

## ***Introduction***

Recent times have been both challenging and exciting, in terms of the crucial commercialisation activity being undertaken by the company, and also due to a difficult economic climate.

As Optiscan faces important transitions from an R&D company to a sales and marketing focused organisation, we recognise the need in these circumstances to maintain increased communication to shareholders.

Consequently the content of recent updates released to market (including this one) and the content of today's AGM presentation will be more detailed and specific than updates issued during the slower R&D phases of the company.

This shareholder update will cover:-

- A brief review of our products and how they will be developed and brought to market
- Market information and current marketing activities
- A brief update on our continuing development activities
- A review and update on some corporate issues

## ***Optiscan's Live Micro Imaging Technology***

Optiscan's technology uses a unique and patented combination of lasers, optical fibres and scanning technology to enable the production of miniaturised microscopic scanners which can be placed against living tissue to obtain live images at cellular detail.

The devices offer ~1000 fold magnification and can reveal cellular details at or just beneath the surface against which they are placed. The images appear as layers, or "optical sections" in real time on a computer screen, without the need for any surgical removal of tissue.

The technology offers views of live tissue never before seen, with implications for research, pharmaceutical monitoring and cosmetics.

We believe the existence of these devices has the capacity to change the way clinicians think about obtaining cellular level information from tissue.

Over time, the ability to detect, observe, characterise and monitor patients' tissues in this way offers major benefits in their management by clinicians.

Non-invasive detection of early stage disease and better monitoring of therapies holds the key to better outcomes for patients and long term cost savings to health systems.

## ***Optiscan's Patents***

Optiscan holds key patents in fibre optic confocal microscope systems, and the main patented feature is the use of the optical fibres themselves to make such systems miniaturisable.

Our preferred implementation works as follows. A single optical fibre is used to project a pinpoint of laser light into a specimen. Light emanating from the focused point is recaptured back into the same optical fibre, and returned to a detector. Light from outside the focused spot is not recaptured into the fibre and is therefore rejected from detection. In short, the detector can only "see" the focal plane illuminated by the fibre.

The image is then built up by scanning the fibre tip under control of a computer which also collects and displays the detector signal, mapping a picture onto the screen in real time as the laser spot scans the tissue.

Optiscan has also patented several key refinements and associated mechanisms required to implement these systems, including the scanning mechanism itself.

## ***Longer term patent protection***

As will be discussed later in this update, Optiscan engineering efforts have led to scanning mechanisms small enough to be inserted into the tips of flexible medical endoscopes.

Patents in this area have been taken out as recently as the past two years and offer significantly extended patent protection life to 2019 for Optiscan's most advanced implementations of the original concept.

The Optiscan patent portfolio now numbers twelve patent families and we believe this confers on Optiscan a strong intellectual property base and high degree of exclusivity in both the underlying technology, as well as specific improvements which enable all of the products anticipated for the foreseeable future.

As shareholders are aware, we successfully resolved alleged patent infringements with upfront fee and royalty bearing licences from the six major confocal microscope manufacturers. It is important to note that these relate to desktop microscopes only and specifically preclude the licensees from producing endoscopes.

We believe that Optiscan's Intellectual property base is one of its most valuable and commercially important assets.

## ***Selection of medical applications***

Optiscan's advancing patent portfolio represents a strong platform which could be exploited in numerous medical applications.

Virtually any tissue of the body which can be accessed by the miniature scanners potentially offers applications and access to a market segment within the associated medical speciality.

Optiscan has selected several key applications for product development, and is prioritising these on an ongoing basis.

The approach is to strategically balance issues of progress in miniaturisation, time-to-market, regulatory hurdles, potential market size and competition.

### ***Instrument Development Pipeline***

Consequently, Optiscan has for some time pursued two very specific product lines, and with recent progress, a strategy for the third is now emerging.

