BIOSCEPTRE INTERNATIONAL LIMITED

NEWSLETTER JUNE 2020

Unique Opportunity to Invest in Next Generation Cancer Therapy

Dear investor

We hope you are keeping safe and well during these difficult times. Despite the challenges of COVID-19, Biosceptre continue to make significant progress both scientifically and in preparations for the new CAR-T clinical and GMP (good manufacturing practice) facilities in Sydney. We will provide more information on that in the next newsletter.

We would like to draw your attention to other aspects of Biosceptre that make this an exciting investment including details on the recent, successful completion of a phase 1 vaccine trial.

One of Biosceptre's great strengths is their solid patent wall around all aspects of the cancer target nfP2X$_7$. This has been reinforced by the recent deal with Carina Biotech (a South Australian CAR-T company). Essentially, this transaction takes out the only other player in the market that was looking at CAR-T with Biosceptre's target, considerably improving their IP position and creating a much greater moat around the use of CAR-T and their target. Any FTO (Freedom to Operate) will now be difficult for someone coming into this space.

Biosceptre currently have a patent portfolio of 186 patents in 14 families. Biosceptre will lodge considerably more IP in this space via both a divisional strategy under the two patents they have now negotiated from Carina Biotech and via new patent applications over the next 6-12 months. The deal also ensures that Carina will not compete in the nfP2X$_7$ space. The only work they will do is in collaboration.

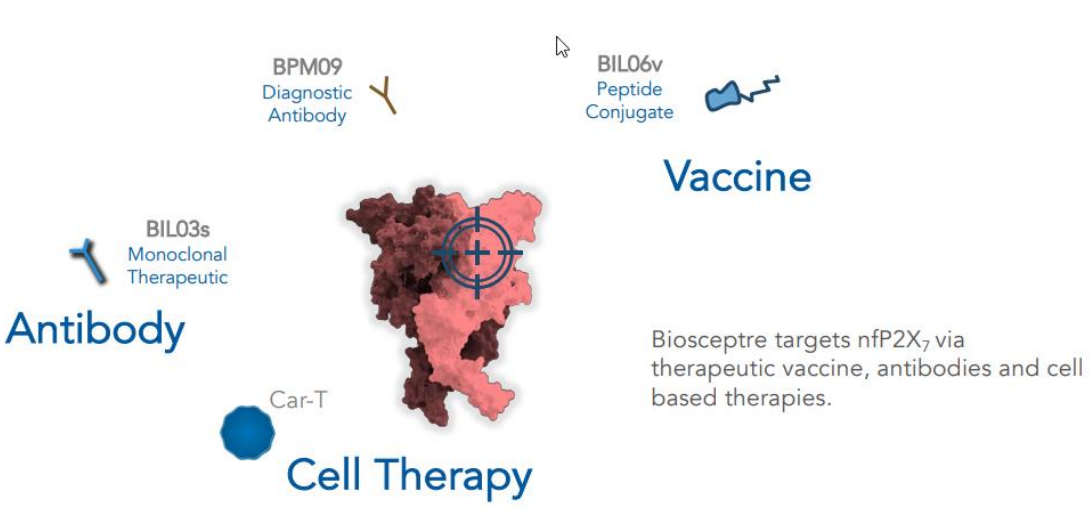
Before moving onto the multiple applications covered within Biosceptre's patent portfolio there are some terms that are important to understand that are used to assess whether a trial has been successful or not. These are expressed below in lay terms and not strictly scientific terms:

Affinity is how tightly a drug binds to its target; the targets often being referred to as receptors. It is rather like the attraction a magnet has to a metal.

Efficacy is the level of desirable response seen when the drug binds to its target e.g. killing of a cancer cell or, for a vaccine, the level of immune response produced by the vaccine. In clinical trials, efficacy can also relate to clinical outcomes.

Clinical trials: The primary objective in a phase 1 clinical trial is to demonstrate the therapy is safe, usually by using an escalating level of the therapeutic. Phase 2 & 3 trials are used to demonstrate the clinical efficacy of the therapy. Sometimes important indications of efficacy are also observed in phase 1 trials as demonstrated in the Biosceptre trials below.

Biosceptre's patent portfolio covers multiple applications which includes:



CAR-T Therapeutics:

