



Phosphagenics

news

FEBRUARY 2016



Welcome to the third instalment of the new Phosphagenics newsletter - the first for 2016. Since our last newsletter issued in October 2015, there has been a considerable amount of news flow and activity. We have reported results from the oxycodone patch trial and the weaner pig feed efficiency trial of TPM[®] in our Animal Health & Nutrition business, as well as initiating a second trial in grower pigs. There has also been considerable progress made in the background, with the reformulation of the TPM[®]/Oxymorphone patch proceeding well, positive progress on our plans to expand our sales base and our manufacturing capability and numerous business development discussions.

This increase in pace is a direct reflection of the structural changes put in place in the third quarter of 2015. Although we have only been operating in our new form (with both the new Board and new structure) for six or so months we have really benefited from the focus on clearly defined areas of endeavour, de-risking the impact of any one binary outcome for shareholders, while also

optimising synergies across the separate but related business areas. While the restructuring of the business has meant that staffing levels have been reduced considerably, I am pleased to report that these have had little if any impact on our speed or focus on key projects. Long-term, these reductions are designed to considerably decrease our fixed overhead costs, extending our ability to fund and achieve our short to medium term commercial goals. These savings should begin to become evident midway through 2016 once the impact of redundancy commitments and other one off factors have concluded.

Since starting in early 2015, I have worked to create a business for shareholders with a healthy spread of "risk to reward" and a balance of short, medium and longer-term goals. Each program has been designed to produce data to inform potential partners and achieve the milestones of commercial and later stage development agreements. We are making real progress in this respect with increasing partner interest, however there is still work to be done. Our active portfolio of businesses and products are shown below.

Human Health:

- | | |
|--|---|
| • TPM [®] /Diclofenac Gel | Commercialised (additional partner discussions ongoing) |
| • TPM [®] /Oxycodone Patch | Phase 2a (trial complete) |
| • TPM [®] /Oxymorphone Patch | Phase 1 (undergoing reformulation) |
| • TPM [®] /Daptomycin Injectable | Partnered (in late phase development*) |
| • Multiple TPM [®] /injectable candidates | Various stages of early development |

Animal Health & Nutrition:

- | | |
|---|---|
| • TPM [®] Pig Feed additive | One study completed and one in progress |
| • TPM [®] feed additive (additional species) | To initiate trialling in 2016 |

Production & Personal Care:

- | | |
|----------------------------|--|
| • Vital ET [®] | Commercialised and in further partner assessment |
| • TPM [®] GMP | Incorporated into Human Health products |
| • TPM [®] non-GMP | Commercialised: Animal feed and Personal Care products |

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Each item in the list on the previous page has attracted external interest from potential partners over the past three to four months, with the recent announcements bolstering those discussions. We continue to discuss the potential for partnerships across the portfolio.

As shareholders are aware, we currently have two arbitrations underway. The arbitration with ProPhase is now wrapping up, with the formal arbitration hearing held in New York in December and January. We now await the arbitrator's decision which will hopefully be received within the next three to six months, although the actual delivery is at the discretion of the arbitrator.

We have also commenced arbitration proceedings against Mylan Laboratories Limited. Previously we have not been able to provide much detail on this project due to contractual constraints. The product under development with Mylan, daptomycin, is an injectable antibiotic marketed by Merck & Co. as Cubicin[®], with annual revenues of around US\$1 billion. Cubicin[®] was launched and initially marketed by Cubist Pharmaceuticals which was taken over in late 2014 by Merck. The relevant Cubicin[®] patents were due to expire in 2016, 2019 and 2020; however, the validity of these patents was challenged by generic manufacturers and the latter two patents have been recently voided. This means that the product is now due to come off patent protection in mid-2016.

Unlike simple generic versions, Phosphagenics' TPM[®]/Daptomycin product (developed in collaboration with Agila Specialties and Mylan) has multiple technical advantages to commercially differentiate it from Cubicin[®] and other generic daptomycin competitors. We believe this differentiation supports the potential for significantly improved market share and revenue. This TPM[®]/Daptomycin product is at present in late stage development towards a 505(b)(2) regulatory

filing in the USA. We have asserted in our arbitration notices that Mylan/Agila Specialties has breached several provisions under our agreements related to TPM[®]/Daptomycin. Despite the arbitration proceedings, Phosphagenics' existing commercial agreement with Mylan remains in full force and effect pending the Arbitrator's decision. The arbitration hearing, which is taking place in Singapore, is expected to be scheduled for late 2016 with a judgement expected sometime in 2017.

