April 18, 2024

Benitec Biopharma Reports Positive Interim Clinical Trial Data for First OPMD Subject Treated with BB-301 in Phase 1b/2a Study

-First efficacy signals demonstrated for a gene therapy under development for Oculopharyngeal Muscular Dystrophy (OPMD) which affects ~15,000 patients worldwide-

- BB-301 facilitated improvements across multiple measures of swallowing function in the first Phase 1b/2a clinical study subject as compared to pretreatment assessments conducted during the observational natural history portion of the study-

-Virtual R&D Day being held today at 9:00 am EDT, details below-

HAYWARD, Calif., April 18, 2024 (GLOBE NEWSWIRE) -- Benitec Biopharma Inc. (NASDAQ: BNTC) ("Benitec" or "Company"), a clinical-stage, gene therapy-focused, biotechnology company developing novel genetic medicines based on its proprietary "Silence and Replace" DNA-directed RNA interference ("ddRNAi") platform, today announces positive interim clinical data from the 90-day timepoint following the administration of BB-301 to the study's first subject (Subject 1) treated in the BB-301 Phase 1b/2a single-arm, open-label, sequential, dose-escalation cohort study (NCT06185673) in Oculopharyngeal Muscular Dystrophy (OPMD). BB-301 has been granted Orphan Drug designation by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP).

"To date, no clinical studies have systematically demonstrated a clinical improvement in OPMD patients across both objective and subjective measures of swallowing. We are, therefore, pleased to report positive interim clinical data from multiple radiographic measures as well as subject-reported outcome measures from the first subject treated with BB-301," said Jerel A. Banks, M.D., Ph.D., Executive Chairman and Chief Executive Officer of Benitec. "We are highly encouraged by these early clinical trial results and for the hope that they may offer to patients and caregivers, and we look forward to reporting additional results and continuing to treat patients as they enter the dosing portion of the study from the Natural History observational lead-in period."

BB-301 Interim Clinical Study Results:

During the OPMD Natural History Study, which represents the pre-dose observational period for each subject, Subject 1 experienced progressive worsening of dysphagia as demonstrated by the results of the videofluoroscopic swallowing studies (VFSS), the cold water timed drinking test, and the key subject-reported outcome measure (the Sydney

Swallow Questionnaire). Videofluoroscopic swallowing studies represent the gold standard analytical method for the quantitative assessment of dysphagia (swallowing difficulty) in the clinical setting.

At the 90-day timepoint following the administration of BB-301, Subject 1 demonstrated improvements in key videofluoroscopic assessments which correlated with the observation of similar improvement in the key subject-reported outcome measure as compared to the average values for the respective assessments completed during the pre-dose observational period (as summarized in Figure 1). Notably, the results of many assessments completed at the 90-day timepoint demonstrated improvements over the initial measurements assessed at the subject's first visit for the natural history observational study which occurred more than 12 months prior to the 90-day assessment.

The most significant VFSS improvements at Day 90 were observed for swallowing tasks centered on the evaluation of pharyngeal constrictor muscle function and swallowing efficiency in the context of the consumption of thin liquids, solid foods and thick, non-solid foods (e.g., yogurt or pudding) (Figure 1). The VFSS improvements correlated with an improvement in the key subject-reported outcome measure the Sydney Swallow Questionnaire, indicating an improvement in swallowing function as reported by Subject 1 (Figure 1).

Figure 1: Improvement in All Outcomes at 90-Days Post-BB-301 Injection*

Radiographic Assessments of Pharyngeal Area at Maximum Constriction to Determine Pharyngeal Constrictor Muscle Function During Swallowing

	OPMD Natural History Study	Phase 1b/2a BB-301 Dosing Study	
	Pre-Dose Period	Post-Dose Period	
Barium-Containing Food Items	Average PhAMPC During Swallowing	Day 90 PhAMPC During Swallowing	Improvement in Pharyngeal Closure During Swallowing After BB-301 Dose
Thin Liquid	9.1	3.9	5.2 Units (-57.1%)
Moderately Thick Liquid	20.0	14.8	5.2 Units (-26.0%)
Extremely Thick Liquid	21.8	18.5	3.3 Units (-15.1%)
Solid Food	18.0	10.9	7.1 Units (-39.4%)

Radiographic Assessments of Pharyngeal Residue (i.e., food or liquid material) Remaining Post-Swallow to Determine Swallowing Efficiency

	OPMD Natural History Study	Phase 1b/2a BB-301 Dosing Study	
	Pre-Dose Period	Post-Dose Period	
Barium-Containing Food Items	Average Pharyngeal Residue Remaining Post-Swallow	Day 90 Pharyngeal Residue Remaining Post-Swallow	Reduction in Post-Swallow Pharyngeal Residue After BB-301 Dose
Thin Liquid	4.9	0.9	4.0 Units (-81.6%)
Moderately Thick Liquid	18.2	11.0	7.2 Units (-39.6%)
Extremely Thick Liquid	21.5	11.9	9.6 Units (-44.7%)
Solid Food	19.0	12.3	6.7 Units (-35.3%)

