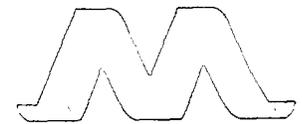


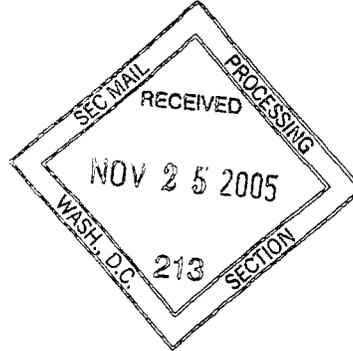


05012913



metabolic

16 November, 2005



SUPPL

Securities and Exchange Commission  
Division of Corporate Finance  
Office of International Corporate Finance  
450 Fifth Street, N.W.  
Washington D.C. 20549  
U.S.A.

EXPRESS POST

Dear Sir/Madam,

Re: Metabolic Pharmaceuticals Limited (FILE NO. 82-34880)  
submission of information filed with Australian Stock Exchange (ASX)  
and Australian Securities and Investment Commission (ASIC)  
pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934

Please find attached copies of announcements lodged with the ASX and ASIC:

Date of Announcement/Lodgement	To:	Title	No of Pages
4 November 2005	ASX	CEO to present at Healthcare Conference in New York	28
16 November 2005	ASX	Phase 1 Clinical Trial for Pain Drug – Positive Results	5

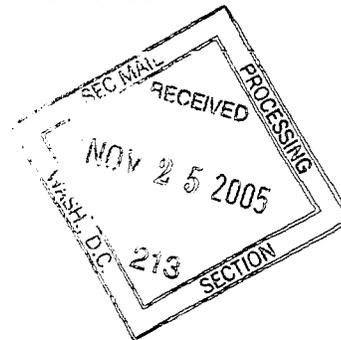
Yours faithfully,  
Metabolic Pharmaceuticals Limited

Belinda Shave  
Financial Controller & Company Secretary

PROCESSED

NOV 30 2005

THOMSON FINANCIAL



Australian Stock Exchange Limited  
 ABN 98 008 624 691  
 Exchange Centre  
 Level 4, 20 Bridge Street  
 Sydney NSW 2000

PO Box H224  
 Australia Square  
 NSW 1215

Telephone 61 2 9227 0334

Internet <http://www.asx.com.au>  
 DX 10427 Stock Exchange Sydney

**FACSIMILE**

**Department: COMPANY ANNOUNCEMENTS OFFICE**

**DATE:** 04/11/2005  
**TIME:** 14:42:30  
**TO:** METABOLIC PHARMACEUTICALS LIMITED  
**FAX NO:** 03-9860-5777  
**FROM:** AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office  
**SUBJECT:** CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

**MESSAGE:**

We confirm the receipt and release to the market of an announcement regarding:

CEO to present at Healthcare Conference New York

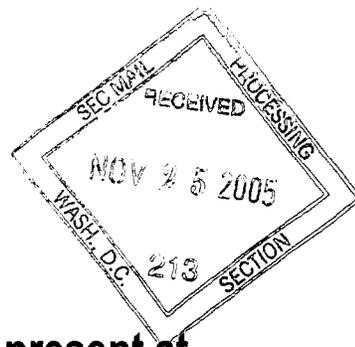
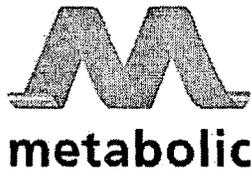
**If ASX considers an announcement to be sensitive, trading will be halted for 10 minutes.**

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## Metabolic Pharmaceuticals CEO to present at Healthcare Conference in New York

4 November 2005

The CEO of Metabolic, Dr Roland Scollay, will be making a presentation at the Rodman & Renshaw Techvest 7<sup>th</sup> Annual Healthcare Conference, in New York at 4.35pm, Monday, 7 November 2005, New York time. The program and details are available at:  
<http://www.rodmanandrenshaw.com/rodman.asp?link=Conferences7/ConferenceSchedule&bgcolor=wht>.

The presentation gives an overview of Metabolic's business including an explanation of its two high potential, clinical stage drugs, AOD9604 and ACV1. Dr Scollay will address the current development status, and the markets and competitive environment for each of these drugs.

