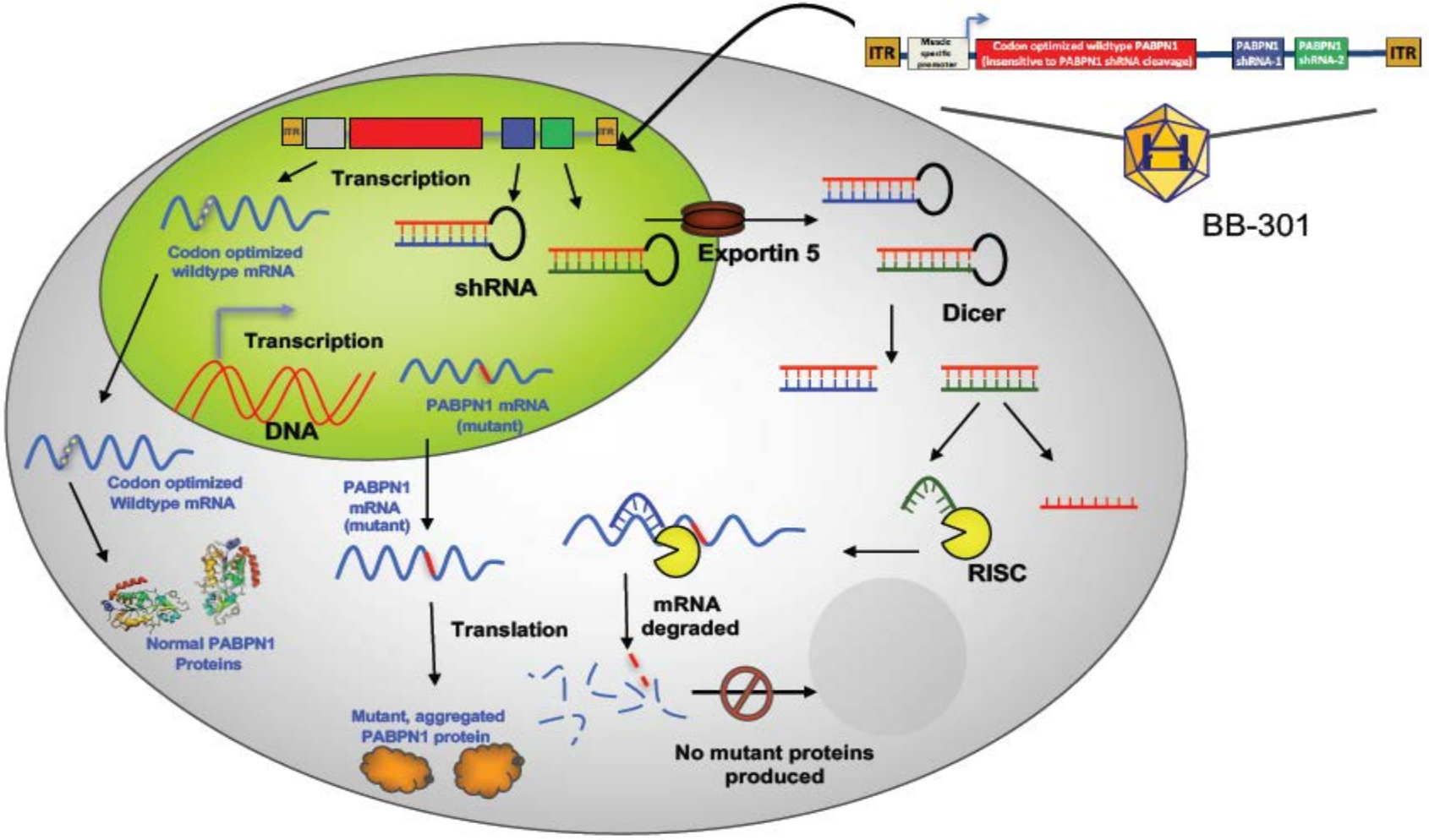
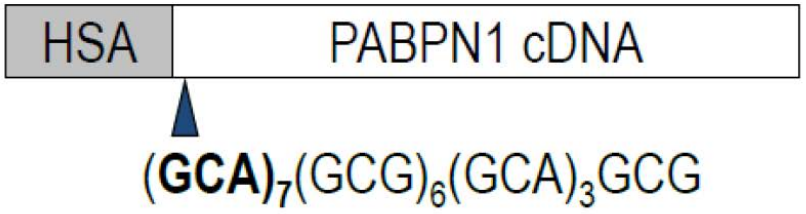


An Animal model of OPMD: The 'A17' mouse



- 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

Nature Medicine **11**, 672 - 677 (2005)
Published online: 1 May 2005 | doi:10.1038/nm1242

Doxycycline attenuates and delays toxicity of the oculopharyngeal muscular dystrophy mutation in transgenic mice

Janet E Davies[1], Lin Wang[1], Lourdes Garcia-Oroz[1], Lynnette J Cook[1], Coralie Vacher[1], Dominic G O'Donovan[2] & David C Rubinsztein[1]