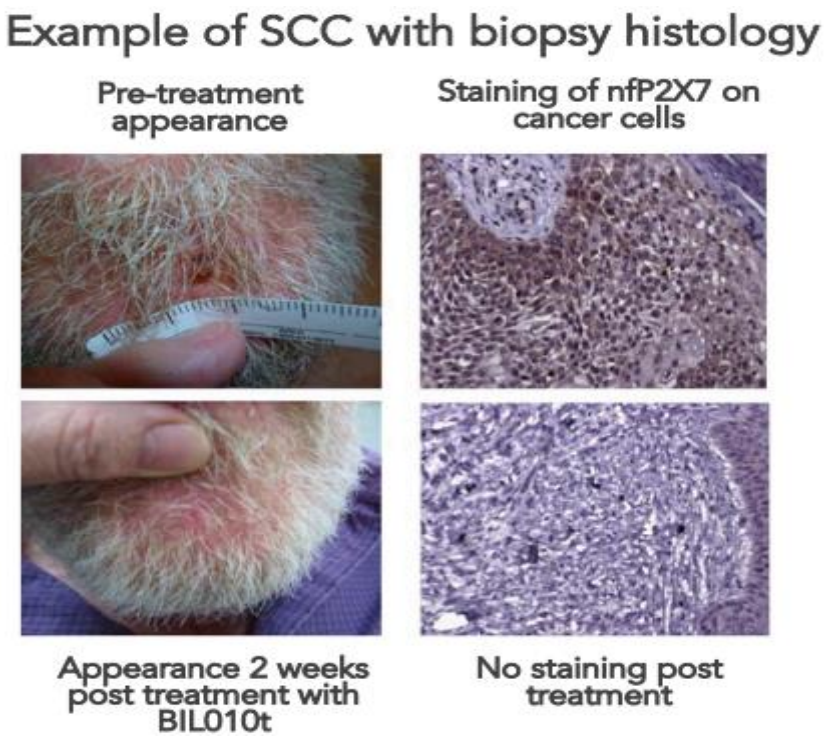
This will be the principal focus of the company as it promises the greatest benefit both clinically and financially and overcomes the issues of affinity seen with monoclonal antibodies. However, the following applications are all of value and could be potentially be divested or developed further in the medium term.

Monoclonal antibodies (MAbs) to nfP2X$_7$:

Monoclonal antibodies are the largest group of pharmaceuticals, by revenue, sold world-wide and are among the leading cancer therapeutics. Biosceptre have developed MAbs to nfP2X$_7$ but further work is required to improve the affinity of the antibody and that work is ongoing in collaboration with Professor Daniel Christ at the Garvan Institute of Medical Research in Sydney, Australia. Professor Christ is a former colleague of Sir Gregory Winter NL and he participated in the foundation of Domantis Ltd (sold to GSK for £230 million in 2006). In 2007, Professor Christ joined Garvan as Head of Antibody Therapeutics, translating structural and genomic advances into drug candidates and treatments for cancer and inflammatory conditions.

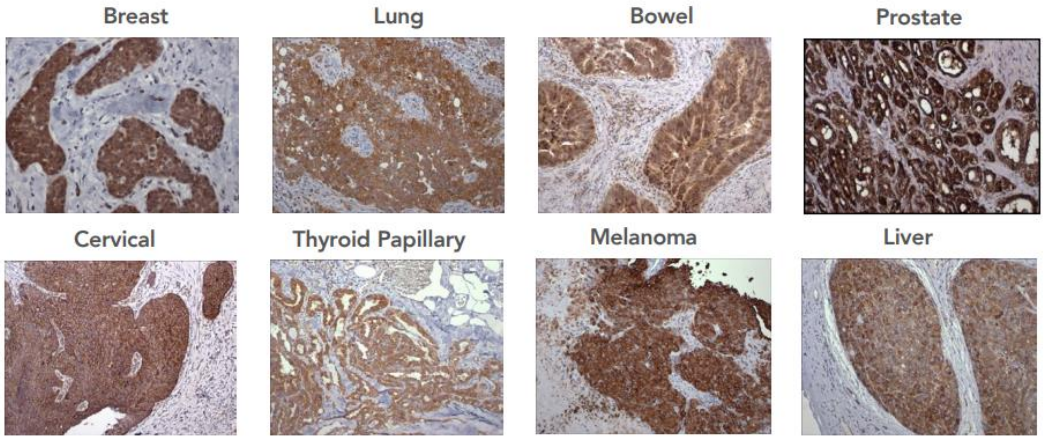
Polyclonal antibodies:

In a phase 1 FDA trial Biosceptre's topical administration of an ointment containing 10% sheep polyclonal anti-nfP2X$_7$ antibodies (BIL 010t) to primary basal cell carcinoma lesions demonstrated an excellent safety profile and indications of efficacy with 65% of subjects showing regression of surface lesions. A phase 1 trial is designed to show safety only, but the study is important in that it shows the efficacy of treatments targeted to nfP2X$_7$. Again, this is a promising application, but the financial and intellectual resources of the company will be focused on CAR-T.



Diagnostic antibodies:

One of the challenges in cancer diagnosis is detecting rare tumour cells in a tissue under the microscope. Modern methods include using a monoclonal antibody (where affinity is far less of an issue than in therapeutic MAbs). The antibody is labeled with a dye so the tumour cells can be visualized. However, this requires an antibody for a specific target on each tumour type and, unfortunately, most targets are found on normal cells and are just over expressed on cancer cells. The unique feature of nfP2X$_7$ is that it is only seen on cancer cells and is found in a large range of cancer types making it an ideal diagnostic target. Examples are shown below where the brown staining in the tissue section indicates cancer cells in the primary tumour.