The first product is the Optiscan Stratum. This device features a hand-held scanner for skin examination, for which we have just received our first sales orders in the US. Skin examination was targeted first to balance time to market with minimal requirements for miniaturisation.

The second product is the flexible endoscope. A major technical milestone for Optiscan has always been to miniaturise the devices to the extent that they can be incorporated into clinically usable flexible endoscopes. This was achieved during the past year. There are now clinical grade prototypes and formal clinical work is expected to begin shortly.

As is discussed later in this update, we believe that there is a very large market for this device and we are progressing steadily with a path to commercialisation.

Finally, now that the above miniaturisation in scanning mechanisms has been achieved, Optiscan has the capability to easily and rapidly develop further devices with different shaped scanners for different applications. Plans are in place to perform pilot clinical studies in orthopaedic surgery (eg knees), examination of the cervix, and head and neck cancer in the near future.

### ***Market Development Strategy***

Parallel development of these products is important given that introducing new medical technology requires a multistage, strategic process.

The benefits of LMI must be established to gain acceptance.

Market uptake begins with clinical research by early adopters, and must transition to mainstream clinical usage through medical education.

This is the basis of Optiscan's marketing strategy.

Specifically, the key steps are:-

Step 1 - Pre-sales marketing and preliminary "proof of concept" clinical work

Step 2 - Regulatory approvals (FDA)

Step 3 - Establishment with market leaders

Step 4 - Initial sales to early adopters

Step 5 - Maturation of applications, and promotion of results by users

## Step 6 - Mainstream sales and marketing to broader market

It is difficult to predict the exact point at which the market is likely to mature. It is anticipated to be approximately 2 years, during which time sales can be achieved, but such sales would represent only a fraction of the greater market potential. After this time, the market should be mature and sales growth should rise markedly.

### ***The Stratum***

Skin examination was targeted for our first medical device product due to ease of miniaturisation and accessibility of the clinical applications. The Stratum features a hand held scanner which is placed into contact with the skin to reveal surface and subsurface cellular detail at approximately 1000X magnification. Images appear in real time on the computer screen and are digital.

Applications of the device include cellular examinations of diseases which include skin cancer, psoriasis and other inflammatory conditions, examination of penetration, localisation and effects of pharmaceuticals, cosmetics research, and a multitude of general dermatology research applications.

The potential benefits relate to the ability for a non-invasive, earlier detection of changes at the cellular level. The determination of what these actual benefits are, and their magnitude and significance will depend on each of the diseases being studied.

We received an FDA exemption which classifies the Stratum as a medical examination (imaging) device. This classification permits sale of the device in the US for any application desired by the user, but does not provide for any specific diagnostic claims. Hence we are at the point of achieving initial sales with early adopters and establishment of the technology with opinion leaders in dermatology. The list price for sale of the Stratum in the US is approximately US \$75,000.

### ***Clinical Trial Output***

An important step in the introduction of the Stratum was the collection of a image atlas (Australian clinical trials) of a substantial list of lesion types. This serves to demonstrate the imaging capability of the product in the one of the main areas of clinical interest - sun damaged skin and skin cancer.

The atlas demonstrates the characteristic appearance of the layers of normal skin, for comparison with the characteristic cellular differences observed in a variety of skin lesions.

The list of lesions examined and sample images for each type can be found on the Optiscan web site ([www.optiscan.com](http://www.optiscan.com)). Importantly, every lesion examined was biopsied and the lesion type established by conventional pathology. At this stage, the atlas forms an instructive demonstration of some of the capabilities of Stratum, and indeed this has stimulated interest resulting in the first purchase orders and further sales prospects. The determination of what the actual benefits of

Stratum are (and their magnitude and significance) will depend on each of the diseases being studied.

In some cancers for example which spread (or metastasise) early on then very early detection is vital.

In others, early detection may be of less importance. However, finding the margin for guiding surgical excision could improve the cosmetic and health outcomes for the patient.

