



Phosphagenics

news

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- Increased market value as a result of commercial strategy

Welcome to the latest instalment of the Phosphagenics newsletter and the last one for 2016. The company has had a very busy and productive second half of the year culminating in a number of announcements this month. Since our last newsletter, there have been several significant developments and announcements that I would like to highlight to our shareholders.

R&D ACTIVITIES

In late 2nd quarter 2016 Phosphagenics agreed to grant **Terumo Corporation** a six month exclusive option to undertake technical/scientific and commercial due diligence on both the TPM[®]/Oxymorphone and TPM[®]/Oxycodone patches for the Japanese market. Terumo Corporation is a leading Japanese healthcare company with a market capitalisation in excess of ¥1.4 trillion and an eye to expand further into both the Japanese and broader international markets.

Following six months of extensive due diligence, including a joint International Scientific Advisory meeting in New York City, Terumo requested further time to complete its assessment. In November, we announced we had agreed to grant Terumo Corporation an extension to this exclusive option for an additional three months.

During the next phase of discussions, Phosphagenics and Terumo will work together to conclude the assessment and move towards a potential development and licensing agreement. Any such agreement will typically start with a

term sheet which would outline the terms of payment by Terumo to Phosphagenics followed by a more comprehensive agreement. We look forward to updating shareholders of any such developments as soon as they occur.

Phosphagenics and Terumo already have a broader strategic R&D alliance related to three additional pharmaceutical products (including the TPM[®]/Propofol injectable), in which Terumo is reimbursing Phosphagenics for any work undertaken. This has now been in operation for over six months with the collaboration and R&D continuing to progress well.

Phosphagenics in conjunction with tesa Labtec GmbH, the German transdermal formulation specialists, have very recently completed the **reformulation of the TPM[®]/Oxymorphone patch**. Taking into account Phosphagenics' growing relationship with Terumo, this reformulation program was expanded to ensure that any formulation improvements had the flexibility to address key technical differences noted between the requirements for the Japanese pain market compared to the North American market. We are pleased to report that this effort appears successful and the new reformulation candidates have attributes designed to address both markets. The reformulation enhances physical aspects of our proprietary patch while maintaining or surpassing the established delivery profile in-vitro. We see this as a critical milestone as we continue to engage with licensing partners, such as Terumo, and further the development of this asset.

Themis Medicare continue the **TPM®/Diclofenac gel** expansion, now targeting 17 markets. The product is now on-market in both India and Georgia with regulatory packages being submitted for approval in several of the other countries under license. The additional attention Themis has given the product has already produced the highest quarter sales for the product, and this is expected to grow further as the TPM®/Diclofenac becomes available in the other countries.

Another recent development is the long-awaited verdict in the **ProPhase arbitration**. This arbitration was initiated against Phosphagenics by ProPhase Labs Inc in October 2014. It was related to a joint venture (established in 2010) between Phosphagenics and ProPhase to develop a range of Over-the-Counter (OTC) pharmaceutical applications utilising the TPM® technology. ProPhase had claimed that Phosphagenics breached the OTC licence granted to the joint venture entity. The arbitration ruling handed down in November 2016 through the American Arbitration Association determined that the full use and ownership of the licence for OTC pharmaceutical applications for TPM® be returned to Phosphagenics. No cash damages were awarded to either party. We believe the outcome is a good result for the company, and that the potential OTC pharmaceutical applications of TPM® are significant. Retaining full ownership of the licence represents a valuable opportunity for Phosphagenics shareholders.

I would like to take this opportunity to thank Phosphagenics shareholders for their patience in awaiting the ProPhase arbitration decision and reiterate that the costs of the arbitration have already been fully expensed through the 2015/2016 accounts.



The ProPhase arbitration decision also clears the way for Phosphagenics to progress with the **sale of the BioElixia® brand**. The decision to sell the brand and focus our limited resources on our core businesses was made in early 2015, however the actual sale was not able to progress prior to the conclusion of the ProPhase arbitration process. We are confident we can conclude a sale of this brand in the very near future, as we are presently in active discussions.

