



# PHOSPHAGENICS

**May 2010**

**Delivering More...**

Through Innovation in Transdermal Delivery

Listed on the Australian Stock Exchange (POH) and OTCQX (PPGNY)

# Safe Harbor

This presentation contains forward-looking statements based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialise, actual results could vary materially from the Phosphagenics' expectations and projections. Risks and uncertainties include general industry conditions and competition; economic conditions, such as interest rate and currency exchange rate fluctuations; technological advances and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; domestic and foreign health care reforms and governmental laws and regulations.

# Overview

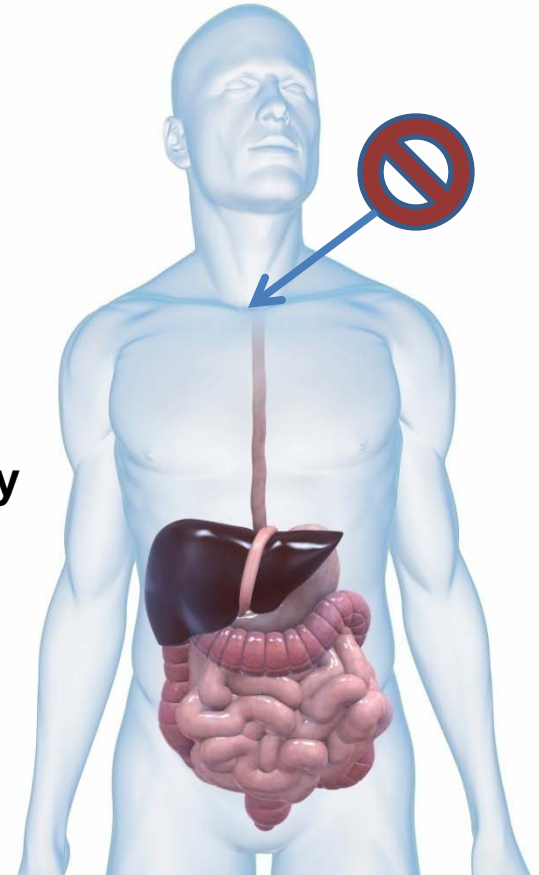
- Headquartered in Australia
  - Corporate development in U.S.
- Clinically validated transdermal  $\alpha$ -tocopheryl phosphate mixture (TPM) drug delivery technology
- Creating value by leveraging TPM<sup>™</sup> technology across diverse markets with partners
- Strong intellectual property
- Listed on the Australian Stock Exchange (POH) and OTCQX (PPGNY)

# Transdermal Benefits

## For the patient:

- Eliminate first pass metabolism
- Provide steady delivery/blood levels
- Increase compliance/convenience
- Reduce systemic drug interactions
- Minimise abuse/diversion

