BENITEC BIOPHARMA

NASDAQ: BNTC | ASX: BLT

OPMD WEBINAR

15 May 2018

MEETING AGENDA

- Welcome and opening remarks (Greg West)
- Corporate overview (Greg West)
- OPMD overview (Bernard Brais)
- OPMD unmet medical need (Georgina Kilfoil)
- BB-301 – Benitec's OPMD therapeutic (David Suhy and Georgina Kilfoil)
  - Mechanism of action
  - Nonclinical silence and replace
  - Pathway to the clinic
  - Planned clinical program
  - Market potential
- Wrap-up (Greg West)

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SAFE HARBOR STATEMENT

If we make any forward-looking statements, we note that such statements involve risks and uncertainties relating to the difficulties in our plans to develop and 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 the ability to procure additional sources of financing.

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CORPORATE OVERVIEW

Greg West, Chief Executive Officer

BUSINESS OVERVIEW

Proven Technology

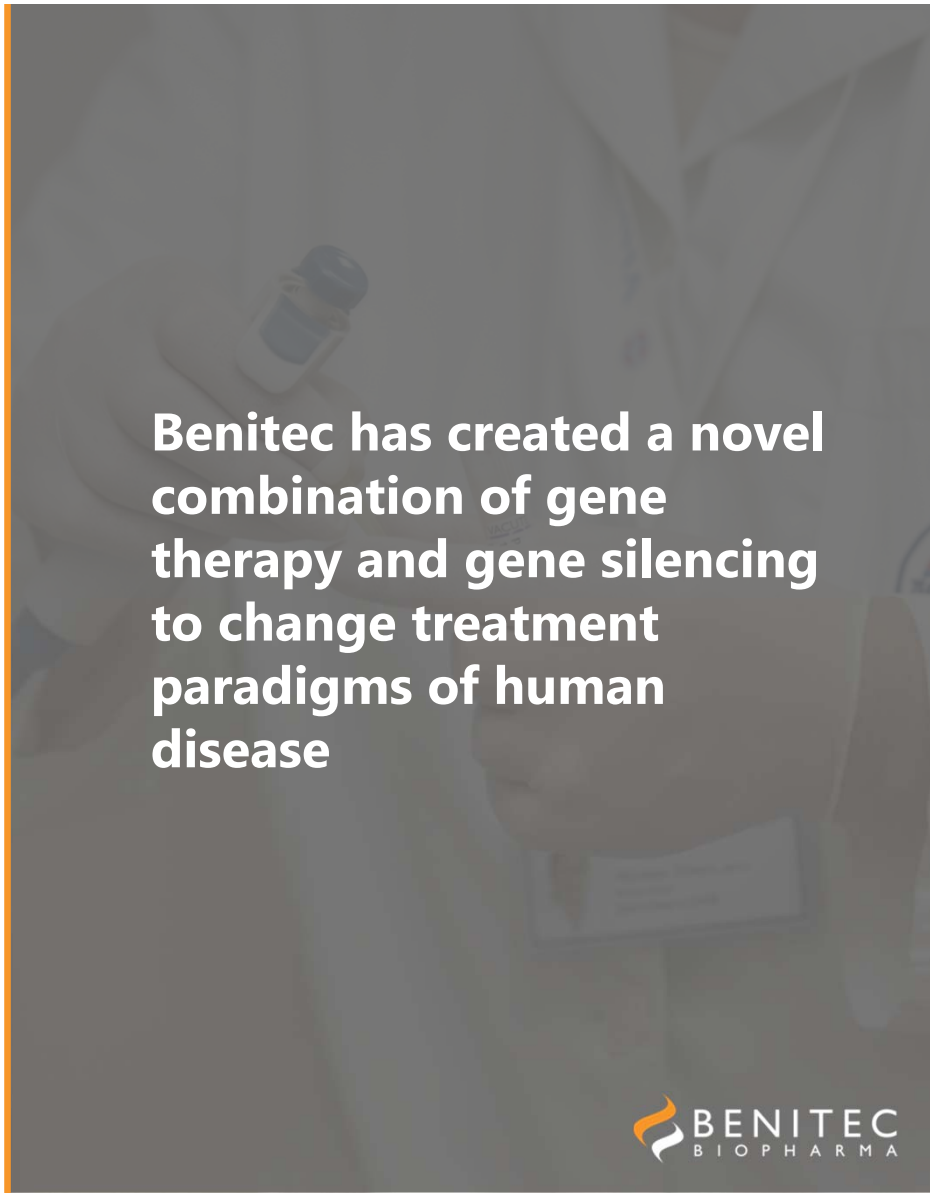
First company into human clinical studies under a US IND with systemically delivered non-withdrawable RNAi (TT-034)

Robust Pipeline

Assets in oncology (Phase 2 entry, 1Q18), orphan genetic disorders (Phase 1/2a entry, 1Q19), retinal disease, and infectious disease.

Valuable Products

Human therapeutic products for commercialization, partnering, and collaborations



HIGHLIGHTS

Programs advancing to clinic	**EGFR-targeted gene silencing therapy confirmatory Phase 2 trial initiated in Q1 2018**	**Unique 'silence and replace' therapeutic designed to treat OPMD with IND filing in Q1 2019**	**Other programs could be clinic-ready in late 2019**
Capital markets access	**Listed on ASX (2002, BLT) and NASDAQ (2015, BNTC)**	**US$50M capital raised since 2014**	**US shelf registration statement filed June 2017**
Strong in-house capabilities	**19 staff with scientific operations in Hayward CA, including 9 PhDs with deep gene therapy expertise**	**In-house manufacturing expertise for process optimization and scalability**	**Extensive commercial and drug development expertise**

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DIVERSE PROGRAM PIPELINE

Program	Delivery	Discovery	Preclinical	IND-Enabling	Early stage clinical (IND – Ph 2)	Late stage clinical (Ph 2 – Ph 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
Infectious disease – hepatitis B (HBV)*							
HBV BB-103	AAV Intravenous						Global
Retinal disease - wet age-related macular degeneration (AMD)							
AMD BB-201	Novel AAV Intravitreal						Global

*Continued development dependent on partnership or funding

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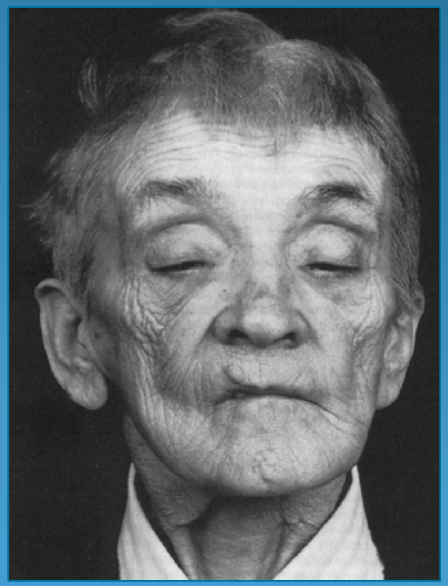
Oculopharyngeal muscular dystrophy (OPMD)

Bernard Brais M.D.C.M., M.Phil., Ph.D., FRCP(C)
Professor of Neurology and Genetics
Co-Director, Rare Neurological Diseases Group
Montreal Neurological Institute
McGill University
Bernard.Brais@Mcgill.ca

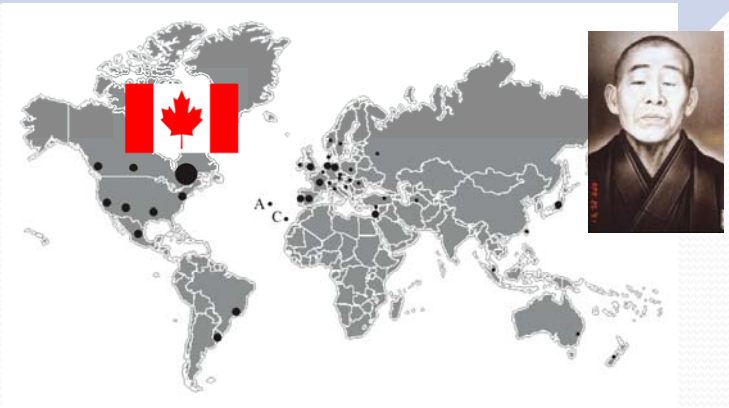


Outline of presentation

- OPMD prevalence
- OPMD diagnosis
- Progression and treatments of OPMD
- End of life in OPMD

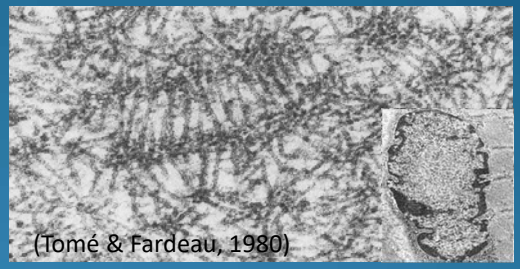
OPMD is a world wide late-onset muscular dystrophy with variable prevalences

Northern UK	France	South-West USA	Quebec	Bukhara Jews in Israel
>1:100000	1:100000	1: 15000	1:1000 (>1500 (GCN)n + cases)	1:600

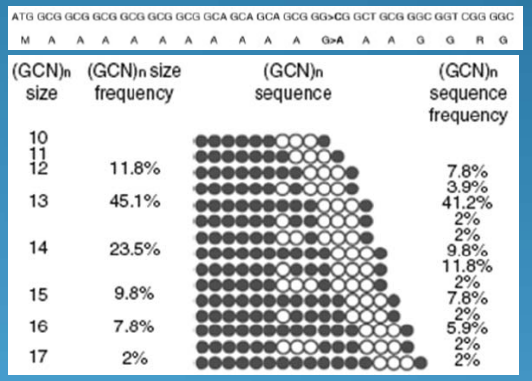


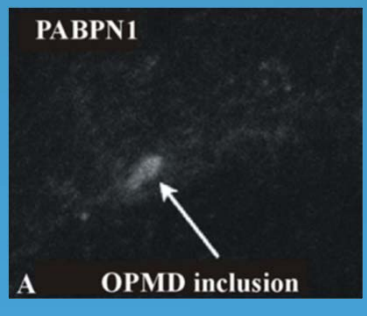
Diagnosis of OPMD


(Taylor, 1915)


(Tomé & Fardeau, 1980)

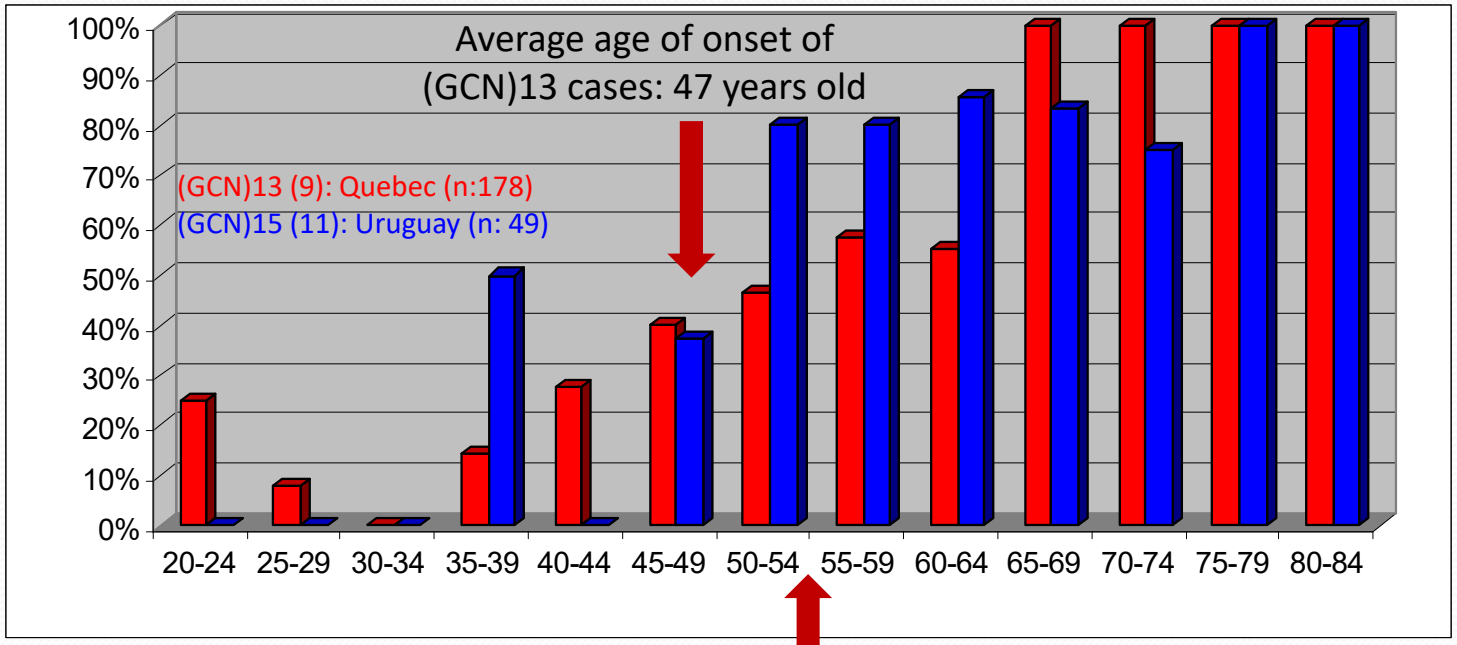
- 1915: First French Canadian families (Taylor)
- 1962: Victor and Adams name OPMD the disease affecting a Ashkenazi Jewish family, *New England Journal of Medicine*. OPMD is a dominant dystrophy that presents with eyelid drooping and dysphagia that starts in the late forties-early fifties
- 1980: Description of a diagnostic pathological marker: Intranuclear inclusions (INI) by Tomé and Fardeau
- 1995: objective dysphagia in OPMD: Bouchard's Cold Water test defined as swallowing 80ml of cold water >7 seconds as supporting the diagnosis of OPMD
- 1998: Brais et al. in *Nature Genetics* describe the cryptique (GCN)n/Alanine repeat mutations in *PABPN1* as the cause OPMD worldwide