Phosphagenics is also involved in an **arbitration with Mylan** arising from a partnership agreement to develop a TPM® enhanced daptomycin injectable. Due to confidentiality regulations in the Singapore Arbitration rules, I cannot provide any more details at this time other than to say that we continue to pursue our rights in this matter and will provide shareholders with an update when and if appropriate.

OUR HUMAN HEALTH PORTFOLIO

Product	Formulation	Therapeutic Area	Partner	Research	Development	Marketed
Diclofenac	Gel	Pain (NSAID)	Novartis (India) Themis (17 countries)	★		
Oxycodone	Patch	Pain (opioid)	Terumo Corporation	★		Option for Japan
Oxymorphone	Patch	Pain (opioid)	Terumo Corporation	★		Option for Japan
Daptomycin	Injectable	Antibiotic	Mylan (Global)	★		
Propofol	Injectable	Anesthetic	Terumo Corporation	→		Global
2 additional products*	Other	Pain	Terumo Corporation	→		Global
5 additional products*	Injectable	Assorted		→		

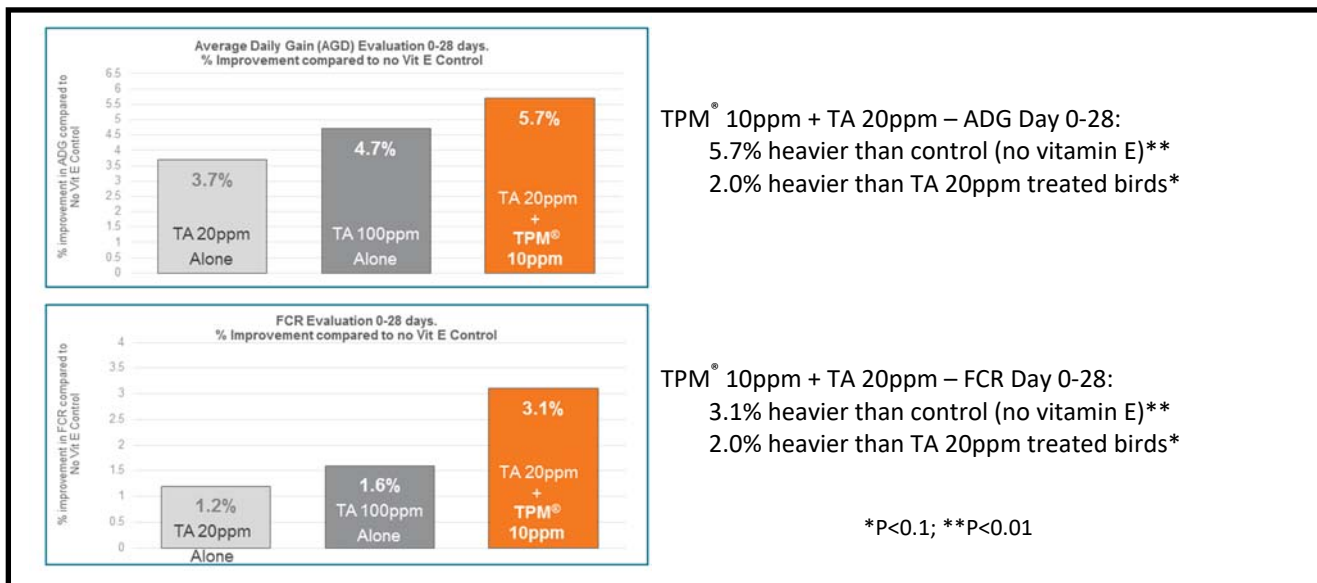
■ Partnered
■ Not Partnered
 Option pending
★ Clinical POP achieved
* undisclosed product

Our internal Human R&D has significantly progressed over the second half of 2016. Key developments have been made in the area of **TPM® injectables**. When combined in a formulation with selected drugs, our proprietary TPM® technology has been shown to enhance the solubility and/or stability of these drugs. This property of TPM® has now become a key focus for our R&D and we have already initiated work to develop TPM® enhanced injectable forms of multiple drugs. Our initial focus has been a TPM®/Propofol injectable for development with our Japanese partner Terumo, but this has already expanded. We believe there is significant value in the TPM® injectables business with multiple lucrative end markets. We expect to be able to provide shareholders with more news flow in this area during 2017 as our lead injectable candidates enter development. To better explain the rationale behind our injectable strategy, I have asked our CSO (Dr Paul Gavin) to put together a couple of paragraphs that will hopefully help you the shareholder, to better understand our thinking behind this opportunity. Please see that section at the end of this newsletter.