**Versus  
Oral  
Delivery**



**PHOSPHAGENICS**

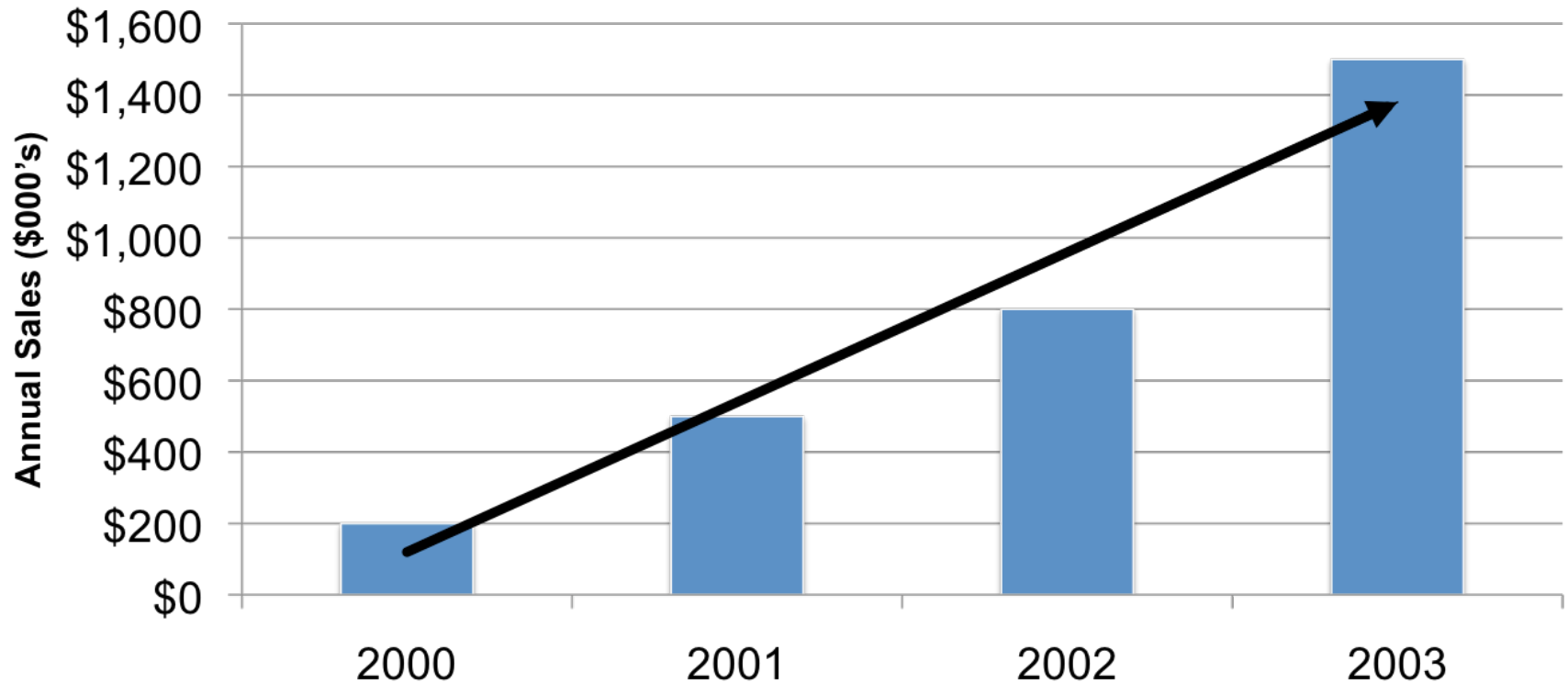
# Transdermal Benefits

## For the pharmaceutical industry:

- Replace lost sales as R&D productivity continues to decline
- Extend product life cycle in the face of generic competition
- Manage the escalating costs of developing new products
- Conversion of injectable only drugs to more convenient transdermal products
- Delivery options for NCEs (increase bioavailability, large molecules not suitable for oral delivery, etc.)

# Example of Success

The 72-hour Duragesic® transdermal patch revolutionized the use of fentanyl in chronic pain management and reached over \$2 billion in sales before patent expiry in January, 2005



# Transdermal Summary

- Transdermal drug delivery systems provide low cost / reduced risk opportunities for product life cycle extension
- As a “novel” technology, the upside potential for transdermal delivery of new molecules in almost all therapeutic categories is still very significant
- $\alpha$ - Tocopheryl Phosphate Mixture (**TPM**) is uniquely suited to provide access to larger molecules and select peptides
- TPM<sup>TM</sup> delivery technology can deliver both small and large molecules into the dermis and across the skin (transdermal) without causing any disruption, irritation or damage

# Technology Overview

- TPM™ is a multi-component, multi-functional delivery system
- TPM™ is comprised of  $\alpha$ -TP and  $\alpha$ -T<sub>2</sub>P
- $\alpha$ -TP is the signaling form of vitamin E and is associated with specific cellular transport
- TPM™ enhances the absorption and solubility of compounds in the body
- TPM™ is non-invasive, non-irritant and has unique properties
- TPM™ is GRAS approved

**TPM™ does not alter the active compound, but instead alters the lipidic structure of the stratum corneum allowing for the specific, controlled delivery and enhanced absorption of small molecules or peptides into the skin (locally) or systemically**

# TPM Delivery Platform - Vesicular Encapsulation

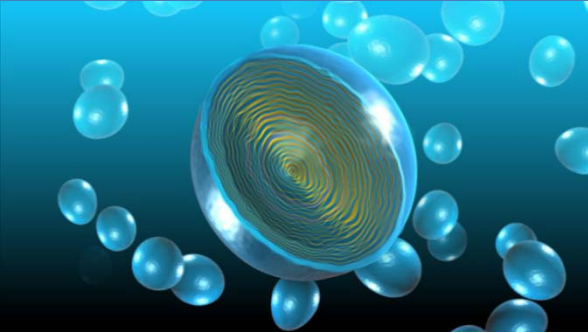


Figure a) Close-up of a TPM vesicles showing its multi-layered interior.

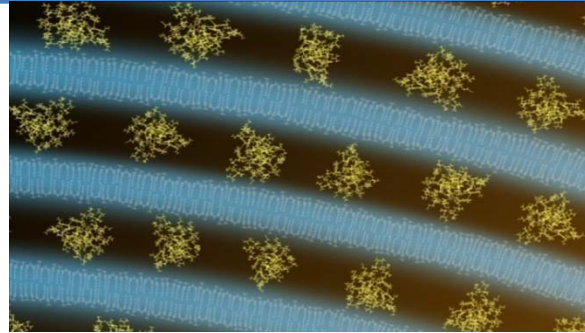


Figure b) Inside view of the TPM vesicle, showing how the drug to be delivered ("the active") may be positioned within the layers of the vesicle.



Figure c) An example of where and how the TPM/active gel may be applied to the skin.

