Interim Clinical Data Summary: A Phase 1b/2a Open-label, Dose Escalation Study to Evaluate the Safety and Clinical Activity of Intramuscular Doses of an AAV9-based gene therapy (BB-301) Administered to Subjects with Oculopharyngeal Muscular Dystrophy (OPMD) with Dysphagia

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October 12, 2024

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Except for the historical information set forth herein, the matters set forth in this presentation include forward-looking statements, including statements regarding Benitec's plans to develop and commercialize its product candidates, the timing of the completion of pre-clinical and clinical trials, the timing of the availability of data from our clinical trials, the timing and sufficiency of patient enrollment and dosing in clinical trials, the timing of expected regulatory filings, and the clinical utility and potential attributes and benefits of ddRNAi and Benitec's product candidates, and other forward-looking statements.

These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: the success of our plans to develop and potentially commercialize our product candidates; the timing of the completion of preclinical studies and clinical trials; the timing and sufficiency of patient enrollment and dosing in any future clinical trials; the timing of the availability of data from our clinical trials; the timing and outcome of regulatory filings and approvals; the development of novel AAV vectors; our potential future out-licenses and collaborations; the plans of licensees of our technology; the clinical utility and potential attributes and benefits of ddRNAi and our product candidates, including the potential duration of treatment effects and the potential for a "one shot" cure; our intellectual property position and the duration of our patent portfolio; expenses, ongoing losses, future revenue, capital needs and needs for additional financing, and our ability to access additional financing given market conditions and other factors, including our capital structure; the length of time over which we expect our cash and cash equivalents to be sufficient to execute on our business plan; unanticipated delays; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; determinations made by the FDA and other governmental authorities and other regulatory developments; the Company's ability to protect and enforce its patents and other intellectual property rights; the Company's dependence on its relationships with its collaboration partners and other third parties; the efficacy or safety of the Company's products and the products of the Company's collaboration partners; the acceptance of the Company's products and the products of the Company's collaboration partners in the marketplace; market competition; sales, marketing, manufacturing and distribution requirements; greater than expected expenses; expenses relating to litigation or strategic activities; the impact of, and our ability to remediate, the identified material weakness in our internal controls over financial reporting; the impact of local, regional, and national and international economic conditions and events; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission. The Company disclaims any intent or obligation to update these forward-looking statements.

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03 Pathophysiology of Dysphagia in OPMD

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06 Q&A Session with Professor Emily Plowman, PhD, CCC-SLP, FASHA

Professional Biography:

Emily Plowman, PhD, CCC-SLP, FASHA

Professor, Department of Otolaryngology - Head and Neck Surgery, The Ohio State University College of Medicine

Emily Plowman, PhD, CCC-SLP, FASHA, Professor, Department of Otolaryngology – Head and Neck Surgery, The Ohio State University College of Medicine is Director of the Aerodigestive Research Core across its two sites at the Ohio State University and University of Florida and Director of the Wexner Medical Center Dysphagia Program. She is an internationally recognized expert in the field of dysphagia who has held uninterrupted funding from the National Institutes of Health (NIH) since commencing her academic career in 2009. Her current research at OSU and UF are supported by the National Institute of Aging, National Institute of Nursing Research, National Institute of Cancer, Department of Defense, and the ALS Association. Dr. Plowman has authored over 85 peer-reviewed scientific manuscripts, given over 600 lectures worldwide, and obtained over 30 external research grants. In addition to her own research, Dr. Plowman is passionate about mentoring the future generation of clinician scientists and her mentorship efforts were recently recognized by the National Institutes of Health with the NINDS Story Landis Award for Outstanding Mentorship by a Neuroscientist (2022) and the University of Florida Doctoral Mentor of the Year award (2021). She was inducted into the American Speech and Hearing Association as a Fellow in 2022 and was elected to be the incoming President of the international Dysphagia Research Society for 2026.

Disclosures: Clinical advisor and consultant to Benitec Biopharma Inc

Key Data Findings

- Two subjects have received the lowest-dose of BB-301 (1.2e13 vg/subject), and there were no Significant Adverse Events.

- Dysphagic symptoms at baseline for Subject 1 (7-years post diagnosis) were more severe than those of Subject 2 (6-years post diagnosis) as assessed by pre-dose SSQ and TPR results, but both Subjects experienced significant levels of clinical benefit per the post-dose SSQ scores and TPR results.

- The SSQ Total Scores and SSQ Sub-Scores correlate strongly with the VFSS TPR results.

- Subject 1 experienced clinically meaningful improvement in post-dose Sydney Swallow Questionnaire Score at Day 270 driven by corresponding reductions in Total Pharyngeal Residue values.

- Subject 2 experienced clinically meaningful improvement in post-dose Sydney Swallow Questionnaire Score at Day 180, with a score representative of a normal swallowing profile, driven by a corresponding reduction in the frequency of pathologic low-volume sequential swallows.

- These data represent the first reported successful improvements in swallow function using a novel gene therapy for OPMD.

Oculopharyngeal Muscular Dystrophy: Clinical and Pathophysiological Overview

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OPMD: A Chronic, Progressive Disease With No Approved Therapeutics

- Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant, chronic, myopathic disorder with a typical age of onset in the 40s-50s
- OPMD results from a trinucleotide repeat expansion within exon 1 of the polyadenylate binding protein nuclear 1 (PABPN1) gene

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

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

- OPMD has been diagnosed in at least 33 countries, and currently impacts an estimated 15,000 patients in North America Europe, and Israel
  - Large patient cohorts exist globally as verified by the literature and specific patient/population databases (e.g., the University of New Mexico Patient Data-Base comprises several hundred subjects)

Country/Province/Region	Estimated Population	OPMD Prevalence Estimate	Estimated OPMD Patient Population
United States	333,000,000	0.00001	**3,330**
Quebec	8,500,000	0.001	**8,500**
Europe	742,000,000	0.00001	**7,420**

OPMD: Clinical Presentation

- OPMD typically presents with:
  - Ptosis (eyelid drooping) which can be asymmetric at onset
  - Choking during meals (dysphagia), leading to prolonged mealtimes and avoidance of specific food
- A retrospective chart review was conducted at the Saguenay Neuromuscular Clinic (Quebec, Canada) to screen for and characterize their OPMD population
  - Dysphagia was present in 96.6% of subjects
  - Pharyngeal pooling of thickened secretions was present in 74.1% of subjects
- Dysphagia worsens over time and, as a result, patients can develop malnutrition and aspiration pneumonia which can lead to death

TABLE 1 Population characteristics (n = 333)

Characteristics	n (%)
Sex	
Male	166 (49.8)
Female	167 (50.2)
Transmission (n = 321)	
Paternal	167 (52.0)
Maternal	154 (48.0)
PABN1 test source	
Patient	254 (76.3)
Family member	80 (23.7)
First degree	56 (16.8)
Second degree	16 (4.8)
Third degree	5 (1.5)
Fourth degree	3 (0.9)
Ptosis (n = 332)	
Present	321 (96.7)
Absent	11 (3.3)
Dysphagia (n = 329)	
Present	318 (96.6)
Absent	11 (3.4)
Lower limb proximal weakness (n = 331)	
Present	287 (86.7)
Absent	44 (13.3)
Fatigue (n = 250)	
Present	220 (88.0)
Absent	30 (12.0)
Dysphonia	
Present	168 (50.5)
Absent	165 (49.5)
Pharyngeal pooling of thickened secretions (n = 220)	
Present	163 (74.1)
Absent	57 (25.9)

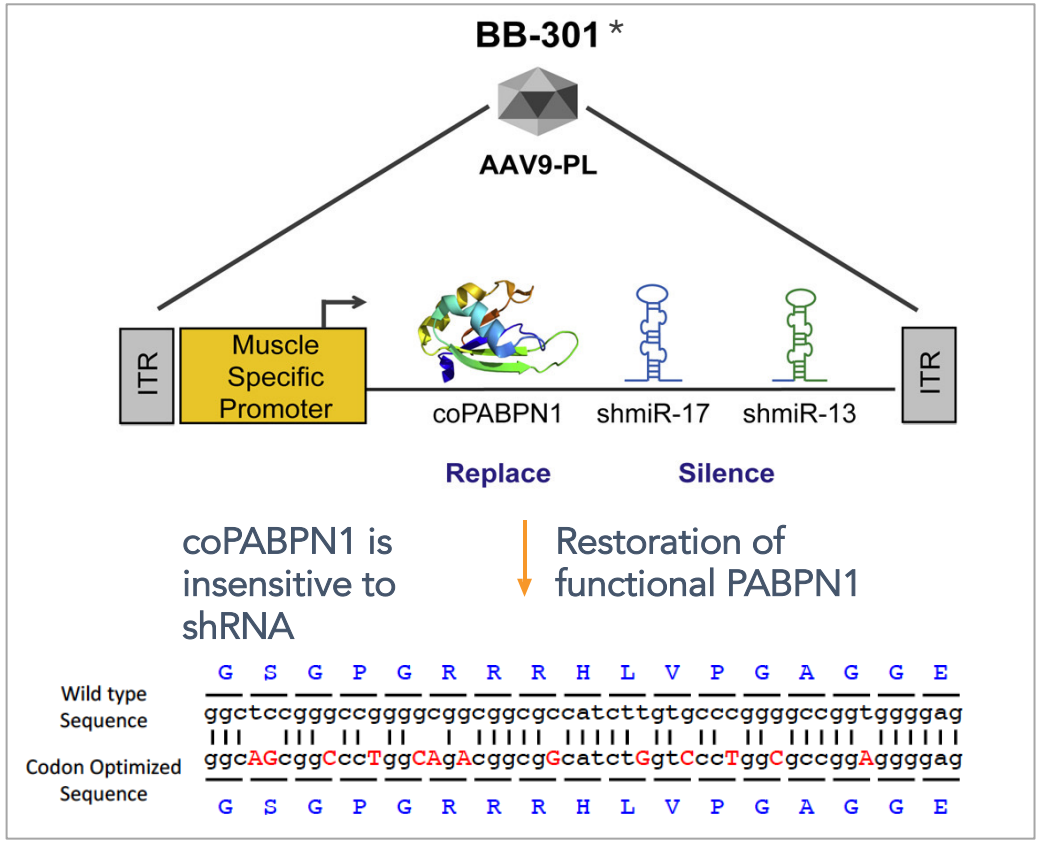
Brisson, JD, Muscle & Nerve, 2020

Current Clinical Management Strategies for Dysphagia Do Not Prevent Disease Progression

- Nutritional recommendations including dietary texture/consistency modifications
- Surgical Interventions for moderate to severe dysphagia have temporary effects and may require repeated administration/application:
  - Cricopharyngeal muscle paralysis with botulinum toxin injection
  - Cricopharyngeal muscle dilation
  - Cricopharyngeal myotomy
- In all cases, the pharyngeal constrictor muscles continue to atrophy, leading to progressive loss of pharyngeal propulsion/clearance of food and liquid into the esophagus

BB-301 Inhibits the Production of the key Disease-Causing Protein in OPMD and Delivers a New, Fully-Functional Version of the Protein

- BB-301 is a gene therapy designed by Benitec Biopharma Inc. to accomplish two goals:
  - Reduce the production of the mutant form of the PABPN1 protein in the muscles of the pharynx
  - Deliver a new, functional gene to the muscles of the pharynx that will drive production of the wildtype form of the PABPN1 protein
- In preclinical proof-of-concept studies carried out in the A17 mouse model, direct intramuscular injection of BB-301 facilitated:
  - Increases in muscle cross-sectional area
  - Increases in muscle mass
  - Increases in muscle force generating capacity
  - Clearance of intranuclear inclusions within the muscle cells