Progression of OPMD

Dysphagia



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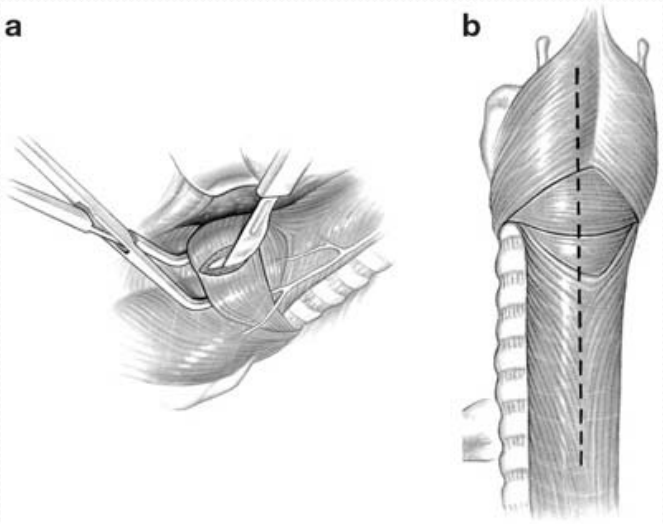
Aspiration pneumonias

Treatments for dysphagia

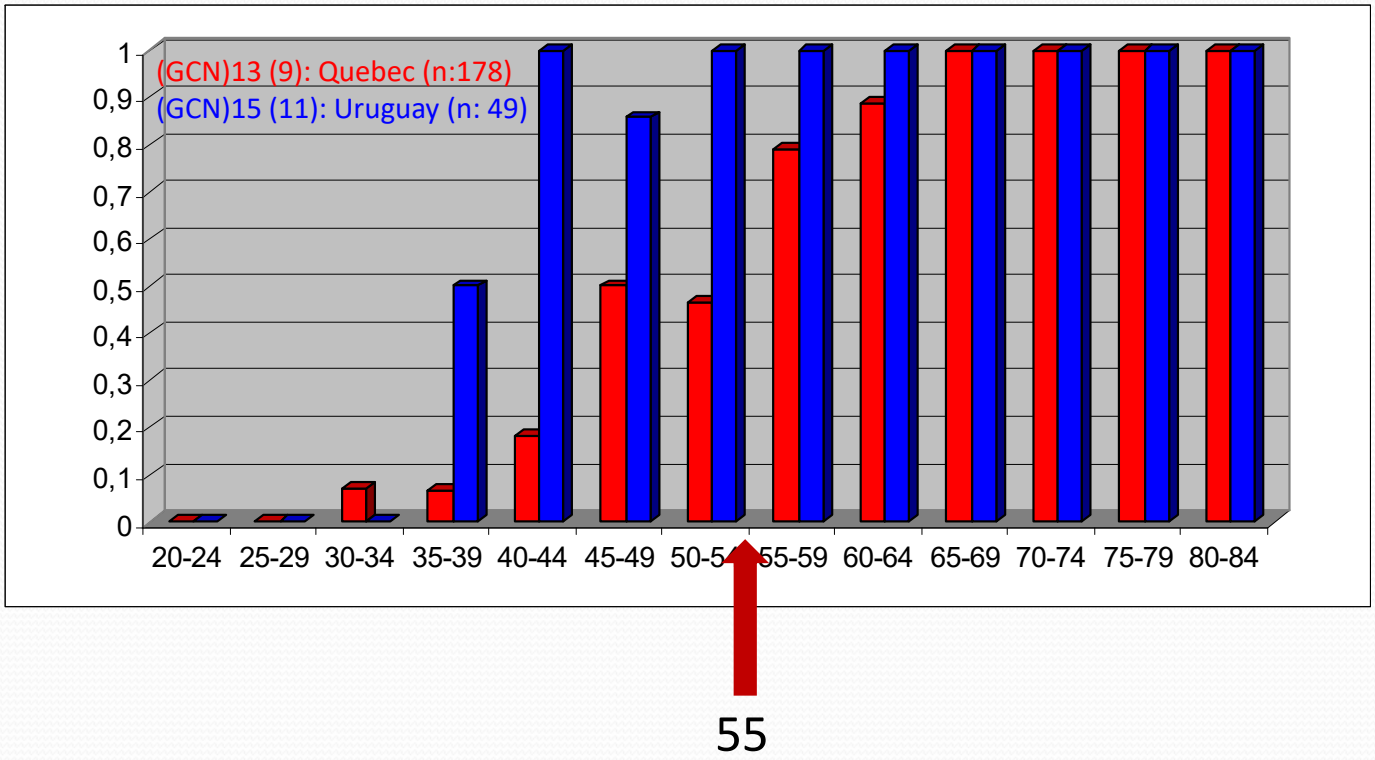
- Indications: moderate to severe dysphagia
- Cricopharyngeal dilatation (needs to be repeated)
- Cricopharyngeal myotomy (morbidity and mortality)
- Cricopharyngeal paralysis with Botox (unproven)



Cricopharyngeal myotomy

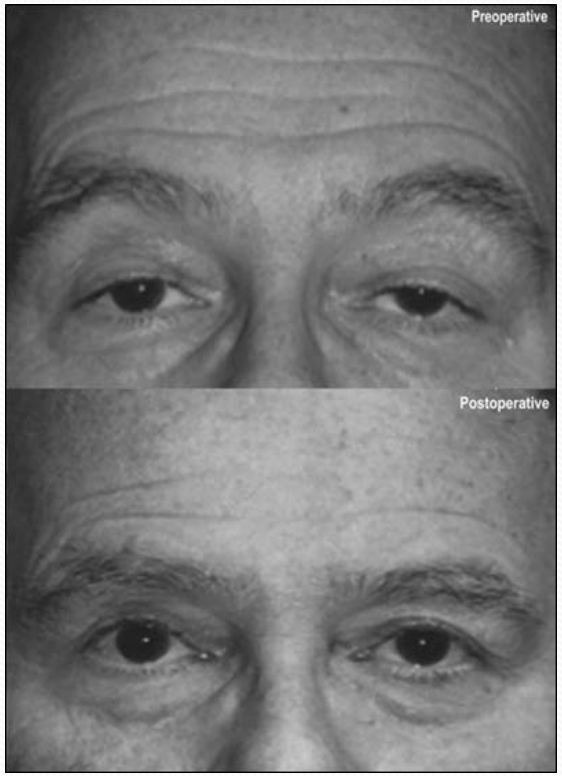
Progression of OPMD

Eyelid Ptosis



Treatment of the eyelid ptosis

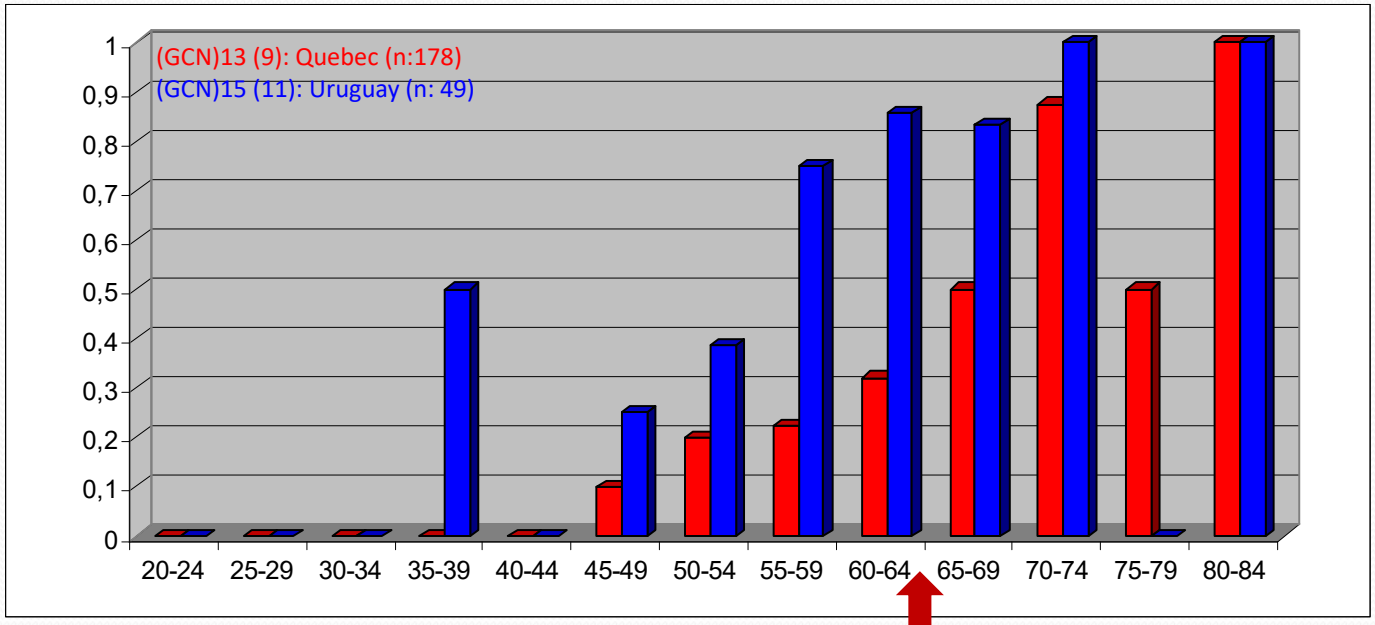
- Indications: More than 50% coverage of pupil, night driving more difficult and cervical pain
- Frontal suspension is the permanent solution



Kalin-Hajdu, E., et al., Codere, F. *Ophthalmic Plastic & Reconstructive Surgery*. 2017.

