BENITEC BIOPHARMA

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CORPORATE PRESENTATION

January 2024

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Investment Highlights

Novel Technology Platform

- Benitec's DNA-directed RNA interference (ddRNAi) platform combines gene therapy with RNA interference (RNAi) to simultaneously silence & replace disease-causing genes permanently, following a single administration
- Platform has application in diseases that cannot be treated with gene silencing or gene therapy alone

Lead Asset Entered Clinical Evaluation in Orphan Disease in November 2023

- BB-301 is being developed to treat dysphagia (inability to swallow) in subjects with Oculopharyngeal Muscular Dystrophy (OPMD). There are no therapies approved for the treatment of OPMD. The estimated prevalence in the US, Europe, Canada & Israel is 15k subjects.
- Compelling preclinical data demonstrated complete restoration of muscle function in vivo via a murine disease model
- The Investigational New Drug (IND) application for BB-301 was approved to proceed by the FDA in June 2023, and the first study subject was safely dosed in the BB-301 Phase 1b/2a clinical trial (NCT06185673) in November 2023

Significant Near-Term Milestones

- Preliminary clinical safety data and clinical efficacy data for the BB-301 Phase 1b/2a clinical trial are expected in mid-2024

Seasoned Management Team

- Benitec's management team has broad expertise in gene therapy development, biological manufacturing and capital allocation

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Experienced and Efficient Management

Jerel A. Banks, MD, PhD
CEO & Executive Chairman

- Healthcare investment professional with over 15 years of experience
- Former Vice president & co-portfolio manager at Franklin Templeton Investments
- M.D., Ph.D. Brown University; A.B. Princeton University

Megan Boston
Executive Director

- CEO & managing director of multiple ASX-listed entities
- Chartered Accountant with over 20 years of experience
- Held senior executive roles at various banking institutions in risk and compliance as well as PricewaterhouseCoopers

Claudia Kloth, PhD
SVP of Manufacturing

- Over 20 years of cGMP manufacturing & process development experience in therapeutics
- Led process development group at Lonza Viral Therapeutics
- Developed, optimized, and transferred robust viral-based products (Ad5, AAV, lentivirus) to cGMP manufacturing
- Guided process transfer & validation activities of Yervoy (BMY)

PRINCETON UNIVERSITY BROWN pwc Bristol Myers Squibb™ Lonza

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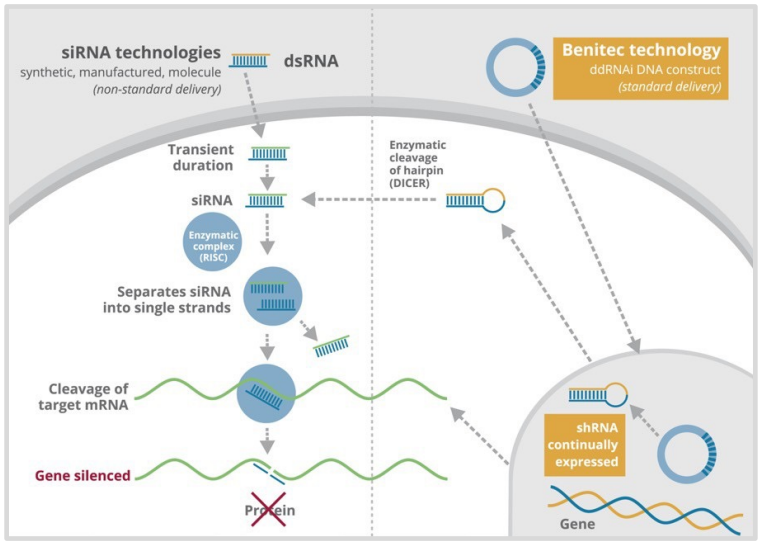
ddRNAi Platform Enables Both Permanent Silencing AND Replacement of Mutated Genes in the Target Tissue

Limitations of Current siRNA Technologies:

- Requires repeated administration
- Enables only transient silencing of mutated gene
- Silencing capacity restricted to a single gene



Advantages of the ddRNAi Platform:

- Long-term therapeutic potential from a single administration
- Constant, steady-state levels of shRNA expression enables permanent silencing of mutated gene
- Provides permanent expression of wildtype gene where activity is necessary for function or viability
- Silence a single gene or multiple genes simultaneously