Diagnosis of inflammatory conditions is often difficult, and rarely warrants the surgical invasiveness of a biopsy. Non-invasive LMI would be desirable for such situations.

Proving these benefits is the continuing goal of collaboration with our early adopters.

### ***Stratum clinical & research partners***

We are pleased to report that we have now established several clinical research sites, comprising some of the highest calibre cancer institutes and dermatological research schools in the US.

These include key users at Memorial Sloan Kettering Cancer Institute in NY, University of California, Davis and the Medical College, of Wisconsin. With the assistance of the key clinicians, researchers and pathologists at these sites we will be developing our standardised workflow for *in vivo* fluorescent imaging of skin and skin lesions.

Incorporation of such work into medical education material will form the basis of wider uptake and future market development activity.

We feel that the enthusiasm expressed by these prestigious groups and their desire to work with us is a positive indicator that our technology has good prospects of becoming an important tool in mainstream dermatology.

### ***Initial Market for Stratum***

Given the need to develop the awareness of the diagnostic efficacy of LMI in mainstream dermatology, it makes sense to target the research market initially and then feed into the clinical market as the technology gains market awareness through the work of opinion leading centres.

The customers in the short term will therefore be:-

- Leading dermatology research institutes
- Pharmaceutical companies
- Cosmetics companies

Sales are therefore expected to grow modestly over the next two years while the utility of the product in each application area is demonstrated by respected early adopters leading to broader market uptake.

## **Stratum Market Information<sup>1</sup>**

In the longer term, the market potential for Stratum in dermatological diagnosis is very large. The market need is compelling and economically driven, with substantial healthcare expenditure attributable to delayed or inaccurate diagnosis.

There are around 13,700 dermatologists practicing in the USA, and 75,500,000 visits to doctors for skin examinations per year (33,000,000 of which are to dermatologists<sup>1</sup>).

In the USA there are 1.3 million new cases of skin cancer each year, 51,400 of which are melanoma. Basal cell carcinoma (BCC) & squamous cell carcinoma (SCC) account for more than 1 million new cases each year. 9,800 people die each year from skin cancer (7,800 from melanoma)<sup>1</sup>

The direct medical costs of new skin cancers is \$US2.7B each year and indirect costs, mainly related to lost productivity, are \$2.6B per year<sup>1</sup>.

Psoriasis is also one of the major conditions seen by dermatologists, with more than 7 million sufferers in the USA, where direct costs of therapy are estimated to be US \$2.9 billion<sup>2</sup>.

Thus the market for Stratum could be very large if its role in the diagnosis and monitoring of these conditions can be defined and established in the mainstream.

### **\*\*Footnotes**

<sup>1</sup>Estimated by US Dept of Health and Human Services for 1999.

<sup>2</sup> National Psoriasis Foundation (USA)

## **Stratum Production**

Optiscan anticipates that production capacity at the present facility will be adequate to meet the foreseeable demand for the Stratum.

As of 8 November we will have built 13 Stratum units., and we have initiated a run of a further 8 units to feed into the early stage sales. Subsequent production runs are planned to be from 8 to 25 units based on need for next 1 to 2 years.

Production capacity is currently around 200 units per annum. This could be increased if required.

## **Medical Devices Markets**

Global markets for all medical devices are dominated by the USA and Western Europe.

The USA accounts for 45% of global sales, and EU for 30%, (10% is attributable to Germany, Austria and Switzerland).

Australia accounts for less than 5% but is an important market due to its accessibility to us and the high calibre of its medical practices and research.

Clearly, Optiscan must assume an international focus if it is to maximise value from the commercialisation of its technology.

### ***Stratum Sales & Distribution***

Geographically we will target Australia, USA, Europe and possibly Japan.

Recent activities have involved the Australian sales and marketing group conducting US based conference exhibits and roadshows to prospective customers by extensive travel to the US.

This activity has been successful in securing early sales prospects, establishing opinion leading reference sites and obtaining the first sales purchase orders.