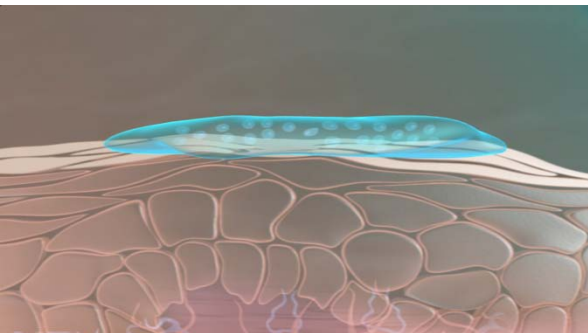


Figure d) Close-up of the TPM/active gel, showing the vesicles in suspension.

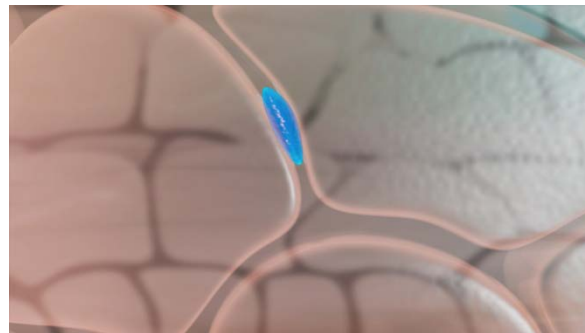


Figure e) Close-up showing how the TPM/active vesicles' flexibility allows them to squeeze between the skins cells and travel towards the more vascular, deeper layers of the skin.

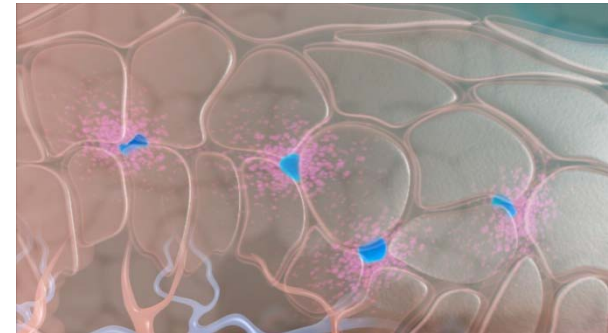
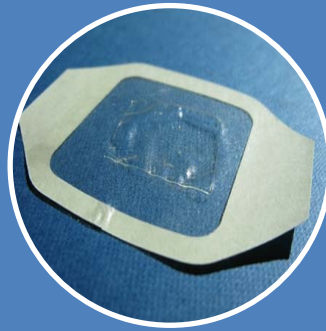


Figure f) A representation of TPM vesicles delivering the active to the site of action, in this case the deeper layers of the skin.

