



Phosphagenics

news

NOVEMBER 2014



UPDATE FROM THE CEO

2014 has been a busy period for Phosphagenics as we progress our various programs, including late-stage trials for our pioneering pain patches and acne product and move closer towards their commercialisation. The recent oversubscribed capital raising provided a demonstration of the high regard in which our expanding platform technology is now held, with \$19.3 million raised through a successful placement and subsequent Share Purchase Plan.

The capital raising puts the Company in a strong position to fulfil our primary objectives of funding vital Phase 2 clinical trials for the two transdermal opioid patches, the TPM®/Oxymorphone patch for moderate to severe chronic pain and the TPM®/Oxycodone patch for peripheral pain indications.

The TPM®/Oxymorphone patch has passed the most critical hurdle by demonstrating that it can deliver oxymorphone into plasma in concentrations consistent with therapeutic levels. This was validated in two separate clinical trials, with each of the 27 subjects involved in both trials achieving therapeutic levels of oxymorphone. As previously reported, the Company plans to commence a Phase 2 clinical trial of its TPM®/Oxymorphone patch in the United States in 2015, while a proof-of-concept Phase 2a TPM®/Oxycodone patch will be conducted in Australia.

The Company has achieved a number of significant milestones in 2014, including:

- The completion of a proof-of-concept Phase 2 clinical trial on the TPM®/Tretinoin gel for the treatment of acne vulgaris with very encouraging results;
- Completion of a single dose pharmacokinetic clinical trial for the TPM®/Oxymorphone patch that established the drug elimination parameters and reproducibility of the product;
- Both Novartis and Themis launched a prescription topical diclofenac gel in India. Voveran® TPM® gel was launched by Novartis and Themis launched its Instanac® TPM® gel. Both products are formulated with our TPM® drug delivery system;
- The launch of a customised cellulite/toning cream specifically formulated and sold by Phosphagenics to our South Korean partner, the Korean Drug Company;
- Acquisition of Le Métier de Beauté Inc by a US-based private equity company keen to exploit our TPM® technology to grow sales; and
- Positive results from a proof-of-concept study on the use of the TPM®/Oxycodone patch to treat shin bone soreness in racehorses by our animal health partner, Veterinary Research Australia (part of the Integrated Animal Health group).

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As well as these achievements and while remaining focused on its opioid programs, when time permitted the Company continued to develop its next generation of products referred to in the March newsletter including;

- The continued optimisation of the TPM®/Diclofenac patch to a stage where it may be assessed by potential partners;
- The continued development of a TPM®/Lidocaine patch;
- The development of a further TPM®/NSAID product, specifically an Ibuprofen gel;
- The TPM®/Ketoconazole program has been deferred while we determine the strategic direction of our dermatological program. Following the excellent results obtained in the recent trial of our TPM®/Tretinoin product, we have commenced out-licensing discussions with several parties.

Notwithstanding the success we continue to have with TPM® applications across our portfolio, our two transdermal opioid patches demonstrate the greatest commercial potential and remain our main focus.

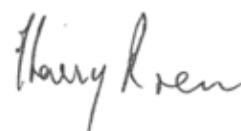
The TPM®/Oxymorphone patch program is gearing up to file an Investigational New Drug (IND) application with the US FDA, a precursor to the commencement of a US-based Phase 2 trial. This trial will be an important milestone on the road to gaining FDA registration of the patch in the USA and will be of interest to potential partners. With the US market

accounting for approximately 70% of the world's opioid consumption, the benefits of undertaking the study in the USA are clear.

At the same time, we have strengthened our management team to help oversee the critical stages of our Opioid Patch Program and to steer our first two patches towards commercialisation. Mark Gawel was recently appointed as Senior Project Manager. Prior to joining Phosphagenics, he performed a similar senior project management role at CSL. Later in this newsletter, as will become a feature in future newsletters, we will introduce our shareholders to two members of our exceptional team, Alisha Smith and Peter Lynch.

I am grateful to our team's dedication to our Company and would like to sincerely thank all the Phosphagenics staff who have shown great loyalty to me and the Company since my return from the USA. They are our most important asset.