Progression of OPMD

Lower limb weakness



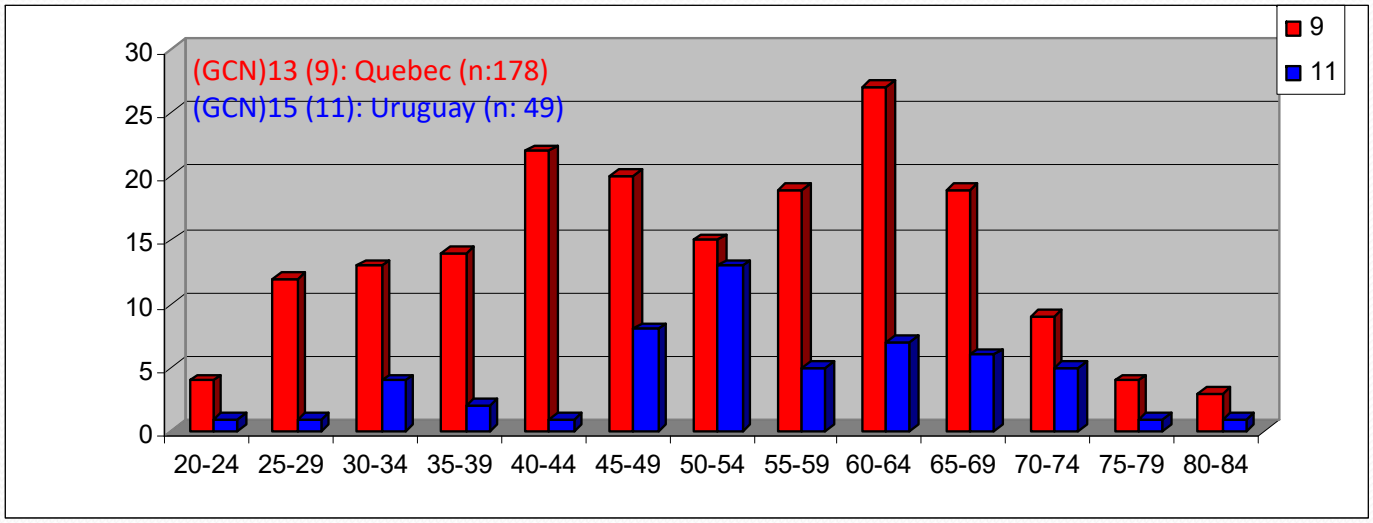
No treatment for the progressive limb girdle weakness

65

Loss of walking is rare

Progression of OPMD

End of life in OPMD



Increasingly poor quality of life past 65 with a reasonably normal life expectancy.

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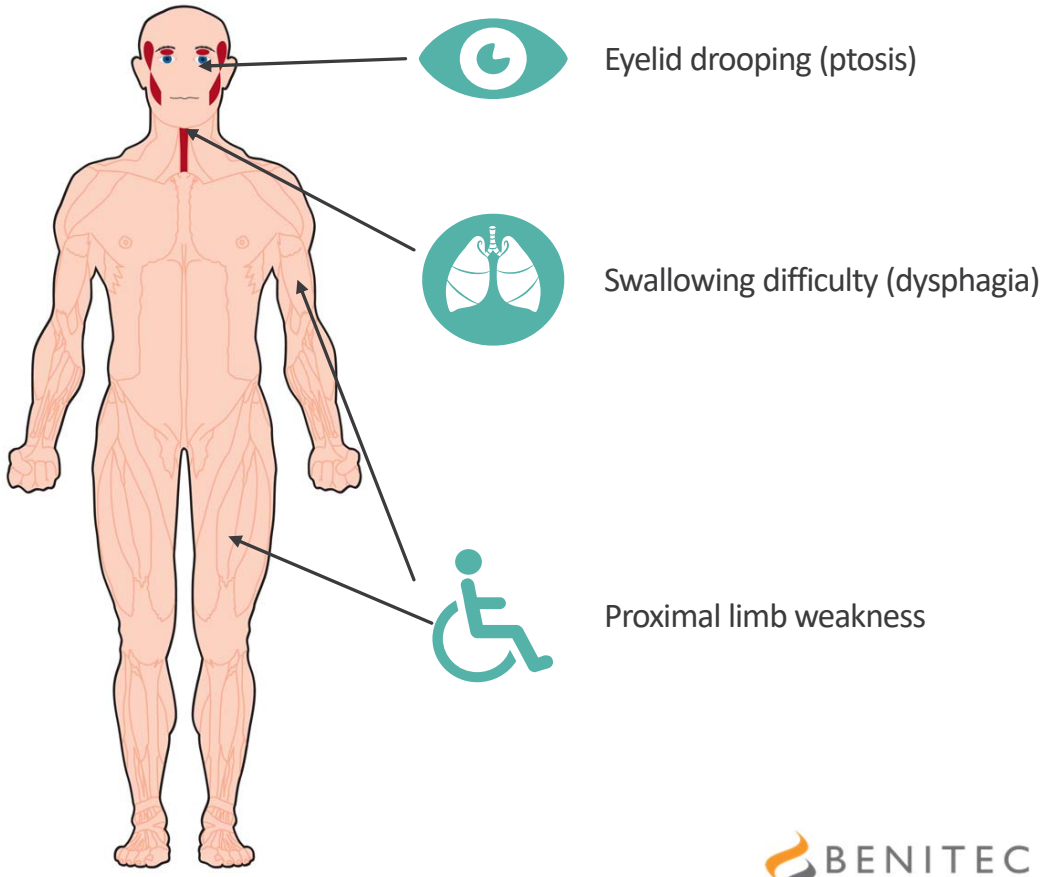
OPMD
UNMET MEDICAL NEED

Georgina Kilfoil, Chief Development Officer

LIVING WITH OPMD

- Slow progressing muscle wasting disease
- Rare autosomal inheritance
- Caused by a defect in the PABPN1 gene
- Typical age of onset is 40s or 50s
- Available therapies limited to palliative care



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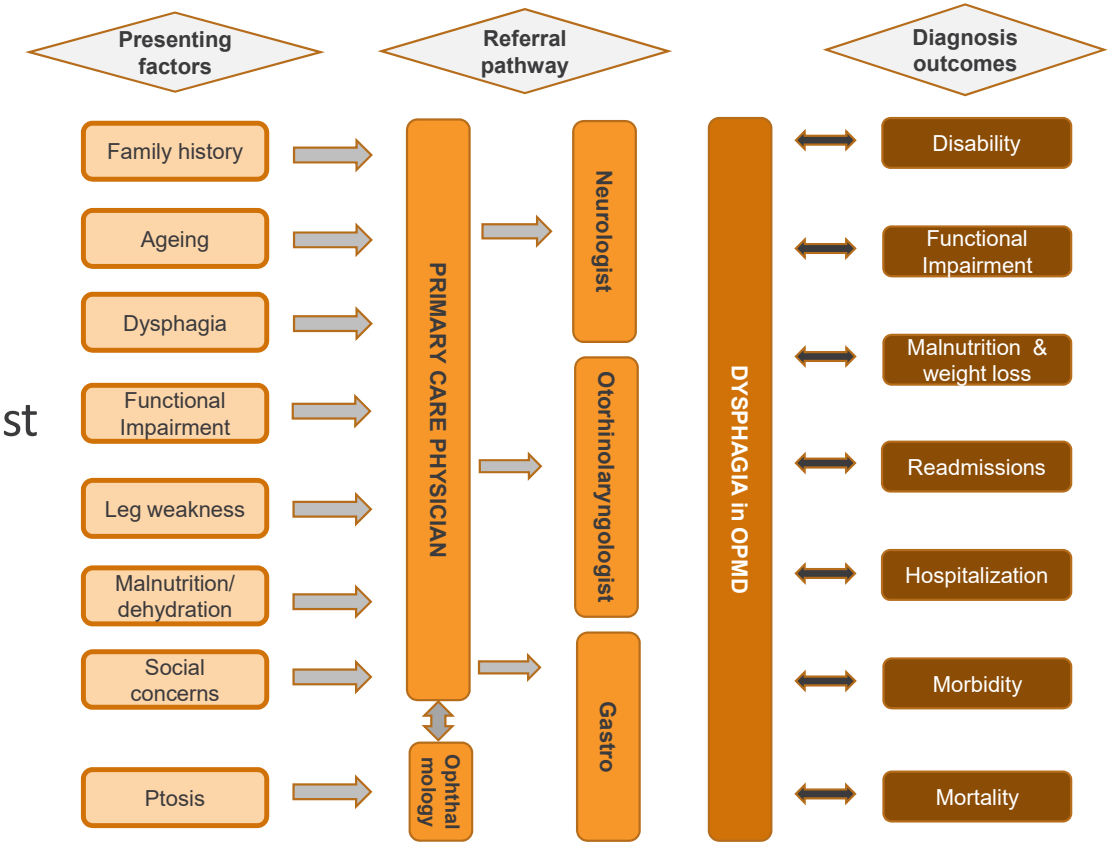
OPMD PATIENT PRESENTATION & DIAGNOSIS

Initial Presentation

- Specialty depends on triggering symptom

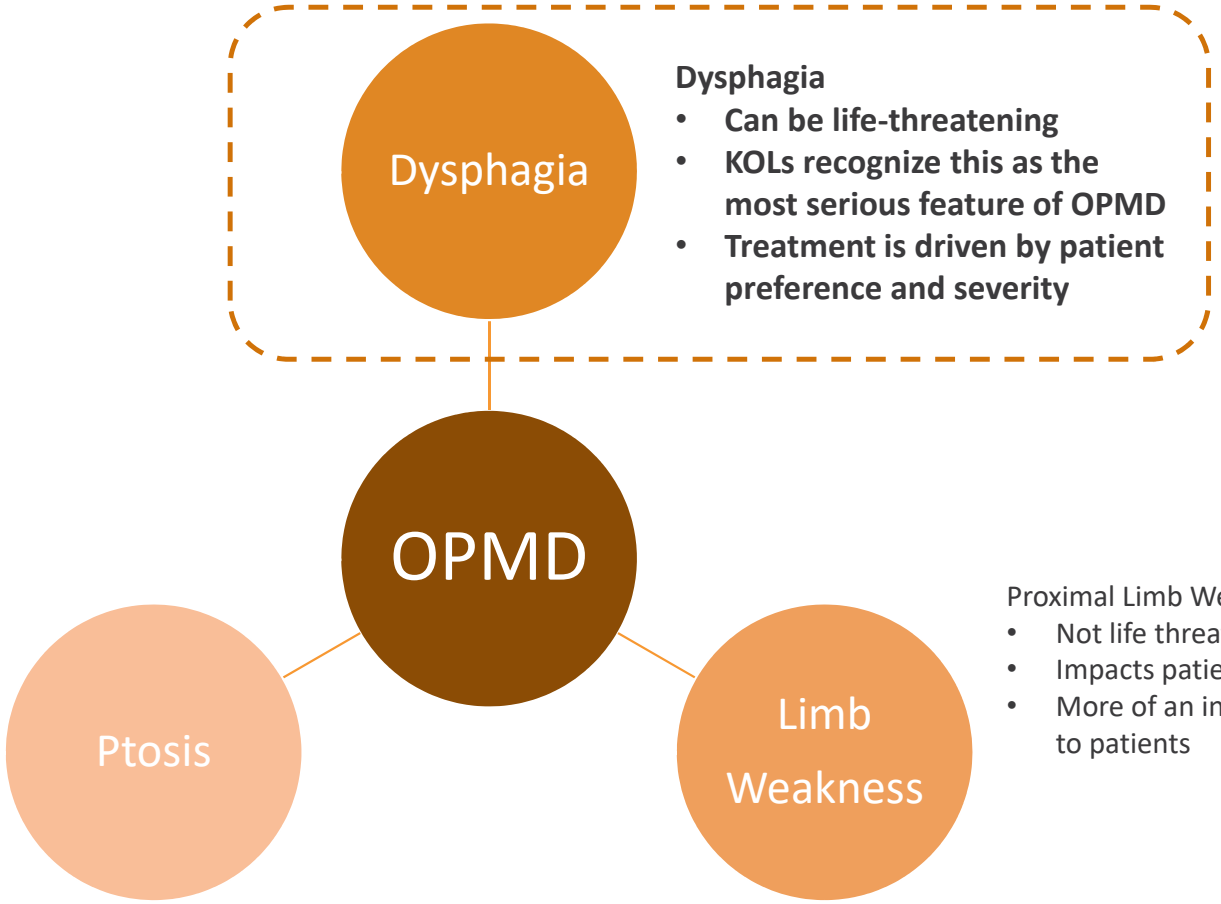
Diagnosis

- Performed by neurologist or geneticist



Source: GlobalData Report Oct 2017

DYSPHAGIA - MOST SERIOUS FEATURE OF OPMD



Dysphagia
- **Can be life-threatening**
- **KOLs recognize this as the most serious feature of OPMD**
- **Treatment is driven by patient preference and severity**

Ptosis
- Often the symptom that motivates patient to seek care
- Satisfactorily fixed with corrective surgery (frontal sling highly preferred vs blepharoplasty)

Proximal Limb Weakness
- Not life threatening
- Impacts patient's QOL
- More of an inconvenience to patients

