CALDERA HEALTH

Newsletter to Shareholders

8th August, 2014

Caldera is in a busy phase with our scientific team heads down in the lab. Clinical Study 2 is under way and proceeding according to plan and budget. There will be little to report in the way of outcomes until the results of the study start to come together later this year or in the first half of 2015.

New Investment

Subscriptions of $515,720 were received by Caldera when the pro-rata offer of Series D to shareholders closed on 30 May 2014. Since then three new shareholders have invested a further $360,000 in Series D, giving a total receipts of $875,720. The Mercy Ascot Hospital Group is a new investor, through their subsidiary Integrated Hospitals Limited.

With the R&D grants, this total will carry Caldera into the very early part of next year. Your directors currently plan to keep the Series D issue open until funding is assured through to the end of Clinical Study 2.

R&D Grants from Callaghan Innovation

Last year the Government announced new grants aimed at promoting R&D expenditure in young companies developing new market products as well as encouraging more mature businesses to spend significant funds on their R&D. Caldera applied for an R&D Growth grant which is a three-year grant that provides 20 per cent public co-funding for a qualifying firms' eligible R&D expenditure, capped at $5m per annum. Caldera has just been informed its application has been successful and will be funded from July 1, 2014 initially for three years.

After two years of funding, Caldera may be granted a two-year extension of funding.

Clinical Study 2

Dr Genevieve Johnston is leading the organisation and management of this trial to determine the range of patient samples that could be used for prostate cancer diagnosis, from urine and blood to biopsies and other surgically removed tissue (prostatectomy). We have been given full Ethics approval for the study which is always a large amount of work, and Gen has organised physicians and donors throughout Auckland to help us in this study. And of course the staff have done a lot of work getting all the processes for the study stream-lined and refined.

Malaghan Institute

We will also be collaborating with Professor Graham Le Gros and his team in the Clinical study to use their sophisticated flow cytometry to actually characterise prostate cancer cells in urine. The Malaghan Institute is New Zealand's leading medical research institute based at Victoria University in Wellington. The Institute also has a major cancer programmes based around developing a novel immunotherapy cures for cancer.

Accounting

The Annual Accounts for the year ended March 2014 are ready for audit. Ernst and Young will carry out the audit over the next two months following the return of our Accountant Reg Schierling from overseas. Over the coming months Caldera will be updating its accounting system to use the New Zealand developed Xero software.

New Premises

Auckland University has given notice that they want to terminate our lease August 31, 2014. We are awaiting a decision on our application for suitable laboratory and office space, shared kitchen and meeting room facilities in the Callaghan Innovation building located in Balfour Street, Parnell. As a backup we have also looked at a range of other buildings with suitable space for our facilities

Staff

In June we welcomed Robin Kelly to the Caldera team. Robin has joined us from a research laboratory at the University of Auckland, where he completed his BSc with first-class Honours. Apart from a passion for molecular biology and clinical science, Robin also knows a little of the world of start-up business, being the founder and managing director of Last Tapes Theatre Company – a boutique theatre production company based in central Auckland.

Chiasma

Chiasma is an Auckland University student-led organisation that fosters connections between science and business, connecting university students to high-tech industries. Chiasma addresses New Zealand's need for innovative and professionally developed scientists to create our knowledge-based economy's next generation of leaders. Chiasma encourages innovation particularly in the field of biotechnology and creates links and networks between the University's biotech community and the New Zealand biotech sector. As part of the promotion of biotechnology, Chiasma runs "Synapse", New Zealand's science career fair for tertiary students. This gives graduate students a chance to interact with leaders and exhibitors from New Zealand's top science companies. On August 4th, Caldera was one of some 20 young companies that showcased their innovative science to students to highlight the importance of innovative science in New Zealand's future. This took place in the Auckland University Business School and was extremely well attended and a very successful evening.

Over the next few newsletters we will be including some Opinion Pieces about Prostate Cancer, written by Jim Watson. The first of these is appended.