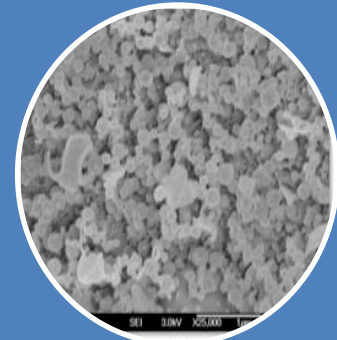
# Formulation Examples



reservoir patch



matrix patch



vesicle formulation



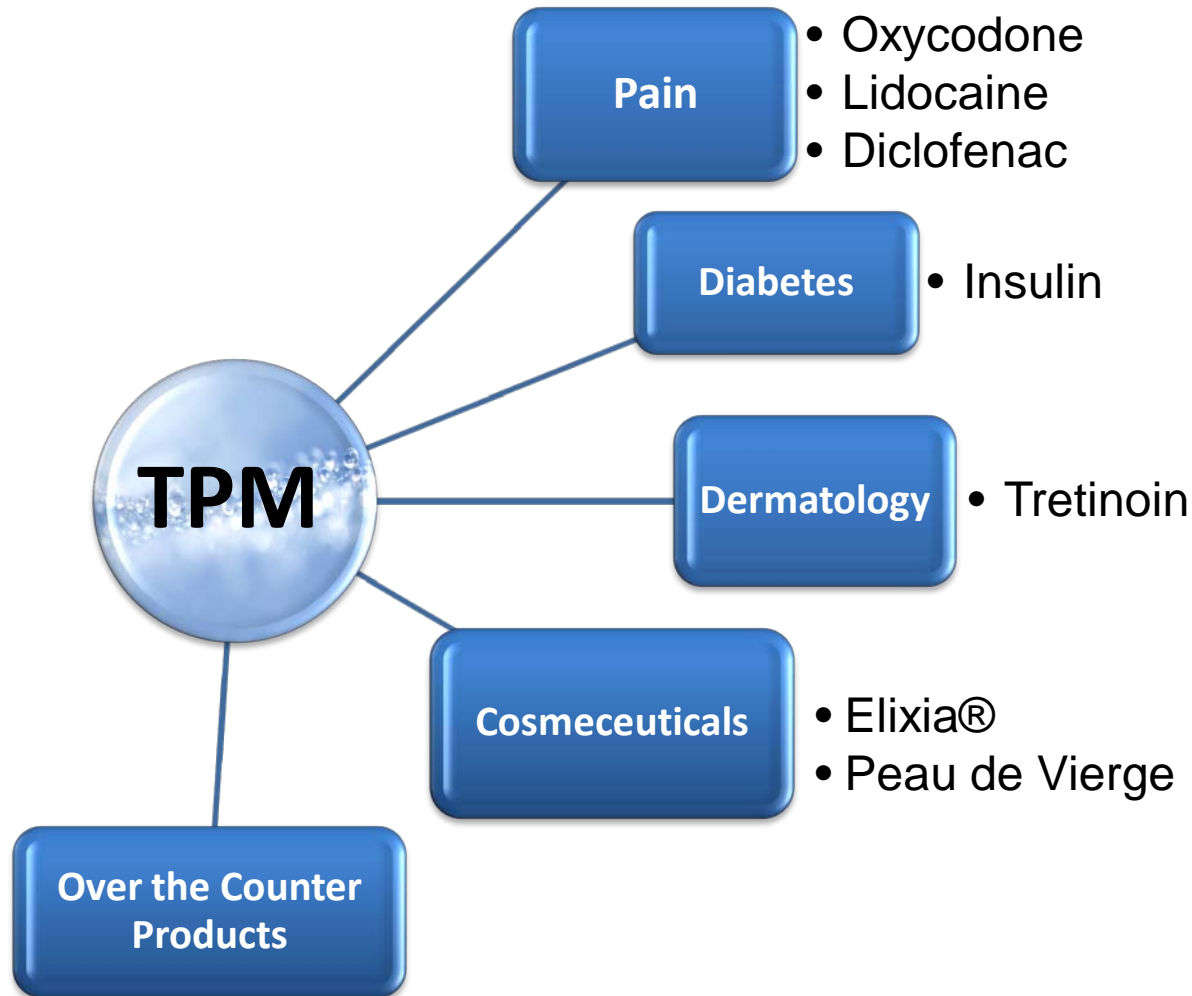
**TPM™ technology**



# Collaborations



# Validated Technology



# Phase I Study: Oxycodone

- TPM/oxycodone has the potential to be the first transdermal oxycodone – currently there is a very large unmet medical need for non-invasive, non irritating sustained release opioid delivery
- Completed all preclinical studies
- Developed patch systems in house
- Phase I Repeat Insult Patch Test completed in June 2009 with no significant erythema and no sensitization
- Phase 1B Repeat dose application completed in Q4/2009

# Phase 1 B: Summary

Results summary:

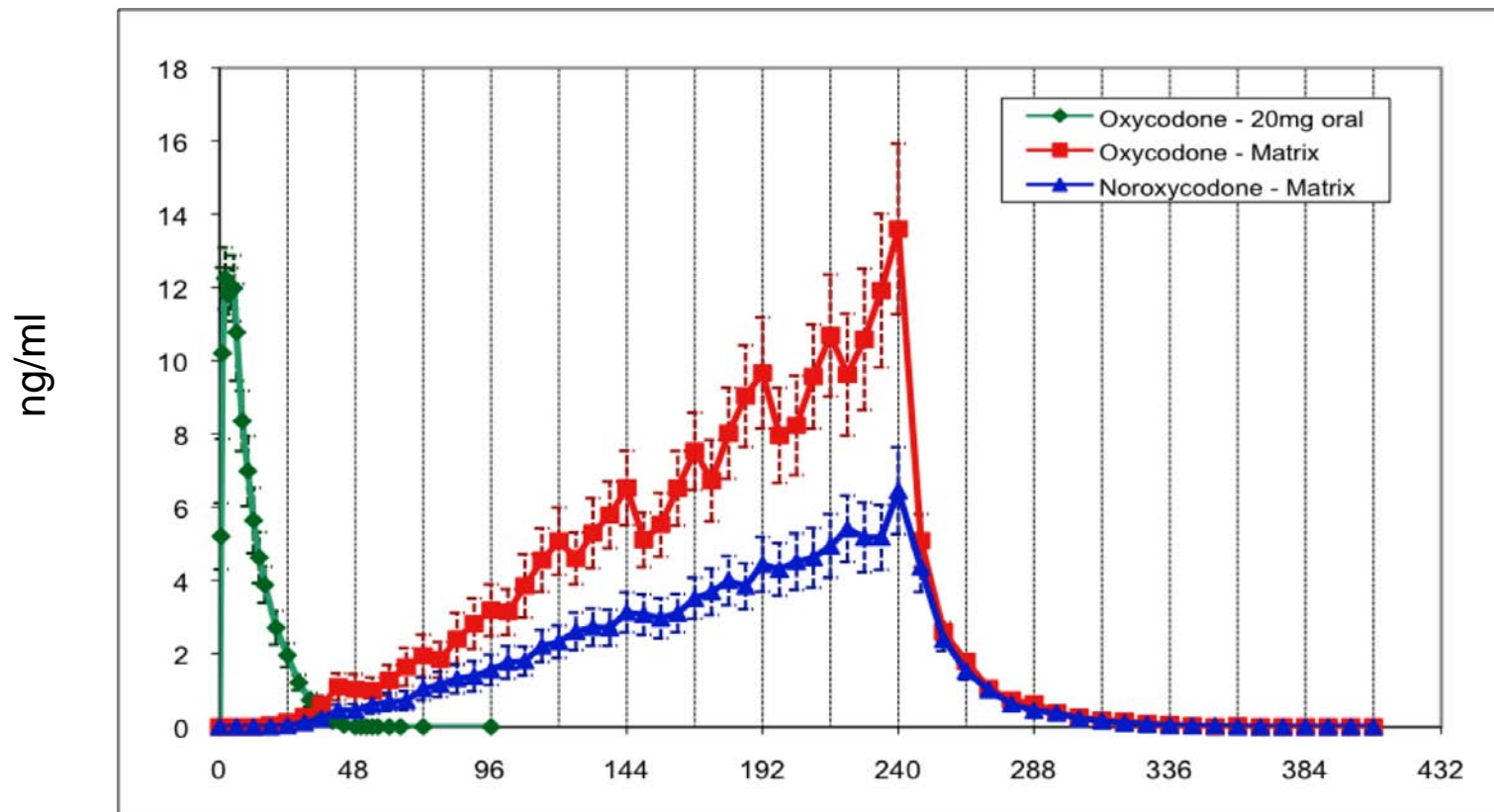
- Therapeutic levels (  $>8\text{ng/ml}$ ) achieved with repeat dosing
- Sustained release profile - no peaks and troughs
- Matrix patch more superior than reservoir patch system
- No irritation observed



