ASX/NASDAQ ANNOUNCEMENT

Benitec in-licenses clinical program for head and neck cancer from NantWorks

- Returns Benitec to clinical stage company
- Clinical proof of concept achieved via demonstration of durable anti-tumor activity in advanced head and neck cancer patients
- Continued development under planned research collaboration with NantWorks

Sydney, Australia, 23 December 2016: Benitec Biopharma Limited (ASX:BLT; NASDAQ: BNTC; NASDAQ: BNTCW) today announced that it has executed an exclusive, world-wide sublicensing agreement that will enable Benitec, in collaboration with NantWorks, to develop a clinical stage asset to treat Head and Neck Squamous Cell Carcinoma (‘HNSCC’) using a gene silencing approach that targets the Epidermal Growth Factor Receptor (EGFR).

According to GlobalData (Head and Neck Squamous Cell Carcinoma – Opportunity Analysis and Forecast to 2024, February 2016), approximately 64,000 new patients will be diagnosed annually in the US with HNSCC and 50% of the patients are expected to develop recurrent or metastatic disease, with approximately 13,000 annual deaths expected in the US from HNSCC.

Benitec’s Chief Executive Officer, Greg West said: “Squamous cell carcinoma of the head and neck is a debilitating and hard-to-treat disease associated with a very poor prognosis. We are excited to be able to continue the clinical development of this promising asset. As we move into the 2017 calendar year, our team remains steadfast in its commitment to generate shareholder value through the use of gene silencing technology to develop clinical stage assets. Completing this sublicense is a key step in our continued engagement with NantWorks, one that I believe to be extremely important as we move our company into its next phase. I look forward to providing further updates on this, and other initiatives in the new year.”

The asset is comprised of a DNA plasmid which produces an antisense RNA to silence EGFR (referred to here as ‘EGFR-AS’). EGFR is a well validated oncology target and has been shown to be a key driver of the growth of HNSCC lesions with more than 80% of HNSCC lesions exhibiting significantly elevated levels of EGFR versus concentrations found in non-malignant tissues. The collaboration between Benitec and Nantworks is anticipated to also include the development of a novel compound utilising Benitec’s proprietary ddRNAi gene silencing platform against a related family of therapeutic targets underlying the core pathophysiology of HNSCC.

INITIAL CLINICAL RESULTS WITH THE EGFR-AS ASSET

The anti-tumor efficacy of EGFR-AS has been explored in patients with advanced HNSCC with lesions that were unresponsive (‘refractory’) to standard anti-cancer therapies (Lai, et al., Journal of Clinical Oncology, 2009). The Phase I study, comprised of 17 evaluable patients with advanced, refractory HNSCC, evaluated the safety and efficacy of the EGFR-AS following direct injection into the cancerous lesions.

- Five patients (i.e. 29% of the evaluable Phase I study patients) achieved ‘Objective Responses’ with reductions in the sizes of their tumors by at least 30% of the original size.
Two of these patients experienced ‘Complete Responses’ (i.e. reductions in the sizes of the injected malignant lesions of 100% by Response Evaluation Criteria in Solid Tumors or “RECIST” criteria) and three Phase I study patients experienced “Partial Responses” (i.e. reductions in the sizes of the injected malignant lesions of ≥ 30% by RECIST criteria).

Two additional patients achieved ‘Stable Disease’ (i.e. a change in the sizes of the injected malignant lesions of -29% to +19%), leading to an overall “Disease Control Rate” of 41% for the 17 patients.

Importantly, the $\text{EGFR-AS}$ was only administered to target malignant lesions once per week for four weeks. Yet, in the seven patients that achieved Complete Responses, Partial Responses, and Stable Disease, the median duration of the observed anti-tumor response was 6.5 months.

No Grade 3 or Grade 4 toxicity or Dose Limiting Toxicity was noted in the Phase I study.

Collectively, these clinical data clearly illustrate $\text{EGFR-AS}$-driven anti-tumor activity.

COMPARISON TO OTHER EGFR-TARGETED ANTI-CANCER THERAPIES IN DEVELOPMENT

The current efficacy profile of the $\text{EGFR-AS}$ compares favorably with that of other EGFR-targeted anti-cancer therapies that have been evaluated for the treatment of HNSCC.

In a Phase II, 115 patient, multicenter Phase II study evaluating erlotinib (an EGFR receptor tyrosine kinase inhibitor) for the treatment of recurrent or metastatic HNSCC, Souileres, et al. (Journal of Clinical Oncology, 2004) reported that no Complete Responses were observed among the study patients and only 5 patients in the study achieved a Partial Response (i.e. 4.3% of patients achieved Objective Responses). The median duration of the erlotinib-driven anti-tumor response was 2.4 months.

Vermorken, et al. (Journal of Clinical Oncology, 2007) conducted a multicenter Phase II study evaluating cetuximab (a monoclonal antibody against EGFR, and currently approved for use in HNSCC) in 103 patients with recurrent or metastatic HNSCC that failed to respond to platinum-based chemotherapy and reported that no Complete Responses were observed among the study patients and 13% of patients achieved Partial Responses (i.e. 13% of patients achieved Objective Responses). The median duration of cetuximab-driven anti-tumor response was 4.1 months.