Last week, our Animal Health & Nutrition division announced the completion of our **poultry feed efficiency study** in broilers. The study undertaken, at a large research facility in Australia tested a broad range of

TPM® doses. The study tested 8 different treatment groups (5 containing TPM®), each with 72 birds divided amongst 12 replicate cages (6 birds per cage). The study produced a range of promising results that paralleled our findings from the previous weaner pig study. This data package will now be used to demonstrate the value potential of TPM® for potential partners.

As outlined in the announcement, the “TPM® enhanced feed” (containing 20ppm Vitamin E and TPM® at 10 and 20ppm) was able to significantly improve the average live weight (LW at Day 28) and average daily gain (ADG; Day 0-28) of the test broilers (at a level of $P < 0.05$). The “TPM enhanced feed” with 10ppm TPM® was the “optimal TPM enhanced feed” and produced the largest numerical improvement in LW, ADG and feed conversion rate (FCR) across all test groups without a significant change in total average feed intake. FCR is a primary performance measure in the livestock industry. Key results are shown graphically below:



Although the magnitude of these improvements in FCR may appear relatively modest the potential is quite significant. A recent local poultry industry report indicated that for every 1% improvement in FCR, the financial savings to the Australian industry is ~\$9.4 million, a saving that would be 100-fold greater if applied to the global meat production. (Cowieson A.J. and Selle P.H, *The environmental impact of low feed conversion ratios in poultry, Recent Advances in Animal Nutrition – Australia (2011)*). Poultry is now the second livestock species to demonstrate a positive response to TPM® as a feed additive.

The other major study which remains ongoing within the Animal Health and Nutrition business is the **dairy cattle trial**. It continues to progress well with January 2017 marking the midpoint of this study. It remains on-track for reporting out on time in the second half of 2017.

OTHER ACTIVITIES

In September, the company completed a strategic review of its **long term incentive** arrangements for its employees and directors. The Board of Phosphagenics has made a decision to replace its previous long term incentive scheme with a three year Conditional Options Scheme which more appropriately aligns employee performance to the creation of shareholder wealth. Shareholders will be asked to formally approve this scheme at the company's next Annual General Meeting to be held in May 2017.

Revenue from sales of Vital ET and TPM has had its challenges over the last half of 2016. Orders for Vital ET/TPM from our two largest historical customers were down in the second half of the year compared with the same period in the previous year. This shortfall was primarily due to our largest Vital ET customer Ashland putting ordering on hold for the half year as they worked through previously stockpiled inventory and a significant company restructure. This was compounded by no sales to Integrated Animal Health (IAH). Recognising that poor sales can always be a potential scenario, the company has made great strides over 2016 to build a broader customer base, expand sales with existing partners and to increase our efforts to contain costs where possible. Despite considerable effort, it is expected that "sales revenue" for 2016, will be lower than last year. However, we have been able to make up some of the shortfall with increased revenue from our smaller partners Themis and Le Metier, who have increased their TPM orders, delivering increased royalty payments to Phosphagenics.

As of January 2017, **Phosphagenics will move** its headquarters from 11 Duerdin St, Clayton and consolidate it with our manufacturing site at Hallmarc, Unit A8 2A Westall Road, Clayton. A limited number of Laboratory staff will remain at Duerdin St. This consolidation will benefit the company in a number of ways and provide considerable financial savings in the order of \$200,000 per year.



As you will have noted by the number of announcements this year we increased our **Business Development** intensity over 2016 and intend to build this further through 2017. I will be travelling to San Francisco USA in early January for the JP Morgan Healthcare conference and will follow this up with a number of Business Development and Investor meetings. I look forward to providing you with news from this trip and a 2016 CEO's review and summary of our key financial metrics for the financial year ending 31 December in our next newsletter due to be released in 1st Quarter 2017.

