BARD1 CANCER VACCINE STUDY RESULTS

- **Completion of collaborative cancer vaccine study with IRH to evaluate a potential BARD1 vaccine**
- **Significant effect of a 5-peptide BARD1 vaccine showing delayed tumour growth, prolonged survival and induced immune response in a malignant mesothelioma mouse model**
- **No effect of the same 5-peptide BARD1 vaccine in lung, colon or breast cancer mouse models**
- **Results are encouraging but will require further research to evaluate different BARD1 antigens, vaccine formulations and doses to determine best cancer vaccine strategy**

Perth, Australia, 15 February 2019: BARD1 Life Sciences Limited (ASX:BD1), a medical technology company developing non-invasive cancer diagnostics, today announced results that showed a significant vaccine effect in malignant mesothelioma supporting further research to develop a potential BARD1 vaccine using an optimised vaccine strategy.

While BARD1's core business is the development and commercialisation of cancer diagnostics, it is also interested in exploring the therapeutic potential of its technology for future collaboration or licensing purposes.

Objectives

The cancer vaccine study was an exploratory research program undertaken in collaboration with the Institute for Respiratory Health (IRH) to evaluate a potential BARD1 peptide vaccine for the prevention and/or treatment of cancer in mouse models. The study examined the effect of a vaccine formulation containing five different BARD1 peptides at a total 100 µg or 200 µg dose, using both preventative and therapeutic approaches on tumour size, tumour growth and immune response in four different mouse models of cancer.

Results

BARD1 previously reported encouraging initial results showing delayed tumour growth in a malignant mesothelioma mouse model in a Company Presentation released in November 2018. The final results are set out below and confirm a significant but moderate vaccine effect on tumour growth, survival and immune response using a 5-peptide BARD1 vaccine in the AB1 malignant mesothelioma mouse model.

Malignant mesothelioma model

Analysis of prophylactic experiment-1 (vaccination given before tumour cell inoculation) using a 200 µg dose of the 5-peptide BARD1 vaccine in eight AB1 inoculated mice (4 vaccinated: 4 controls) showed a significant vaccine effect with 76% reduction of tumour growth rate (p=0.02), prolonged survival (p=0.03) and positive likelihood ratio (LR) test[1] (p=0.03) compared to controls in a cancer model of malignant mesothelioma. The prophylactic experiment was repeated in Experiment-2 which was performed in 16 mice (8V:8C) but the difference between tumour growth rate in vaccinated and control mice was not significant. However, when prophylactic experiment-1 and -2 was combined (12V:12C) there was an overall significant effect on tumour growth rate with 58% reduction (p=0.04). A therapeutic experiment (vaccination given after tumour cell inoculation) in twelve mice (8V:4C) showed a significant but moderate vaccine effect in prolonged survival (p=0.02) and positive likelihood ratio (p=0.04), see **Error! Reference source not found.**.

Statistics / Vaccine	Growth rate ratio Vacc/Control		Tumor volume 1st endpoint Vacc/Control		Survival time to endpoint Average days Vacc minus Control		TumGrowth package analysis
	Ratio	***p-value***	***Ratio***	***p-value***	***Difference (days)***	***p-value***	***ANOVA II Likelihood Ratio (LR) test p-value***
Prophylactic exp.1	0.24	0.02	0.54	0.11	4	0.03	0.03
Prophylactic exp.2	0.56	0.25	0.85	0.59	2	0.48	0.24
Proph. exp. 1 & 2 combined	0.42	0.04	0.86	0.56	2	0.41	0.06
Therapeutic exp.	0.58	0.32	0.47	0.07	7	0.02	0.04

Table 1. BARD1 vaccine results in malignant mesothelioma mouse model (AB1 cell line). Probability or *p* value < 0.05 is considered significant. See endnote for description of measurements[2].

The immune response was also assessed with a well characterised *in vitro* assay (ELIspot) using immune cells isolated from vaccinated and control mice. A moderate but significant specific immune response ($p<0.05$) was observed in vaccinated animals. The response was strongest for peptides specific for isoforms BARD1α, BARD1δ, and BARD1η.

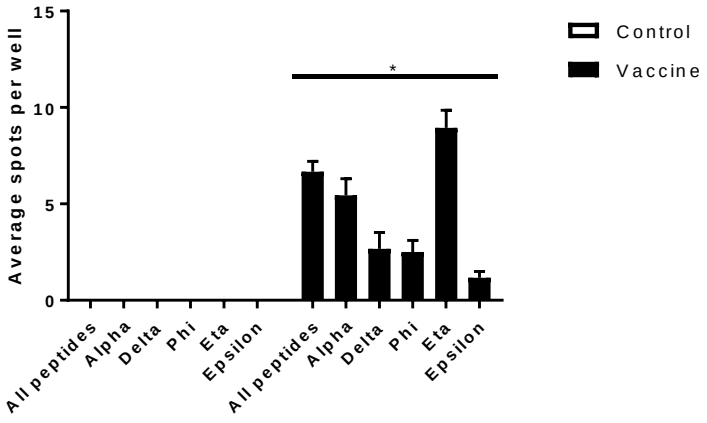

Figure 1. ELIspot assay showing IFN-γ production in T-cells isolated from 3 vaccinated and 3 control mice when exposed to BARD1 peptides separately or combined, n=6 for each mouse, * $p< 0.05$.

Lung, colon and breast cancer models

Analysis of both prophylactic and therapeutic experiments showed no significant effect of the same 5-peptide BARD1 vaccine at either 100 µg or 200 µg dose on tumour growth rate, tumour size, survival or likelihood ratio in the other lung (LINE 1 cells), colon (CT26 cells) or breast (4T1 cells) cancer mouse models tested. However, individual mice showed reduced tumour growth rate and prolonged survival. These results suggest that tumours induced by these cell lines escaped the immune response in the majority of vaccinated animals.