***Ideal product profile for chronic pain management***

# Phase 1 B Study: Oxycodone

Plasma oxycodone concentration over time following repeated application of the TPM/oxycodone patch systems. A representative curve for 20mg oral Oxycontin has been included for comparison. Bars represent SEM, n=20

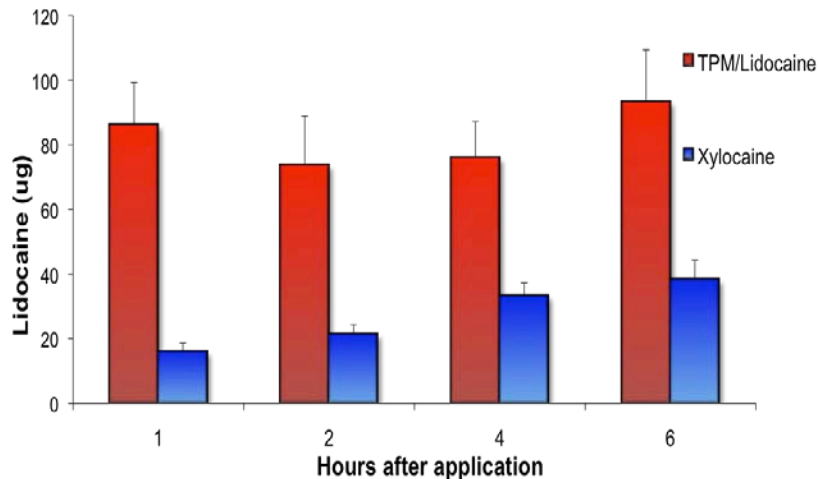


# Development Milestones

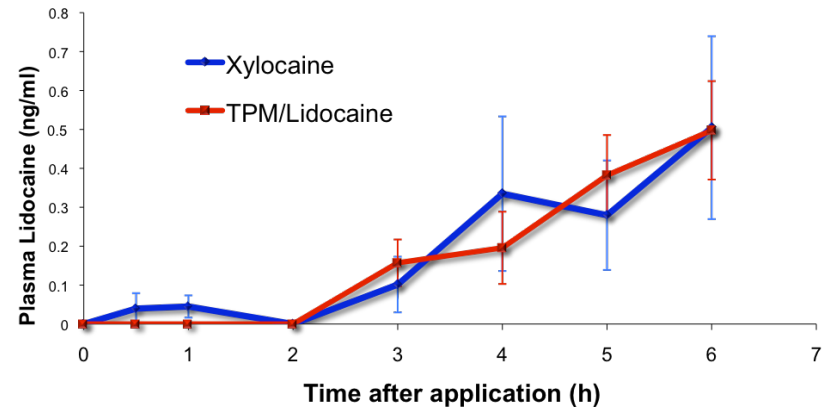
- Optimize patch design for various dose forms: Q2'10
- Initiate further product development studies (ie, patch rotation, +10 days application to achieve steady state): Q3'10
- Complete IND filing in the USA: Q4'10
- Phase 2/3 Study: Q1'11
- Expected approval date: H2'13

# Phase I Data: Lidocaine

- Equivalent dose of Xylocaine 5% ointment and TPM/lidocaine.
- 21 tape strips taken at each time point. Results from strips pooled
- N = 11 healthy volunteers, bars represent SEM (Graph on left)
- Graph on right shows equivalent Plasma levels demonstrating no spill over into the blood



TPM/lidocaine significantly increased dermal absorption in-vivo compared to Xylocaine ( $p < 0.001$ ).