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

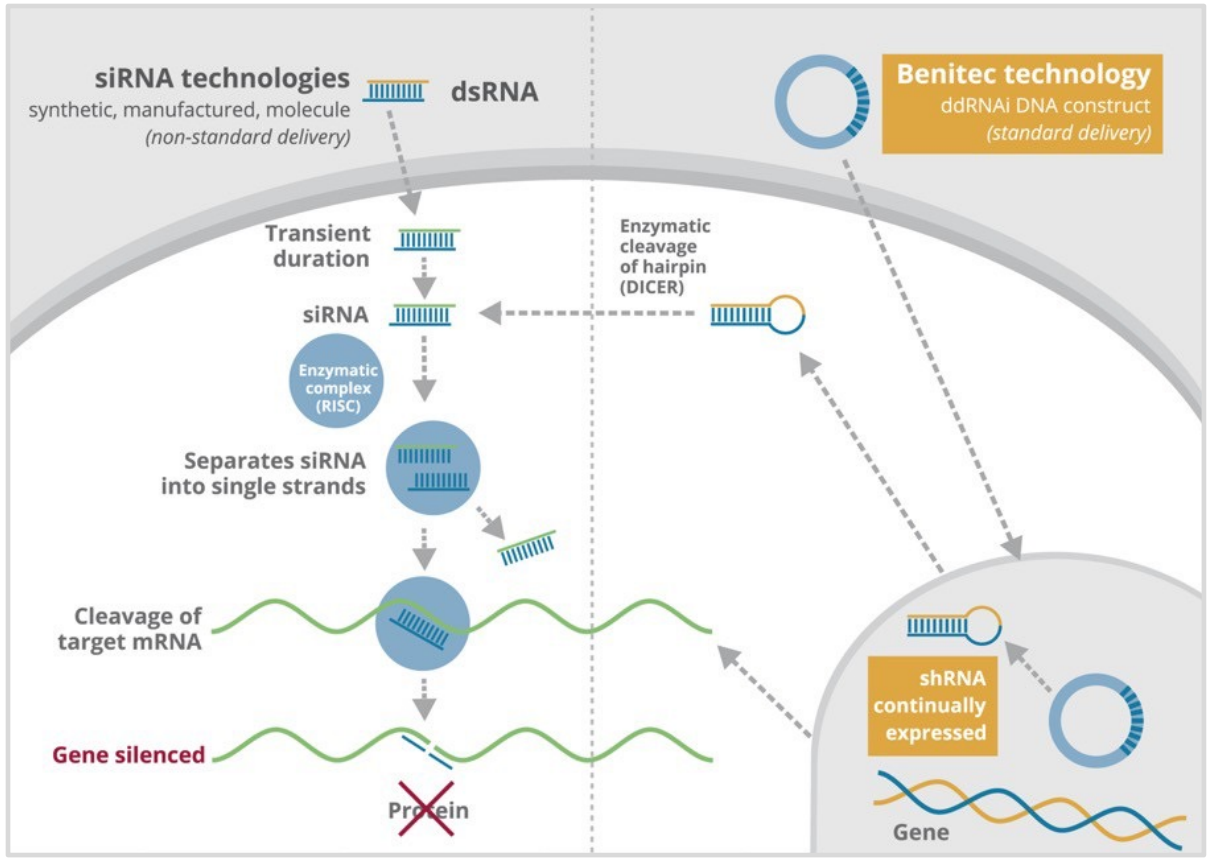
ddRNAi Platform Enables Both Permanent Silencing AND Replacement of Mutated Genes in the Target Tissue

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

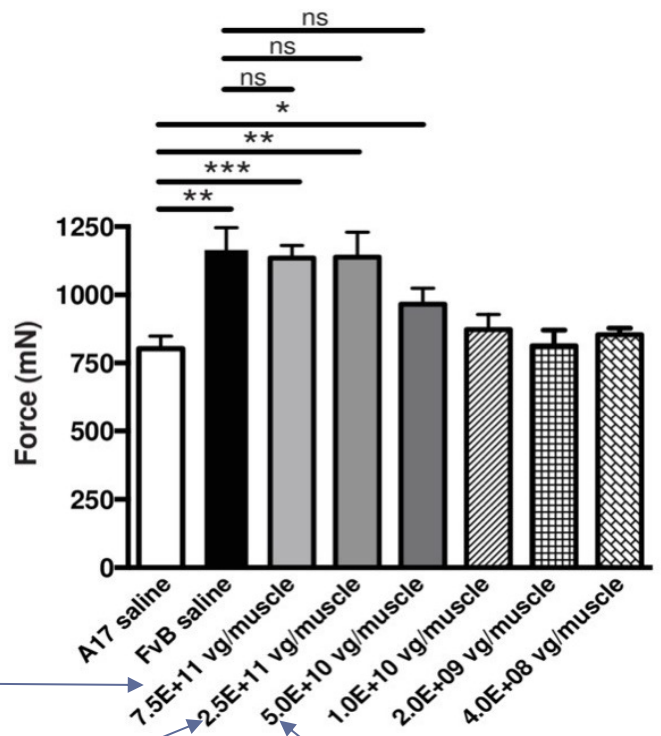


BB-301 Demonstrated Robust Molecular Activity and Complete Restoration of Muscle Strength in the OPMD A17 Mouse Model

- Improvements in Muscle Strength in A17 mice were observed at the Lowest Gene Replacement Level
- The lowest effective dose tested in the A17 mouse model is currently being evaluated in the BB-301 Phase 1b Study

Muscle Response (150 Hz)

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



BB-301 Dose (vg)		"Silence" Inhibition of PABPN1	"Replace" coPABPN1 Expression
7.50 x 10^{11}	Phase 1b Cohort 3 Analog	86%	63%
2.50 x 10^{11}	Phase 1b Cohort 2 Analog	75%	26%
5.00 x 10^{10}	Phase 1b Cohort 1 Analog	31%	2%
1.00 x 10^{10}		32%	1%
2.00 x 10^{9}		14%	0%
4.00 x 10^{8}		0%	0%

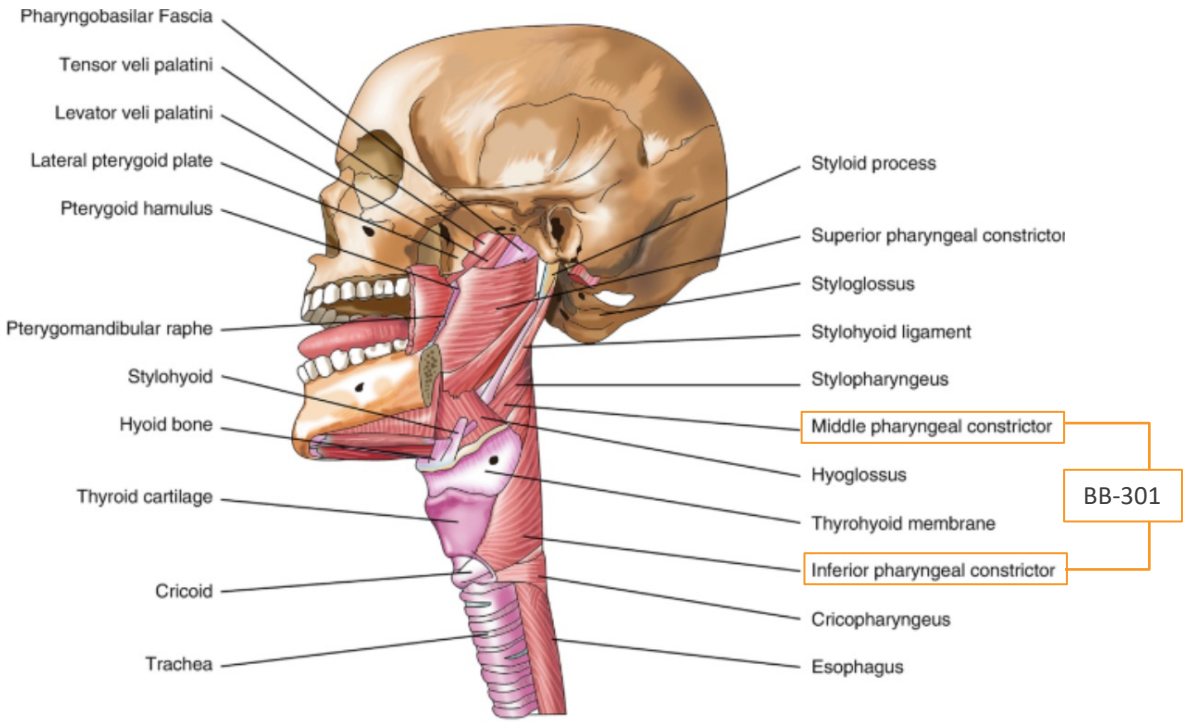
Data from Strings-Ufombah, et al., Molecular Therapy: Nucleic Acids, Vol. 24, 67-78, June 2021

Swallowing Overview and The Rationale for BB-301 in OPMD

OPMD Drives Disordered Swallowing

- In OPMD, the pharyngeal constrictor muscles are weakened and atrophic and unable to support the propulsion of food or liquid towards the esophagus
- In the current clinical study, BB-301 is delivered to the pharyngeal constrictor muscles via direct intramuscular injection in the operating room
- Potential BB-301-derived increases in muscle cross-sectional area, muscle mass, and muscle force should generate excess capacity in the pharyngeal constrictor muscles of OPMD patients to enhance the functional capacity of the muscles, thereby reducing dysphagia

Anatomical Structures of the Pharynx and BB-301 Injection Sites



Muscles Of Pharyngx: Lateral view

Pathophysiology of Dysphagia in OPMD

Distinct Drivers of Dysphagia Noted in the OPMD Study Population

- OPMD subjects enrolled into the OPMD Natural History Study and the BB-301 Phase 1b/2a Clinical Study have been shown to be impacted by excessive accumulation of pharyngeal residue post-swallow

- OPMD subjects enrolled into the OPMD Natural History Study and the BB-301 Phase 1b/2a Clinical Study have also been shown to be impacted by increased frequency of pathologic low-volume sequential swallows (i.e., rapid contractions of the pharyngeal muscles during the consumption of low volumes of thin liquids)

Impaired Pharyngeal Clearance Leads to Aspiration, Aspiration Pneumonia, and Death

Approximately one third of subjects had respiratory diagnoses listed as the cause of death:

- Impaired swallowing (dysphagia) can lead to aspiration pneumonia
- Pneumonia can result from the aspiration of food and/or liquid
- Pneumonia can also result from the aspiration of thickened pharyngeal secretions

	n (%)
Diseases of the respiratory system	34 (31.5%)
Aspiration pneumonia	18 (16.7%)
Influenza or pneumonia of unspecified etiology	12 (11.1%)
Other respiratory disease	3 (2.8%)
Chronic lower respiratory disease	1 (0.9%)
Neoplasms	19 (17.6%)
Diseases of the circulatory system	9 (8.3%)
Heart failure	5 (4.6%)
Cardiac problem	3 (2.8%)
Cerebrovascular disease	1 (0.9%)
Others	9 (8.3%)
Hip fracture complications	3 (2.8%)
OPMD not otherwise specified	2 (1.9%)
Malnutrition	1 (0.9%)
Suicide	1 (0.9%)
Hepatic cirrhosis	1 (0.9%)
Urinary tract infection	1 (0.9%)
Unknown	37 (34.3%)
Total	108 (100%)

Brisson, JD, Muscle & Nerve, 2020

Sequential Swallowing is a Normal Physiologic Process Observed in Healthy Subjects During the Consumption of Large Volumes of Thin Liquid (e.g., ≥90 mL of Water)