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OPMD: A Progressive, Chronic Disease With No Approved Therapeutics

- Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant, chronic, myopathic disorder characterized by ptosis (drooping of the upper eyelid) and progressive dysphagia (loss of the ability to swallow) due to impairment of the muscles of the eyelids and throat.
- Typical age of onset in the 40s-50s, and affects approximately 15k adults in the US, Canada, Europe and Israel.
- Progressive dysphagia increases the risks of severe malnutrition and potentially life-threatening aspiration pneumonia.
- In OPMD, a genetic mutation results in trinucleotide repeat expansion within exon 1 of PABPN1 producing an expanded poly-alanine tract at the N-terminal end of the PABPN1 protein:

Wildtype: ATG $(GCG)_6$ ---------- $(GCA)_3$ GCG GGG GCT GCG…

OPMD Mutant: ATG $(GCG)_6$ $(GCG)_{1\text{-}7}$ $(GCA)_3$ GCG GGG GCT GCG…

Patient with OPMD

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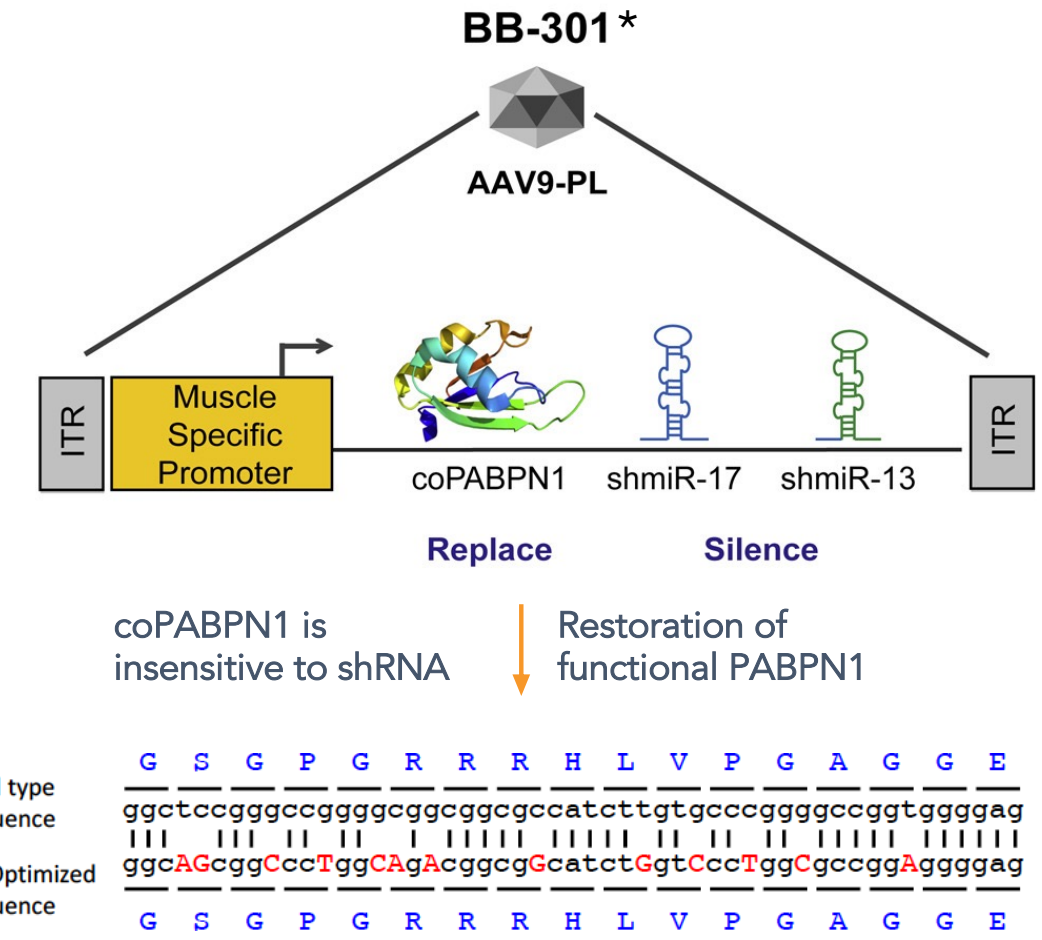
BB-301 Simultaneously Silences Mutant PABPN1 & Delivers Wildtype PABPN1 To Restore Normal Myocyte Function