Concurrent with this, we have established a US office which will now take over sales and support activity. This will maintain continuity in the market place, nurture our reference sites, and pursue further early adopter sales. We have now received three sales orders in the USA, and the units have been shipped this week. Installation is expected to be completed over the next two weeks.

It remains our long term goal to take on distribution partners as the market matures, or at such time that our growing presence enables us to attract favourable terms from an appropriate partner.

Optiscan's initial direct sales and marketing activities have resulted in substantial interest from potential distributors in other regions. We are pleased to report that this has led to the completion of a distribution agreement with Lawrenz Instruments of Germany, covering distribution rights for Germany, Austria and Switzerland. Under the terms of this deal, Lawrenz will directly engage all marketing and market development activities in these countries. The company has successfully completed Optiscan's distributor training program and will take delivery of its first unit in the near future.

### ***Flexible Endomicroscope***

As described earlier, we have recently made significant breakthroughs in the miniaturisation of our scanning technology.

This has enabled integration with the tip of a conventional medical endoscope for clinical endoscopic applications.

This is an important milestone and represents an extreme exploitation of our enabling intellectual property base.

The device was exhibited at the world's largest gastroenterology conference, International Digestive Diseases week attended by over 20,000 delegates in Atlanta, USA in May 2001.

This generated a great deal of interest from gastroenterologists, clinical researchers and endoscope companies alike, particularly for the ability to image internal structures at the cellular level without biopsy. Potential applications in gastroenterology include diagnosis and early detection of colon cancer, inflammatory conditions, Barrett's oesophagus and gastric cancer. Although not yet a product, we have produced clinical grade prototypes for trials.

### ***Rigid Endomicroscopes***

Having achieved the miniaturisation of the scan mechanism, it has now become a straightforward exercise to package the device in various ways for different applications.

Consequently, we now have two designs of clinical grade rigid endoscope prototypes, with potential applications in gynaecology, orthopaedics, head and neck cancer, urology and keyhole surgery.

In the short term, pilot clinical work has been planned for applications in orthopaedics gynaecology, and head and neck cancer examination. This work should further clarify priorities in extending the product range.

### ***World First examination of human colon***

The success in miniaturisation has allowed the first imaging of the human colon in vivo, demonstrating the viability of performing such procedures.

Clear stable images of colonic mucous crypts were visualised in cellular detail. Formal clinical trials are now being planned to assess the viability of using these devices to detect pre-cancerous tissue in high risk colon cancer patients.

### ***Endo-Microscope Market Information<sup>1</sup>***

There is an enormous market potential for flexible and rigid endo-microscope to provide microscopic images of early changes in internal structures at the cellular level.

The incidence rate for colorectal cancers in the leading industrialised countries of the world appears to be increasing each year both on an age adjusted basis and with the increasing age demographics.

The mortality rates for colorectal cancers, while trending downward due to better detection and improved treatment, are still very high and there is a real gain to be made here with the introduction of a more accurate and earlier detection techniques. The faecal occult blood test (FOBT) is notoriously inaccurate as a screen test and follow-up examination by standard colonoscopy at present looks for macroscopic

changes which are often only observed late into the development of the colon cancer. We believe that a confocal endo-microscopic examination can detect cellular changes far earlier.

Total annual sales of endoscopes and minimally invasive surgery devices is US \$4.2 B<sup>1</sup> of which 17% or US \$714 M sales relates to gastroenterology applications. About half these sales relates to the accessories leaving about US \$357 M annual sales for the endoscope devices which average US \$20,000 per endoscope, thus accounting for around 18,000 unit sales of endoscopes globally per year, or around 8,100 unit sales per year in the US (ie 45% of global).

We believe that a significant proportion of these current sales could involve the incorporation of a confocal insert at a price premium.

