Newsletter to Shareholders

9th April, 2014

Where we have been

At the May 2013 Shareholder Meeting Caldera presented its strategy for the development of a molecular diagnostic prostate test based on next-generation sequencing technology (NGS). To achieve execution of the strategy, the following actions were laid down:

- Completion of Clinical Study 1 to validate RNA biomarkers and utilisation of an NGS technology platform for high throughput diagnostic purposes;
- Acquisition by Caldera of Illumina MiSeq NGS analyser;
- Appointment of a managing director with extensive medical diagnostic experience;
- Establish a process for the commercialisation of Caldera's prostate cancer diagnostics through partnering with one or more multinational diagnostic companies.

Since the July 2013 installation of the Illumina MiSeq sequencer, Caldera staff have had the in-house capability to validate the selected RNA biomarkers with prostatectomy tissue from samples stored at Diagnostic MedLab (Sonic Health) in Auckland. This work has comprised Clinical Study 1 and was completed in March 2014. The primary endpoints for this study were to:

- Validate the use of Caldera's RNA biomarker amplicon sequencing technology (RBAS) for multi- RNA biomarker analysis using human prostate cancer samples;
- Develop a "reference standard" that can be used to measure levels of RNA biomarkers in prostate cancer samples to replace the practice of using adjacent tumour tissue as a source of healthy tissue to measure increases or decreases in cancerous tissue samples from the same donor;
- Analyse RNA biomarker expression patterns in prostatectomy samples with Gleason scores ranging from 3+3 to 5+5 to determine differences that correlate with changing Gleason scores.

With the data from this now complete, Clinical Study 1 has demonstrated the following:

- Of the 85 RNA biomarkers we selected for the clinical study, 59 showed significant differential expression of RNA biomarkers in cancerous samples;
- We have established the first reference standard to be used as an independent control standard for interpretation of results from cancerous samples;
- We can distinguish RNA biomarkers that identify gene expression changes which are common across all stages of prostate cancer as reflected in Gleason scores;
- We can also identify RNA biomarkers that identify gene expression changes which are unique to certain stages of prostate cancer.

Where we are today

As advised at the recent March 2014 Annual Meeting the objectives set out at the May 2013 Shareholder Meeting and described above in "Where we have been" have been achieved.

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Clinical Study 1 has validated Caldera's gene signatures for the diagnosis of prostate cancer using stored prostate tissue. This now provides the basis to move forward to Clinical Study 2 which is designed to advance to a commercial diagnostic test by confirmation of which patient sample material (prostate tissue, blood, and urine) can be used for a commercial diagnostic test. Clinical Study 2 will also:

- Confirm the robustness and reproducibility of Caldera's RBAS technology;
- Optimise data processing by Caldera's unique analytical software to provide clinically usable results;
- Refine a reference standard as required for a laboratory diagnostic process.

Staff numbers have been increased with Dr Kristen Chalmet as Chief Scientist, reporting to Dr Jim Watson the Director of Science, and Dr Genevieve Johnston who joined in March this year as Clinical Study Manager responsible for the coordination of Clinical Study 2, beginning May, 2014.

Where we are going

While the data developed in Clinical Study 1 confirms our diagnostic process and the correlation of Caldera's biomarker patterns to Gleason scores in stored prostate tissue, more advanced data needs to be developed in order to demonstrate the utility of Caldera's technology as a reliable and accurate diagnostic test in a medical laboratory setting.

Clinical Study 2 is designed for this purpose and also examines the possibilities of using urine or blood sampling in addition to prostate tissue. Caldera will work with Auckland and Hamilton urologists to access their patient sample materials and it is projected that 9 to 12 months will be required to assemble this body of data.

Caldera management has previously described the significant opportunity environment for an accurate prostate test, given the inadequacies of the current PSA (prostate specific antigen) test. This test is controversial with medical opinion due to false positive and false negative reporting. This leaves a huge unmet clinical need, which in turn provides significant commercial opportunity.

Realisation of Caldera's RNA biomarker technology to complement or replace microscopic analysis of biopsy prostate tissue to diagnose and stage prostate cancer, would be a significant step forward in the management of the disease in cancer patients. However, the ability to use urine samples would result in a non-invasive test and consequently high clinical uptake.

Caldera will also determine if the RBAS technology can be transitioned to other epithelial cancers such as breast and lung.

The way forward

It is important to understand that the prostate cancer diagnostic is not a multipurpose technology with a large number of applications and customer groups. It is a product with a tightly defined application and market, being medical diagnostic laboratories, with local examples being Auckland Hospital Laboratory and LabTests which both process samples requested by doctors. Accordingly the market and its potential are readily identified.

However, access to this identified customer group is dominated by a limited number of large international diagnostic companies who have multi-year analyser / test reagent contracts with the laboratory customer. This makes it difficult, if not impossible in many cases, to readily access the customer. This in turn means volume can only be achieved by participation with one or more of the major players in the global diagnostic business.

Caldera is now engaged with two international diagnostic companies. However the ability of Caldera management to advise on the details of the meetings and communications to date is constrained by confidentiality agreements in place with these two companies. I can advise however that a face-to-face meeting took place in mid-March in San Francisco involving Jim Watson, myself, and two Caldera scientists. Our audience comprised senior management, global business development and senior research and development staff. A further meeting is scheduled for April 16 in Singapore with the management of the second diagnostic company we are engaged with.

What is clear is that there is a real interest expressed by these potential partners in the NGS prostate diagnostic under development at Caldera. What must be done to advance the interest to a commercial collaboration/ partnership is to move forward to completion of Clinical Study 2.

In summary:

- The customer group and market potential is identified;
- The commercial pathway to the opportunity is clear and understood;
- Initial R&D for Caldera's prostate test has been completed with Clinical Study 1;
- In Clinical Study 2 we move from research to development;
- Caldera is engaged with two international diagnostic companies who have confirmed interest in our unique technologies;
- To advance the interest to collaboration/partnership Caldera needs the data that is designed to be generated by Clinical Study 2.

Caldera now must focus on three strategic priorities

- Remain engaged with potential partners;
- Complete Clinical Study 2.
- Source the funding necessary to support and make possible the completion of Clinical Study 2.

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