PABPN1 in OPMD

- PABPN1 is a ubiquitous protein that controls the length of mRNA poly(A) tails, mRNA export from the nucleus & alternative poly(A) site usage.
- The PABPN1 mutant protein underlying OPMD is aggregation prone due to an N-terminal expanded poly-alanine tract of up to 18 contiguous alanine residues, and drives the formation of intranuclear inclusions (INIs) in the myocytes.
- INIs also sequester wildtype PABPN1 and may contribute to the "loss of function" phenotype associated with OPMD.



* Strings-Ufombah, et al., Molecular Therapy: Nucleic Acids, Vol. 24, 67-78, June 2021

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BB-301: Overview of Gene Therapy for OPMD

- BB-301 targets the genetic cause of the disease by both silencing the mutant PABPN1 gene and delivering a wildtype PABPN1 gene to restore production of functional protein with a single intramuscular administration.
- Orphan drug designation has been granted for BB-301 in both the US and EU.
- The IND application for BB-301 was approved to proceed by the FDA in June 2023, and the first study subject was safely dosed in the BB-301 Phase 1b/2a clinical trial (NCT06185673) in November 2023.
- The BB-301 Phase 1b/2a clinical trial is designed to enroll up to 30 subjects.
- Benitec retains global rights to BB-301, with prevalence estimates and established global reimbursement paradigms for orphan and gene therapies supporting a multi-billion dollar commercial opportunity over the life of the product.
- Benitec's Intellectual Property portfolio includes both indication-specific and technology-focused patents.

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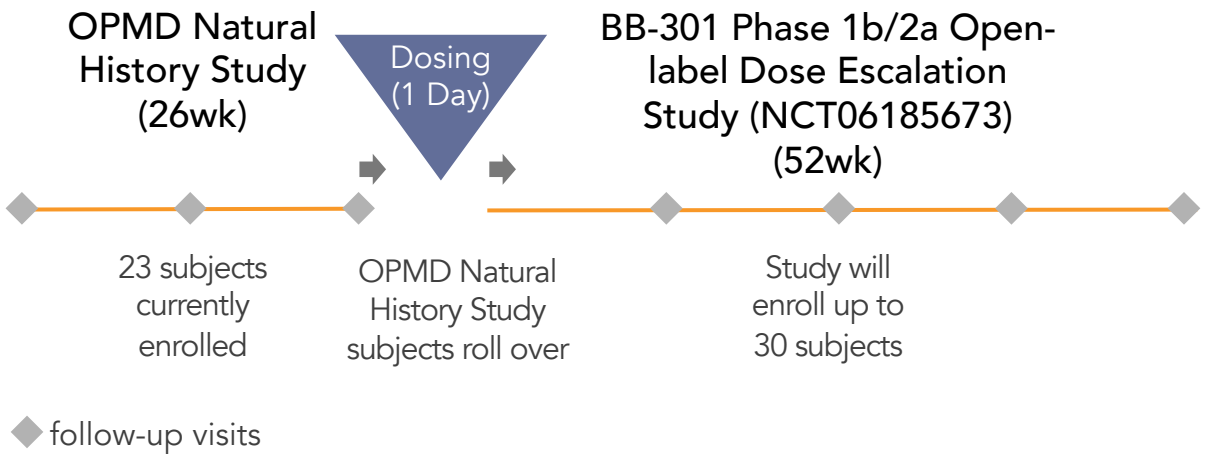
BB-301 Clinical Development Program in OPMD

Characterization of OPMD subject disposition at baseline assessing:

- Rates of progression of dysphagia via quantitative radiographic measures of global swallowing function and target pharyngeal constrictor muscle function (including Videofluoroscopic Swallowing Studies (VFSS))
- 23 subjects enrolled as of January 2024



- Every 90 days, subjects are assessed for key safety and efficacy endpoints
- First subject entered the Phase 1b/2a Clinical Trial (NCT06185673) in 4Q23