- Sequential swallowing is defined as the completion of two or more consecutive swallows in rapid succession where the hyolaryngeal complex (HLC) does not return to rest and the pharynx lacks complete patency between swallows[1]
- Under normal physiologic conditions, sequential swallowing occurs during continuous drinking of large volumes (90 mL or greater) of thin liquids via straw, cup, or bottle (for reference, one can of a soft drink has a volume of approximately 355 mL of thin liquid)
  - 90 mL of Thin Liquid administered by cup[1]
  - 300 mL of Thin Liquid administered by straw in 10-second tasks[2]
  - 150 mL of Thin Liquid administered by cup and soda bottle[3]
- Distinct from the pharyngeal swallowing patterns observed for large volumes of thin liquids (i.e., 90 mL or greater), low-volume thin liquids (approximately 15 mL or less) progress through the pharynx via discrete swallows characterized by coordinated, peristaltic, sequential contractions and relaxations of the pharyngeal muscles moving from the cranial to the caudal direction towards the UES
  - At the conclusion of each discrete swallow of low-volume thin liquid, the pharyngeal muscles relax completely, and following the closure of the UES, the HLC returns to rest, and pharyngeal patency is restored prior to the initiation of the subsequent wave of peristaltic pharyngeal muscle contractions

[1]Ambrocio, K. R., et al., Dysphagia (2023) 38:1497–1510; [2]Daniels, S.K., Journal of Speech, Language, and Hearing Research, Vol. 47, 33–45, February 2004; [3]Chi-Fishman, G. and Sonies, B., Journal of Speech, Language, and Hearing Research, Vol. 43, 1481–1492, December 2000

During VFSS Assessments, Pathologic Sequential Swallowing was Detected for OPMD Subjects During the Consumption of Low Volumes of Thin Liquids (i.e., <15 mL of Thin Liquid)

- For the BB-301 Phase 1b/2a Study, the achievement of physiologic pharyngeal muscle relaxation during the swallowing of low-volume thin liquid is verified on VFSS by the identification of the the "Swallow Rest Frame"
    - Swallow rest is the terminal event of each discrete swallow, identified as the first VFSS frame showing the pyriform sinuses at their lowest position, relative to the spine, prior to any hyoid burst or laryngeal elevation for a subsequent subswallow[1]
- In diseases for which dysphagia is a core symptom (e.g., OPMD), during the consumption of low volumes of thin liquids (e.g., thin liquid swallowing tasks of less than 15 mL employed in the BB-301 Phase 1b/2a Study), physiologic pharyngeal muscle relaxation is not always achieved, and a subject instead experiences pathologic sequential swallows when consuming low volumes of thin liquids
- Pathologic low-volume sequential swallows are experienced by the subject as multiple swallows and are detected during VFSS as a series of rapid contractions of the pharyngeal muscles interrupting the discrete peristaltic contraction pattern typically observed during swallows of low-volume thin liquids

[1]Steele, C., et al., Journal of Speech, Language, and Hearing Research, Vol. 62, 1338–1363, May 2019

BB-301 Clinical Development Program

BB-301 Clinical Development Program (Estimated Timeline for Cohort 1)

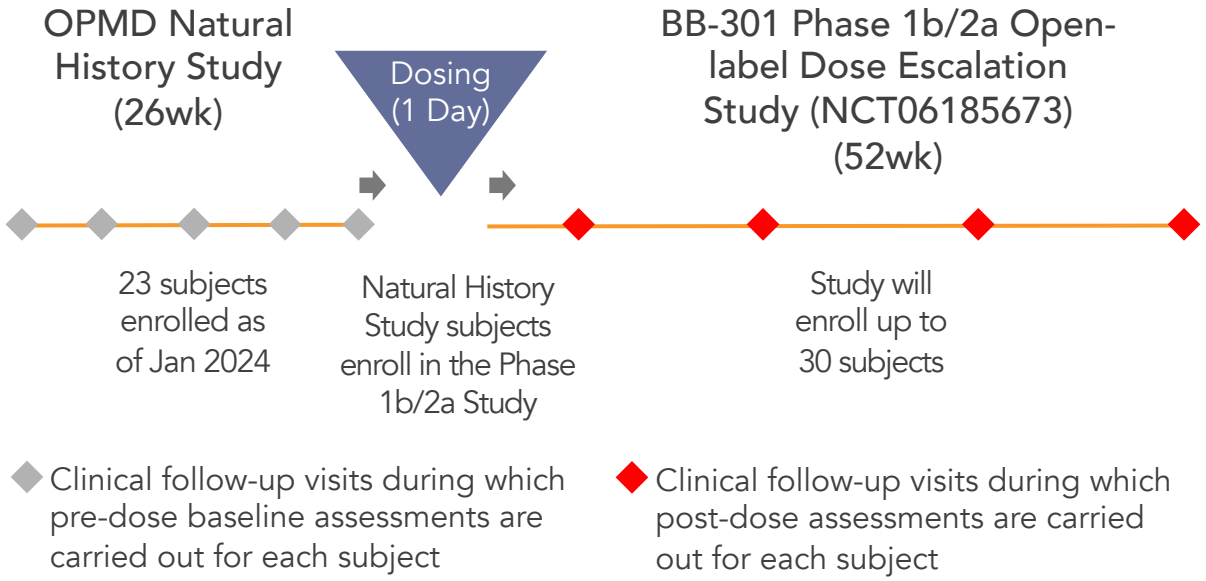
Subject	(2024) October	(2024) November	(2024) December	(2025) January	(2025) February	(2025) March	(2025) April
1 (Treated 4Q2023)							
2 (Treated 1Q2024)							
3	Projected Dosing						
4			Projected Dosing				
5					Projected Dosing		
6							Projected Dosing

- First subject entered the Phase 1b/2a Clinical Trial in 4Q23, and the second subject was enrolled in 1Q24
- Subsequent subjects in Cohort 1 may be treated as projected above, pending confirmation of site and subject availability
- Treatment of subjects in Cohort 2 is anticipated to begin in June 2025
- Efficacy endpoints are defined statistically as the change from Baseline at Day 90, Day 180, Day 270, and Day 360

BB-301 Clinical Development Program and Key Assessments

Characterization of patient disposition at baseline:

- Degree of, and rates of, progression of dysphagia are assessed using the Sydney Swallow Questionnaire (SSQ) and Videofluoroscopic Swallowing Studies (VFSS) over a 6-to-12 month period
- 23 subjects enrolled as of January 2024



Endpoints

- **Primary:**
  Safety and tolerability*
- **Secondary:**
  SSQ
  VFSS
- 2 subjects enrolled as of February 2024

*Incidence of DLTs in phase 1b, and Incidence of AEs according to NCI CTCAE v5.0
(The clinical and analytical methods employed exclusively for the assessment of Subject safety in studies BNTC-OPMD-NH-001 and BNTC-OPMD-BB-301-01 represent globally-established standards of care for human subjects (e.g., clinical chemistries, hematologic assessments, thyroid function testing, and urinalysis)).

Key Subject-Reported and Videofluoroscopic Endpoints

The key secondary endpoints of the OPMD Natural History Study and the BB-301 Phase 1b/2a Clinical Study (NCT06185673) facilitate serial characterization of:

- Subject-Reported Oral-Pharyngeal Dysphagia (via the use of a validated 17-item patient reported outcome instrument, SSQ)
- Swallowing Efficiency (by assessment of Total Pharyngeal Residue via the use of videofluoroscopic swallowing studies, VFSS)

Sydney Swallow Questionnaire (SSQ)

The SSQ is employed to evaluate the chronic severity of dysphagia as reported by the subject at each clinic visit:

- The SSQ is a 17-item self-report inventory assessing subjective symptoms of oral-pharyngeal dysphagia
- The SSQ has demonstrated strong content, construct, discriminant, and predictive validity and test-retest reliability in a range of patient populations
- The SSQ evaluates a range of domains, including: difficulty swallowing specific food types/consistencies, frequency of choking during ingestion of specific food types/consistencies, and the requirement for multiple swallows during ingestion of food and liquid

Videofluoroscopic Swallowing Studies (VFSS)

VFSS are employed to analyze Swallowing Efficiency at each clinic visit, with imaging results reviewed and rated via a standardized process:

- Central review of the respective fluoroscopic images by multiple independent Speech Language Pathologists is used for all assessments
- Individual reviewers are assigned fluoroscopic studies to review and rate images with no knowledge of the other rater's scores
- The ratings are completed in full by each rater, and any discrepancies are resolved during a consensus meeting

Swallowing tasks employed during the conduct of the VFSS (e.g., Total Pharyngeal Residue assessments) are not impacted by the effort of the subject

All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

Subject-Reported Oral-Pharyngeal Dysphagia: Sydney Swallow Questionnaire (SSQ)

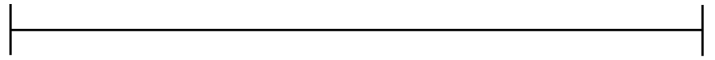
Subject-reported oral-pharyngeal dysphagia as assessed by the SSQ:

- The questionnaire uses a 100-mm long visual analogue scale for all but 1 question
- Possible scores range from 0 to 1700, with higher scores indicating greater swallowing difficulty

Key SSQ Example Questions

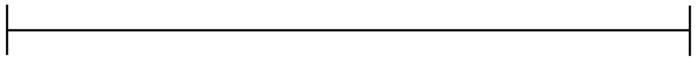
2. How much difficulty do you have **swallowing <u>THIN</u> liquids**?
(eg: tea, soft drink, beer, coffee)

NO DIFFICULTY AT ALL — UNABLE TO SWALLOW AT ALL



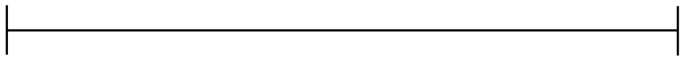
3. How much difficulty do you have **swallowing <u>THICK</u> liquids**?
(eg: milkshakes, soups, custard)

NO DIFFICULTY AT ALL — UNABLE TO SWALLOW AT ALL



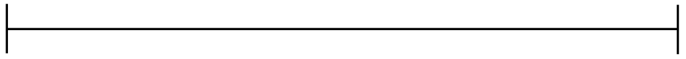
5. How much difficulty do you have **swallowing <u>HARD</u> foods**?
(eg: steak, raw fruit, raw vegetables)

NO DIFFICULTY AT ALL — UNABLE TO SWALLOW AT ALL



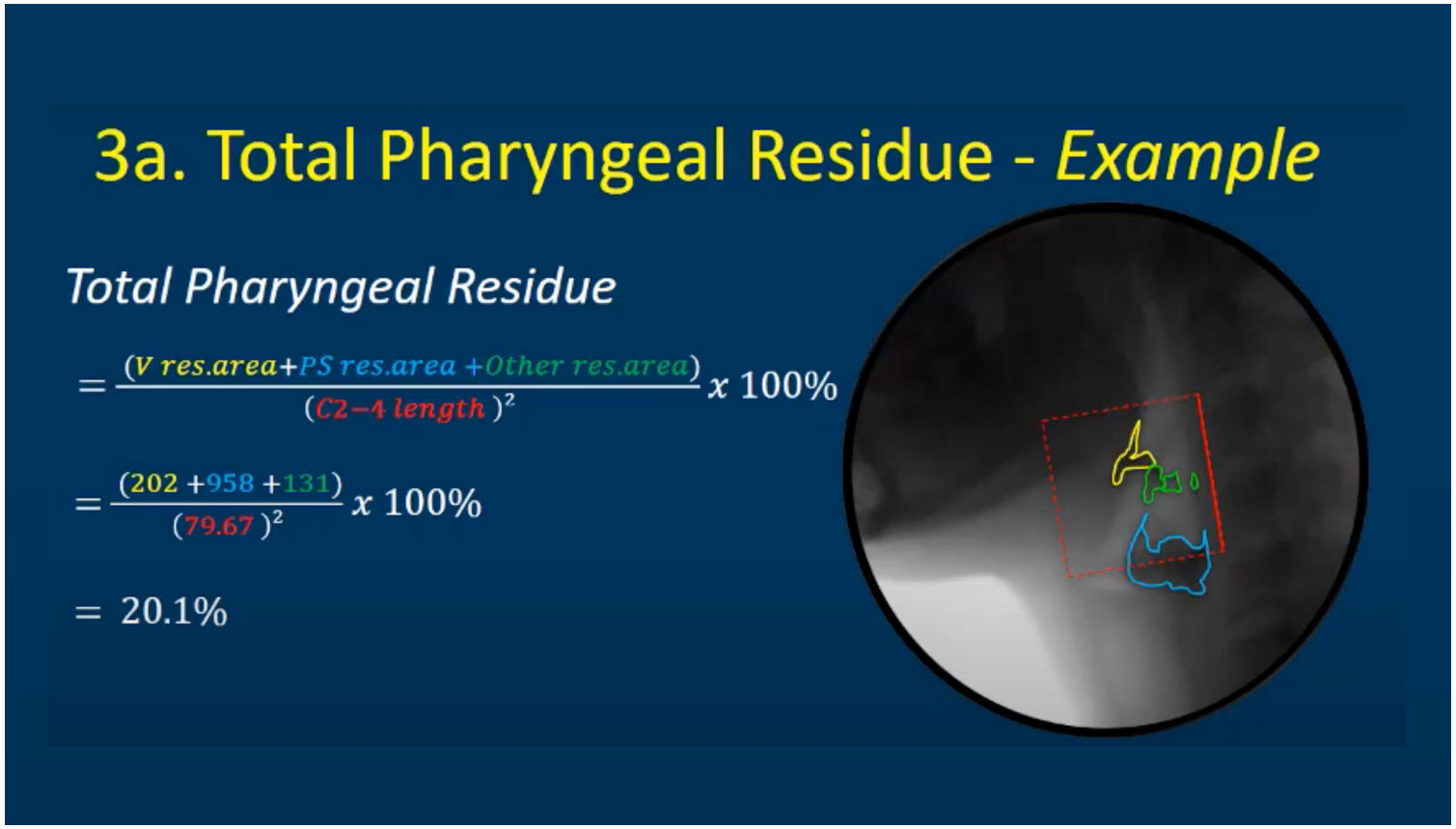
6. How much difficulty do you have **swallowing <u>DRY</u> foods**?
(eg: bread, biscuits, nuts)