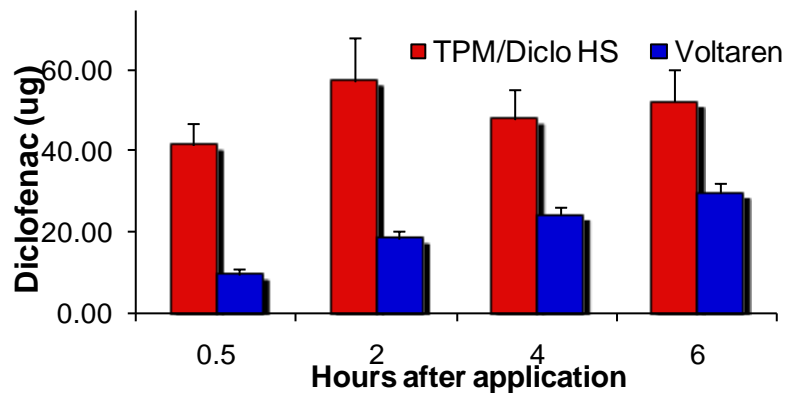


No difference in plasma lidocaine concentrations despite TPM/lidocaine significantly increasing the amount delivered to the skin

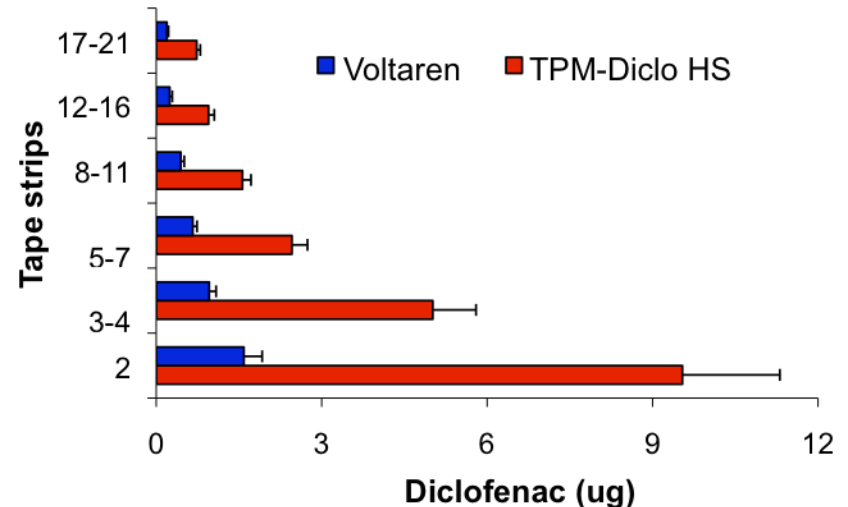


# Phase I Data: Diclofenac

- Dermal penetration of diclofenac 30 minutes after topical application
- N=21 tape strips taken at each time point. First strip discarded
- N = 12 healthy volunteers, bars represent SEM
- Graph on right – demonstrates depth of penetration in skin layers



TPM/diclofenac delivered on average over four times more ( $p < 0.001$ ) diclofenac into the stratum corneum, than Voltaren® gel.



TPM/diclofenac significantly increased the depth of penetration, with 380 percent ( $p < 0.001$ ) more diclofenac in the deepest layers of the skin sampled.