– Harry Rosen, CEO



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NEW WEBSITE LAUNCHED

Today, Phosphagenics launched its revitalised brand and new corporate website. This represents a significant advancement for the Company in terms of branding and online identity. The previous company logo had been a part of Phosphagenics since 2004.

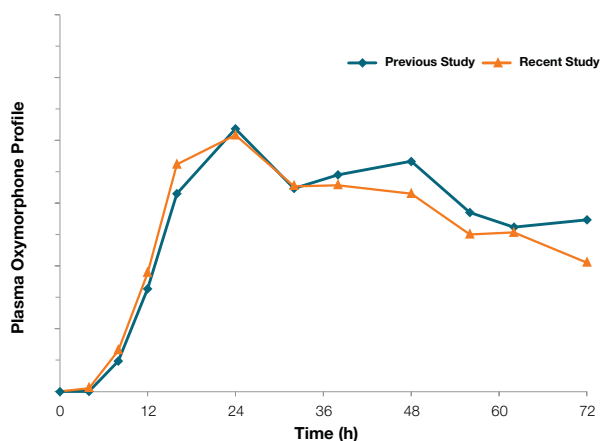
We encourage shareholders to visit the website at www.phosphagenics.com where the full details of the Phosphagenics brand update can be found. We hope that shareholders will find our new online presence a vast improvement on the previous website.

PAIN PROGRAM UPDATES

ADDITIONAL TRIALS FOR THE TPM®/ OXYMORPHONE PATCH

In July we initiated the first of two trials to examine the principal design and pharmacokinetic characteristics of the TPM®/Oxymorphone patch required for the submission of an IND to the US Food and Drug Administration (FDA). 'Pharmacokinetic' refers to the manner in which the body processes a drug, including the rate of drug absorption, metabolism and excretion.

The first of these 'characterisation trials' was a three week study conducted at the Linear facility in Perth involving 15 healthy volunteers. In August we announced the results of the trial which highlighted several exceptional outcomes, the most noteworthy being the uncanny reproducibility of the previous results announced in October 2013. Furthermore all 15 subjects achieved therapeutic plasma concentrations of oxymorphone, making it a 100% positive result in all 27 subjects used in our two studies.



The second study is an open label pharmacokinetic and safety trial using multiple site single dose applications to demonstrate that delivery from different parts of the body (eg flank, thigh, chest or arm) are consistent, and to determine the rest period required before safely reapplying patches to the same anatomical site. This information is critical for developing the protocol of administering patches to patients and also determining key labelling information.

We recently received ethics approval for this 6-week trial involving 20 healthy volunteers in the lead



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up to the Phase 2 trial. The information from both trials, together with an animal toxicology study, will inform the IND that is planned to be filed with the FDA next year. This clinical trial (and all later stage trials) will use patches manufactured by our contract manufacturer (CMO) in the US. It will commence as soon as technical transfer from us to the CMO has been completed and we receive the clinical supplies from them. Manufacturing reproducibility and scale up of the patch is one of the critical elements required to be included in our submissions to the FDA before an IND is approved.

The timing and details of the US-based Phase 2 clinical trial will become clear once we conduct our pre-IND meeting with the FDA. We expect the US Phase 2 trial will enroll approximately 200-240 chronic pain patients at multiple clinical sites, with the pain indication likely to be for chronic lower back pain (CLBP).

Phosphagenics is confident that this US-based trial represents the most timely and effective means of presenting a complete package to the FDA, and increasing commercial interest in our continuing discussions with potential development and licensing partners.

TPM®/OXYCODONE PATCH PROOF-OF-CONCEPT TRIAL

Our TPM®/Oxycodone patch program will achieve a significant milestone with the launch of a Phase 2 proof-of-concept trial to validate the ability of topically applied oxycodone to reduce localised neuropathic pain. The trial will test the hypothesis that inflammation caused by peripheral nerve injuries up-regulates opioid receptors in the skin, thereby allowing a peripherally delivered opioid agonist (such as oxycodone) to provide non-systemic pain relief.