NO DIFFICULTY AT ALL — UNABLE TO SWALLOW AT ALL



Szczesniak, M., et al, Dysphagia, 2014

Swallowing Efficiency: As Measured by Total Pharyngeal Residue



- C2-C4 length act as an anatomical scalar
- "Total Pharyngeal Residue" measurement comprises the amount of material remaining in the pharynx after the first swallow of the bolus
- Measurement (yellow, green, and blue) occurs on the first frame showing pyriform sinuses at lowest position
- Normal Total Pharyngeal Residue values should be close to zero

Steele, C., et al. ASHA 2019 Convention Session on the ASPEKT C Method of Videofluoroscopy Analysis

What Constitutes Clinically Meaningful Improvements in Swallowing?

Clinical researchers and caregivers report clinically meaningful improvement would be defined by:

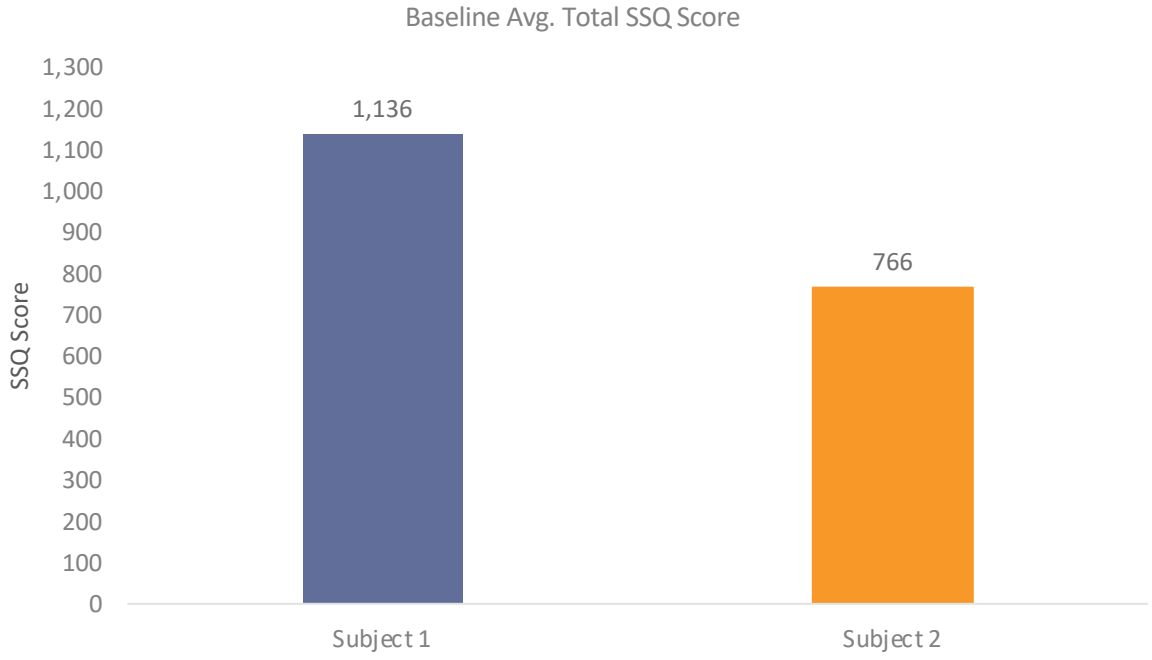
- Improvement in Subject-Reported Outcomes post BB-301 dose (i.e., reductions in the Sydney Swallow Questionnaire ["SSQ"] Total Scores)
  - Swallowing is a core element of the "Activities of Daily Living" for all subjects diagnosed with OPMD
  - Swallowing activities occur consistently over the course of a 24-hour cycle, and include food consumption, liquid consumption, and salivary clearance from the pharynx. Therefore, the study subject is best positioned to accurately assess changes in the level of difficulty associated with swallowing activities (i.e., dysphagia) over the course of a 6-month or 12-month period

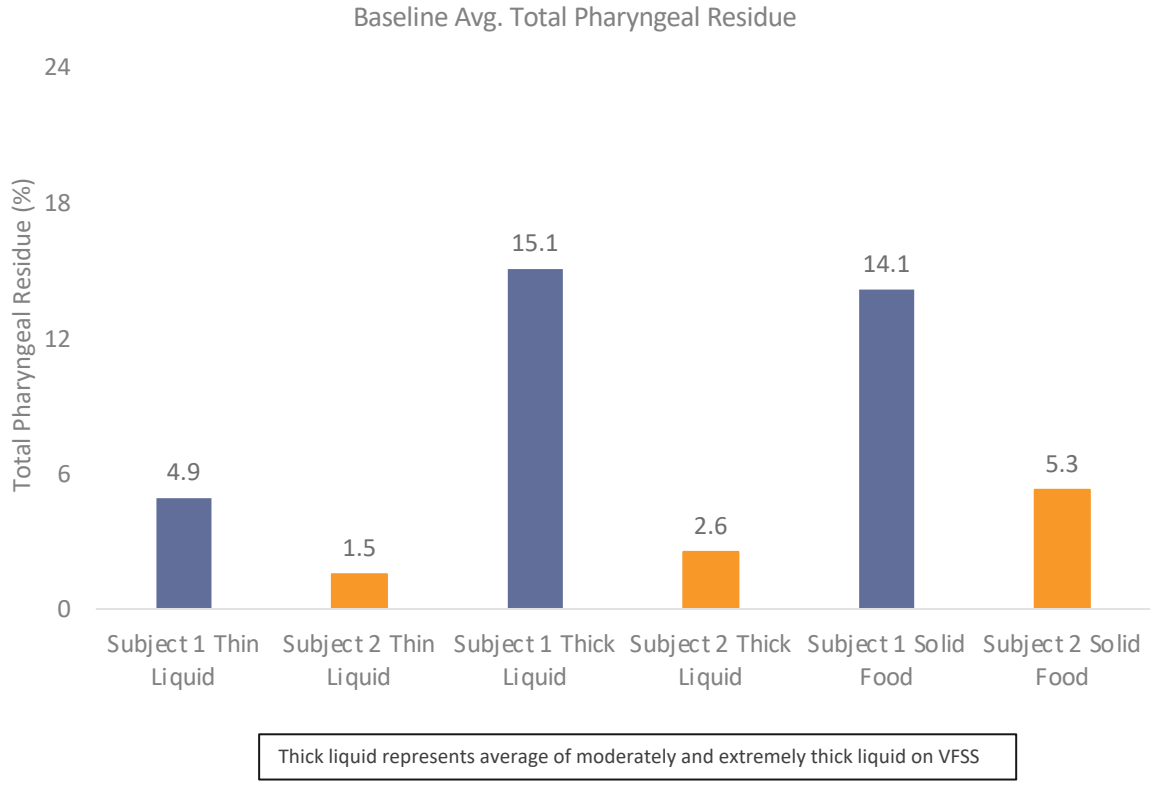
- Reductions in Total Pharyngeal Residue ("TPR") as assessed via VFSS post BB-301 dose (i.e., reductions in the total amount of solid food or liquid material remaining in the pharynx at the completion of swallowing)
  - TPR is objectively characterized via VFSS which evaluate the complete swallowing process for each subject in the context of distinct food and liquid types/consistencies (i.e., Thin Liquid, Thick Liquid, and Solid Food)
  - Regarding the liquid consistencies: Thin Liquid is similar to water, Thick Liquid is similar to a smoothie or yogurt

Interim Low-Dose BB-301 (1.2e13 vg/subject) Phase 1b Clinical Data Summary for the First Two Study Subjects Demonstrates Strong Correlations Between Videofluoroscopic Swallowing Study Results and the Sydney Swallow Questionnaire Scores

Pre-Dose Characteristics of Subject 1 and Subject 2 Demonstrate Strong Correlations Between SSQ Scores and VFSS TPR Results

- Milder Dysphagic Symptoms Noted for Subject 2 vs. Subject 1 Based on SSQ Scores and VFSS TPR Results
- Global inefficiency of swallowing for Solid Food, Thin Liquid, and Thick Liquids Drives Dysphagia for Subject 1
- Pathologic low-volume sequential swallowing for thin liquid and inefficient swallowing of Solid Food Drives Dysphagia for Subject 2





Thick liquid represents average of moderately and extremely thick liquid on VFSS

All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

Subject 1: Key SSQ Questions and Pre-Dose SSQ Sub-Scores Correlate Directly with VFSS TPR Assessments

VFSS TPR Correlate	SSQ Question	Average Pre-Dose SSQ Sub-Score	SSQ Sub-Score Comments
Thin Liquid (Thin 5 mL)	**Question 2:** ***How much difficulty do you have swallowing THIN liquids (e.g., tea, soft drink, beer, coffee)?***	**46.6** (out of 100)	• Prior to BB-301 dosing, Subject 1 reports the least difficulty swallowing Thin Liquid
Moderately Thick Liquid and Extremely Thick Liquid	**Question 3:** ***How much difficulty do you have swallowing THICK liquids (e.g., milkshakes, soups, custard)?***	**77.8** (out of 100)	• Prior to BB-301 dosing, Subject 1 reports significantly greater difficulty swallowing Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, Subject 1 reports approximately the same level of difficulty swallowing Thick Liquids and Solid Food
Solid Food	**Question 5:** ***How much difficulty do you have swallowing HARD foods (e.g., steak, raw fruit, raw vegetables)?***	**71.2** (out of 100) **Solid Food Average of 74.3 (out of 100)**	• Prior to BB-301 dosing, Subject 1 reports significantly greater difficulty swallowing Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, Subject 1 reports approximately the same level of difficulty swallowing Solid Food and Thick Liquids
Solid Food	**Question 6:** ***How much difficulty do you have swallowing DRY foods? (e.g., bread, biscuits, nuts)?***	**77.4** (out of 100)	