Endpoints

- **Primary:** Safety and tolerability
- **Secondary:** Radiographic measures of global swallowing function and pharyngeal constrictor muscle function compared to analogous assessments conducted in the OPMD Natural History Study

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Outcome Measures for the OPMD Natural History Study and the BB-301 Phase 1b/2a Clinical Study (NCT06185673)

Videofluoroscopic Swallowing Study Assessments

Global Swallowing Function

Dynamic Imaging Grade of Swallowing Toxicity Scale

Pharyngeal Constrictor Muscle Function

- Pharyngeal Area at Maximum Constriction
- Pharyngeal Constriction Ratio

Swallowing Efficiency

- Total Pharyngeal Residue
- Vallecular Residue
- Pyriform Sinus Residue
- Other Pharyngeal Residue
- Normalized Residue Ratio Scale

Clinical Assessments

Other Assessments

- Clinical measures of swallowing capacity & dysphagia (including timed-based and volume-based drinking tests)
- Patient-reported measures of dysphagia

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Key Preclinical & IND-Enabling Studies

BB-301 Silenced and Replaced PABPN1 Over a Broad Range of Doses in the A17 Mouse Model of OPMD

Varying levels of inhibition of PABPN1 expression, when coupled with partial replacement of wildtype PABPN1, significantly:

- Reduced INIs
- Increased muscle force generation
- Corrected disease phenotype

	"Silence"	"Replace"
BB-301 Dose (vg)	Inhibition of PABPN1	coPABPN1 Expression
7.50×10^{11}	86%	63%
2.50×10^{11}	75%	26%
5.00×10^{10}	31%	2%
1.00×10^{10}	32%	1%
2.00×10^{9}	14%	0%
4.00×10^{8}	0%	0%

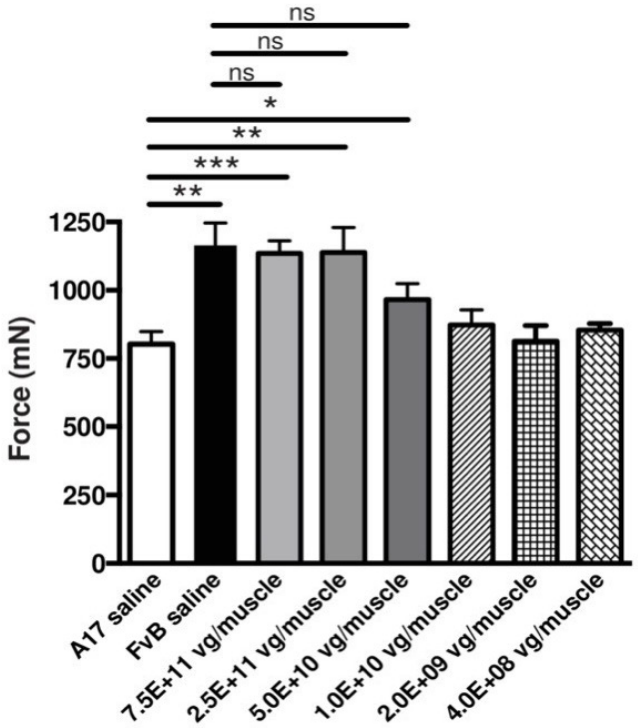
PABPN1 inhibition levels of ≥31% led to complete resolution of OPMD disease symptoms and correction of histological hallmarks

Data from Strings-Ufombah, et al., Molecular Therapy: Nucleic Acids, Vol. 24, 67-78, June 2021
VG = Viral Genomes