There are a range of large life-science companies, distinct from therapeutic pharmaceutical companies, that will be very interested in this technology as it fits into the cytology and histopathology diagnostic market growing at 13.6% CAGR and is estimated to reach $34.5 Billion by 2027[1].

Vaccine:

The purpose of a vaccine to nfP2X$_7$ is to induce the patient's body to develop immune response to that target on cancer cells. The company has completed a phase 1 trial whose primary aim was to demonstrate safety of the vaccine. The data are currently being analysed but two features stand out:

1. The trial passed the phase 1 criteria of safety
2. Despite being immunocompromised, patients mounted an immune response to the vaccine

Vaccine
BIL06v

Phase Ib Trial – 29 patients recruited

Biosceptre

Patients	29 (2 cohorts (1000 and 1500mg dose) containing 10 and 19 patients respectively)
Trial Centers	2 Australian centres recruiting competitively – • Sydney Adventist Hospital (Wahroonga, Sydney NSW) • Sydney Southwest Private Hospital (Liverpool, Sydney NSW)
Patient Inclusion	Basket trial – primary focus on prostate, colorectal, and lung
Method	Subcutaneous Injection (BIL06v mixed 1:1 with Alhydrogel® 2%)
Study Objectives	• Primary – safety and serological immunogenicity. • Secondary – evaluate Dose Limiting Toxicity (DLT), determine Max Tolerated Dose (MTD) and/or Recommend Phase 2 Dose (RP2D), disease control rate (SD+PR+CR at 12 weeks), and Progression Free Survival (PFS) • Exploratory – QoL, overall survival, serum tumour biomarkers, cellular immunogenicity (*in vitro* restimulation)

SYDNEY ADVENTIST HOSPITAL

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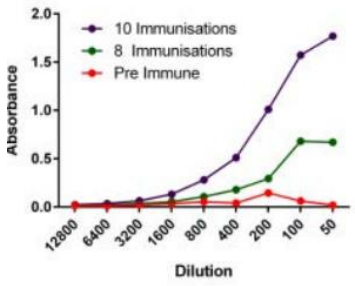
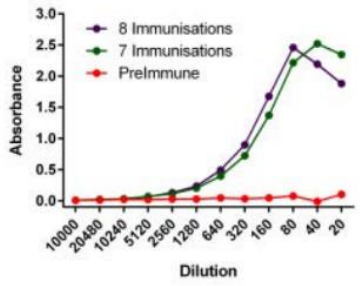
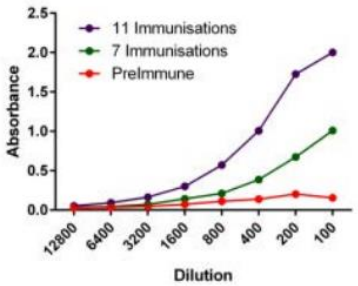
Memorial Sloan Kettering Cancer Center

Clinical Trial Design
Dr. Bob Li

As is common for a phase 1 study, this study was conducted in patients with advanced disease, usually with metastases. Such patients have a short life-expectancy and are usually highly immunocompromised. Nevertheless, those patients that survived the minimum 12-week period all mounted an immune response. As examples in the graphs below, the y axis (labelled absorbance) is an indication of the amount of antibody induced by the vaccine in individual patients.







Confidential

The next stage in Biosceptre's vaccine development would be to evaluate the vaccine for efficacy in patients with a low cancer burden, for instance, those who had undergone surgical removal of the primary tumour. Promising as that would be, Biosceptre is completely focused on delivering CAR-T.

As Dr. Julian Barden, Director of Research at Biosceptre, has commented:

"*In the vaccine trial, the total burden was not so large that you were fighting a forest fire with a garden hose, although there were times it felt like it. With CAR-T the garden hose becomes a giant airtanker dropping retardant in the centre of the conflagration. Moreover, through CAR-T cell expansion, it is like having an airtanker that refuels itself for repeat runs that end only when the fire is extinguished, i.e. when the target epitope is no longer expressed*."

As you can see, Biosceptre's patent portfolio is far reaching with the ability to generate significant revenues via diagnostics and alternative cancer therapies to CAR-T. Understandably, the main focus is on CAR-T[2] as this exciting new therapeutic modality offers the most promising route to clinical success. As an article in the Scientific American expressed *"its cancers most promising new therapy"*[3]. However, potential acquirers will be looking at not only the CAR-T patents but at the overall value of the patent portfolio and future revenue/value from that.

Do get in touch if you have any queries.

The Norcliffe Capital Team

References

1. (Grand View Research https://www.grandviewresearch.com/press-release/global-histology-cytology-market).
2. For more information on CAR-T see Cancer research UK: https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/immunotherapy/types/CAR-T-cell-therapy
3. https://www.scientificamerican.com/custom-media/eureka-frontiers-in-t-cell-therapy/the-unlikely-story-of-cancers-most-promising-new-therapy/