It is clear that the ability to relieve pain by administering opioids topically, with little or no systemic delivery, would create a highly effective breakthrough for complex neuropathic pain conditions such as post-herpetic neuralgia (PHN), as well as other local pain conditions such as osteoarthritic joint pain. Non-systemic delivery would also reduce many of the risks and side effects associated with other routes of administering opioids.

Phosphagenics expects to receive ethics approval for the proof-of-concept Phase 2 trial shortly. The trial will involve 25-30 PHN patients at a number of sites, using a single dose cross-over design (against a vehicle control patch) and pain scores to measure effectiveness. Recruitment for this trial may take several months to complete. However, the trial will only take approximately four weeks to complete once recruitment is finished. As with the oxymorphone patches, these patches will be manufactured by our US CMO and, therefore, requires technical transfer of the manufacturing method to them. GMP patch manufacturing facilities do not exist in Australia.



COMMERCIAL AVAILABILITY OF TPM®/ DICLOFENAC GELS IN INDIA

Early uptake by consumers of two TPM®-based diclofenac gel products in India, the Novartis Voveran® TPM® gel and Themis Instanac® TPM® gel, has been very good. While concrete sales figures are not yet available, TPM® reorders from the manufacturer, Themis Medicare, point to a positive sales trend. Although the low retail price of diclofenac products in the Indian market will limit Phosphagenics' revenues, these reorders indicate a promising level of retail demand for TPM®-based gels.

The packaging of the Novartis product, which was launched earlier this year as a prescription drug, highlights the superior delivery properties of the TPM®-based formulation compared to other diclofenac gels. The packaging also prominently displays Phosphagenics and the TPM® technology. Phosphagenics remains confident of expanding its diclofenac products into other territories, with several companies indicating their interest. With the global market for diclofenac products exceeding US\$1 billion annually, the Indian launch presents an excellent opportunity to leverage our technology into other countries and to other products, especially NSAIDs.



DERMATOLOGY & SKINCARE UPDATES

SUCCESSFUL ACNE TRIAL RESULTS

At the beginning of October 2014 Phosphagenics announced the results of the recently concluded proof-of-concept Phase 2 acne vulgaris trial, which set out to compare the effectiveness and user friendliness of our TPM®/Tretinoin gel against that of the market leader, Retin-A. As an exploratory study, the trial was not powered for statistical significance, but the results surpassed all our expectations for such a small trial.

There were three formulations used in this study.

- TPM®/Tretinoin gel (0.05% w/w tretinoin);
- An active control, Retin-A (0.05% w/w tretinoin; Valeant); and
- A negative control, a vehicle containing TPM® without tretinoin.

The results demonstrated each of the three formulations produced statistically significant reduction in total (inflammatory and non-inflammatory) lesion counts. The TPM®/Tretinoin formulation had the greatest reduction in lesion count with the difference between it and the negative control (vehicle) being statistically significant. The Retin-A did not show significance compared to the vehicle.

IGA scores are a qualitative assessment of the severity of acne. The trial was conducted on patients suffering with mild-moderate cases (levels 2 and 3). Success is defined as a reduction in 2 points on the IGA scale. The number of patients that achieved a 2-point reduction was similar across the three treatment groups. However, 70% of patients treated with the TPM®/Tretinoin formulation showed an improvement of 1 or 2 points on the IGA scale. Only 42% of subjects treated with Retin-A and 46% treated with the vehicle showed a similar improvement.

The TPM®/Tretinoin formulation has therefore displayed a higher mean acne reduction than Retin-A as measured by both of the major clinical endpoints recognised by the FDA; total lesion count and IGA score.