We expect that the Mylan arbitration could be a notable cost to the Company and have already built an allowance into our 2016 and 2017 budget for this. Having said that, we also believe that we have a strong claim and a favourable outcome would provide a resolution to the claimed breaches in addition to the revenues that are expected to flow to Phosphagenics from the existing agreement.

Phosphagenics' full year accounts are due for release at the end of February 2016. While it is not appropriate to make comments prior to the directors signing off the accounts, I can say that the cash position as at 31st December 2015 was around \$12.5 million (with additional \$2.4 million due this quarter from the R&D tax rebate).



HUMAN HEALTH

Dr Ross Murdoch & Dr Paul Gavin

It was with mixed emotions that we announced in January the outcomes from the recently completed **TPM[®]/Oxycodone** PHN study.

It was clearly disappointing to announce that the study did not meet its primary endpoint; however the study included some strong positives: the patch's performance and an encouraging result from the "post-hoc subpopulation analysis". Both of which have generated considerable interest from potential partners.

As this has already been the focus of both an announcement and a previous teleconference, I will not go into great detail here other than to reiterate that the study was designed to answer two separate but equally important questions:

1. *Does the patch perform in patients as desired and as predicted from the previous studies: deliver oxycodone to local tissue at the site of application, producing minimal blood concentrations with an appropriate safety and side effect profile? and*
2. *Can oxycodone delivered topically to the perceived site of PHN pain effectively manage the neuropathic pain experienced by patients?*

All the answers to question 1 were positive, with the study confirming that we have produced a viable patch that can deliver drug to a local site in the desired quantities over three days without significant systemic exposure and with a user friendly profile that mimics our targeted commercial profile for tolerability, side effect, delivery and skin adhesion. It provided the data we needed to be confident when talking to potential partners that the patch has a compelling product profile and the potential to be efficacious in other local pain indications.

Unfortunately, despite positive patch performance, the results of this study indicate that topically delivered oxycodone does not appear to be an effective treatment for neuropathic pain across the broad PHN population – a result reflected in the primary endpoint not reaching significance. PHN is a notoriously complicated disease with sufferers divided into a collection of distinct sub-groups with different underlying causes for their pain and different responses to common therapies. Our initial data appears to



support the theory that we too saw significant differences within our study population, with the TPM[®]/Oxycodone patch potentially providing pain relief to one but not all subgroups. Unfortunately, with only nine patients from that sub-group in the trial, this effect was not sufficient to push the overall result to significance, however it has been well received in discussions with potential partners.

We believe we have a strong foundation on which to undertake further development and licensing discussions for the TPM[®]/Oxycodone patch. The data package now includes tolerability and efficacy data from multiple preclinical animal models, strong robust physical and chemical stability, evidence of reproducible patch performance, dermal tolerability, an absence of opioid side effects and (albeit limited) efficacy from our Phase I and Phase 2a studies. Partnership discussions are ongoing.

The impressive physical performance of the TPM[®]/Oxycodone patch also bodes well for the ongoing work to develop a commercially acceptable **TPM[®]/Oxymorphone** patch. The reformulation effort is progressing well. Tesa Labtec GmbH is currently deconstructing the Phosphagenics TPM[®]/Oxymorphone patches in order to understand how they deliver drugs so efficiently and which components can be altered in future iterations while preserving the current product performance. Up to three new TPM[®]/Oxymorphone patch candidates are targeted to go into stability testing in the third quarter of 2016, with the best to be taken forward into further development.

Finally, recognising the advantages that TPM[®] has added to Daptomycin, the Human Health business is moving forward to investigate a number of other injectable candidates. While too early to announce these individually, we are undertaking formulation feasibility on a number of potential candidates selected from both “existing injectables” and “drugs where an injectable form has not been possible as yet but where there is a genuine clinical and commercial driver”.

Three publications are undergoing the final internal approval steps and are expected to be submitted to key journals in the first quarter of 2016.

ANIMAL HEALTH & NUTRITION **Dr Roksan Libinaki**

The Animal Health & Nutrition business has been extremely active with studies to assess the effectiveness of TPM[®] in livestock growth promotion. In the past three months we have completed and reported the first of our pig studies (a weaner study) and initiated a second pig study (a grower/finisher study). Additional studies in another species (likely to be either poultry or cattle) are also planned to start in 2016.