 Source: GlobalData Report Oct 2017

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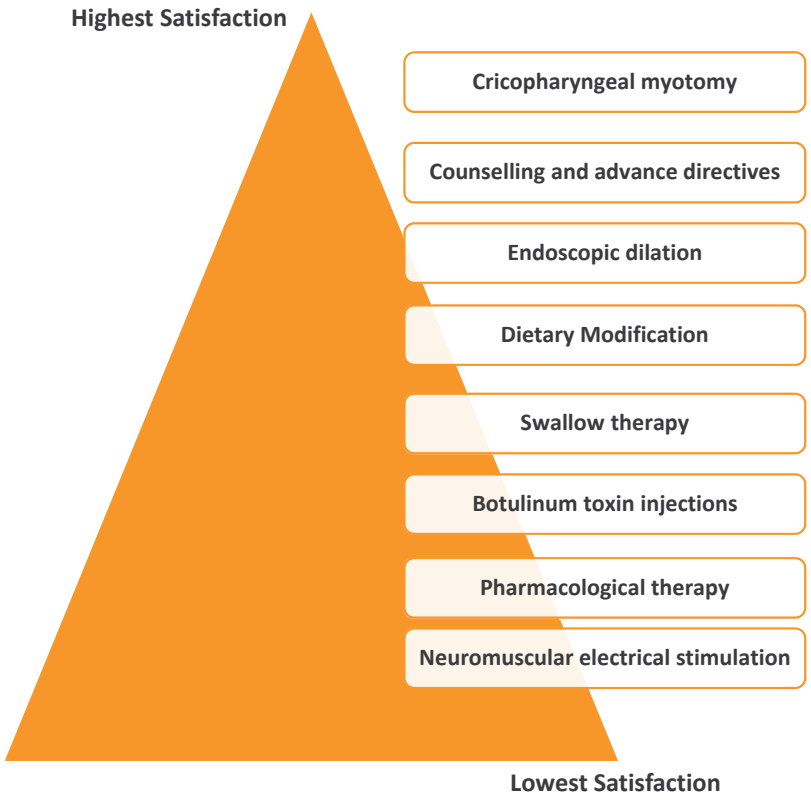
MUCH ROOM FOR IMPROVEMENT WITH CURRENT INTERVENTIONS FOR DYSPHAGIA



	Advantages	Disdvantages
Cricopharyngeal myotomy	Often effective	Expensive, may need repeat, irreversible
Counselling and advance directives	Inexpensive	Not a solution
Endoscopic dilation	Often effective, not as invasive as surgery	Not permanent, may need frequent repeat, not effective in everyone
Dietary Modification	Inexpensive and extremely important, and sometimes effective	Hard to stay compliant, not always effective
Swallow therapy	Not invasive, and relatively inexpensive	Time consuming, need for frequent visits
Botulinum toxin injections	Effective for some	Expensive, temporary, need for frequent visits
Pharmacological therapy	Potential in the future	None available
Neuromuscular electrical stimulation	Non-invasive	Uncomfortable, temporary, need for frequent visits

While CP myotomy and counselling are the most satisfactory treatments, there is much room for improvement

Source: GlobalData Report Oct 2017

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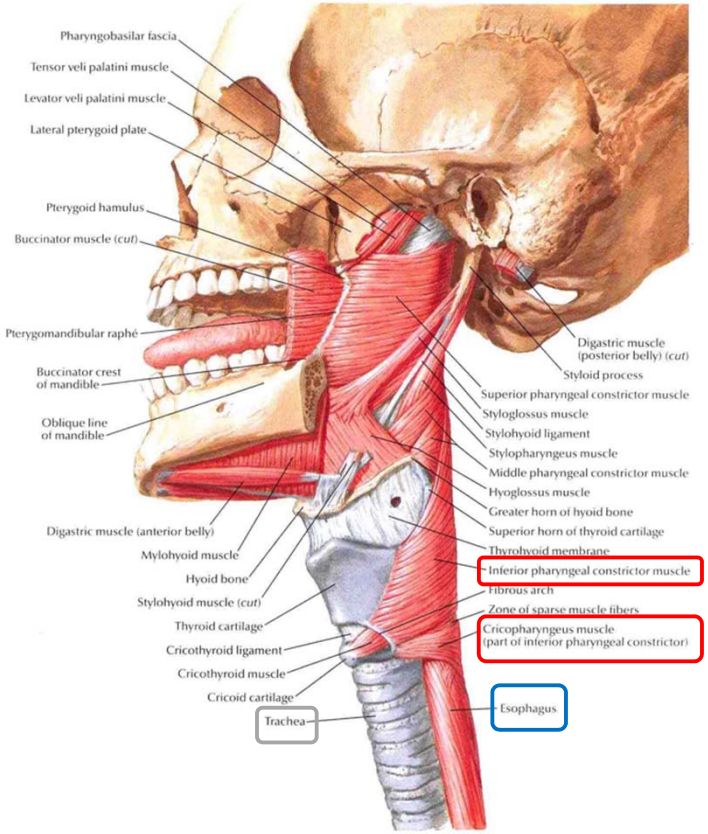
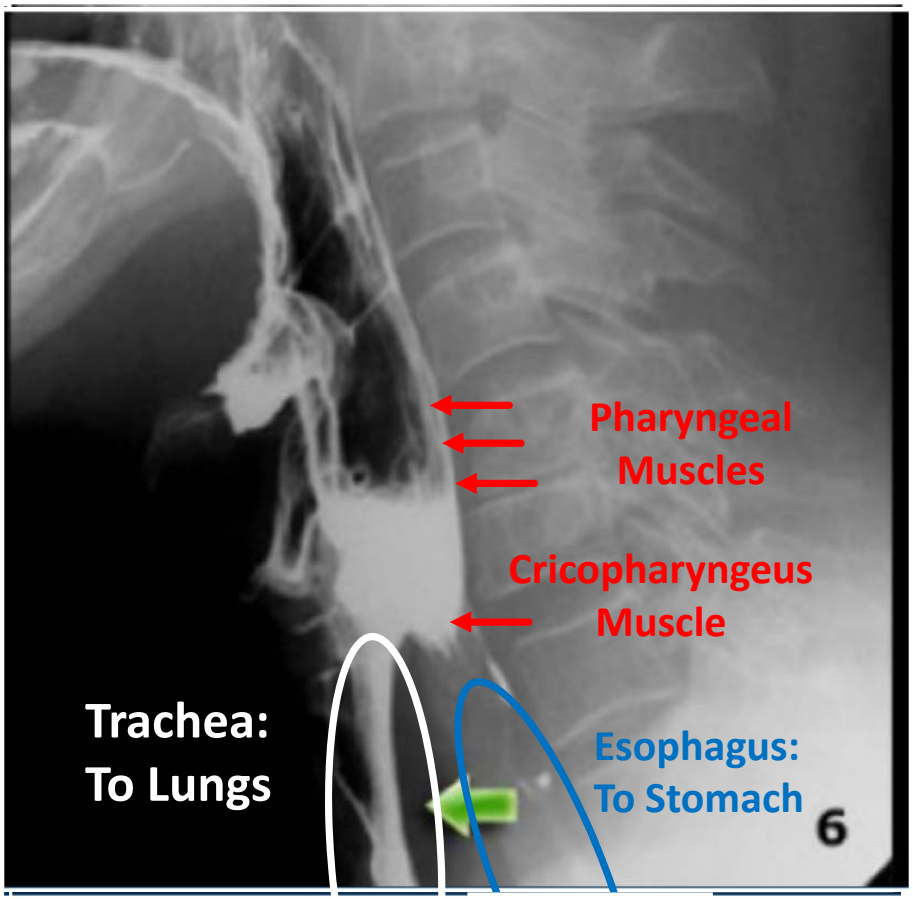
BB-301
OPMD THERAPEUTIC

David Suhy, Chief Scientific Officer

Georgina Kilfoil, Chief Development Officer

ASPIRATION FROM DYSPHAGIA

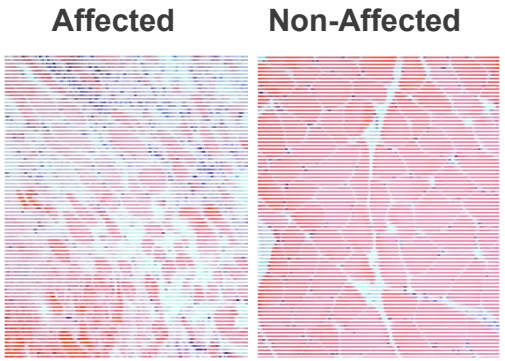




TISSUE AND MOLECULAR ASPECTS OF OPMD

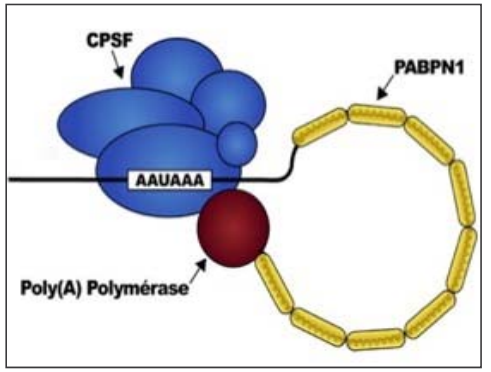
Histopathology:

- Decrease of muscle fiber number
- Variation in the size of muscle fibers
- Fibrosis (connective tissue)
- Net effect: decrease in muscle force



PABPN1:

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



In OPMD:

- An autosomal dominant mutation results in trinucleotide repeat expansion in PABPN1

Normal	**ATG $(GCG)_6$ ---------- -$(GCA)_3$ GCG GGG GCT GCG…**
OPMD	**ATG $(GCG)_6$ $(GCG)_{1-7}$ $(GCA)_3$ GCG GGG GCT GCG…**

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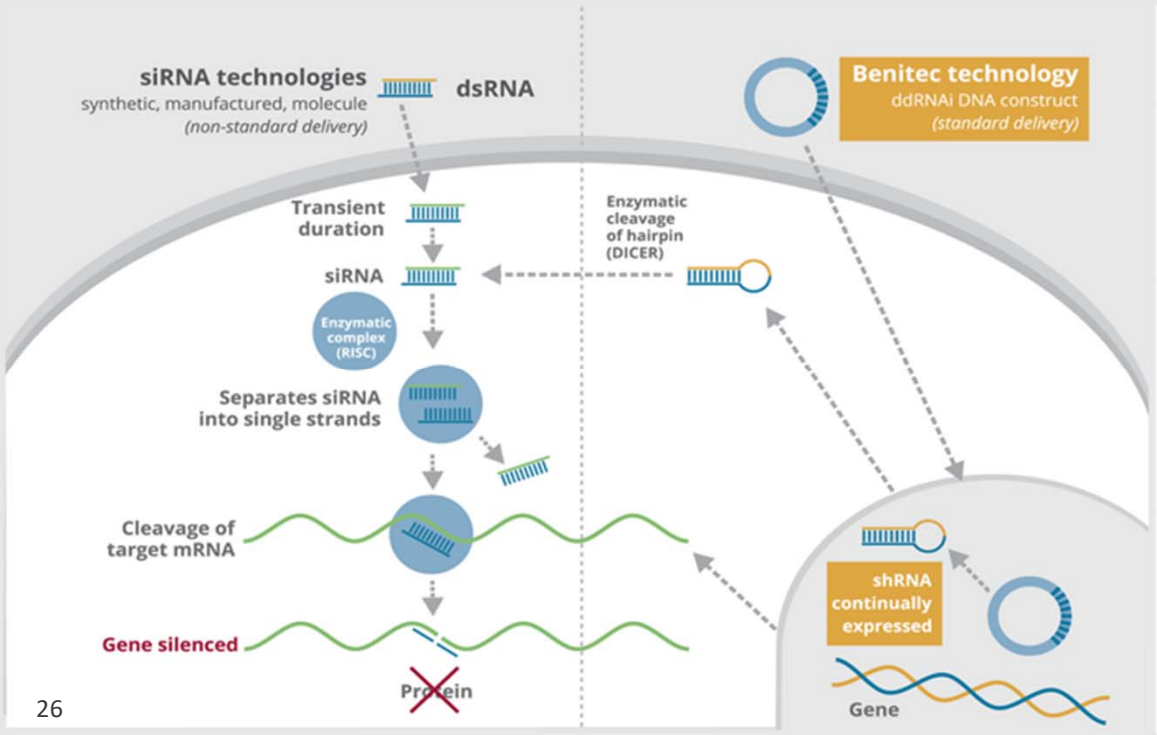
PERMANENT GENE SILENCING