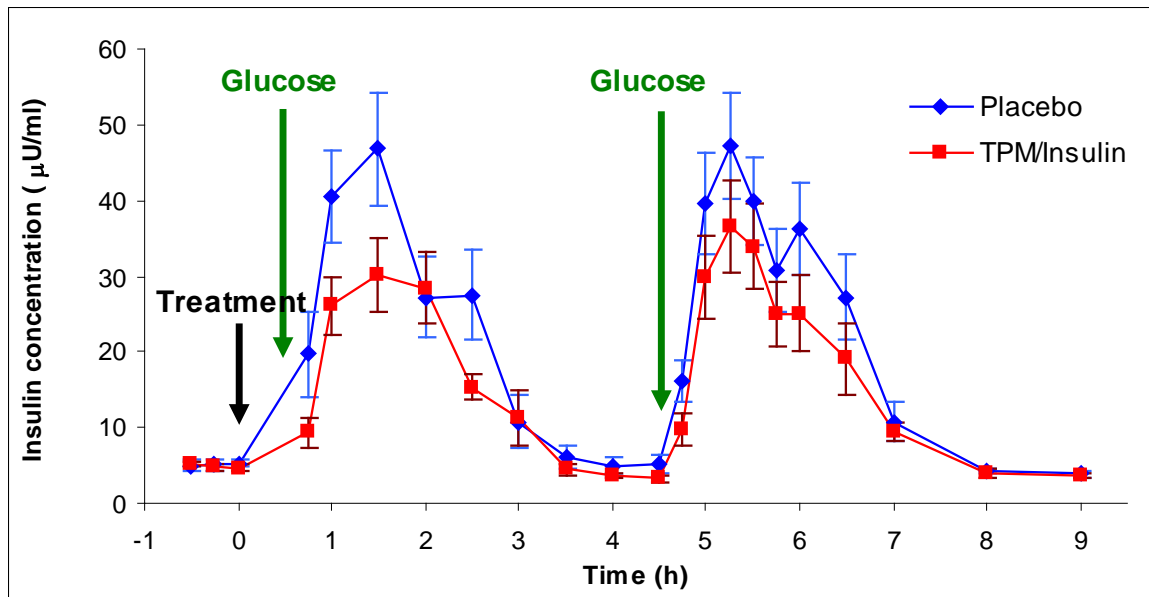
# Phase I Study: Insulin

- Safety and pharmacodynamic activity was established in healthy subjects in 2 Phase I studies
- Number of subjects = 40; one T.D application per subject
- Dose 45 units insulin/kg body wt; skin area of application = 15 x 30 cm
- Two Oral Glucose Tolerance Tests (OGTT) 4 hours apart
- Significant reductions in blood glucose, insulin and C-peptide levels from a single application of TPM/insulin
- No irritation observed
- Conducted in Australia in collaboration with the Joslin Diabetes Centre/ Harvard Medical School, Boston

# Phase I Data: Insulin

Significant changes in insulin concentration

Parameter	1 <sup>st</sup> OGTT		2 <sup>nd</sup> OGTT		Significance
	Active	Placebo	Active	Placebo	<i>p</i>
Insulin AUC <sub>0-1h</sub> (mU.h.L)	20.2 ± 6.5	32.5 ± 12.3	23.7 ± 10.3	31.2 ± 14.1	<b>0.010</b>
Insulin AUC <sub>0-2.5h</sub> (mU.h.L)	52.5 ± 17.0	72.9 ± 29.0	55.1 ± 23.5	74.1 ± 32.5	<b>0.013</b>



Mean (±SE) concentrations.

Time 0 h = dose applied.

OGTTs given at the arrows



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# Insulin Project update

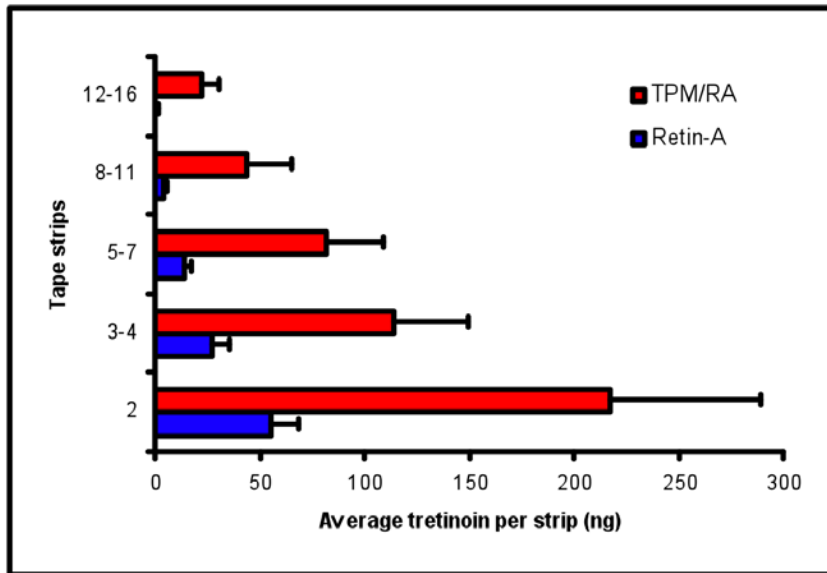
## TPM/Insulin Patch system:

- Patch development work is currently underway. Matrix patch system using TPM/insulin is being optimized in diabetic rats
- Initial preclinical data demonstrates that the single application of TPM/insulin matrix patch can reduce blood glucose for up to +5 hours
- Further studies are currently underway to assess the glucose lowering activity of repeat dose application TPM/insulin patch system
- Repeat dose application of TPM/Insulin patch system will provide:
  - Sustained basal glucose regulation
  - Less variability
  - Overall better management of disease state