In comparison, the Objective Response rate of 29%, with a 12% Complete Response rate, and duration of anti-tumor response of 6.5 months following treatment with the $\text{EGFR-AS}$ asset in the Phase I study demonstrates a significantly higher response rate and more durable, anti-cancer activity.

Importantly, biomarker analyses conducted in a subset of the 17 patients from the initial $\text{EGFR-AS}$ Phase I study suggest a strong correlation between the level of EGFR present in the HNSCC tumor tissue at baseline (i.e. prior to the administration of the $\text{EGFR-AS}$ injection) and the magnitude of the clinical anti-tumor response observed in the Phase I study patients. Thus, the use of molecular diagnostics for early biomarker analyses suggest that testing might identify HNSCC patients that are likely to respond to the $\text{EGFR-AS}$ injection prior to the initiation of therapy.
For a disease like HNSCC, in which significant patient morbidity is derived from locoregional tumor growth and tumor progression within the confines of small anatomical spaces comprising the head and neck (e.g. difficulty speaking, difficulty chewing and swallowing solids and liquids, oral pain, throat pain), therapies that can facilitate durable tumor size reductions or complete eradication of malignant lesions could, potentially, help to meaningfully improve the quality of life and clinical outcomes for patients suffering from this disorder.

Dr Jerel Banks, Chief Investment Officer of Nant Ventures, commented, “NantWorks has pioneered the development and commercialization of an industry-leading suite of molecular diagnostics focused on the use of genomic and quantitative proteomic data to guide therapeutic interventions (‘GPS Cancer’), and the use of a paired drug and diagnostic strategy employing our proprietary technology during the continued clinical development of the EGFR-AS asset should be employed. This strategy could support the potential for a rationally-designed and highly efficient clinical development program and bolster the commercial exclusivity of the EGFR-AS asset.”

**FOLLOW-ON CLINICAL STUDIES WITH EGFR-AS**

Finally, the EGFR-AS asset was subsequently evaluated in a follow-on clinical study that enrolled 6-patients with advanced HNSCC to explore potential EGFR-AS-driven improvements by its addition to a pre-existing multi-agent anti-cancer treatment regimen comprised of cetuximab along with Intensity-Modulated Radiotherapy. The combination of cetuximab with radiation therapy, approved for treatment of locally or regionally advanced HNSCC, has a demonstrated Objective Response rate of 74%.

- In combination with the radiation and cetuximab, the addition of EGFR-AS resulted in five of the six patients (83%) experiencing Objective Responses, with three patients experiencing a Complete Response and the two others achieving a Partial Response.
- Additional combination studies, using significantly higher number of patients, are likely to be explored in the upcoming clinical development plan.

Benitec will work with NantWorks to finalize the terms of its scientific collaboration with a targeted date for execution of 27 January, 2017. Benitec expects to be in a position to release further details following execution of that agreement. As the terms of the scientific collaboration are subject to the execution of a definitive agreement, there can be no assurance that such an agreement will be entered into or as to what these terms will be. The sublicensing agreement is an exclusive royalty bearing license with related development milestone payments.
About Head and Neck Cancer:
Cancers that are known as head and neck cancers usually begin in the squamous cells that line the moist mucosal surfaces inside the head and neck, such as inside the mouth and the throat. In 2016, approximately 64,000 new cases of head and neck cancer are estimated to be diagnosed in the U.S., resulting in more than 13,000 deaths. Head and neck cancers are more than twice as common among men as they are among women. Squamous cell carcinoma of the head and neck accounts for more than 90% of all head and neck cancers, and more than 50% of HNSCC patients present with Stage III or higher disease (locally advanced or metastatic), which has higher potential for progression and recurrence. The relative five-year survival rate for metastatic head and neck cancers is <38%, and can be as low as 4% for recurrent or metastatic Stage IV disease. Total drugs sales in the HNSCC markets in the seven major markets (United States, France, Germany, Italy, Spain, United Kingdom and Japan) will increase from $386 million in 2014 to $1.53 billion in 2024, at a Compound Annual Growth Rate (CAGR) of 14.8%.

Reference: GlobalData Report (February 2016): Head and Neck Squamous Cell Carcinoma – Opportunity Analysis and Forecast to 2024

About Benitec Biopharma Limited:
Benitec Biopharma Limited (ASX: BLT; NASDAQ: BNTC; NASDAQ: BNTCW) is a biotechnology company developing innovative therapeutics based on its patented gene-silencing technology called ddRNAi or ‘expressed RNAi’. Based in Sydney, Australia with laboratories in Hayward, California (USA), and collaborators and licensees around the world, the company is developing ddRNAi-based therapeutics for chronic and life-threatening human conditions including hepatitis B, wet age-related macular degeneration and OPMD. Benitec has also licensed ddRNAi to other biopharmaceutical companies for applications including HIV/AIDS, Huntington's Disease, chronic neuropathic pain, cancer immunotherapy and retinitis pigmentosa.

Safe Harbor Statement:
This press release contains “forward-looking statements” within the meaning of section 27A of the US Securities Act of 1933 and section 21E of the US Securities Exchange Act of 1934. Any forward-looking statements that may be in the press release are subject to risks and uncertainties relating to the difficulties in Benitec’s plans to develop and commercialise its 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 Benitec’s product candidates, potential future out-licenses and collaborations, the intellectual property position and the ability to procure additional sources of financing. Accordingly, you should not rely on those forward-looking statements as a prediction of actual future results.