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

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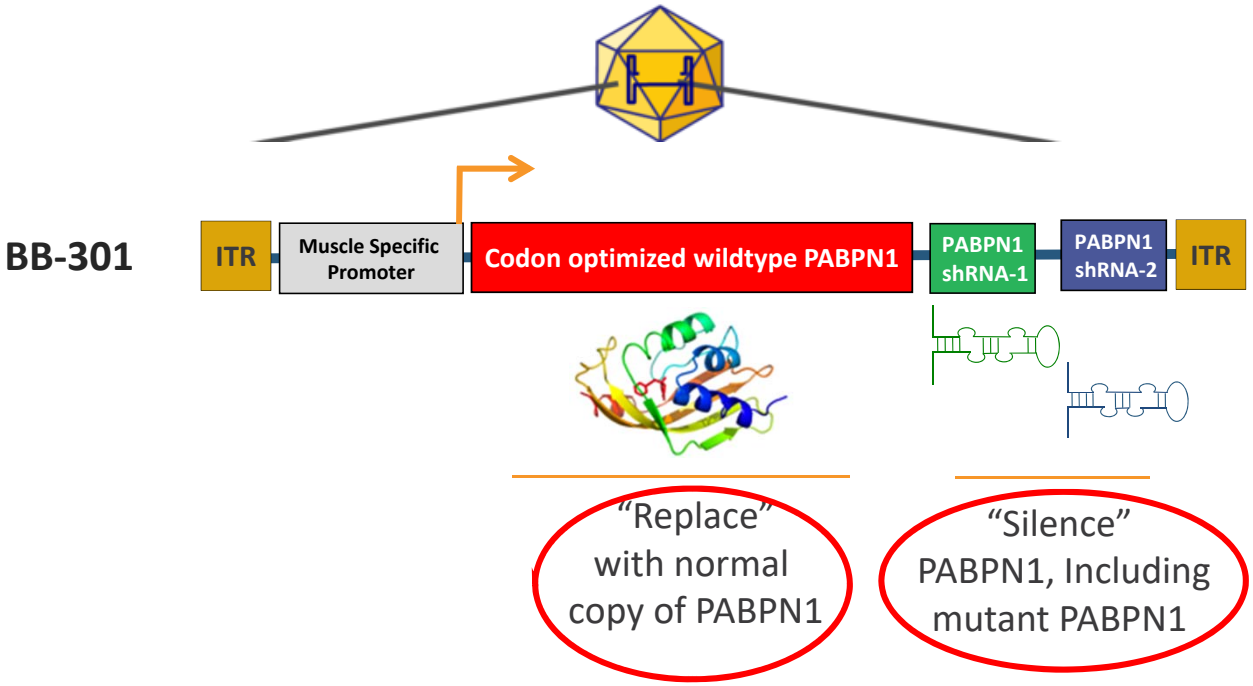
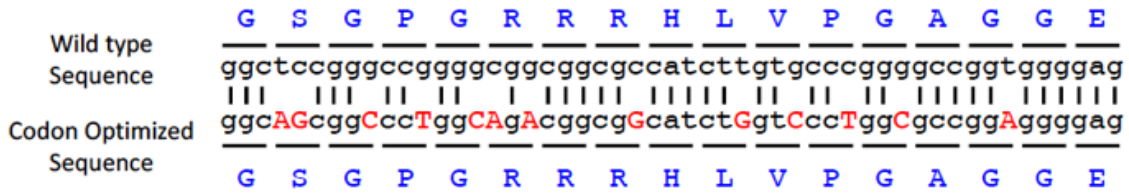
BB-301: A 'SILENCE AND REPLACE' BASED APPROACH





← Insensitive to shRNA

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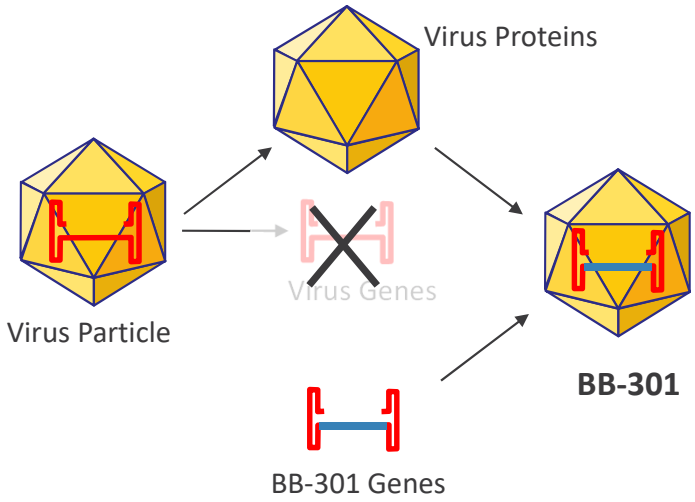
BB-301: HOW DOES A GENE THERAPY SOLUTION WORK?

- Use methods to produce the virus proteins without producing the virus genes
- Design the BB-301 genetic sequences that are designed to treat OPMD
- A manufacturing process is used to insert the BB-301 genes into the protein shell
- BB-301 is injected into the body. For the initial clinical trial BB-301 will be injected into the cricopharyngeal muscle
- BB-301 enters into the muscle cells and starts producing the genes that may help with the mutant PABPN1



AAV

- Non-integrating, non-pathogenic viral delivery
- To date, AAV has been used in 204+ clinical trials
- Sustained expression (years) following single injection

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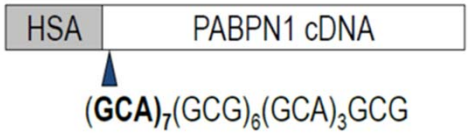
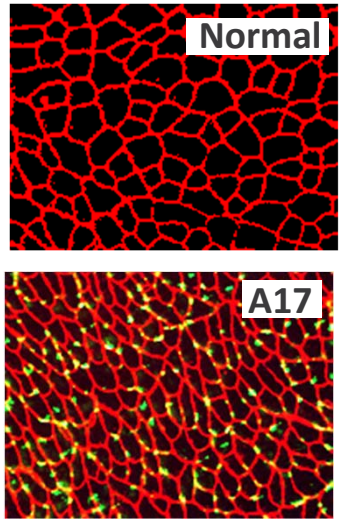
PRE-CLINICAL MODEL OF OPMD: THE 'A17' MOUSE

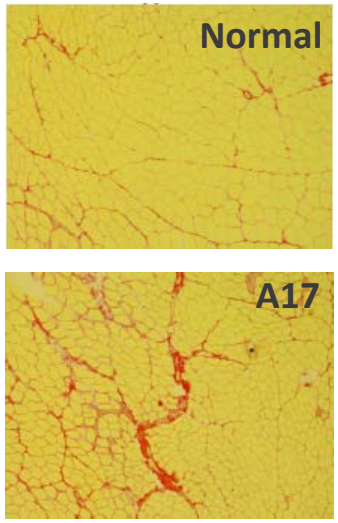


- Transgenic mouse: express a mutated bovine PABPN1 driven by the human skeletal actin promoter in addition to the endogenous PABPN1
- Recapitulates severe muscle atrophy
- Mimics many of the disease pathologies

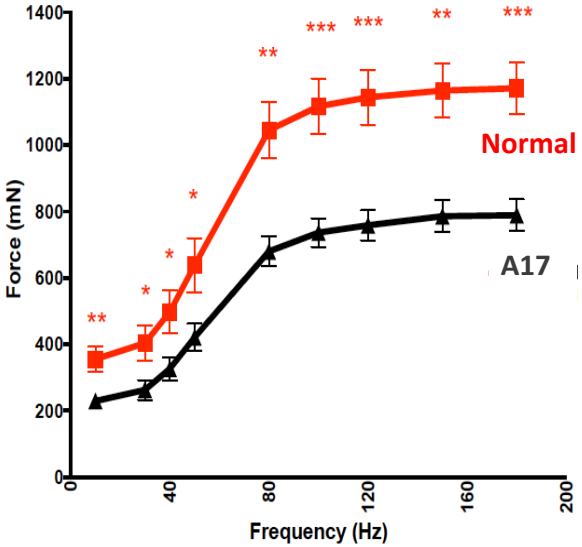
Intra Nuclear Inclusions (INI)