*\*\*Footnotes*

<sup>1</sup>*Theta Report No. 711.*

### ***Flexible Endoscopes - path to market***

The flexible endoscope market is very different from the dermatology market in that it serves a well defined market segment which routinely invests heavily in capital equipment.

Furthermore, the optimal path to market which we anticipate for flexible devices is impacted greatly by the fact that the scanner must be integrated with a conventional endoscope for use in common procedures.

We strongly believe, therefore, that the most efficient path to market for this technology involves partnering with an endoscope manufacturer to perform at least some of the final manufacturing process which yields the integrated device.

We have already entered into early but active discussions with major international endoscope manufacturers.

Our strong patent portfolio combined with the market awareness surrounding our technical success in producing the first devices has attracted significant interest from relevant parties.

### ***Rigid Endoscopes - path to market***

The production of the Stratum now serves as a platform for the development of rigid endomicroscopes. These would require only comparatively minor product development to accept alternative forms of scanner. Such scanners would serve various applications, being small enough to be viable as arthroscopes (eg knee examination), proctoscopes (rectal examination) or colposcopes (cervical examination).

Therefore, most of the Stratum development effort would be reused without change for each of several possible rigid endomicroscope products.

Unlike the flexible device, the rigid endomicroscopes do not require integration with existing devices, so product development would be completely within Optiscan's control and capability.

Ultimately, delivering the product to market would be best achieved in partnership with a rigid endoscope manufacturer.

However it is our intention in the short term to continue clinical evaluation of several potential applications before prioritising product development in line with commercial opportunity.

Our ability for rapid development should not be underestimated in this market. Using the Stratum platform, slightly different shaped scanners can be developed to meet numerous applications and therefore new market segments.

### ***Medical Advisory Board***

Further to the list of reference sites for the Stratum, specific members from these sites and other clinicians representing other specialties have agreed to act for a medical advisory capacity for Optiscan.

The advisory board's function is to steer our development efforts and in so doing, optimise the utility of our technologies in clinical medicine.

As our list of applications and clinical interest grows, we will be adding to this board to ensure that all applications are represented.

The list is published on our web site ([www.optiscan.com](http://www.optiscan.com)) and is expected to be extended in the near future as we progress into clinical evaluation of applications including orthopaedics, Obstetrics and gynaecology, and head and neck examination.

### ***Competition***

Optiscan core protected intellectual property relates to its miniaturisation technology.

There are presently no other vendors offering confocal microscopy miniaturised to endoscopic or even hand held dimensions.

However Lucid Technologies has produced a reflectance mode bulk optical confocal microscope for dermatological microscopic imaging. Although not miniaturised, the company actively promotes the role of skin microscopy in dermatology and is therefore complementary in terms of market development.

We believe that the hand held configuration of Stratum represents its key competitive advantage.

Our further miniaturised devices, the flexible and rigid endomicroscopes are unique and there are no directly competing products. There are however, concerted research efforts to exploit Optiscan fibre optic approach so as to achieve in vivo cellular imaging. This validates the market need for such capability, however we do not believe that any implementations could presently be commercially implemented without infringement of one or more of Optiscan's patents.

### ***Consumables and Disposables.***

There are several forms of products associated with the use of Optiscan's devices which offer substantial follow up business.

We believe that the use of contrast agents (fluorescent agents which enhance image contrast) hold the key to repeatable and easy to interpret images. So far, this has involved the use of common clinical contrast agents. The intent is that these would be packaged for single procedure use. The production of such a product is presently under consideration with the manufacturers of the contrast agents, and is not yet an Optiscan product.

However we believe that this area offers exciting growth in Optiscan's product portfolio and ability to generate revenues per procedure. There would be potential for several products associated with various medical procedures.

In the longer term, there is also the potential for use of very specific contrast agents which may tie in with therapies. An example of this would be to monitor the production of highly specific proteins in cancer cells, which may be the target of a therapy. We have recently published two papers in peer reviewed journals on preliminary work underpinning this potential application.