Graham Watt
Managing Director

Jim Watson
Director of Science

Alastair MacCormick
Chairman

Caldera Health Limited
P: 09 5710310 F: 09 5272011 E: reception@caldera.co.nz
P.O.Box 11664, Ellerslie, Auckland 1542, New Zealand
Building 734, Ground Floor, Auckland University Tamaki Innovation Campus, 261 Morrin Rd., St. Johns, Auckland 1072

A Scientists View of Prostate Cancer

Part 1

I'm not a cancer physician, I am a scientist who has spent a life trying to understand what makes a cell a cancer cell. I am going to give you my view in the next several newsletters of the journey of our company in developing and marketing novel and more informative prostate cancer diagnostics than we have today.

The need for these diagnostics is reflected in the dramatic action of the United States Preventive Services Task Force (USPSTF) in downgrading the use of the PSA test for prostate cancer diagnosis to a "D" in May of 2012. A "D" grading means there is moderate or high certainty that the PSA test has no net benefit or that the harms outweigh the benefits.

The USPSTF was convened in the United States several decades ago to rigorously evaluate clinical research in order to assess the merits of preventive measures, including screening tests, such as the PSA test, counselling, immunizations, and preventive medications. It has become globally respected for the work it has done and continues to do. That is why their grading of the PSA test to a D has been taken very seriously worldwide. The statement recognises that prostate cancer is a spectrum of diseases, not just one disease, and why one biomarker, PSA, cannot diagnose the many stages of prostate cancer that form this spectrum.

We use the word cancer rather loosely to reflect an extraordinary range of diseases from very aggressive cancers like pancreatic cancer at one end of the spectrum, to more indolent cancers or non-life threatening cancers at the other. Prostate cancer as a disease spans this entire spectrum.

If a man lives long enough he is almost certain to grow a few cells in the prostate gland that look like prostate cancer under the microscope. While a diagnosis of prostate cancer may be used to describe such lesions, the vast majority of them are completely indolent and would never have caused any symptoms or threat to life had they not been diagnosed. Conversely, high risk or aggressive prostate cancer kill more men in New Zealand than any cancer, with lung cancer a close second, and is a major public health issue at the national level.

Physicians do their best to treat men according to the risk of the cancer they may carry. The cancer is staged and is one of the most important factors in choosing treatment options and predicting a man's outlook. The clinical staging is based on the prostate biopsy results (including the Gleason score), the PSA level, and any tests that were done to find out how far the cancer has spread. There are hundreds of scientific and clinical papers over the years that have studied these risk features.

As a result there are now universally accepted guidelines that are used to group men into low, intermediate, and high-risk disease. The Gleason Score we hear so much about is based on microscopic analysis of cell and tissue architecture from biopsies, and yields a cancer grade which reflects the development of the disease in the prostate. Prostate cancer staging goes

further to categorize the risk of cancer having spread beyond the prostate. This involves evaluating the size of a tumour, the extent of involved lymph nodes, and any metastasis (distant spread) and also takes into account cancer grade from the biopsy. As with many other cancers, these are often grouped into four stages (I–IV) from Stage I, a cancer that is found incidentally in a small part of the sample when prostate tissue was removed to Stage IV disease where the cancer has spread to lymph nodes or other organs.

The problem is there is really a very wide heterogeneity within low risk, intermediate risk and high risk categories. You can have two men, for example, in the intermediate group that have a completely different risk of dying of prostate cancer.

So these risk stratifications are not very satisfactory. We've known for many years that we need to move past the risk groups. Because there is no way to distinguish indolent or low risk cancer from aggressive prostate cancers, it is inevitable that the USPSTF have concluded that low risk disease is over-treated and that high-risk disease under-treated. This is a major problem for men with prostate cancer and the cost of health services.

Then the question is how do you determine cancer risk in other way?

Caldera is one of a small number of companies taking a new approach which involves analysing prostate cancer tissue and cells using the new science of cancer genomics. Several other well-known companies and institutions are taking similar paths, for example, Myriad Genetic Health, Genomic Health and major cancer centres at the University of California and the University of Michigan. We have in common looking at various genes in the cancer tissue itself to see which genes are up and down regulated (in other words, turned on and turned off in cancer cells.) But we are using different pathways to get there. The goal is to give us better insight, thus novel diagnostic tests, into which cancers that look low risk but will actually progress and, which cancers that look high risk may actually not progress.

In the next newsletter I will go on to discuss what we are doing that differs from other groups and why. This will give you better insight into our clinical study and its importance to our pathway to market.

J.D.Watson
7 August, 2014