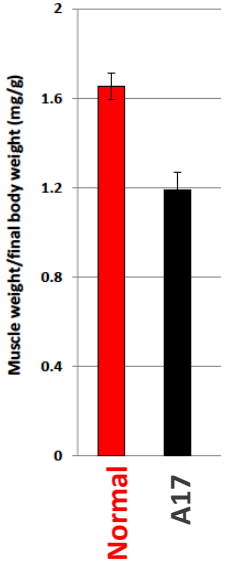
Fibrosis



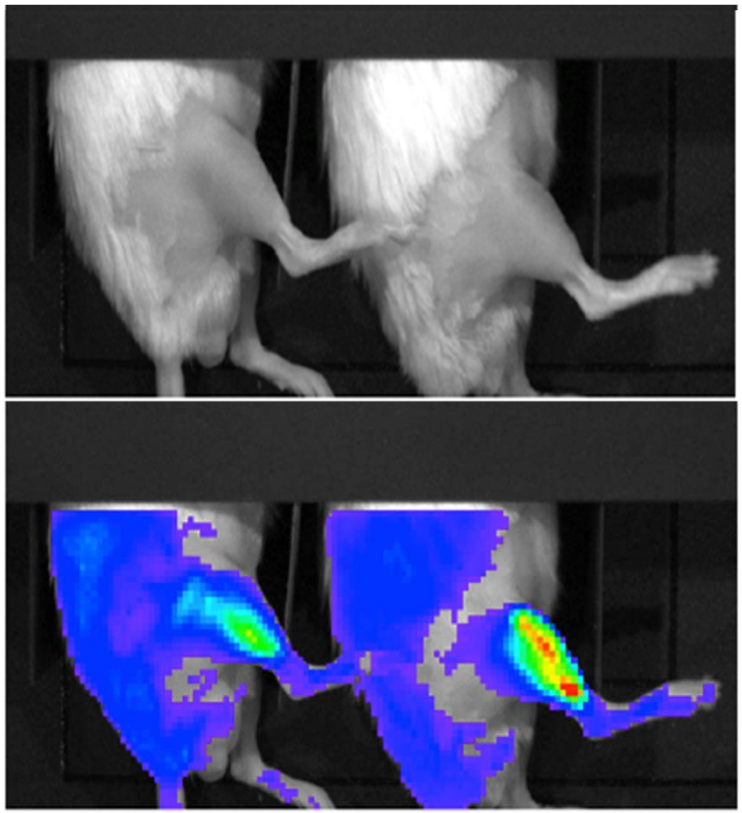
Muscle Force

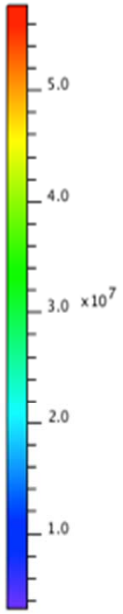


Muscle Weight

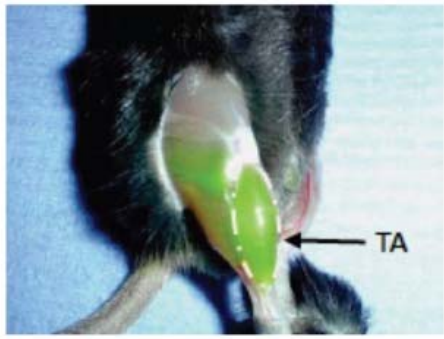


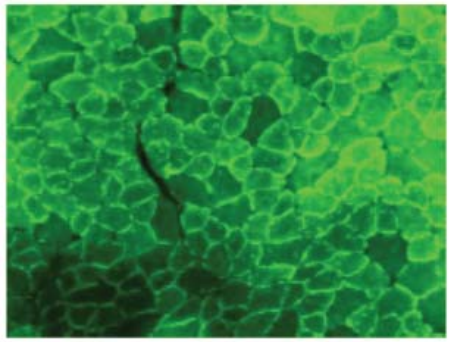
AAV TRANSDUCTION OF MUSCLE BY LOCAL INJECTION





muscle expressing GFP
1 year + post injection





Courtesy of G. Dickson, RHUL

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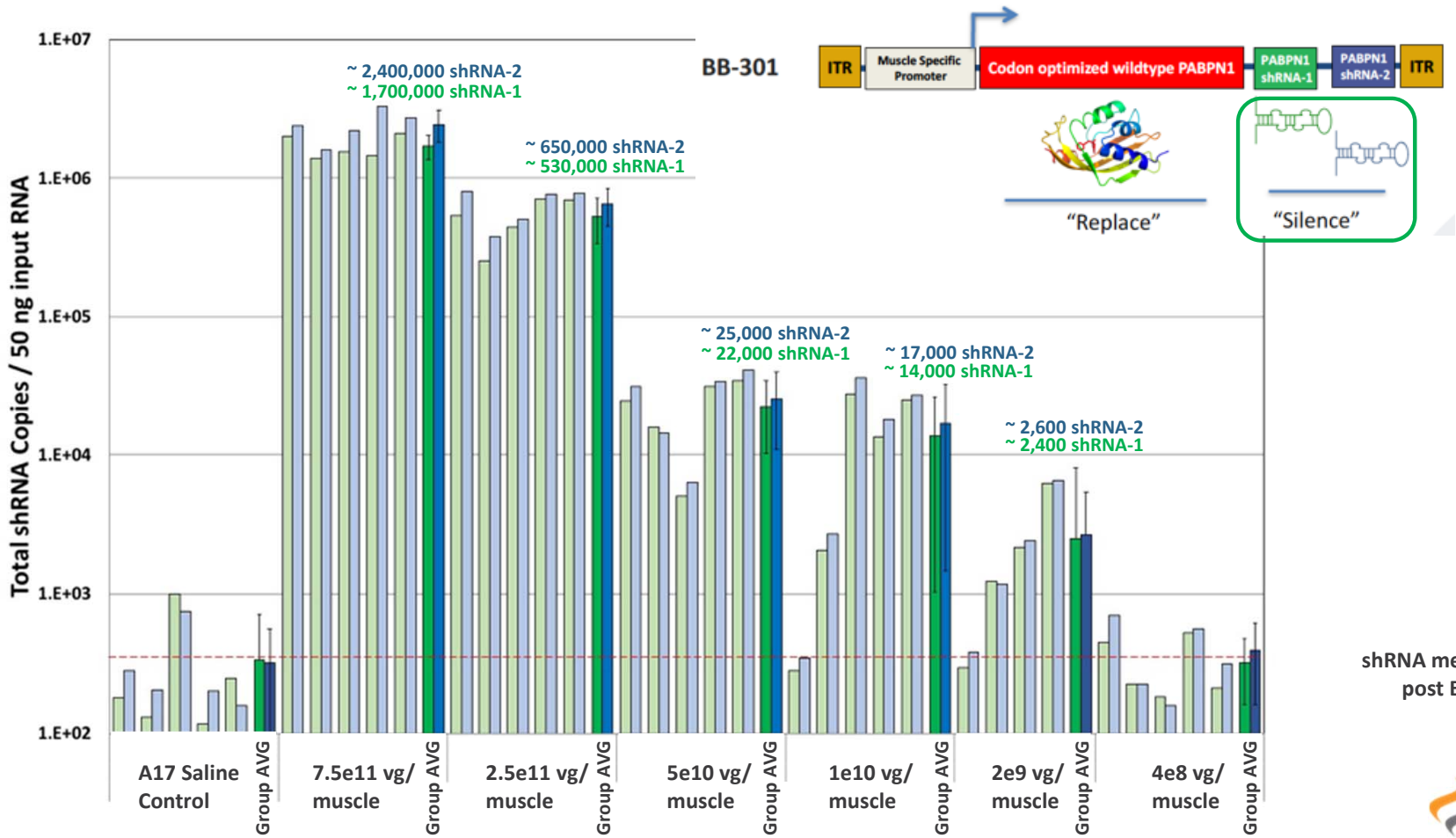
BB-301: DOSE RANGE FINDING STUDY - OVERVIEW

- Single doses of BB-301 across broad range: 4e8 vg/muscle up to 7.5e11 vg/muscle
- Each cohort had N=5 animals
- 2 doses per animal – left/right TA muscle
- Transgenic animals were 10-12 weeks at dosing with established OPMD phenotypes

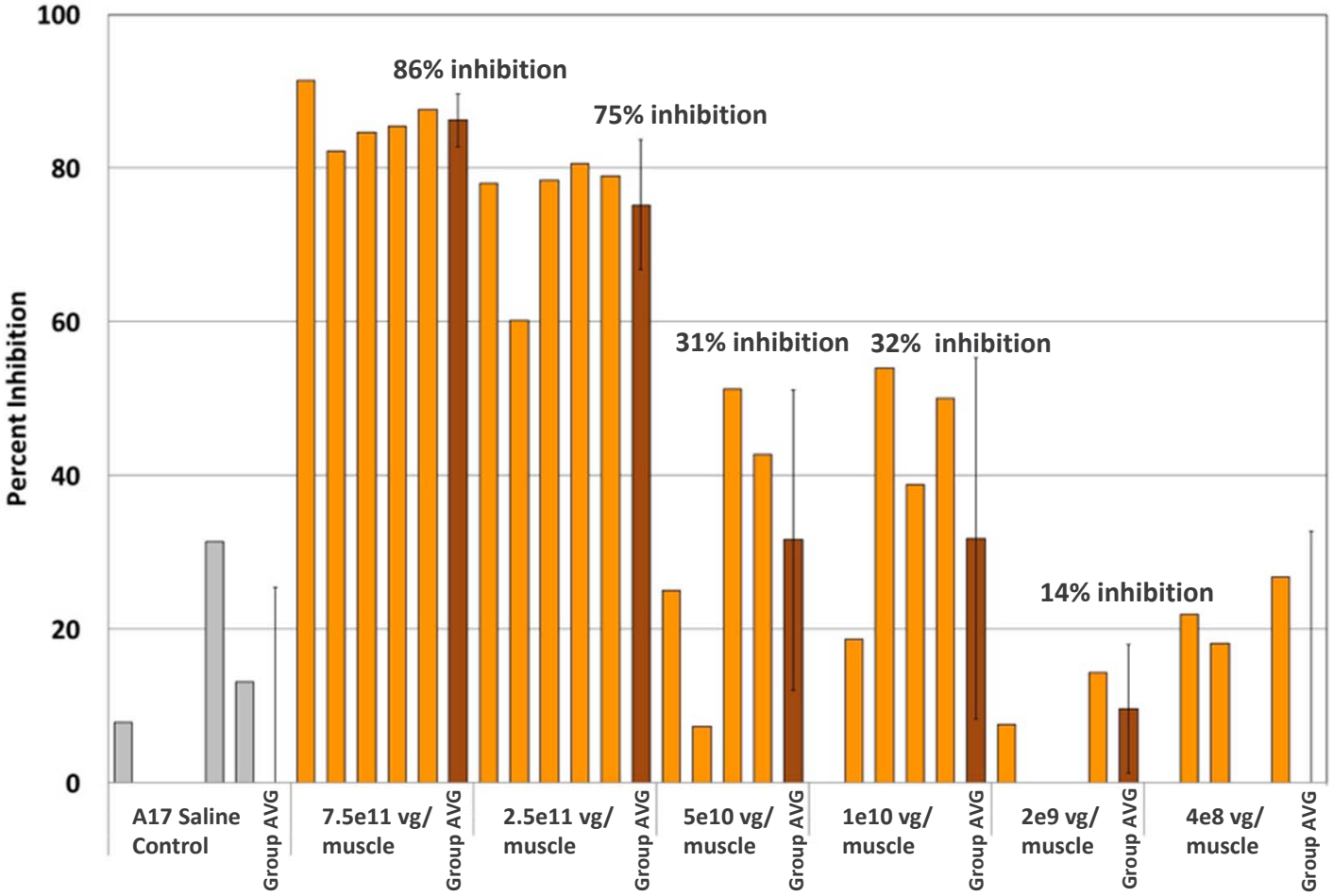
- Endpoint parameters monitored 14 weeks post dosing
- Individual muscles used for INIs, strength, weight
- Paired Muscles measured for shRNA production, codon optimized PABPN1 expression

BB-301: EXPRESSION OF SHRNA IN TA MUSCLES OF A17 MICE



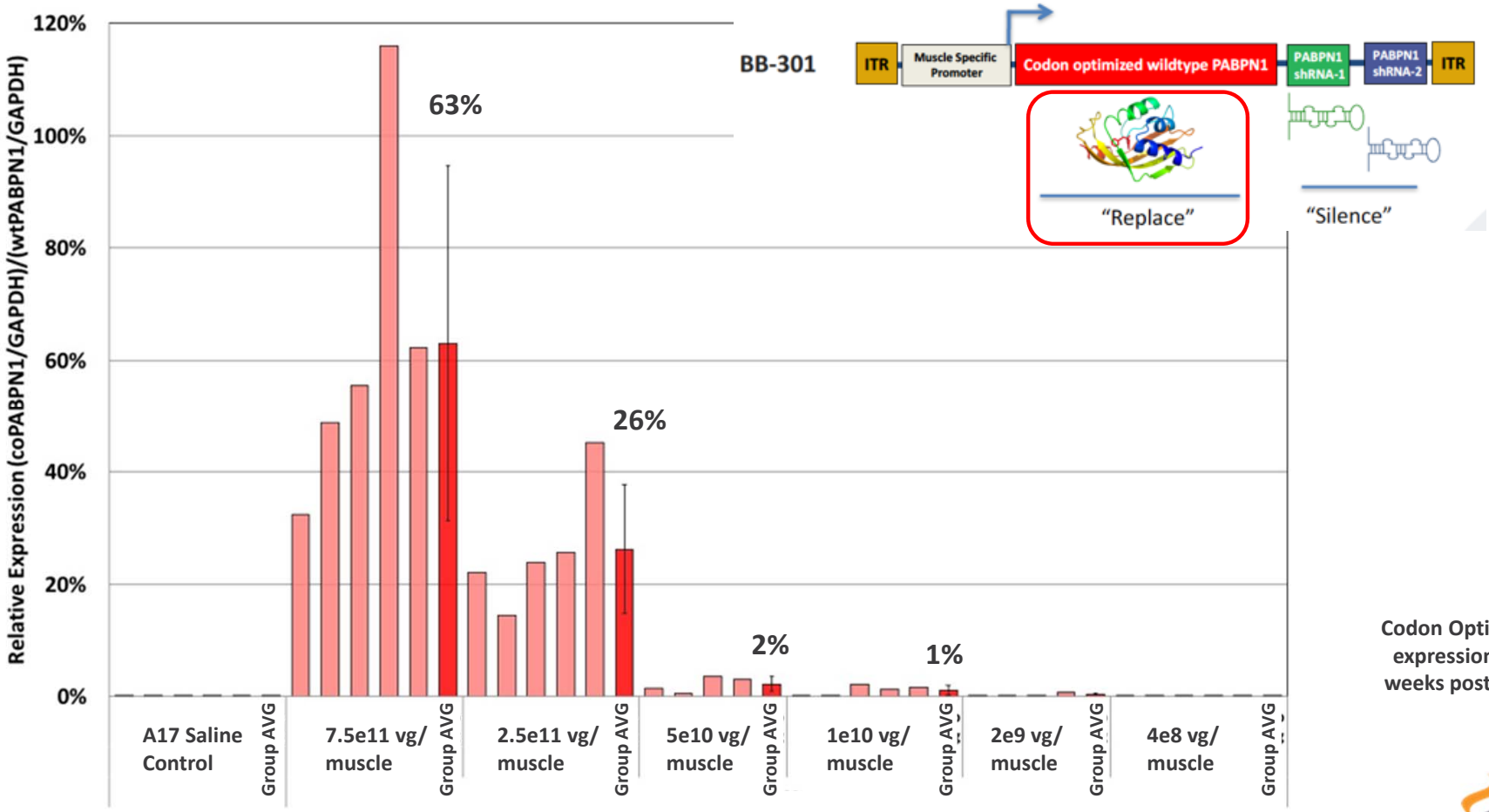
shRNA measured 14 weeks post BB-301 dosing

BB-301 SILENCES PABPN1 EXPRESSION (INCLUDING MUTANT PABPN1) IN AN OPMD MOUSE MODEL



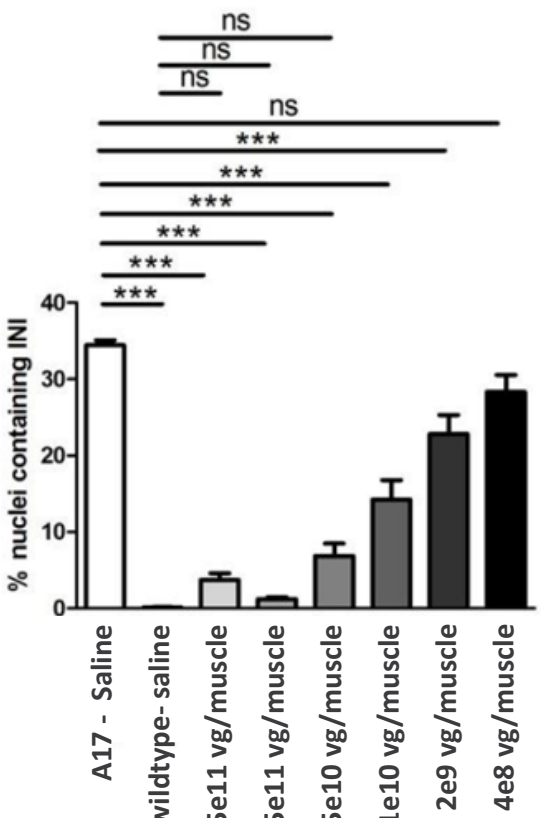
PABPN-1 Inhibition measured 14 weeks post BB-301 dosing