Muscle Atrophy and Restoration of Specific Force Treated A17 mice

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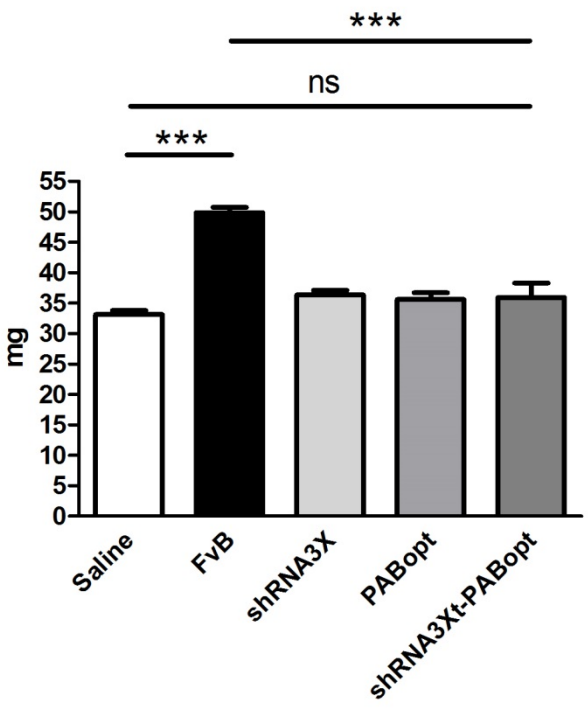
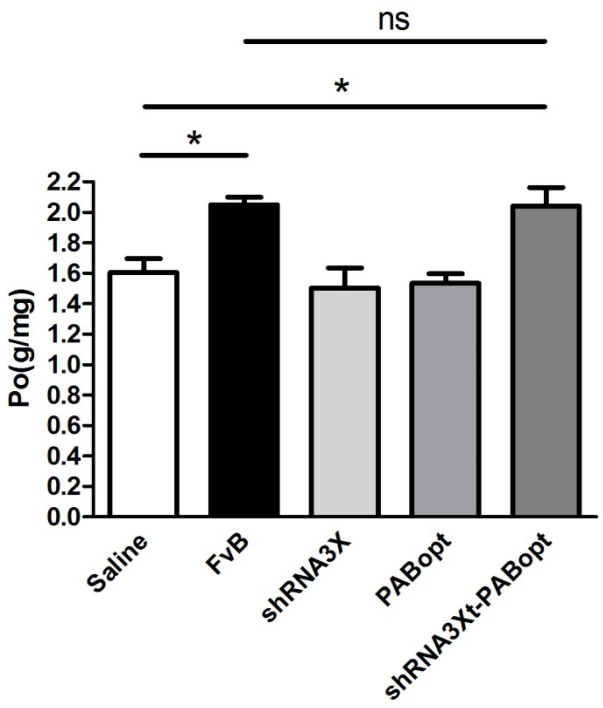
Muscle weight



Reduced Fibrosis +
Partial Reversal of Atrophy

Specific Force



Specific force calculated by normalizing maximal force for muscle weight

OPMD Program Highlights

- Rare orphan indication, potentially accelerates clinical development and commercialization
- ddRNAi construct design highlights unique ‘silence and replace’ therapeutic strategy for monogenic disease
- *In vivo* study demonstrates correction of disease phenotype
- Next steps: further characterization of clinical candidates for *in vivo* efficacy on-going

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Financial and News flow

Company financial snapshot

Key Financial Details	ASX: BLT NASDAQ: BNTC NASDAQ: BNTCW
BNTC Share Price as of 31st Dec, 2016:	USD 1.53
Market Capitalization as of 31st Dec, 2016:	USD 14.1M
Issued Securities as of 31st Dec, 2016: Ordinary shares Options	 175,834,915 34,626,202
Cash Balance as of 30th Sept, 2016:	USD $9.8M
Registered Office	Sydney, Australia

Multiple Shots on Goal
Expected Milestones 2017-2019

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	2017	2018	2019
Hepatitis B BB-103	• Pre-IND meeting • IND-enabling studies	• Phase 1/2 initiation	• Phase 1/2
AMD BB-201	• Preclinical POC • Pre-IND meeting	• IND enabling studies • Phase 1/2 initiation	• Phase 1/2
OPMD BB-301	• Preclinical POC • Pre-IND meeting	• IND enabling studies • Phase 1/2 initiation	• Phase 1/2
HNSCC BB-401 (EGFR-AS)	• FDA meeting • IND filing	• Phase 2 initiation*	• Phase 2 completion
HNSCC BB-501 (ddRNAi EGFR)	• Discovery • Preclinical POC	• IND-enabling studies	• Phase 1/2 initiation
CAR-T	• Preclinical POC		
Non-viral Delivery	• Discovery • Preclinical POC		

* possible Phase 2/3 pending FDA dialog

Investment Highlights

Novel application of gene silencing technologies to build a focused product pipeline to address unmet medical needs across numerous indications

NOVEL GENE SILENCING TECHNOLOGY	ddRNAi has demonstrated broad applicability to address high unmet needs
FOCUSED PIPELINE	Superior efficacy in preclinical animal models as well as demonstrated long term clinical safety
COMMERCIAL STRATEGY	Demonstrated implementation of business model to diversify ddRNAi pipeline through strategic collaborations (e.g NantWorks)

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NASDAQ: BNTC
ASX: BLT

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