Conclusions

The study concluded that the 'naked' 5-peptide BARD1 vaccine showed a significant but variable vaccine effect on tumour growth, survival and immune response in the malignant mesothelioma model using both prophylactic and therapeutic approaches. However, no significant vaccine effect was observed in the lung, colon or breast cancer models. These findings suggest that the 5-peptide BARD1 vaccine formulation and dose selected in this study is unlikely to be optimal and therefore further studies are required to optimise the therapeutic effects of BARD1 vaccines on tumour growth in different tumour types.

Next steps

BARD1 Executive Director and CSO Dr Irmgard Irminger-Finger said: "These results are consistent with previous independent studies that showed that cancer-specific BARD1 epitopes are immunogenic and protect against tumour progression in a mouse model of colon cancer[3] and subsequent research showing that a BARD1 DNA vaccine decreased tumour progression in a rat model of ovarian cancer[4]. Therefore, it is feasible that with alternative vaccination strategies using DNA or BARD1 isoforms (proteins), improved formulations and optimal dosing, that a BARD1 vaccine has the potential to be an effective cancer vaccine."

"Identifying novel Tumour-Associated Antigens (TAA) or neoantigens is a high priority in cancer research for use in combination with novel immune response-enhancing methods or existing cancer immunotherapies.[5] These early research results suggest that BARD1 is an important TAA and potentially a neoantigen that could be developed as a cancer-specific vaccine in combination with existing methods such as bi-specific antibodies[6], chimeric antigen receptor (CAR) therapies[7] or specific therapies such as PD-1 and PD-L1 inhibitor therapies[8] to treat various cancers."

IRH Associate Professor Steven Mutsaers added: "This was an exploratory research program that showed a small but significant immune response in the BARD1 vaccinated animals compared to the adjuvant controls using a crude vaccine formulation, which requires further investigation to determine its biological importance. Importantly, these findings suggest that different peptide combinations, formulations and doses need to be evaluated to determine the best vaccine strategy for different cancers."

BARD1's core business and focus is advancing the development and commercialisation of its cancer diagnostic pipeline for early detection of breast, ovarian and lung cancers. However, BARD1's tumour marker platform also has potential therapeutic applications. Therefore, the Company will consider the findings from this exploratory study, discuss alternative vaccination strategies with industry experts, and seek to explore the therapeutic potential of its intellectual property (IP) in collaboration with experienced partners to evaluate potential vaccines using BARD1 DNA or proteins for the treatment of specific cancers.

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ABOUT BARD1 LIFE SCIENCES LTD

BARD1 Life Sciences Ltd (ASX:BD1) is an Australian medical technology company focused on developing and commercialising non-invasive diagnostic tests for early detection of cancer. BARD1 owns a proprietary tumour marker platform with potential diagnostic and therapeutic applications across multiple cancers. The pipeline includes BARD1 autoantibody tests in development for early detection of breast, ovarian and lung cancers. Additional diagnostic projects will be evaluated for other cancers. The company also has a cancer vaccine project at research-stage for treatment of cancer. BARD1 is committed to transforming the early detection of cancer to save lives. For more information on BARD1, see www.bard1.com.

ABOUT THE INSTITUTE FOR RESPIRATORY HEALTH

The Institute for Respiratory Health is a collaborative respiratory research organisation. It aims to improve the life of everyone living with a respiratory condition by bringing together world class researchers and dedicated clinicians to investigate, diagnose, treat and prevent respiratory conditions. The Institute conducts and fosters innovative basic and clinical research and translates its work into improved treatments for people with respiratory conditions. The Institute for Respiratory Health campaigns for an increased awareness and investment in respiratory education and research. It focuses on real people and its work gives hope for a better future to those with respiratory disease.

DISCLAIMER

This announcement contains “forward-looking statements” and “forward-looking information”, including statements and forecasts relating to the Company. Often, but not always, forward-looking information can be identified by the use of words such as “plans”, “expects”, “is expected”, “is expecting”, “budget”, “scheduled”, “estimates”, “forecasts”, “intends”, “anticipates”, or “believes”, or variations (including negative variations) of such words and phrases, or state that certain actions, events or results “may”, “could”, “would”, “might”, or “will” be taken, occur or be achieved. Such information is based on assumptions and judgements of management regarding future events and results. The purpose of forward-looking information is to provide the audience with information about management’s expectations and plans. Readers are cautioned that forward-looking information involves known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of the Company and/or its subsidiaries to be materially different from any future results, performance or achievements expressed or implied by the forward-looking information.

[1] The Likelihood Ratio (LR) test in this study is the likelihood that a given result would be expected in an animal with the vaccine compared to the likelihood that that same result would be expected in an animal without the vaccine.
[2] Table 1 legend: *Growth rate ratio* - The ratio between the average tumour growth rate of vaccinated and control mice; *Tumour volume 1st endpoint* - The ratio between the average tumour volume of vaccinated and control mice when the first tumour reached maximum permissible size (1000 mm^3); *Survival time to endpoint* - The average number of days between control and vaccinated mice that it took for the tumours to reach maximum permissible size; *TumGrowth package analysis* - Online tool to analyse complex data sets. Compares tumour growth rate, size and time to reach end point (1000mm^3) to give the likelihood ratio (or probability) that there is a difference between treated and control mice.
[3] Gautier et al. Cancer Research 2000
[4] Feki et al. 2009
[5] Nishimura et al. 2015
[6] Dahlen et al. 2018
[7] https://www.cancer.gov/about-cancer/treatment/research/car-t-cells
[8] Constantinidou et al. 2019