Results from the first weaner (young) pig study were reported last month, with a successful significant improvement in feed conversion rate (FCR) or feed efficiency for the first 14 days post weaning reported. The results from this study were encouraging, particularly considering the importance put on the wellbeing of young pigs during this crucial phase of development. The social and psychological stresses at this stage of development can have profound effects on growth and development of the pigs long-term. Removal from their mothers, transport and placement into new social groups, diet changes and feed transitioning, among others,

can all adversely affect long-term well-being, growth rates or performance. The improvement in FCR in the weaners fed with TPM[®] was reported to be greater than 3% compared to those fed a standard feed and Vitamin E alone. If the benefits observed in the first 14 days can be maintained over the life of the pig, these effects would be of a magnitude considered commercially valuable to the industry. The second part of the study (the subsequent 21 days) unfortunately appeared to have been compromised by changes in the overall health of the pigs in the test facility (i.e. no group had growth rates within what are considered a normal range, contrary to the first 14 days of the study). Discussions with industry experts have confirmed that while unfortunate, this is not necessarily unusual within large commercial piggeries. We await the results from our subsequent grower/finisher pig study, which is underway, to provide a better understanding of the potential applications and benefits for TPM[®] utilisation in pigs. Results from this second study are anticipated in the second quarter of 2016.

While the concept of TPM[®] as a feed additive with vitamin derived nutritive benefits is well known, the challenge for the Company, is to be able to demonstrate to the industry that TPM[®] has additional benefits to enhance performance. In an industry where many competitors claim that their feed additives have growth promotion properties, the “growth promotion noise” has fuelled skepticism and led to third parties demanding larger and more definitive data packages to support claims of commercial value.



We recognise that no one single study can define the full potential of TPM® in this market segment. Therefore we have adopted a pragmatic, step wise approach to our program that will provide commercially relevant information to discuss with prospective partners at each stage, while adding value by building a strong technical data package to substantiate these discussions and regulatory submissions moving forward. The studies we are undertaking have been designed with input from industry experts, as well as potential partners, to ensure they fulfil industry expectations and address global animal nutrition and commercial market opportunities.

Antibiotics are recognised as producing consistent advantages over other growth promotion additives and have therefore been considered a gold standard for this purpose for many years. However, the use of antibiotics as growth promoters is falling out of favour and bans are already in place for the European Union. The USA will follow suit by the end of the year. The need to expand animal-based food production due to a growing global population, along with predictions of high single digit growth for the animal feed additive market over the next decade, means that competition is fierce in this sector but also the commercial opportunity is large. Although improved performance is the key driver for these new offerings, a natural, organic and sustainable image is also highly sought after. As TPM®'s backbone is a vitamin, rather than a hormone or antibiotic, we believe it has the potential to deliver both performance and this user friendly image.

If TPM® continues to deliver a 3-5% improvement in feed efficiency combined with other pluses (when compared with balanced diets without TPM®), it has the potential to be a strong competitor in the growth promoter, feed additive market.

All studies have been designed with broad applications in mind to support the utilisation of TPM® in a global market and facilitate business development discussions with dominant global as well as smaller industry players. Essentially, our goal is to allow TPM®'s potential to be exploited globally. The business unit is putting a considerable effort into fostering and actively pursuing partners who meet these criteria.



BULK PRODUCTION

Greg Moses

This year has commenced very positively with solid first half orders from key customers like Ashland, Themis, Le Métier de Beauté and Integrated Animal Health. These orders are in line with those at the same time last year on a product by product basis.

An ongoing process improvement goal for the Bulk Production group has been to improve the bottom-line return to Phosphagenics from both TPM® and Vital ET® manufacturing. To this end we implemented a process over the second half of 2015 to bring internal costs down and improve production and manufacturing efficiency. A number of specific improvements to the manufacturing plant, production planning process and site set-out have been implemented. These have provided immediate gains in efficiency and should increase capacity in the near term. The improved capacity, combined with improved margin, bode well for performance in 2016. Discussions have commenced with key new and existing partners aimed at developing proactive partnering solutions that can drive mutual volume growth and improved revenues within each of their respective markets.

Expansion opportunities continue to be a priority activity for 2016, particularly in relation to the opportunities emerging in the Animal Health sector. The business remains ready to commence manufacturing expansion works as and when these new opportunities grow closer to materialisation and identified timelines are established.

The details of the next CEO Quarterly Update Teleconference will be released shortly.

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