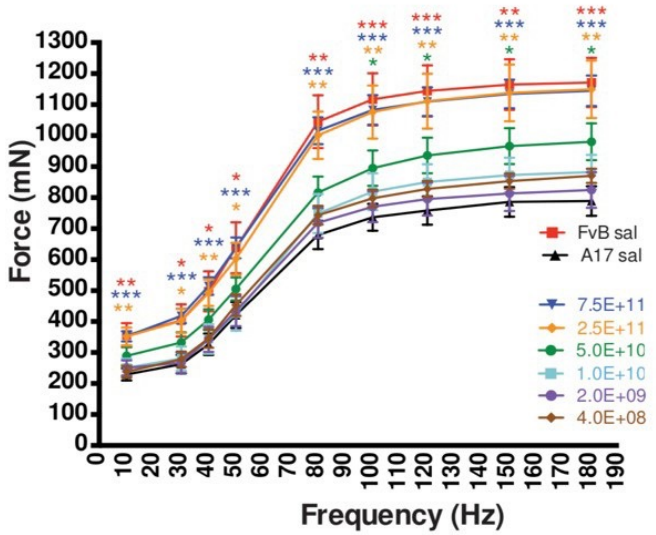
BB-301 Restored Muscle Strength to Wildtype Levels in A17 Model

At 14-weeks post intramuscular administration of BB-301, statistically significant improvements in muscle strength and complete phenotypic correction were achieved at doses ≥ 5.00 x 10^{10} vg

Muscle Response (150 Hz)



Muscle Response (10-190 Hz)



Data from Strings-Ufombah, et al., Molecular Therapy: Nucleic Acids, Vol. 24, 67-78, June 2021

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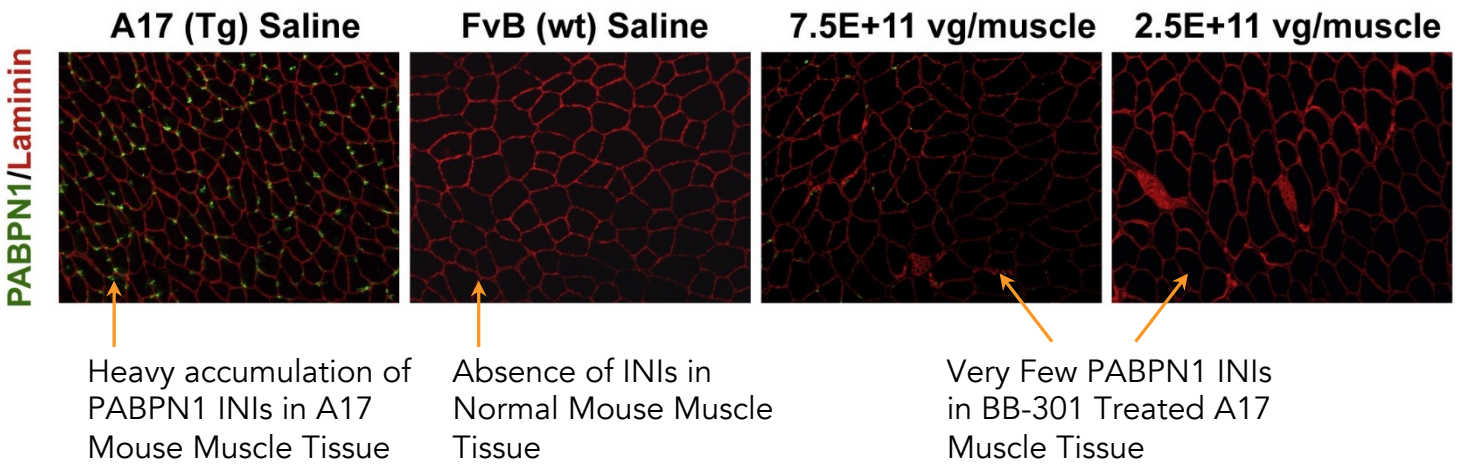
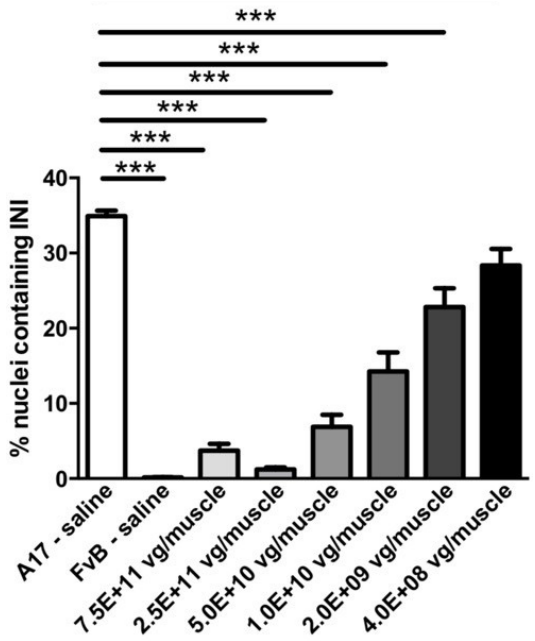
Dose-Dependent Resolution of INIs in Injected Muscles of A17 Mouse Model of OPMD