A copy of the presentation is available at [www.metabolic.com.au](http://www.metabolic.com.au), following the tabs to Investor Relations and then to Presentations. A replay of the presentation will also be available via our website from 10.00 a.m., Tuesday, 7 November 2005 (Melbourne time).

ENDS

### **About Metabolic**

*Metabolic Pharmaceuticals Limited is a biotechnology company based in Melbourne, Australia. The Company was formed and listed on the Australian Stock Exchange (ASX: MBP) in late 1998 and there are 254,410,601 shares on issue. Metabolic has approximately 23 employees. Our mission is to bring to the market innovative drugs which will improve people's lives and return value to stakeholders. Metabolic currently has development programs aimed at treating obesity (AOD9604), and neuropathic pain (ACV1). Metabolic also has discovery programs targeting type 2 diabetes and, in collaboration with Neuren Pharmaceutical Limited, nerve protection and regeneration. For more information, please visit the company's website at [www.metabolic.com.au](http://www.metabolic.com.au).*

### **Background to AOD9604**

*AOD9604 is a 16 amino acid, orally active peptide modelled on one segment of the human growth hormone molecule. Growth hormone occurs naturally in the body and has profound stimulatory effects on fat metabolism. Levels of the hormone are typically suppressed in the obese state and with increasing age. Counteraction of this imbalance by daily dosing with AOD9604 is believed to normalize suppressed fat metabolism in obese individuals, while avoiding unwanted effects of the whole growth hormone molecule. AOD9604 has been through a Phase 2B clinical trial which showed good indications of efficacy and an excellent tolerability profile, and a further low dose study commenced in October 2005, with expected completion in early 2007.*

### **Background to ACV1**

*ACV1 is the first in a potential new class of drugs to specifically treat neuropathic (nerve) pain. Current therapies rely largely on the 'off-label' use of anticonvulsants, antidepressants and local anaesthetics, which have unimpressive efficacy and dose-limiting side effects. The potential range of indications for ACV1 extends to neuropathic pain in diabetics, post-herpetic neuralgia ("shingles"), sciatica and many other neuropathic pain conditions currently underserved by pharmaceutical treatment.*

ACV1 is a 16 amino acid peptide which specifically blocks a subtype of a class of receptors in the peripheral nervous system called neuronal nicotinic acetylcholine receptors (nAChR). ACV1 can be administered by once daily subcutaneous injections providing substantial relief in several animal models of neuropathic pain without apparent adverse effects. A Phase 1 clinical trial began in June 2005 and will be completed before the end of 2005.

**Background information on the drug development process**

The steps required before a drug candidate is commercialised include:

1. Discovery or invention, then filing a patent application in Australia and worldwide
2. Pre-clinical testing, laboratory and chemical process development and formulation studies;
3. Controlled human clinical trials to establish the safety and efficacy of the drug for its intended use;
4. Regulatory approval from the Therapeutic Goods Association (TGA) in Australia, the FDA in the USA and other agencies throughout the world.
5. Marketing and sales

The testing and approval process requires substantial time, effort, and financial resources and we cannot be certain that any approvals for any of our products will be granted on a timely basis, if at all.

Human clinical trials are typically conducted in three sequential phases which may overlap:

**Phase 1**

Initial safety study in healthy human subjects or patients.

Of short duration.

**Phase 2**

Studies in a limited patient population designed to:

- to identify possible adverse effects and safety risks in the patient population (2A); and
- determine the efficacy of the product for specific targeted diseases (2B);
- to determine tolerance and optimal dosage (2B).

**Phase 3**

Trials undertaken to further evaluate dosage and clinical efficacy and to further test for safety in an expanded patient population in clinical study sites throughout major target markets (e.g. USA, Europe and Australia).

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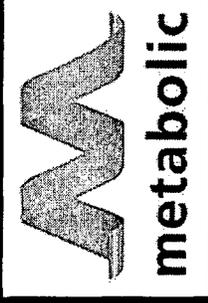
**Contact Information**

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# Metabolic Pharmaceuticals Ltd Melbourne, Australia

Rodman & Renshaw

Techvest 7th Annual Healthcare Conference

November 7, 2005

Presenter: Roland Scollay, PhD, CEO



# Forward Looking Statements

This presentation contains forward-looking statements regarding the company's business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing the company's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercializing drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this presentation. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the Metabolic Pharmaceuticals Ltd Annual Report for the year ended June 30, 2005, copies of which are available from the company or at [www.metabolic.com.au](http://www.metabolic.com.au).