Overall, I am very happy to say that the company has continued to make significant progress in the second half of 2016. We continue to advance our strategic partnerships, the ProPhase arbitration process is behind us, and our core proprietary TPM® technology continues to provide commercialisation opportunities for shareholders. In line with our corporate strategy implemented in late 2015, we continue to apply a commercial filter to all our operations and are committed to ceasing any activities that do not offer an appropriate ROI for shareholders.

In conclusion I would like to wish all shareholders and their families the best for the upcoming Holiday season. I truly believe that 2017 is going to be a great year for Phosphagenics. Given the close proximity to the holidays I have made the decision not to follow this issue with the usual shareholder call. If you have any questions please feel free to contact us and we will attempt to answer you as soon as possible.

Human Health Injectables: by Dr Paul Gavin CSO.

We have previously communicated our intention to explore the benefit that TPM can bring to injectables. The key fundamentals of this strategy are improving the speed with which we can develop licensable assets and reducing our overall development risk profile.

Phosphagenics' current (non-injectable) R&D programs carry relatively high technical and regulatory hurdles. These are typified by Phosphagenics' lead pharmaceutical products; the transdermal matrix patches. Matrix patches are technically difficult dosage forms to develop. They must:

- adhere well for the entire duration of the patch treatment yet peel off easily when removed
- be of minimal size with acceptable patient comfort and tolerability
- be both chemically and physically stable
- most importantly, they must deliver therapeutic amounts of drug over a sustained period of time through skin, a barrier that has evolved to keep material out.

Once you combine these challenges with the opioid problems of abuse and diversion, you can begin to see the challenges the company has had to overcome in bringing forward innovative opioid patches. But "with challenge comes opportunity" and it is these challenges that make the potential upside for the patches so commercially compelling and significant for investors.

Injectable reformulations are a different level of complexity to patches. Injectable drugs do not suffer from problems with delivery into the body (bioavailability). By definition, they are 100% bioavailable, so there is no scope or need for improvement there. There is, however, scope to improve the composition of the formulations themselves. This opportunity is a result of the solubility profile of many injectable drugs.

Injectable formulations are ideally aqueous so that they can mix freely with blood.

Many injectable drugs however, have poor water solubility, and need to be formulated with other ingredients to keep them soluble. These other formulation ingredients, termed "excipients", may be oils, organic solvents or surfactants/detergents and many are not ideal for injection into the blood. Many, such as Cremaphor, bring a range of toxic side effects so bad they can limit the amount of the drug that can be administered, cause anaphylaxis or prevent the drug formulation from being suitable for use in other therapeutic indications. A number of companies are seeking to create next generation injectables, free of these adverse excipients. An example of such a success story is Abraxane; an injectable paclitaxel used for cancer treatment. This reformulated product has become a recent blockbuster by simply removing Cremaphor, the solubilizing agent included in the original product (Taxol) to dissolve paclitaxel.

A big driver for Phosphagenics is that improvements in injectable drugs can be made at the formulation stage. Commercial differentiation can be won quickly and cheaply on the laboratory bench, rather than requiring expensive Phase II/III clinical trials, ultimately providing a quicker path to differentiation, licensing and market. TPM has a long history of successfully encapsulating and solubilising drugs, both in topical and transdermal dosage forms, and in injectable formulations for candidates such as daptomycin and propofol. Recently we have focused our R&D program on evaluating whether TPM can be used to formulate five commercially attractive drugs with poor aqueous solubility.

The chosen drugs all currently require "less than ideal" solubilizing excipients (including Cremaphor) in order to dissolve them for injection and Phosphagenics has explored whether TPM can replace some or all of these harsh solvents. This work has been conducted in conjunction with external experts in the US and has proven very successful. The results of this first round of experiments have demonstrated that TPM can solubilise four of the five selected drugs in the absence of the solubilisers currently used with those products. The plan is now to take one or more of these drugs forward into formal development using the US contractors to generate finished formulations that can ultimately be licensed.

Phosphagenics' move to focus on injectables is designed to take advantage of the quicker path to partnership and market, and should complement the risk/return of the opioid patches. It is hoped that the speed and relatively low cost of this kind of development strategy will allow the generation of multiple licensable assets and compliment the longer-term strategies in play for the high value products such as the opioid patches.

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