Immunofluorescence Staining of INIs in Mouse Muscle Tissue



Quantitative Analysis of INIs in Mouse Muscle Tissue



At higher doses, BB-301 eliminated nearly all PABPN1 INIs in A17 Mouse Muscle Tissue 14 weeks after intramuscular administration

Data from Strings-Ufombah, et al., Molecular Therapy: Nucleic Acids, Vol. 24, 67-78, June 2021

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IND-Enabling Studies for BB-301

Pilot Dosing Study in Beagle Dogs

- 8-week study to confirm the transduction efficiency of BB-301 following direct intramuscular injection into the pharyngeal muscles via the use of an open surgical approach.
- The pharyngeal muscles injected with BB-301 in Beagle dogs (Hypopharyngeal muscles and Thyropharyngeal muscles) correspond to the dosing targets for human OPMD subjects (Middle Pharyngeal Constrictor muscles and Inferior Pharyngeal Constrictor muscles)

Toxicology Study in Beagle Dogs

12-week GLP Toxicology and Biodistribution study in Beagle dogs

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Dose-Dependent BB-301 Tissue Transduction Observed 8 Weeks Following Direct Intramuscular Injection in Beagle Dogs

	Copies of BB-301 (average copies per cell)	
BB-301 Dose (vg/mL)	Hypopharyngeal Muscle	Thyropharyngeal Muscle
3.00×10^{13} vg/ml *High Volume*	5.12	5.66
3.00×10^{13} vg/ml *Low Volume*	3.15	2.70
1.00×10^{13} vg/ml	1.52	2.06

Biologically significant, dose-dependent delivery of the multi-functional genetic construct was achieved in the target pharyngeal muscles of Beagle dogs

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Dose-Dependent Expression of coPABPN1 Observed 8 Weeks Following Direct Intramuscular Injection of BB-301 in Beagle Dogs

	Copies of coPABPN1 (average copies per cell)	
BB-301 Dose (vg/mL)	Hypopharyngeal Muscle	Thyropharyngeal Muscle
3.00×10^{13} vg/ml *High Volume*	61.69	77.26
3.00×10^{13} vg/ml *Low Volume*	27.43	62.89
1.00×10^{13} vg/ml	17.54	30.84

Dose-dependent expression of the replacement wildtype PABPN1 genetic construct was achieved in the target pharyngeal muscle cells of Beagle dogs

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Dose-Dependent Expression of siRNA13, siRNA17 Observed 8 Weeks Following Direct Intramuscular Injection of BB-301 in Beagle Dogs

	siRNA13		siRNA17	
	Hypopharyngeal Muscle	Thyropharyngeal Muscle	Hypopharyngeal Muscle	Thyropharyngeal Muscle
BB-301 Dose (vg/mL)	average copies per cell	average copies per cell	average copies per cell	average copies per cell
3.00×10^{13} vg/ml *High Volume*	340,613	518,329	64,393	112,783
3.00×10^{13} vg/ml *Low Volume*	221,663	303,516	41,787	59,723
1.00×10^{13} vg/ml	83,168	136,812	17,321	30,253

Dose-dependent expression of the silencing moieties of the multi-functional genetic construct was achieved in the target pharyngeal muscle cells of Beagle dogs

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Dose-Dependent Inhibition of PABPN1 Observed 8 Weeks Following Direct Intramuscular Injection of BB-301 in Beagle Dogs

	Average Reported % Inhibition of wtPABPN1	
BB-301 Dose (vg/mL)	Hypopharyngeal Muscle	Thyropharyngeal Muscle
3.00×10^{13} vg/ml *High Volume*	83%	82%
3.00×10^{13} vg/ml *Low Volume*	74%	64%
1.00×10^{13} vg/ml	60%	69%