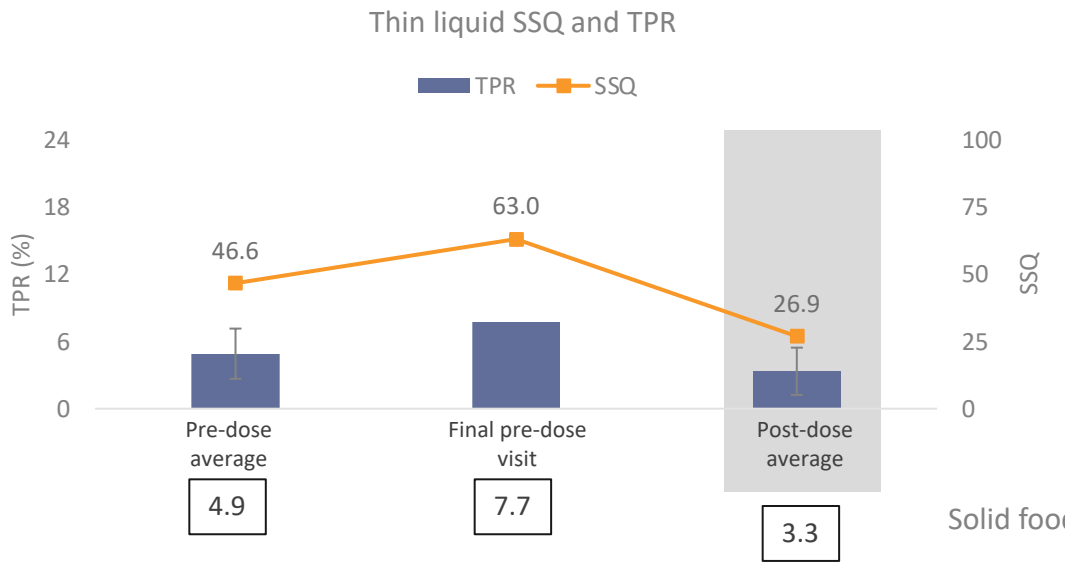
All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

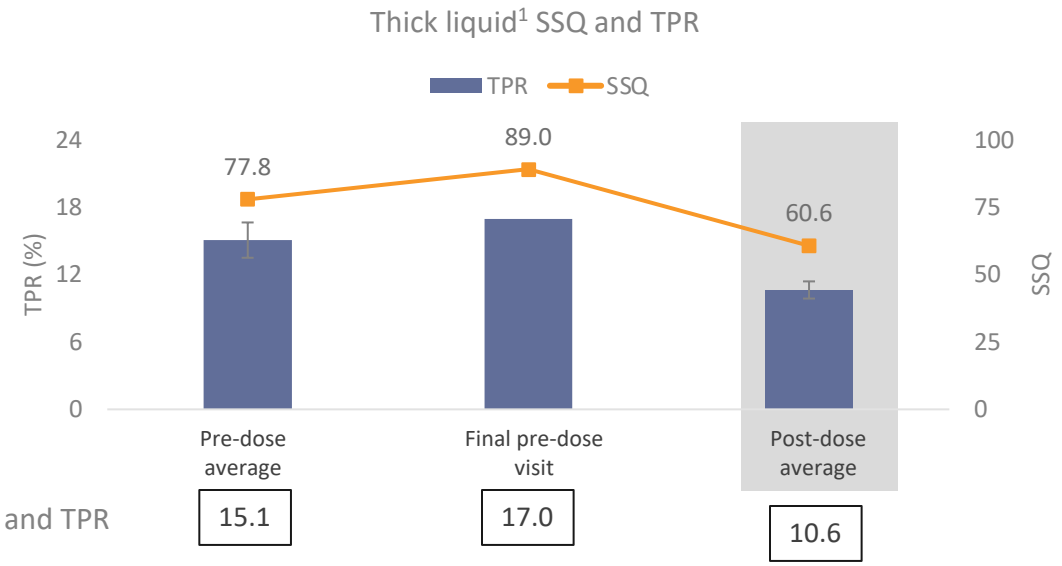
Subject 1: Key SSQ Questions and Pre-Dose SSQ Sub-Scores Correlate Directly with Pre-Dose VFSS TPR Results

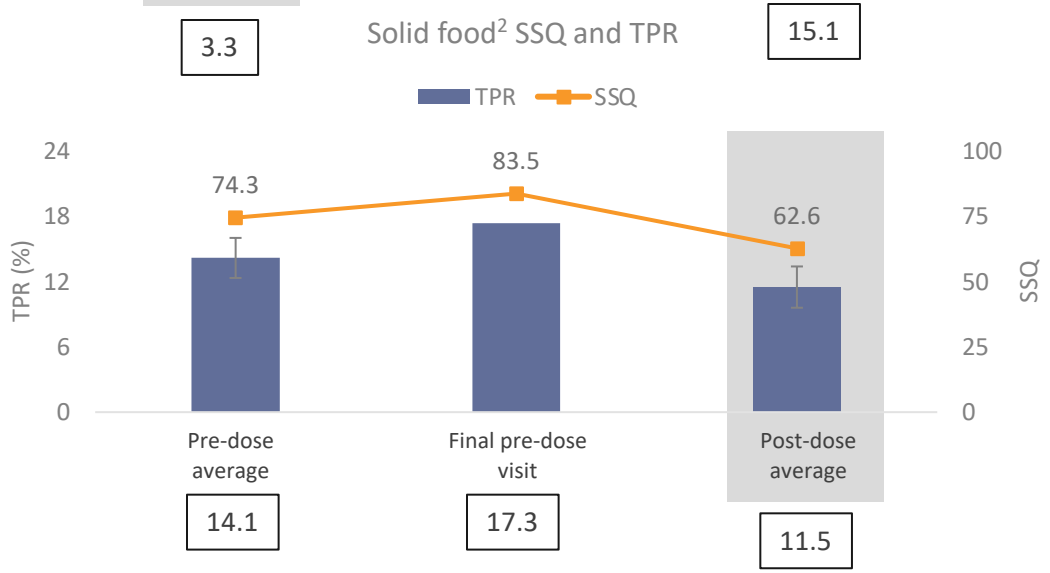
VFSS TPR Correlate	Average Pre-Dose VFSS TPR	VFSS TPR Comments	SSQ Question	Average Pre-Dose SSQ Sub-Score	SSQ Sub-Score Comments
Thin Liquid (Thin 5 mL)	**4.9%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 1 demonstrate the least residue for Thin Liquid	**Question 2:** ***How much difficulty do you have swallowing THIN liquids (e.g., tea, soft drink, beer, coffee)?***	**46.6** (out of 100)	• Prior to BB-301 dosing, Subject 1 reports the least difficulty swallowing Thin Liquid
Moderately Thick Liquid and Extremely Thick Liquid	**12.8%** **Thick Liquids Average of 15.1%** **17.3%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 1 demonstrate significantly greater residue for Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, the VFSS TPR results for Subject 1 demonstrate approximately the same level of residue for Thick Liquids and Solid Food	**Question 3:** ***How much difficulty do you have swallowing THICK liquids (e.g., milkshakes, soups, custard)?***	**77.8** (out of 100)	• Prior to BB-301 dosing, Subject 1 reports significantly greater difficulty swallowing Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, Subject 1 reports approximately the same level of difficulty swallowing Thick Liquids and Solid Food
Solid Food	**14.1%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 1 demonstrate significantly greater residue for Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, the VFSS TPR results Subject 1 demonstrate approximately the same level of residue for Solid Food and Thick Liquids	**Question 5:** ***How much difficulty do you have swallowing HARD foods (e.g., steak, raw fruit, raw vegetables)?***	**71.2** (out of 100) **Solid Food Average of 74.3 (out of 100)**	• Prior to BB-301 dosing, Subject 1 reports significantly greater difficulty swallowing Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, Subject 1 reports approximately the same level of difficulty swallowing Solid Food and Thick Liquids
Solid Food	**14.1%**		**Question 6:** ***How much difficulty do you have swallowing DRY foods? (e.g., bread, biscuits, nuts)?***	**77.4** (out of 100)	

All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

9 Months Post BB-301 Dose: SSQ, VFSS TPR Show Subject 1 Experienced Clinically Meaningful Improvements across all Consistencies





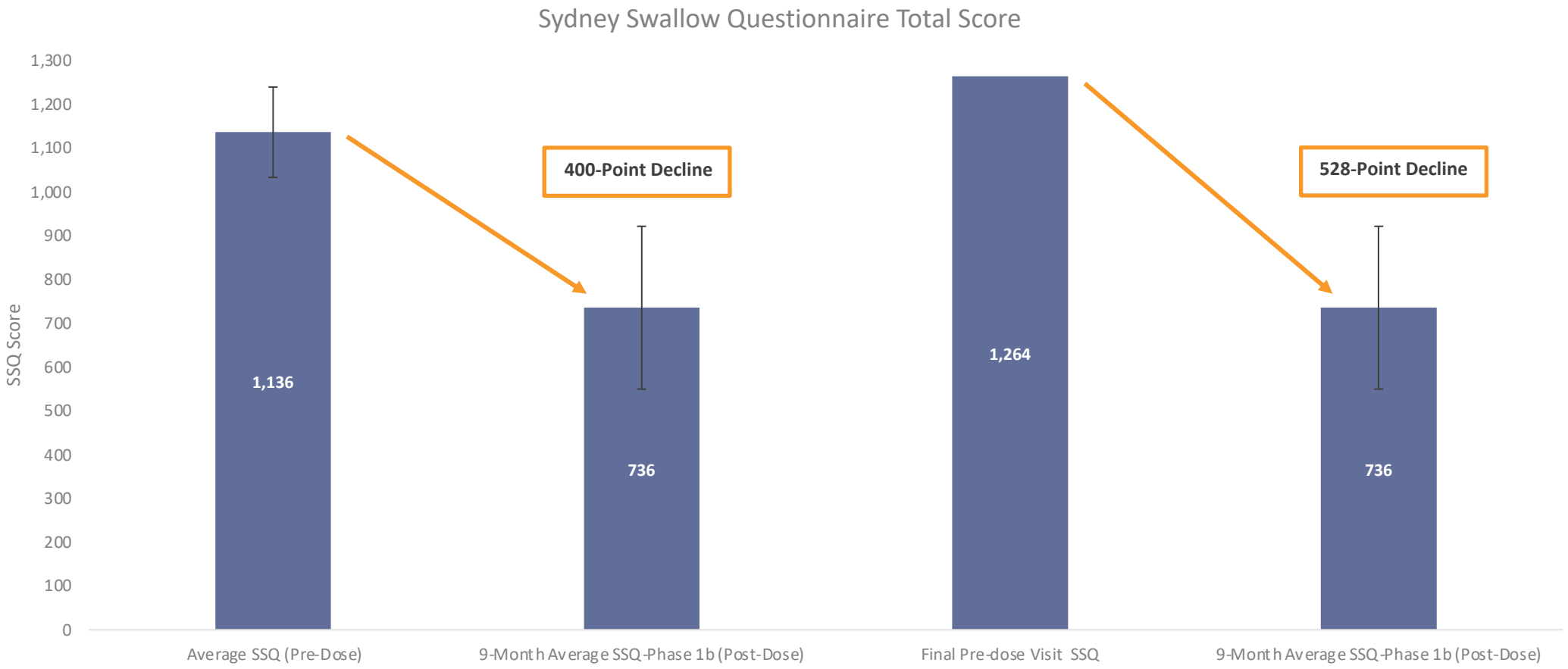


The average American diet consists primarily of Thin Liquids and Solid Food
Pre-Dose period: inefficient swallowing for both Thin Liquids and Solid Food
Post-Dose period: improvement in swallowing efficiency for both consistencies

[1]Thick liquid represents average of moderately and extremely thick liquid on VFSS; [2] Solid food represents average of hard and dry food on SSQ

Subject 1 Experienced Significant Improvement in 9-Month Avg. Post-Dose Sydney Swallow Questionnaire Scores