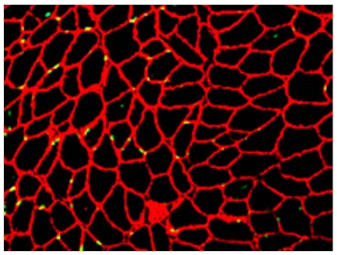
BB-301 RESTORES NORMAL PABPN1 LEVELS IN A17 MOUSE MODEL



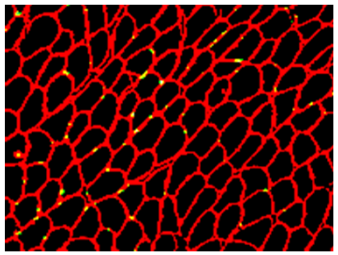
Codon Optimized PABPN-1 expression measured 14 weeks post BB-301 dosing

BB-301 REVERSES INTRANUCLEAR INCLUSIONS IN OPMD MOUSE MODEL

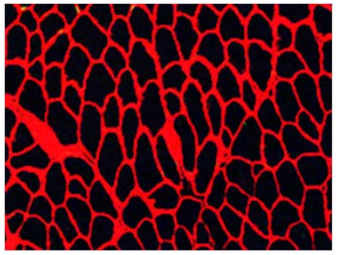




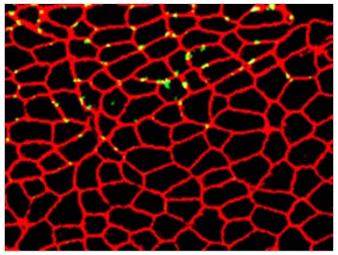
7.5e11 vg/muscle



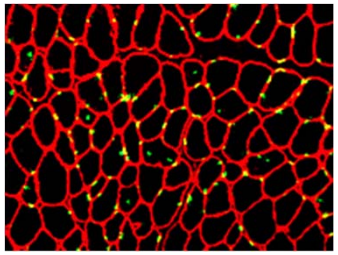
2.5e11 vg/muscle



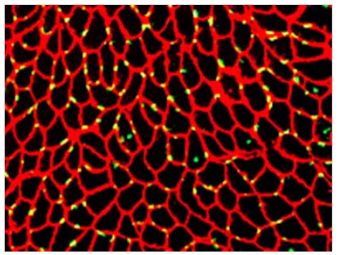
5e10 vg/muscle



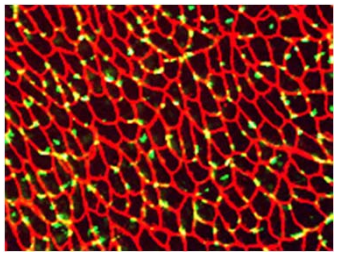
1e10 vg/muscle



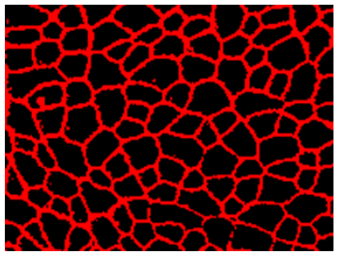
2e9 vg/muscle



4e8 vg/muscle



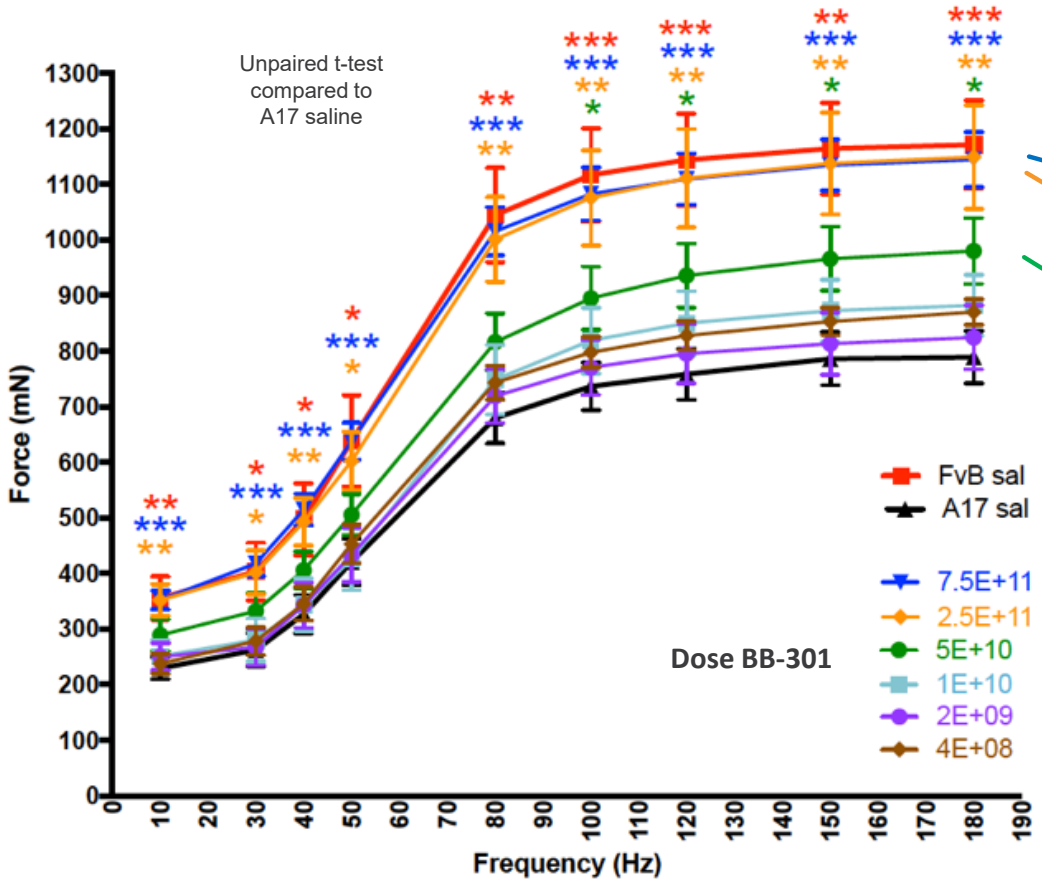
A17 - Saline



Wildtype- saline

INI persistence measured 14 weeks post BB-301 dosing

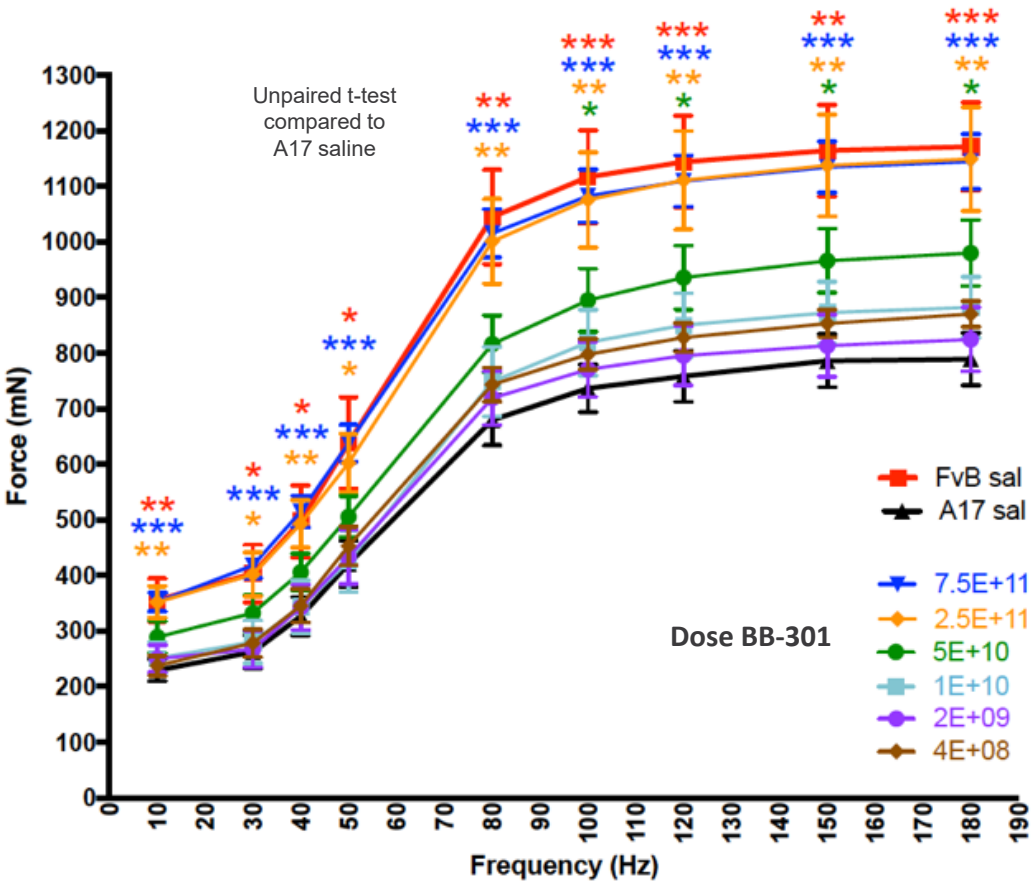
BB-301 RESTORES MUSCLE FORCE IN OPMD MOUSE MODEL

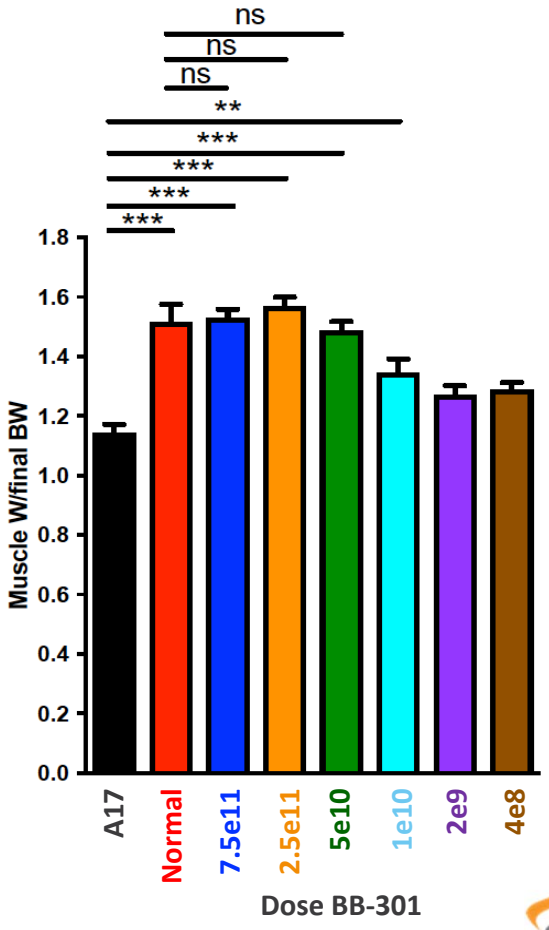


	"Silence"	"Replace"
BB-301 Dose (vg)	Inhibition PABPN1*	WT-PABPN1 Expression
7.5e11	86 %	63 %
2.5e11	75 %	26 %
5e10	31 %	2 %
1e10	32 %	1 %
2e9	14 %	0 %
4e8	0 %	0 %