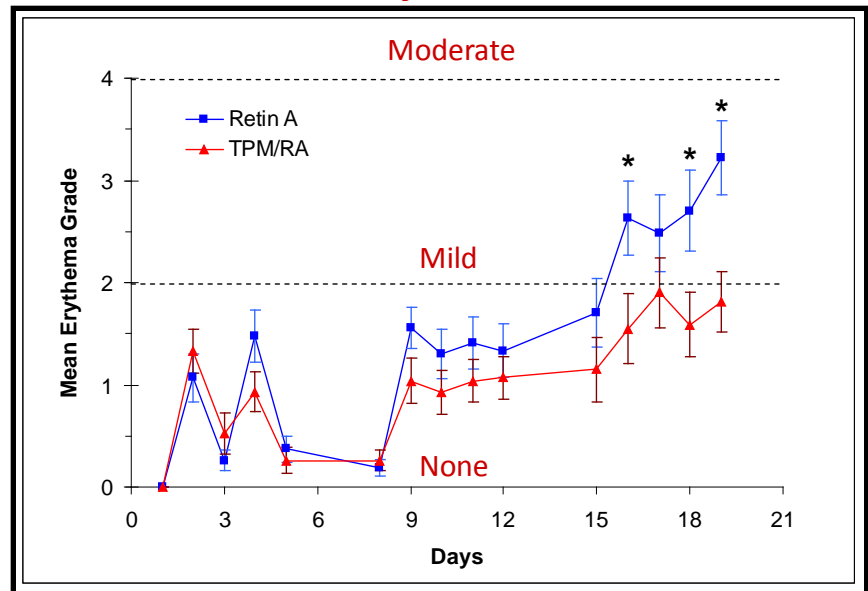
# Phase I Data: Tretinoin

- Human Clinical Trials – Penetration via tape stripping completed in 10 subjects
- Repeat insult patch tolerance (RIPT) test compared Retin-A and TPM/tretinoin
- Patches applied each day for 19 days and erythema and dryness scored
- N = 30 healthy volunteers, bars represent SEM

## Penetration



## Erythema



While significantly increasing the amount of tretinoin delivered, TPM™ was able to reduce the amount of irritation compared to Retin-A



# Cosmeceuticals

- US launch targeting high-end consumers:
- Phosphagenics' TPM™ technology included in new Le Métier de Beauté beauty line, with two products initially (and others in the pipeline for 2010)
- Exclusive launch of Le Métier de Beauté color treatment with TPM™ in Neiman Marcus, Bergdorf Goodman, John Barrett, Jose Eber and Fred Segal
- Peau de Vierge Cosmetic Line
  - Anti-aging Tint Moisturizer
  - Mineral Photo Touch Concealer



Magazine press in December has included WWD, In Style and Harpers Bazaar.

# Cosmeceuticals

- Personal care product under the Brand Name: **ELIXIA®**
- Australian launch through Exclusive Pharmacies (initially six products)
- Launched April 2010
  - Products developed from a topical pharmaceutical delivery platform built around years of scientific and clinical research not hype, which has been applied to the Skincare and Cosmetic Industries
- **Initial Product Range**
  1. Multi V Moisturiser (50ml)
  2. Tinted Multi V Moisturiser with Sun Protection (50ml)
  3. Cleanser (100ml)
  4. Multi V Body Lotion (100ml)
  5. Anti-oxidant Serum (30ml)
  6. Multi action Eye Serum (20ml)



# Attractive Business Model

- Marry our novel TPM™ delivery technology with products through partners
- Generate value from:
  - Development fees
  - Licensing fees
  - Milestone payments
  - Royalties on sales
- Partner at increasingly later stages of product development to maximise value
- Shorter development time from preclinical to product approval compared with NCEs
- Lower risk in reformulating proven, marketed products

# Milestones and Objectives

- Business development
  - Create value by leveraging TPM™ technology and products across diverse markets with partners
- Clinical and regulatory
  - Pharmaceuticals
    - Oxycodone
      - Complete repeat dose study for matrix and reservoir patch
      - Secure IND in USA
      - Partnering discussions
    - Insulin
      - Complete optimization and patch delivery system
      - Initiate clinical trial
- Financial
  - Revenue from skin care products via commercial partners



# Why Invest in Phosphagenics?

- Validated platform delivery technology with proven molecules
- Proof of principle of delivery with molecules transdermally and dermally
- Versatile technology with applications in the pharmaceutical, personal care, nutraceutical and animal health areas translates into reduced investment risk and a larger probability for success
- Marketed products in the Cosmeceutical area
- Multi billion dollar market opportunities in the pharmaceutical area



# PHOSPHAGENICS

***Thank You***

***Delivering More...***

*Through Innovation in Transdermal Delivery*

*[www.phosphagenics.com](http://www.phosphagenics.com)*