8 weeks following administration of BB-301, an average wtPABPN1 inhibition level of 72% was achieved in the target pharyngeal muscle cells of Beagle dogs

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Broad Intellectual Property Portfolio

OPMD-Related Intellectual Property

- OPMD Family 1 anticipated expiry of April 2037
- OPMD Family 2 anticipated expiry of December 2037
- OPMD Family 3 anticipated expiry of October 2039
- OPMD Family 4 anticipated expiry of February 2040

AAV-Related Intellectual Property

AAV Family 1 anticipated expiry of August 2038

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Financial Summary

NasdaqCM Listed: BNTC	Exclusively Nasdaq listed; re-domiciled in April 2020
Shares Outstanding	2,592,434 as of January 3, 2024
Cash & Equivalents	$25.9 million as of September 30, 2023

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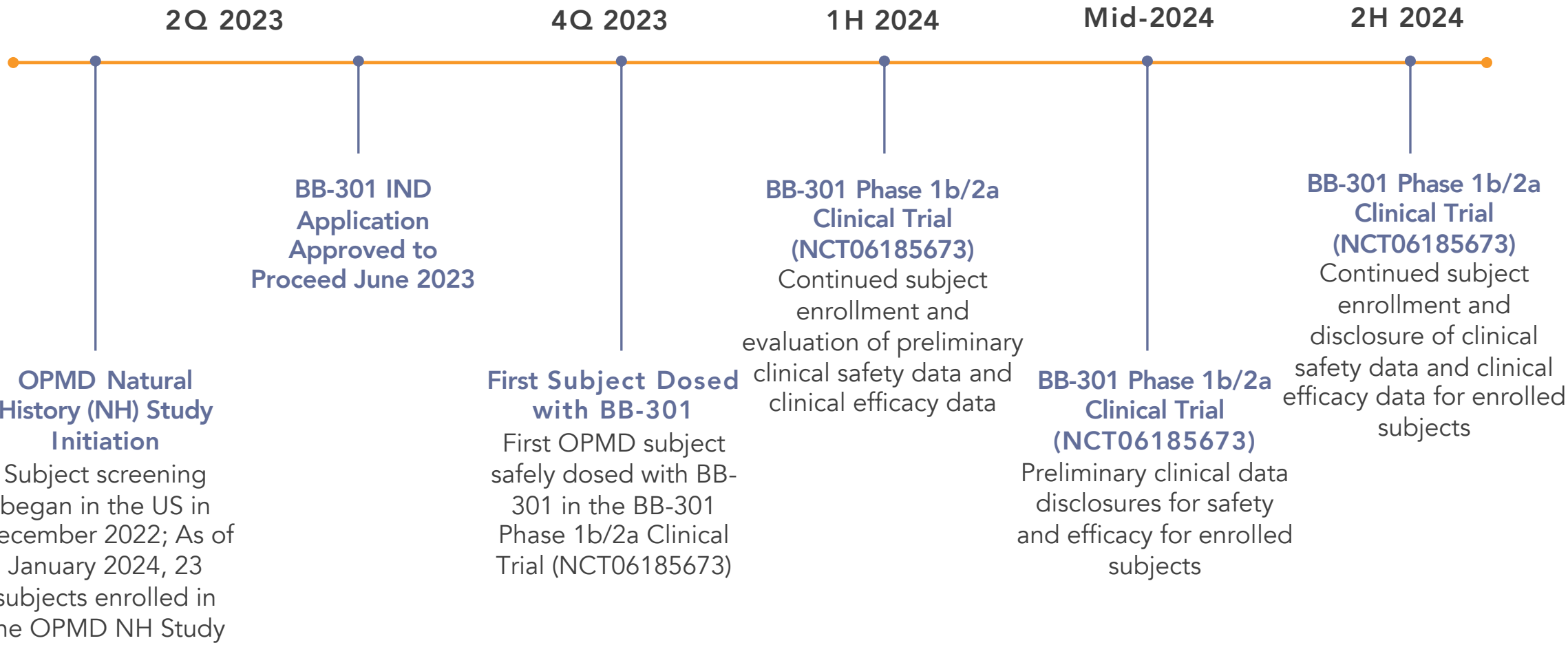
Clinical and Regulatory Milestones



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