Skin reactions such as erythema and dryness are common side effects of topical tretinoin therapy. These can be especially bad in the early weeks-to-months of treatment, before the skin has begun to develop some tolerance to the drug. This is usually the period in which patients discontinue treatment due to the severity of the adverse skin reactions,



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“...a number of studies have confirmed that Vital ET® provides a superior delivery of the renowned anti-inflammatory and anti-erythematous properties of Vitamin E.”



and is therefore a major limitation to topical retinoid therapy. Retin-A performed as predicted in this study with respect to erythema and dryness. The number of Retin-A patients who suffered erythema and dryness increased significantly ($p < 0.05$) after only two weeks of treatment and remained above baseline for the remaining period of the trial. The number of patients suffering erythema and dryness did not increase after two weeks of treatment with TPM®/Tretinoin and remained low for the duration of the study. The TPM® was therefore able to prevent the major limitation of the commercial product, adverse skin effects commonly associated with tretinoin.

Of further interest from the study was the performance of the TPM® Vehicle formulation. The commercial implications of the results produced by the TPM® vehicle are being assessed to consider a TPM® only gel that could be suitable for the OTC market.

Whilst the study was small in patient numbers and exploratory in nature, the performance of the Retin-A was perfectly aligned with published clinical results. This gives us confidence that the relative performance of the TPM®/Tretinoin formulation would be maintained and validated in larger clinical trials, solidifying real commercial benefits to the product.

The prospects for our dermatology programs have been bolstered by the appointment of Dr Geert Cauwenbergh to the Phosphagenics Board of Directors. Dr Cauwenbergh is an industry veteran renowned for his successful track record in developing and commercialising dermatological drugs.

IMPROVED SALES OF VITAL ET®

Vital ET®, Phosphagenics' multi-purpose Vitamin E ingredient, is expected to see annual sales exceed A\$1 million for this year, with most of these sales skewed to the second half of this year. Vital ET®,

a product distributed by our partner Ashland Inc., is a complex form of Vitamin E phosphate. Ashland has conducted human studies that have demonstrated a wide range of potential uses, including the reduction of redness and irritation due to sunburn, acne and shaving. Additionally, a number of studies have confirmed that Vital ET® provides a superior delivery of the renowned anti-inflammatory and anti-erythematous properties of Vitamin E.

NEW PARTNERSHIPS DRIVE DIVERSE SKINCARE OPPORTUNITY

The first half of the year has seen progress made in our two existing arrangements for private label, skin toning formulations. The arrangement with the giant US nutritional company, GNC, saw follow-up orders of the product. Our second partner, the Korean Drug Company (KDC), earlier this year launched its product using the Miss Korea Pageant as the platform for its launch.

The acquisition of Le Métier de Beauté Inc. by a private US company, while retaining the senior management team, has boosted the potential for the premier skincare brand to make greater use of Phosphagenics' TPM® technology. Increased funding for marketing and sales will likely lead to an increased royalty stream from the New York based company, with the new buyer paying the total outstanding royalties of US\$325,000 that was owed to Phosphagenics from 2013.

BIOELIXIA® body shaper

multi purpose
rescue balm

BIOELIXIA®

Sales of BioElixia® skin and body care have stabilised but remain depressed compared to previous years.

Sales to David Jones, Myer and Priceline remain modest but, comparable to last year, in a turbulent and unpredictable retail space. Discussions with the home shopping channel TVSN, where BioElixia® was previously a top selling product, continues with a view to resuming sales through this channel. The resumption of this major source of revenue would be a positive development for our cosmetics division.

To complement its popular BodyShaper range, BioElixia® launched a new product, the Multi-Purpose Rescue Balm, last quarter. Early indications suggest that the product has been well received by retailers and consumers alike. Formulated with our Vital ET® ingredient, the Rescue Balm is a 'supercharged' form of Vitamin E cream with lavender, camomile and rosewater extracts which has proved highly effective in countering the effects of the sun and wind, nappy rash, shaving rashes and dry, uncomfortable skin. Our acne trial results have demonstrated the power of TPM®.

For shareholders who are registered on the BioElixia® website, look out for this exciting new product. To register, go to www.bioelixia.com.

Soothing the
appearance
of irritated
unhappy skin.

With
Vitamin E,
Chamomile,
Lavender
and Rose



ANIMAL HEALTH UPDATE

Our Australian partner in animal health is now consolidated under the control of a single company, Integrated Animal Health (IAH), with a program to rapidly commercialise TPM®-based products for use in animals.