- **The 9-Month Average Post-Dose SSQ Showed a 35% Improvement vs. the Average Pre-Dose SSQ and a 42% Improvement vs. the Final Pre-Dose SSQ**



Subject 2: Key SSQ Questions and Pre-Dose SSQ Sub-Scores Correlate Directly with VFSS TPR Assessments

VFSS TPR Correlate	SSQ Question	Average Pre-Dose SSQ Sub-Score	SSQ Sub-Score Comments
Thin Liquid (Thin 5 mL)	**Question 2:** ***How much difficulty do you have swallowing THIN liquids (e.g., tea, soft drink, beer, coffee)?***	**26.4** (out of 100)	• Prior to BB-301 dosing, Subject 2 reports the least difficulty swallowing Thin Liquid
Moderately Thick Liquid and Extremely Thick Liquid	**Question 3:** ***How much difficulty do you have swallowing THICK liquids (e.g., milkshakes, soups, custard)?***	**38.5** (out of 100)	• Prior to BB-301 dosing, Subject 2 reports greater difficulty swallowing Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, Subject 2 reports less difficulty swallowing Thick Liquids as compared to Solid Food
Solid Food	**Question 5:** ***How much difficulty do you have swallowing HARD foods (e.g., steak, raw fruit, raw vegetables)?***	**56.0** (out of 100) **Solid Food Average of 55.3 (out of 100)**	• Prior to BB-301 dosing, Subject 2 reports significantly greater difficulty swallowing Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, Subject 2 reports significantly greater difficulty swallowing Solid Food as compared to Thick Liquids
Solid Food	**Question 6:** ***How much difficulty do you have swallowing DRY foods? (e.g., bread, biscuits, nuts)?***	**54.6** (out of 100)	

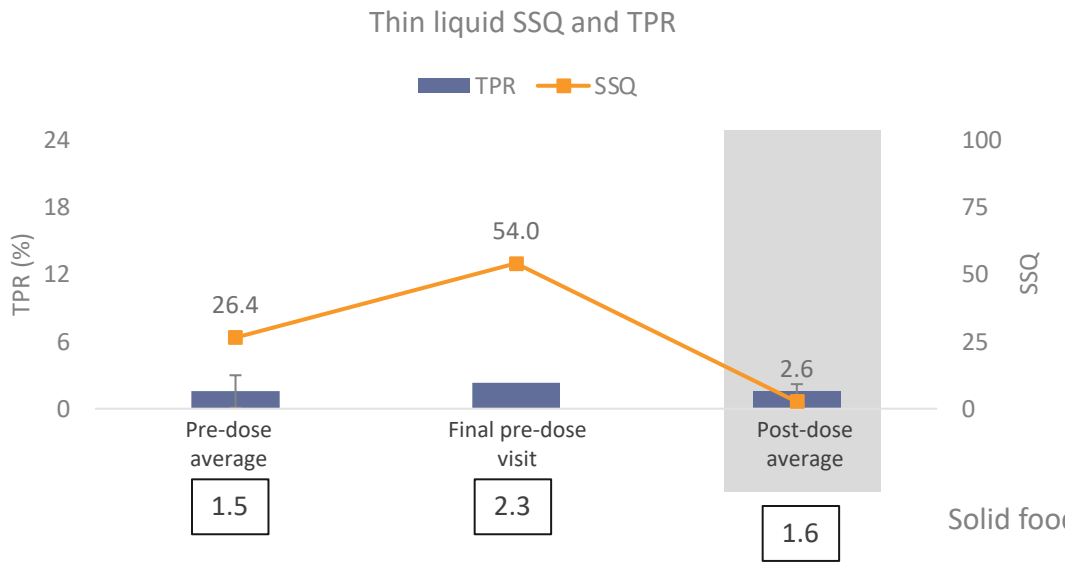
All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

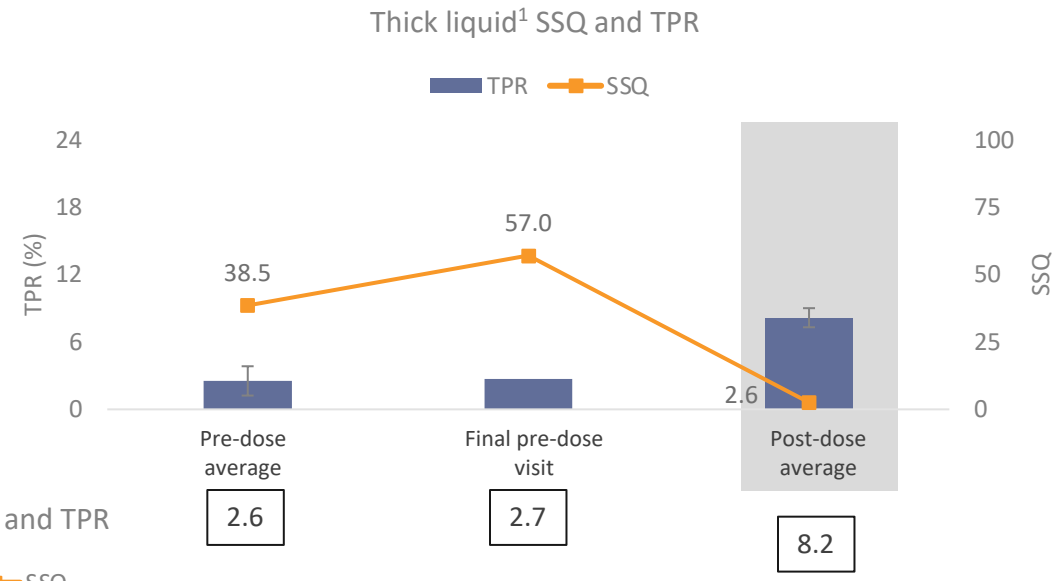
Subject 2: Key SSQ Questions and Pre-Dose SSQ Sub-Scores Correlate Directly with Pre-Dose VFSS TPR Results

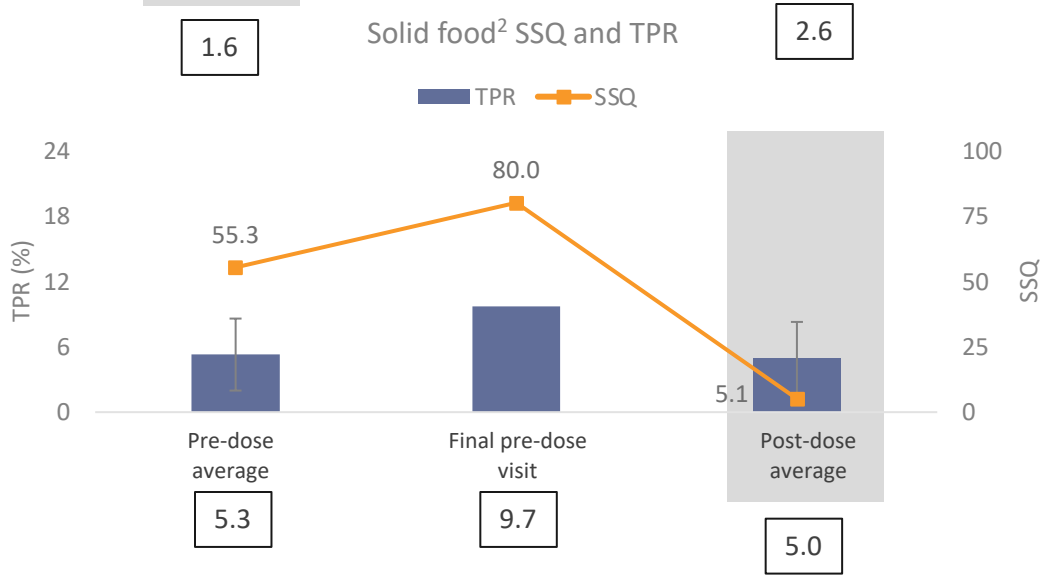
VFSS TPR Correlate	Average Pre-Dose VFSS TPR	VFSS TPR Comments	SSQ Question	Average Pre-Dose SSQ Sub-Score	SSQ Sub-Score Comments
Thin Liquid (Thin 5 mL)	**1.5%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 2 demonstrate the least residue for Thin Liquid	**Question 2:** ***How much difficulty do you have swallowing THIN liquids (e.g., tea, soft drink, beer, coffee)?***	**26.4** (out of 100)	• Prior to BB-301 dosing, Subject 2 reports the least difficulty swallowing Thin Liquid
Moderately Thick Liquid and Extremely Thick Liquid	**1.8%** **Thick Liquids Average of 2.6%** **3.3%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 2 demonstrate greater residue for Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, the VFSS TPR results for Subject 2 demonstrate less residue for Thick Liquids as compared to Solid Food	**Question 3:** ***How much difficulty do you have swallowing THICK liquids (e.g., milkshakes, soups, custard)?***	**38.5** (out of 100)	• Prior to BB-301 dosing, Subject 2 reports greater difficulty swallowing Thick Liquids as compared to Thin Liquid • Prior to BB-301 dosing, Subject 2 reports less difficulty swallowing Thick Liquids as compared to Solid Food
Solid Food	**5.3%**	• Prior to BB-301 dosing, the VFSS TPR results for Subject 2 demonstrate significantly greater residue for Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, the VFSS TPR results Subject 2 demonstrate significantly greater residue for Solid Food as compared to Thick Liquids	**Question 5:** ***How much difficulty do you have swallowing HARD foods (e.g., steak, raw fruit, raw vegetables)?***	**56.0** (out of 100) **Solid Food Average of 55.3 (out of 100)**	• Prior to BB-301 dosing, Subject 2 reports significantly greater difficulty swallowing Solid Food as compared to Thin Liquid • Prior to BB-301 dosing, Subject 2 reports significantly greater difficulty swallowing Solid Food as compared to Thick Liquids
Solid Food	**5.3%**		**Question 6:** ***How much difficulty do you have swallowing DRY foods? (e.g., bread, biscuits, nuts)?***	**54.6** (out of 100)	

All Study Subjects are blinded to their SSQ Total Scores and VFSS (TPR) assessment results, and the Central Reader for the VFSS Assessments is blinded to the SSQ Total Scores and SSQ Sub-Scores for all Study Subjects

6 Months Post BB-301 Dose: SSQ, VFSS TPR Show Subject 2 Experienced Stabilization or Clinically Meaningful Improvement across all Consistencies







The average American diet consists primarily of Thin Liquids and Solid Food

Pre-Dose period: greatest swallowing inefficiency for Solid Food

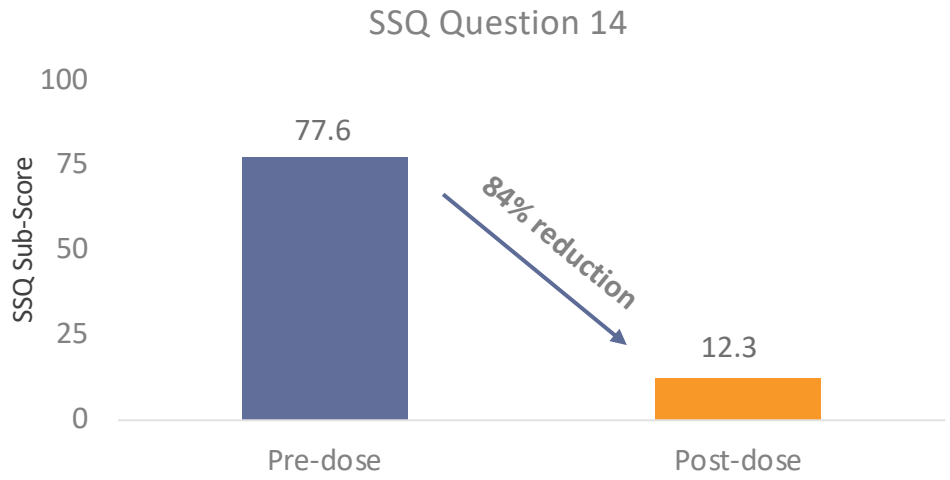
Post-Dose period: outsized improvement in swallowing efficiency for this consistency

[1]Thick liquid represents average of moderately and extremely thick liquid on VFSS; [2] Solid food represents average of hard and dry food on SSQ

Subject 2 Experienced a Significant Reduction in Pathologic Low-Volume Sequential Swallowing 6 Months Post BB-301 Dose

SSQ Question 14: "Do you Ever Need to Swallow More Than Once for Your Food to Go Down?"