# Introduction to Metabolic

- Based in Melbourne
- Formed and listed in 1998
- 23 staff, most activities outsourced
- Ranked most innovative company in Australia in 2004 by the Intellectual Property Research Institute of Australia and IBISWorld
- Current market cap ~US\$105m
- Cash at 30 Sept 2005 ~US\$14m  
(sufficient to fund the current clinical trials)



Sydney  
The Olympics, remember!

Melbourne



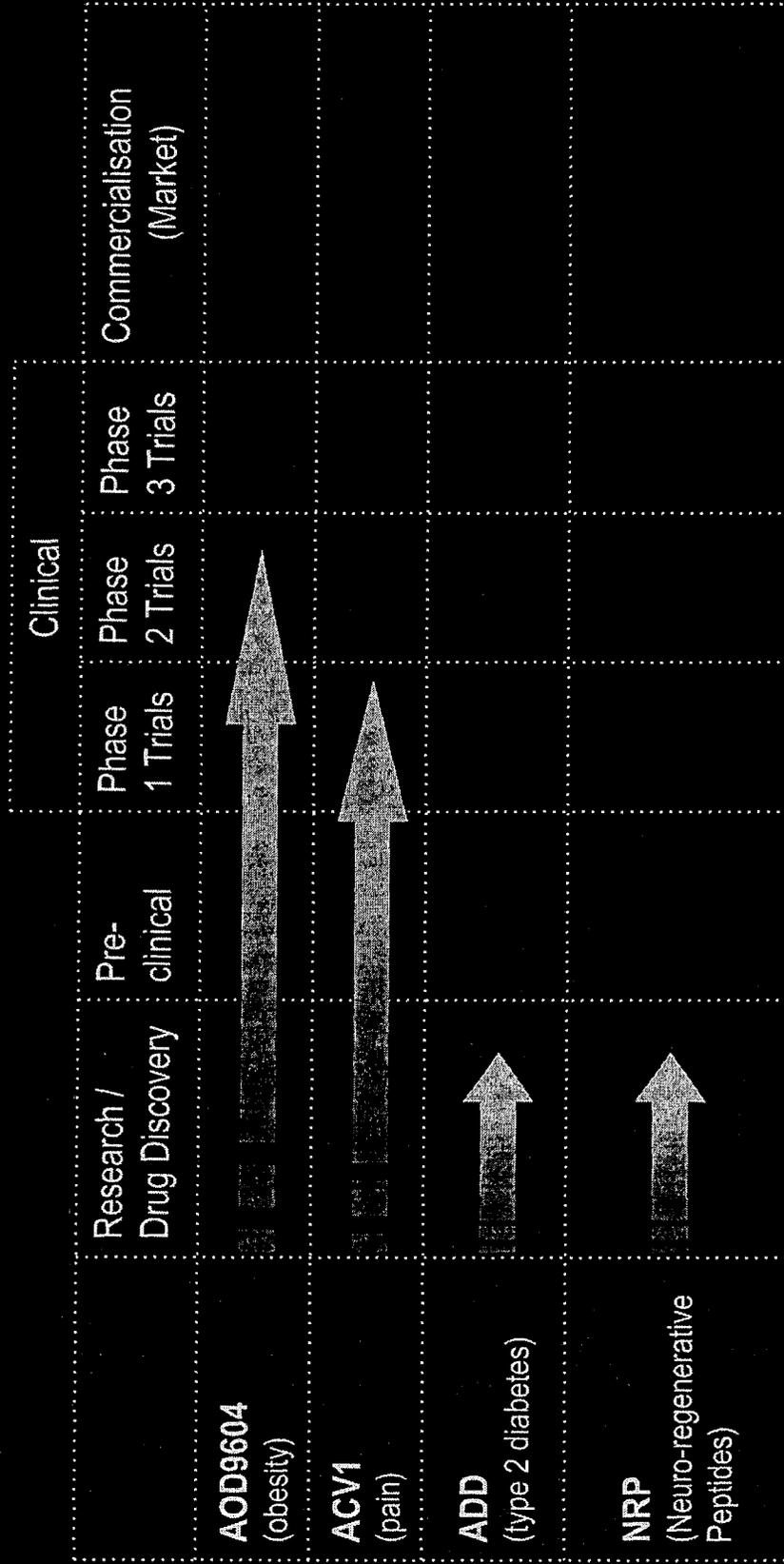
# What does Metabolic do?