Subject Reported Outome Measure: Sydney Swallow Questionnaire or "SSQ" (17-Question Self-Report Inventory Assessing Subjective Symptoms of Oropharyngeal Dysphagia)

OPMD Natural History Study	Phase 1b/2a BB-301 Dosing Study	
Pre-Dose Period	Post-Dose Period	
Average SSQ Score for the Study Subject	Day 90 SSQ Score for the Study Subject	Reduction in SSQ Score After BB-301 Dose
1,136	935	201 Points (-17.7%)

Cold Water Timed Drinking Test: Time in Seconds the Subject Requires to Consume 80 mL of Cold Water

	OPMD Natural History Study	Phase 1b/2a BB-301 Dosing Study	
	Pre-Dose Period	Post-Dose Period	
Barium-Containing Food Items	Average Time (sec) Recorded for the Study Subject	Day 90 Time (sec) Recorded for the Study Subject	Reduction in Total Drinking Time (sec) After BB-301 Dose
Thin Liquid	30	26	4.0 Seconds (-13.3%)

**Company data on file*

Regarding the BB-301 safety profile observed to date, no Serious Adverse Events have been observed for the two subjects that have received BB-301. Transient Grade 2 Gastroesophageal Reflux Disease or "GERD" (i.e., "acid reflux" or "heartburn") was

observed for the two subjects that received BB-301. For both subjects, the GERD resolved following the completion of a short course of common prescription medications approved for the treatment of GERD.

OPMD is a rare progressive muscle-wasting disease caused by a mutation in the poly(A)-binding protein nuclear 1 (PABPN1) gene, for which there is currently no effective drug therapy. The disease is characterized by swallowing difficulties (dysphagia), limb weakness and eyelid drooping (ptosis). Dysphagia worsens over time and can lead to chronic choking, regurgitation, aspiration pneumonia, and in severe cases, death. Available clinical and surgical interventions are limited in scope and effectiveness and do not address the underlying progressive muscle weakness.

Virtual R&D Event Information:
This live virtual R&D Event, featuring two OPMD key opinion leaders, will be held at 9:00 AM EDT today, April 18th, 2024 and can be accessed here. The event replay will be placed on the News & Events tab on the Investor page of the Benitec website.

About BB-301

BB-301 is a novel, modified AAV9 capsid expressing a unique, single bifunctional construct promoting co-expression of both codon-optimized Poly-A Binding Protein Nuclear-1 (PABPN1) and two small inhibitory RNAs (siRNAs) against mutant PABPN1. The two siRNAs are modeled into microRNA backbones to silence expression of faulty mutant PABPN1, while allowing expression of the codon-optimized PABPN1 to replace the mutant with a functional version of the protein. We believe the silence and replace mechanism of BB-301 is uniquely positioned for the treatment of OPMD by halting mutant expression while providing a functional replacement protein.

About Benitec Biopharma, Inc.

Benitec Biopharma Inc. (“Benitec” or the “Company”) is a clinical-stage biotechnology company focused on the advancement of novel genetic medicines with headquarters in Hayward, California. The proprietary “Silence and Replace” DNA-directed RNA interference platform combines RNA interference, or RNAi, with gene therapy to create medicines that simultaneously facilitate sustained silencing of disease-causing genes and concomitant delivery of wildtype replacement genes following a single administration of the therapeutic construct. The Company is developing Silence and Replace-based therapeutics for chronic and life-threatening human conditions including Oculopharyngeal Muscular Dystrophy (OPMD). A comprehensive overview of the Company can be found on Benitec’s website at www.benitec.com.

Forward Looking Statements
Except for the historical information set forth herein, the matters set forth in this press release include forward-looking statements, including statements regarding Benitec’s plans to develop and potentially commercialize its product candidates, the timing of 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, the clinical utility and potential attributes and benefits of ddRNAi and Benitec’s product candidates, the intellectual property position, 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: 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; 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 Company's ability to satisfy its capital needs through increasing its revenue and obtaining additional financing, given market conditions and other factors, including our capital structure; our ability to continue as a going concern; the length of time over which the Company expects its cash and cash equivalents to be sufficient to execute on its business plan; the impact of the COVID-19 pandemic, the disease caused by the SARS-CoV-2 virus and similar events, which may adversely impact the Company's business and pre-clinical and clinical trials; 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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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/a47d2f41-3feb-49a7-a58f-62e5b0dd4332

Source: Benitec Biopharma Inc.

Figure 1



Improvement in All Outcomes at 90-Days Post-BB-301 Injection*