For Subject 2, the Average Post-Dose SSQ Sub-Score was **reduced by 84%** as compared to the Average Pre-Dose SSQ Sub-Score

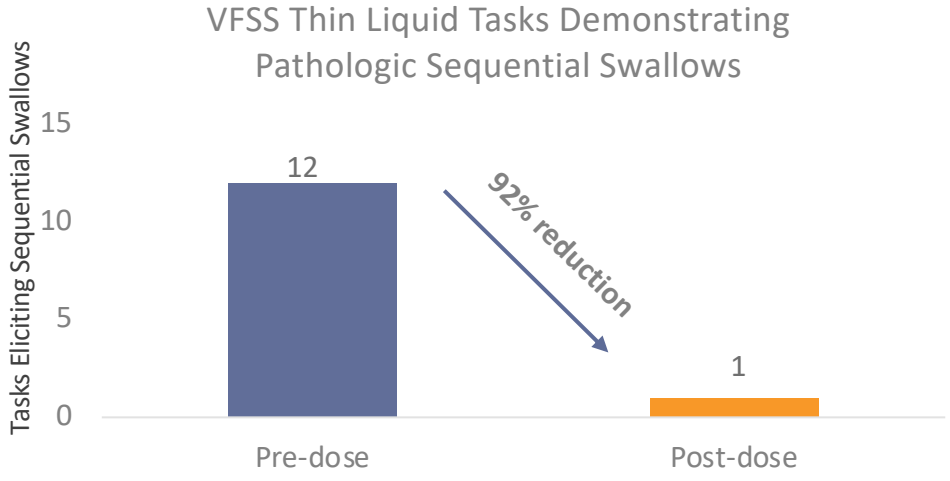


VFSS TPR assessments

For Subject 2, pathologic low-volume sequential swallows for thin liquids were observed:

- **during 12 swallowing tasks** carried out during the pre-dose clinical visits
- **during only 1 swallowing task** carried out during the post-dose clinical visits

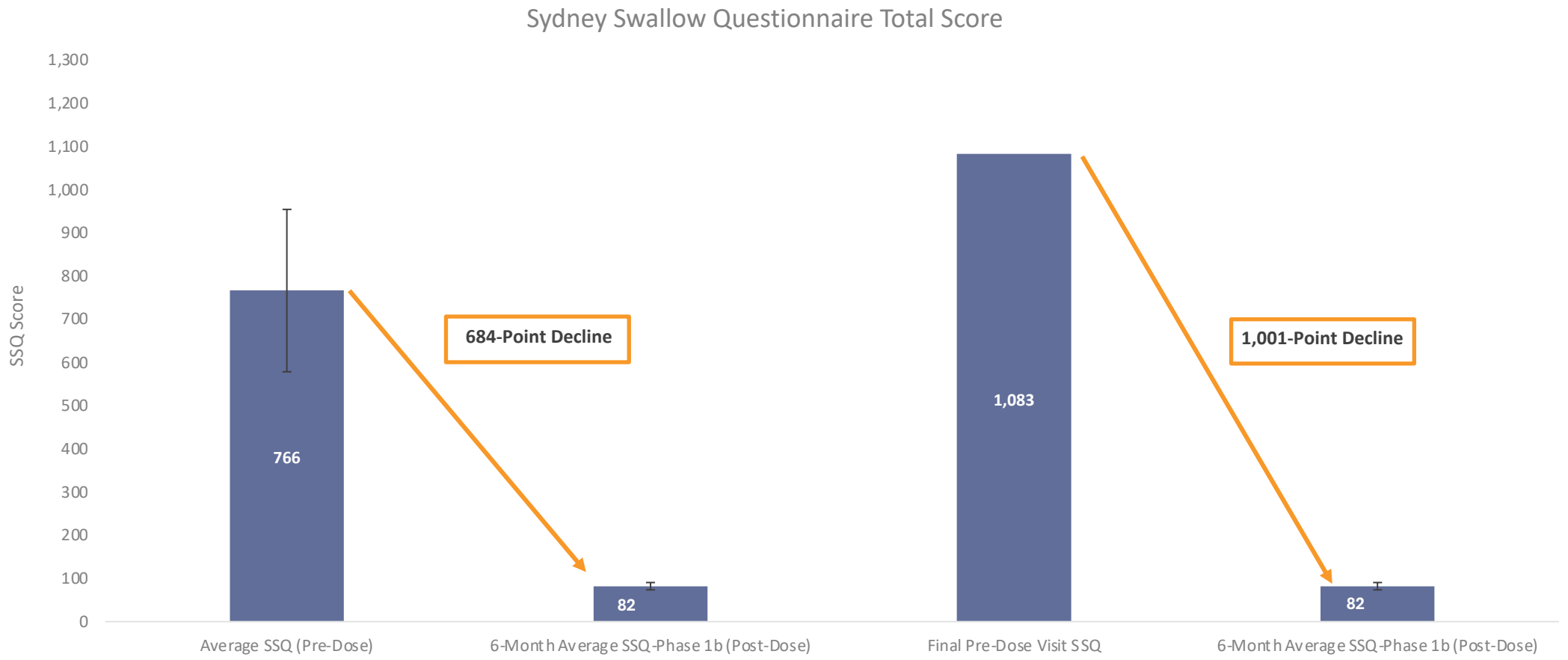
Following BB-301 administration, Subject 2 **experienced a 92% reduction** in the occurrence of pathologic low-volume sequential swallows for thin liquids



The significant post-dose reduction in pathologic low-volume sequential swallows for thin liquid (as demonstrated by the Post-Dose VFSS TPR results and the SSQ Sub-Scores) drove a significant reduction in dysphagia for Subject 2

Subject 2 Experienced a Significant Improvement in Post-Dose Sydney Swallow Questionnaire Scores, Achieving Scores that Represents Clinically Normal Swallowing

- **The 6-Month Average Post-Dose SSQ Showed an 89% Improvement vs. the Average Pre-Dose SSQ and a 92% Improvement vs. the Final Pre-Dose SSQ**



The final 6-month post-dose average SSQ value of 82 units for Subject 2 represents a clinically normal swallowing profile.

Summary and Conclusions

- Two subjects have received the lowest-dose of BB-301 (1.2e13 vg/subject) with compelling clinical impact
  - There were no Significant Adverse Events
  - Both subjects experienced significant levels of clinical benefit per the post-dose SSQ scores
  - Both subjects experienced significant levels of benefit per the post-dose VFSS TPR results
  - The subject with pathologic low-volume sequential swallows at baseline experienced an almost complete resolution of this problem and achieved an SSQ score indicative of clinically normal swallowing
  - **We believe these early data reflect a major impact on the subject's swallowing function and activities of daily living, and represent the first successful improvement in swallowing by a gene therapy in OPMD**

- Dysphagic symptoms at baseline for Subject 1 (7-years post diagnosis) were more severe than those of Subject 2 (6-years post diagnosis) as assessed by pre-dose SSQ and TPR results
  - Despite baseline differences, the SSQ Total Scores and SSQ Sub-Scores correlate strongly with the VFSS TPR results.

- We expect to deepen our understanding of the therapy and the potential impact for patients as we continue the treatment of subjects in the low dose cohort and, subsequently, advance to a higher dose
  - The preclinical proof-of-concept data for BB-301 demonstrated greater improvements in muscle strength at higher doses, and we are optimistic about the potential for improved efficacy as we enter the next dosing cohort

Summary and Conclusions (continued)

- The Total SSQ scores represent the most accurate reflection of the subjects' experiences of their pre-dose and post-dose dysphagic symptoms.
  - The final pre-dose visit is temporally closest to the subjects' post-dose experiences
  - The final pre-dose visit likely represents the most vividly memorable pre-drug dysphagic symptomology for each subject and serves as the ideal comparison for efficacy assessments
  - As a result, we compare the post-dose clinical results with both pre-dose averages and the final pre-dose visit

- Improvements in dysphagic symptoms may relate directly to post-dose improvements in efficiencies of swallowing for the types/consistencies of food and liquid most commonly ingested by the subject or the correction of altered swallowing physiology (e.g., reductions in the frequency of pathologic low-volume sequential swallows)
  - Daily diets consist primarily of thin liquids (e.g., water, juice, tea, coffee, etc.) and solid foods
  - The post-dose reductions in TPR for these types/consistencies of food and liquid should meaningfully reduce the subject's daily dysphagic symptoms and, therefore, Total SSQ scores and the corresponding SSQ Sub-Scores.
  - We expect that improvement for the most adversely impacted consistencies will drive the most significant improvements regarding a subject's SSQ Score and overall swallowing function

Q&A: Videofluoroscopic Swallowing Studies and Subject-Reported Outcome Measures

Emily Plowman, PhD, CCC-SLP, FASHA

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Appendix

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OPMD: A Chronic, Progressive Disease With No Approved Therapeutics

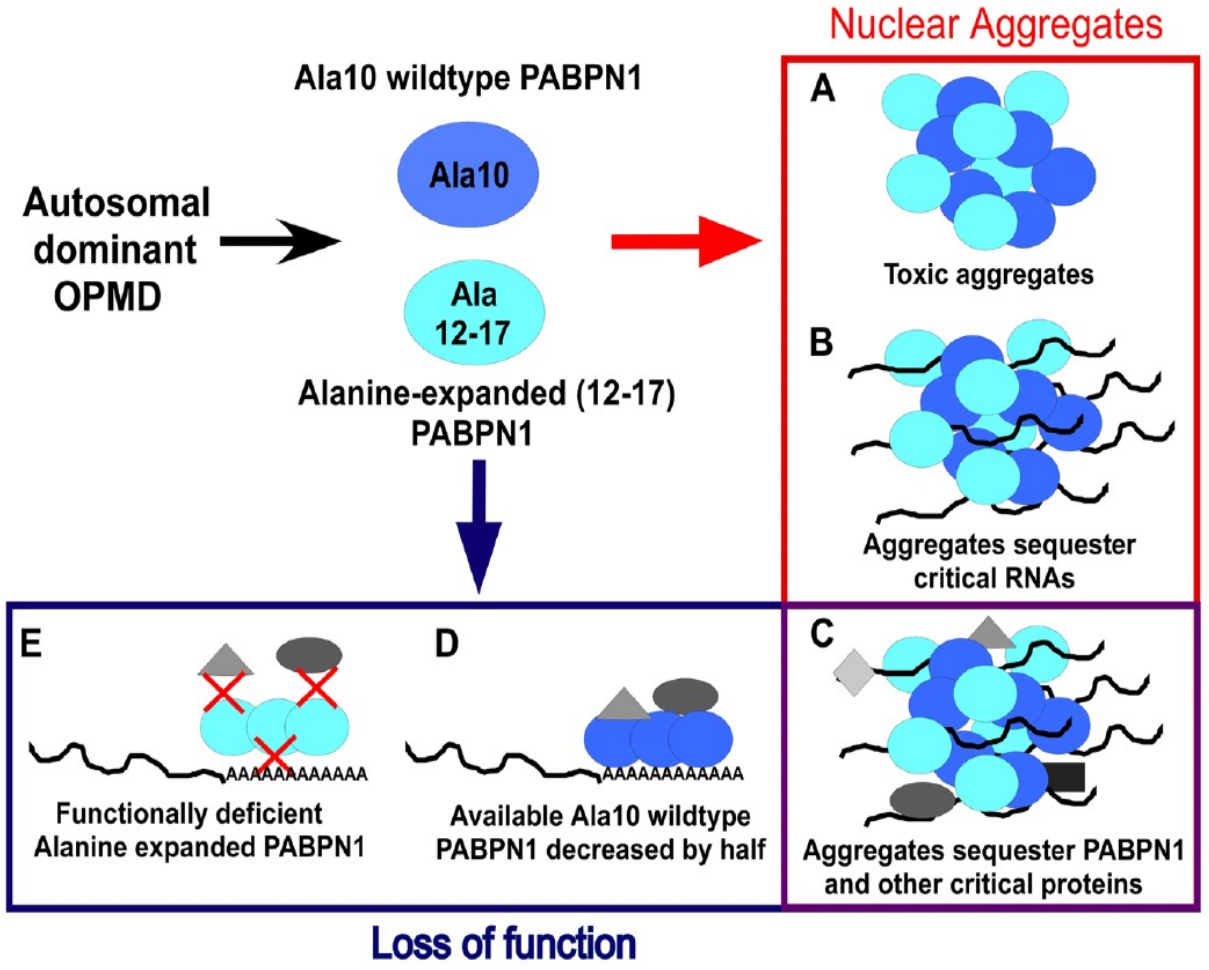
- Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant, chronic, myopathic disorder characterized by ptosis (drooping of the upper eyelid) and progressive dysphagia (loss of the ability to swallow) due to impairment of the muscles of the eyelids and throat.
- Typical age of onset in the 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 of up to 18 contiguous alanine residues at the N-terminal end of the PABPN1 protein; the PABPN1 mutant protein is aggregation prone and drives the formation of intranuclear inclusions (INIs) in the myocytes which can cause cell death and/or loss of function (see appendix for additional information):