Force measured 14 weeks post BB-301 dosing

CORRELATION BETWEEN RESTORATION OF MUSCLE FORCE AND MUSCLE WEIGHT UPON BB-301 TREATMENT

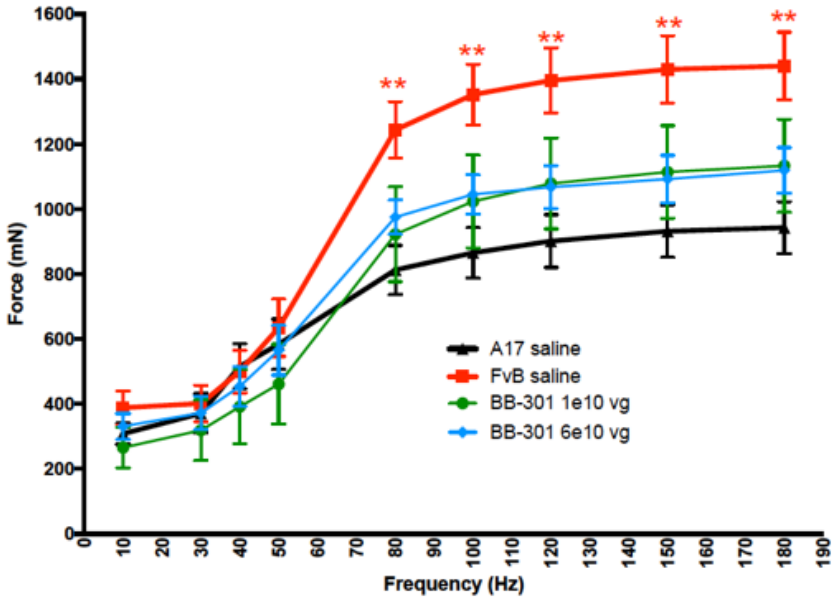




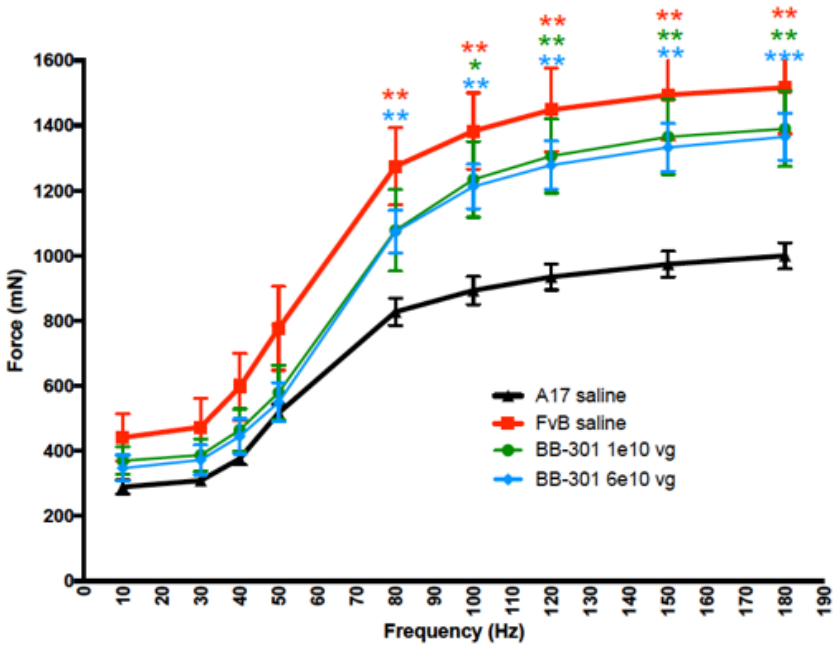
Muscle Weight

BB-301: RESTORATION OF MUSCLE FUNCTION TAKES TIME

14 weeks post BB-301 Dosing

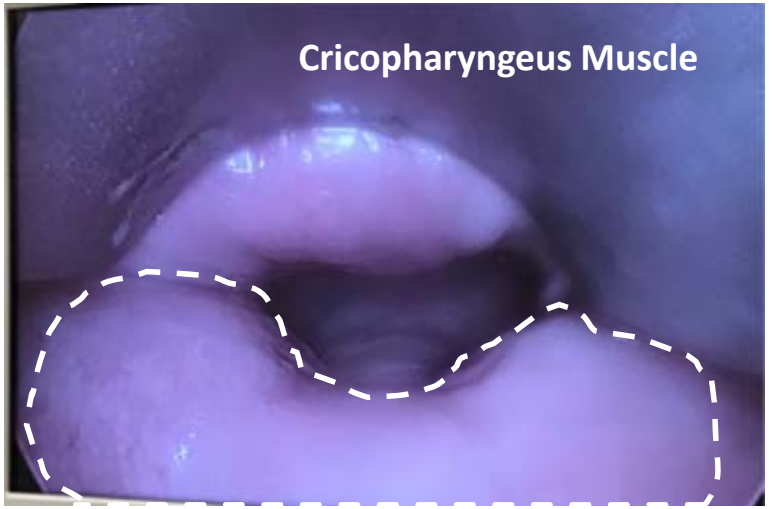


20 weeks post BB-301 Dosing



BB-301 Dose (vg)	Inhibition PABPN1*	WT-PABPN1 Expression
6e10	88 %	91 %
1e10	63 %	13 %

SAFETY STUDIES IN SHEEP: DIRECT INJECTION OF BB-301 INTO IMPACTED MUSCLES



BENITEC BIOPHARMA

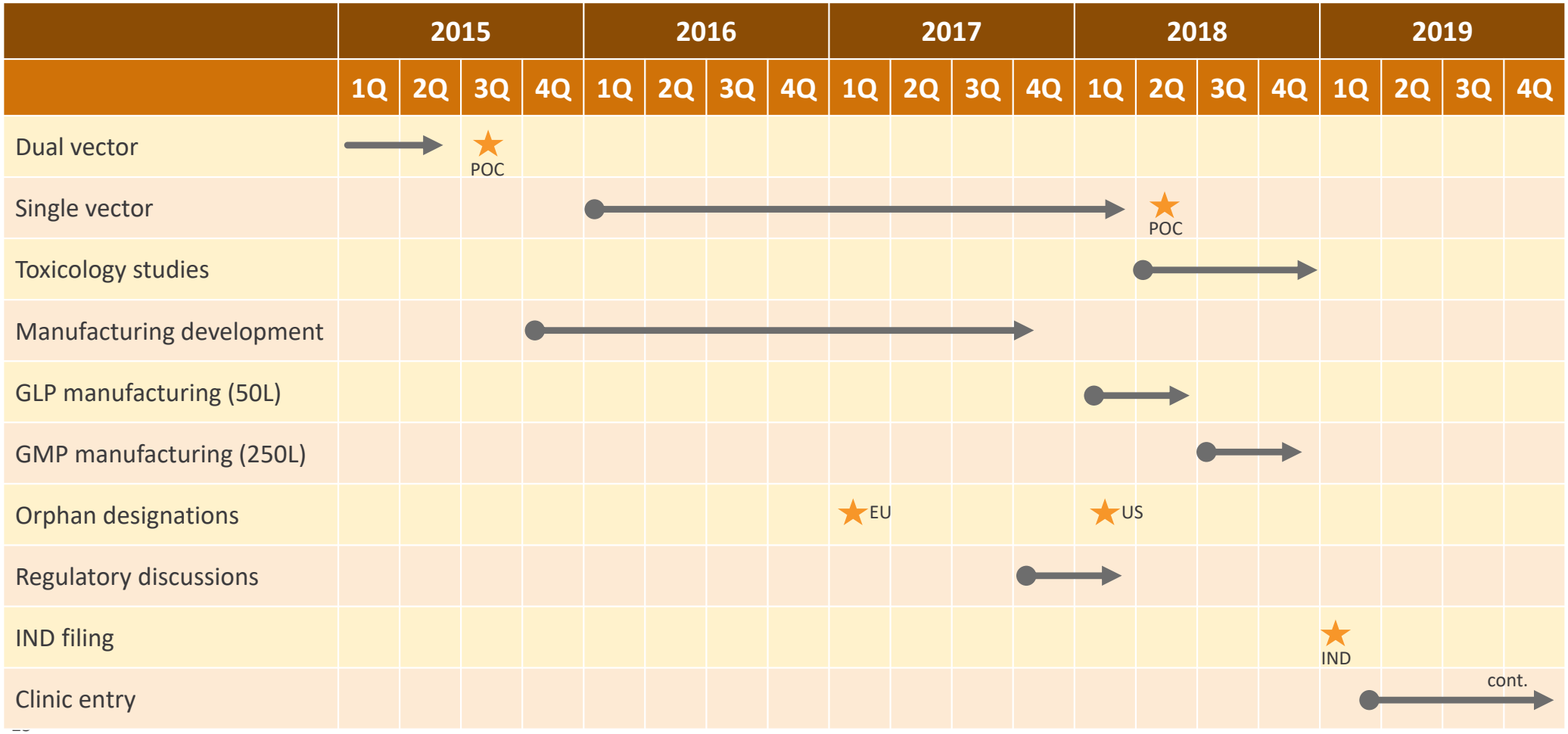
BB-301: SCALABLE MANUFACTURING

50 Liter Reactor

- Produced with scalable baculovirus based methodologies and purification processes to control cost of goods.
- Using a modified AAV capsid for the generation of highly active BB-301 particles
- Benitec has developed a product specific process for producing high titer, highly pure BB-301:
  - Yields exceed 1e14 vector genomes/liter
  - Recovery yields in final product range from 30 – 40 %
- GMP grade clinical material produced at leading Contract Manufacturing Organization
- Currently manufacturing at 50L scale
- Clinical product to be generated at 250L scale

Silver stain of SDS protein gel
showing output of purification steps
(3 capsid bands expected in final product)

BB-301 PATHWAY TO THE CLINIC



BB-301-01: PHASE 1/2A CLINICAL STUDY IN OPMD

Intramuscular BB-301 in OPMD patients with swallowing dysfunction*

Key Entry Criteria

- Aged 35 to 80
- Clinical diagnosis of OPMD
- Genetic diagnosis of OPMD
- Swallowing dysfunction
- No prior myotomy

Multicenter Dose Escalation Study

Cohort 1 – Low Dose
(~3-5 BB-301)

Cohort 2 – Medium Dose
(~3-5 BB-301)

Cohort 3 – High Dose
(~3-5 BB-301)

Maximum Effective Dose
~12 patients BB-301

Endpoints Through 52 Weeks

- Safety & tolerability
- Quantitative clinical improvement in swallowing
- Patient reported improvement in swallowing and quality of life

*Study design and parameters subject to change based on nonclinical toxicology results and clinical and regulatory feedback

BENITEC BIOPHARMA

POTENTIAL FOR EARLY ADOPTION AND HIGH MARKET PENETRATION

- BB-301 has the ability to restore muscle strength and improve symptoms of dysphagia with a single intramuscular administration
- Potential exclusivity through patents and orphan drug designations in US and EU
- Increasing diagnosis of OPMD due to aging population and increased awareness
- BB-301 life cycle opportunities
  - Expansion into earlier stages of dysphagia
  - Systemic administration to treat proximal muscle weakness and ptosis
  - Prophylaxis

BENITEC BIOPHARMA

NASDAQ: BNTC | ASX: BLT

WRAP UP

Greg West, Chief Executive Officer

PROGRAM SUMMARY

BB-401:
Oncology (HNSCC)

- EGFR antisense asset (BB-401) entered clinic in 1Q18 in P2 study in recurrent or metastatic HNSCC
- Discovery stage program using proprietary ddRNAi platform, to develop follow-on anti-EGFR strategies (BB-501)

BB-301:
Orphan disease (OPMD)

- Unique single vector 'silence and replace' mechanism
- Pre-IND meetings complete in US and EU
- IND filing planned 1Q 2019
- Commercial opportunity in excess of US$1 billion

BB-103:
Infectious disease (HBV)

- Preclinical POC with significant reduction in viral load and HbsAg when combined with SOC
- Pre-IND April 2017 informed direct path to clinic entry
- Seeking partnerships to move into the clinic

BB-201:
Retinal disease (AMD)

- Novel viral capsids for delivery to retinal cells via intravitreal injection
- Molecular analyses ongoing from PoC study in NHP – additional work required to progress BB-201 in AMD
- Possible delivery platform for other retinal diseases

BENITEC BIOPHARMA

INVESTMENT HIGHLIGHTS

Novel combination of gene therapy and gene silencing

- BB-401 (oncology) in clinic with Phase 2 study. BB-301 (OPMD) in clinic early 2019
- Validated ddRNAi technology, with human safety data
- Robust pipeline in oncology, orphan genetic disorders, retinal disease and infectious disease

Capital market access

- Listed on ASX (BLT) and NASDAQ (BNTC)
- US$50M capital raised since 2014
- US shelf registration statement filed

Strong in-house capabilities

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

BENITEC BIOPHARMA