With a marketing program targeting nutritionists and dairy farmers, the uptake of products for the dairy industry continues to grow. In New Zealand we have assisted IAH in obtaining the requisite regulatory registrations to complement discussions that are taking place with some of the country's larger dairy companies. New Zealand's herd population is about 2-3 times larger than the Australia market and ownership is more concentrated.

IAH has spent most of the first half of this year putting together an experienced team to focus on the many TPM®-based opportunities that it has developed for the animal health sector.

In May we announced the results of a successful study on the use of TPM®/Oxycodone patches on thoroughbred racehorses suffering from cannon (shin) bone soreness, which showed that complete pain relief was achieved within 24 hours. While the study involved a small number of horses, it provided a proof-of-concept that should help with the development of a suitable product.



Integrated Animal Health™

MANAGEMENT PROFILES

ALISHA SMITH, CLINICAL TRIALS PROJECT MANAGER:

“US trial will show true colours of our incredible pain patch.”



The next year will be a critical time for Phosphagenics, as we move ever closer to the prospect of regulatory approvals for two transdermal pain patches that could bring relief to millions of pain sufferers. It will also be a critical period in the career of our Clinical Trials Project Manager, Alisha Smith, who for the past three years has been overseeing the complex web of logistics, approvals, patients and data that make up the Company's human trial programs.

“I am really looking forward to next year's Phase 2 trial in the United States, which I am confident will show the true colours of the incredible TPM®/ Oxymorphone patch,” says Alisha. “This is a vital step in confirming the efficacy of this unique product and paving the way for its commercialisation in the world's largest pain market.”

Since September 2011 Alisha has been managing the administration of the Company's various human trials, from designing their protocols and liaising with the researchers who conduct them, to recruiting patients and coordinating the statisticians and data managers who analyse the results.

Much of Phosphagenics' business strategy is based on the data and results of these trials, and it is paramount that the integrity of these processes remains above question. The results of these trials will provide the core data for an IND application – the key document required to conduct trials in the US and a prerequisite for approval by the FDA.

Before joining us Alisha gained a wealth of experience at CSL and Acrux where she occupied key management roles in a number of clinical programs. Today all her experience is focused on the prospect of successful clinical trials for Phosphagenics' product portfolio.



PETER LYNCH, REGULATORY AFFAIRS MANAGER:

“Big ideas and bold plans need a regulatory strategy to match”

Since joining the Company as Regulatory Affairs Manager back in January 2014, Peter has been hard at work coordinating and advising on the multiple chemistry and manufacturing controls (CMC), nonclinical and clinical requirements that must be fulfilled to steer our product successfully through an FDA approval process.

But however large the task, Peter relishes the challenge. “Phosphagenics has big ideas and bold plans with the patch, and these require a considered and appropriate regulatory strategy,” he says. “The opportunity to play a key role in helping Phosphagenics commercialise a transdermal pain patch is extremely exciting. We have a fantastic team here, with every member dedicated to doing whatever it takes to achieve our goals.”

Peter holds the primary responsibility for collating and informing the IND application that will be required before commencement of a Phase 2 trial of the oxymorphone patch in the USA. His role includes interpreting FDA regulatory requirements

and working with our internal team and external consultants to provide key inputs to virtually every aspect of the development process – from CMC, animal toxicology and Phase 1 trials through to later stage Phase 2 and 3 trials. An important part of this process is our pre-IND discussions with the FDA and ensuring the implementation of any recommendations from the agency on our opioid patch program.

Peter is well qualified to lead this initiative, having managed several submissions to the FDA as Senior Regulatory Project Manager at CSL Limited. Prior to working at CSL, Peter spent several years at the Therapeutic Goods Administration in Canberra – the Australian equivalent of the FDA - working in various roles in the evaluation of prescription medicines for the Australian market.

Peter is legally qualified with a recently completed post-graduate law degree as well as a Bachelor of Science (Pharmacology).