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

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

Models for OPMD Pathogenesis

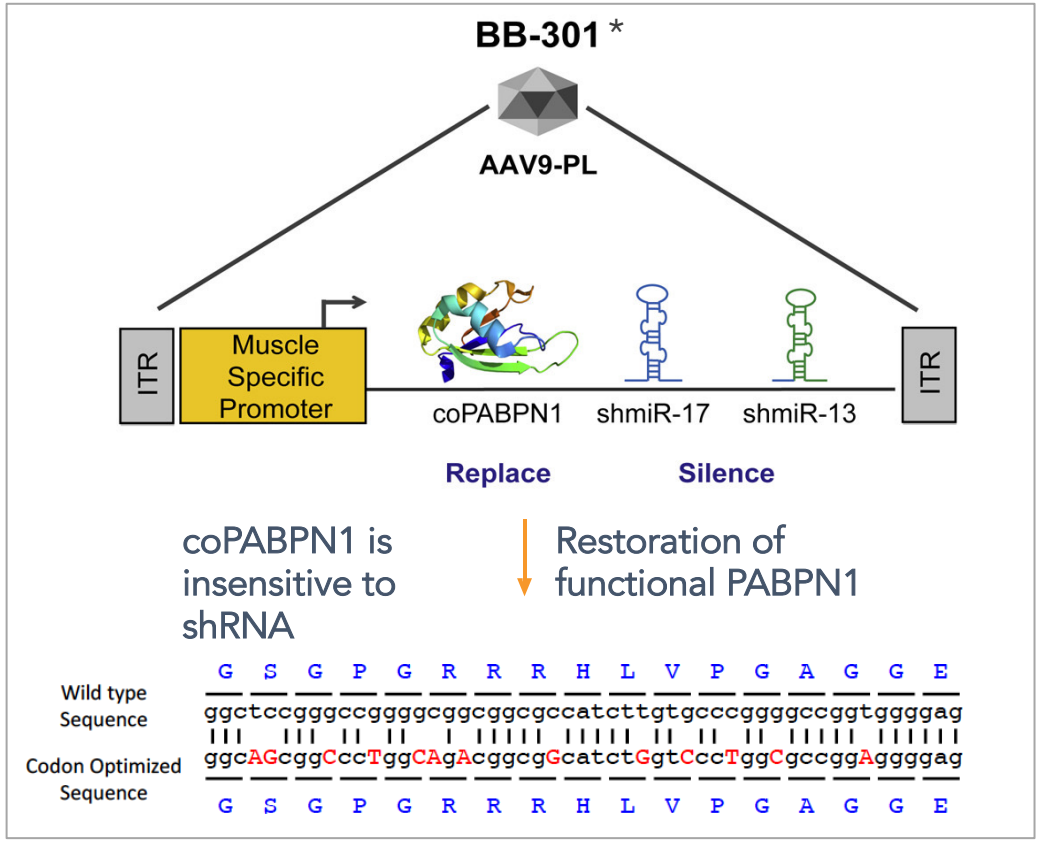
- PABPN1 is a ubiquitous protein that controls the length of mRNA poly(A) tails, mRNA export from the nucleus & alternative poly(A) site usage
- Currently two general models are used to explain how alanine-expanded PABPN1 confers muscle pathology in autosomal dominant OPMD where patients have one normal and one mutant allele of PABPN1
- One model suggests that nuclear aggregates cause disease (right column, outlined in red)
- A second model suggests that loss of PABPN1 function (bottom row, outlined in blue) underlies pathology



Banerjee, A, FEBS J., 2013

BB-301 Inhibits the Production of the key Disease-Causing Protein in OPMD and Delivers a New, Fully-Functional Version of the Protein

- BB-301 is a gene therapy designed by Benitec Biopharma Inc. to accomplish two goals:
  - Reduce the production of the mutant (harmful) form of the PABPN1 protein in the muscles of the throat
  - Deliver a new, functional gene to the muscles of the throat that will drive production of the normal, healthy form of the PABPN1 protein
- BB-301 contains 3 genes, 2 of which serve to reduce the production of the mutant form of the PABPN1 protein in the treated muscles of the throat, and 1 gene that allows the treated muscles to produce the normal, healthy PABPN1 protein
- These 3 genes are placed, or "encapsulated," within a special virus (i.e., AAV9 vector)
- The AAV9 vector used for BB-301 is part of a family of viruses called adeno-associated viruses (AAVs), and AAVs have been evaluated in hundreds of clinical research studies
- In preclinical efficacy studies for BB-301 carried out in the A17 mouse model, direct intramuscular injection of BB-301 facilitated increases in muscle cross-sectional area, increases in muscle mass, and increases in muscle force generating capacity
- In Beagle dog studies, intramuscular injections of BB-301 into the pharyngeal constrictor muscles supported dose-dependent tissue transduction, transgene (coPABPN1) expression, and target gene (mutant PABPN1) knockdown in the injected muscles



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

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

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

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

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

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%

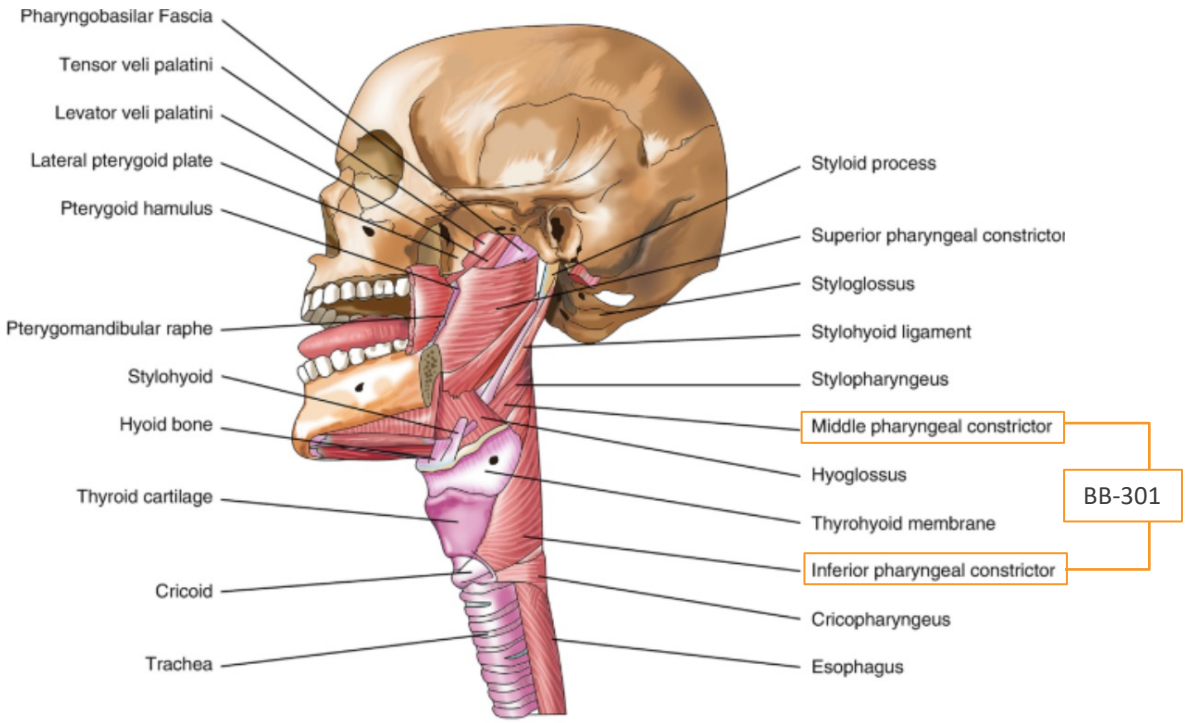
8 weeks following administration of BB-301, an average wtPABPN1 inhibition level of 72% was achieved in the target pharyngeal muscle cells of Beagle dogs

Swallowing Overview and The Rationale for BB-301 in OPMD

Normal vs. Disordered Swallowing

- Under normal conditions, a food bolus leaves the oral cavity and is able to traverse the length of the pharynx, en route to the esophagus, via the propulsive activity of the coordinated constriction of the superior, middle, and inferior pharyngeal constrictor muscles
- As the food bolus nears the opening of the upper esophagus, the subsequent relaxation of the cricopharyngeal muscle allows the bolus to enter the esophagus and travel to the stomach
- In OPMD, the pharyngeal constrictor muscles are weakened and atrophic and are unable to consistently exert the level of force required to support the propulsion of the food or liquid bolus that defines the normal swallowing process
- In the ongoing Phase 1b/2a clinical research study, BB-301 is delivered by direct intramuscular injection to the weakened muscles of the pharynx
- Restoration of muscle fiber size and muscle force generating capacity in the weakened and atrophic pharyngeal constrictor muscles of OPMD patients following BB-301 administration would be expected to meaningfully enhance the ability of the pharyngeal constrictor muscles to support food and liquid bolus propulsion through the pharynx and towards the esophagus, reducing dysphagia in OPMD patients

Anatomical Structures of the Pharynx and BB-301 Injection Sites



Muscles Of Pharyngx: Lateral view

Primary Source Data Verification

- **All safety data are confirmed via a process of Source Data Verification (SDV) approximately monthly**
  - The SDV process entails a clinical representative of the Clinical Research Organization (CRO) visiting the clinical site and reviewing all primary medical data entered into the medical record, the electronic Case Report Forms (eCRF), and/or provided by associated clinical laboratories
  - The Benitec Clinical Team also verifies all safety data (e.g., clinical chemistries, hematologic assessments, thyroid function testing, urinalysis, and physical examination findings)
  - SDV for safety data is performed at this cadence as this is a first-in-human study with safety as the primary endpoint
- **Secondary endpoints (e.g., VFSS) are exploratory, and the assessment of the utility of the exploratory endpoints as fundamental indicators of disease progression or symptomatic improvement will be assessed at month 12 for each Phase 1b/2a Study Subject**
  - In this regard, SDV of the primary data sources (e.g., the primary imaging and analytical data files which are used by the central reading team to populate the eCRF for all subjects screened and/or enrolled into BNTC-OPMD-NH-001 and BNTC-OPMD-BB-301-01) occurs after the month-12 assessment for each subject
  - In preparation for the 2024 World Muscle Society Annual Congress late-breaking oral presentation, the SDV process was initiated early for Subjects 1 and 2