Progression towards procedures in orthopaedics (eg knee surgery), head and neck cancer and gynaecology relate to the use of a rigid endomicroscope requiring a sterile tip. Consequently the rigid endomicroscope has been designed with a removable, sterilisable tip.

For present usage in pilot clinical studies, the tips are manufactured by Optiscan and sterilised for each use.

In the longer term, common medical practices would demand that this would be disposable, potentially representing significant per-procedure revenue streams. The value of this business is dependant on each application or type of procedure, and will form an important consideration for impending product development choices as discussed earlier.

### ***Board and senior executive management***

We are pleased to report that the Board and senior executive management staff of Optiscan has been significantly expanded since our last AGM.

Keith Daniel recently joined Optiscan's Board as a non-executive Director and brings more than 30 years experience at the forefront of Australian Biomedical Technology.

Over nearly 30 years, Keith held positions ranging from design through manufacturing, marketing and CEO with various companies in the Nucleus group (which was acquired by Pacific Dunlop Limited in 1988). He is hence well versed in commercialisation of Australian technology in global markets.

Further details of Keith's career and present involvements can be found on our web site at ([www.optiscan.com](http://www.optiscan.com)).

The executive management team has also been significantly expanded over the last six months.

John Allen brings a wealth of intellectual property management and commercialisation experience to the now full time role of Licensing and IP manager. The other new addition since last years AGM is Russell Thompson, who brings with him many years medical device commercialisation experience. Having worked in senior executive roles at companies including GE medical and Ausonics, he has also joined the team as director of marketing and business development. Again, further details are available on our web site.

The Directors believe that Optiscan has sound management in place to enable it to achieve the company's objectives.

### ***Financial Outlook***

The company incurred an average burn rate of around \$400,000 per month during 2000/2001. By the end of the financial year (30 June, 2001) the cash on hand was just on \$7.0M.

In the first four months of the current financial year, the average burn rate has increased slightly due to increased travel and marketing expenses. However, this will be mitigated somewhat by a decline in the level of inventory spending. We currently hold most of the inventory required to meet our production schedule over the remainder of the financial year.

Cash on hand at 31 October is \$6.3M. This has been bolstered by the final START grant receipt of \$1M. The company had accrued \$600,000 of this amount, and the balance of nearly \$400,000 is an additional grant funding entitlement claimed by the company.

One of the key parameters in the immediate outlook is the 12 million options which are due for exercise in February and March 2002. If all of these options are exercised, they will contribute around \$2.5M in funding. At the present time we anticipate that most if not all options will be exercised.

On this basis, we expect to have around \$5M in June 2002. This would provide funding for much of the following year, until early or mid 2003 without factoring sales revenues. This forecast position will be further enhanced by early Stratum sales (as the build cost has already been covered), but it is difficult to forecast future sales in an immature market with any certainty.

We will continue to pay close attention to our cash position and it will be carefully assessed throughout the course of next year.

## **Summary**

In summary, the directors believe that your company has progressed strongly both technically and commercially.

- The Stratum is now a product.
- We have formed key relationships with several respected sites in the US, received the first purchase orders, and established means of ongoing sales, distribution and support in five countries. There are also positive signs in the skin microscopy figures strongly in future of dermatology.
- We have a rich product pipeline. Flexible endoscopes are now a reality and can enter formal clinical usage. Rigid endomicroscopes of clinical grade have also been built and open exciting new markets for our platform. The emerging new product directions are becoming clearer, and can be prioritised increasingly on commercial priorities rather than technical feasibility.
- We are in a good position for partnering. We have broad patent coverage serving as a barrier to entry into miniaturised microscopic examination devices, demonstrated proof of concept in rigid and flexible endoscopy.
- After four years, we have accumulated losses of around AUD\$10M for bringing our technology to the above described points of commercialisation on several fronts. This is considerably less than the costs some other new technology companies have incurred.

We thank you for your participation in Optiscan and trust that this update has been informative.