- Two drugs in the clinic
  - AOD9604
    - Peptide for obesity and metabolic syndrome
    - Phase 2B complete, dose finding study started in Oct 05
  - ACV1
    - Peptide for pain
    - Phase 1 dosing complete, Phase 2A H106
- Several drug candidates in research
- Expansion of clinical pipeline in progress
- Expansion of pre-clinical pipeline ongoing

# Why invest in Metabolic?

- Two high potential drugs in the clinic, one in advanced Phase 2, each addressing billion dollar markets
- Strong patents with long lives
- Experienced management (CEO with science, management, big pharma, US biotech experience)
- Track record of clinical development (5 trials completed so far, 2 more in 2005)

# Metabolic's Pipeline



# ACV1

Metabolic's innovative pain drug

R&R NY 071105

7



1-3% of the population of the USA and Europe have neuropathic pain. This is expected to double in the next five years.

Less than 50% get relief from current therapies.

From Espicom Business Analysis 2005.

# What is ACV1?

- Peptide derived from the toxins of the cone snail
- Reduces nerve pain in animals
- Also appears to repair the damaged nerves that cause the pain
- Safe and well tolerated in animals

# ACV1 Clinical Update

- Phase 1 clinical trial (safety) started on schedule in June 2005
- Dosing completed on schedule in Sep 2005
- Final results to be announced in Nov 2005
- Phase 2A expected to start first half of 2006, subject to Phase 1 outcome

# The market for pain drugs

- Significant need for new pain killers with new modes of action (e.g. ACV1)
- For neuropathic pain, many people get no relief from existing therapies
- Very large market with limited competition
- Much “off-label” use (e.g. anti-convulsants, anti-depressants)
- Most existing drugs have side effect issues

# Pain market - the people

- 42% of US adults report daily pain
- 89% of US adults report monthly pain
- 15% report severe debilitating pain
- 10% have chronic pain
- 1-3% have neuropathic pain, expected to double in the next 5 years
- Of these about 50% from diabetes, 15% from herpes

# Pain market - the dollars

- Total pain market: US\$40 billion, growing to US\$75 billion by 2010
- Neuropathic pain market: US\$2.5 billion, growing to \$5.5 billion by 2010
- Diabetes, shingles, HIV, immune disorders, toxic neuropathies (e.g. chemotherapy)
- Until recently only one approved drug, clinically effective in only 30% of patients (Neurontin)
- Neurontin sales in 2004 were US\$2.7 billion (about 55% for neuropathic pain)



# AOD9604

## Metabolic's innovative obesity drug

R&R NY 071105

14



If current trends in the USA continue, of the cohort of children born in the year 2000, 50% can expect to have obesity related diabetes in their lifetime.

Centers for Disease Control, USA  
quoted in "Fat Land"  
By Greg Critser, 2003.

# What is AOD9604?

- AOD9604 is a peptide fragment of growth hormone that restores the ability of the body to burn fat and hence reduce weight
- It has the fat burning but not the growth stimulating activities of growth hormone
- Based on studies so far, it appears to be very safe and well tolerated, as expected for a natural hormone molecule
- Once daily oral delivery

# AOD9604 - Clinical history

Trial Phase	Subjects	BMI	Doses tested	Route of admin	Year
Phase 1	15 non-obese males	normal	~3 - 40 mg (1 group)	Intravenous, single dose	2001
Phase 2A	22 obese males	>35	~2 - 10 mg (4 groups)	Intravenous, single dose	2002
Phase 2A	16 obese males	>35	10 - 60 mg (4 groups)	Oral, single dose	2002
Phase 2A	36 obese males	30 - 47	10 - 60 mg (4 groups)	Oral, multiple dose	2002/ 2003
Phase 2B	300 obese male & female	>35	1 - 60 mg (6 groups)	Oral, multiple dose	2004
Phase 2B low dose	480 obese male & female	30-45	0.25 - 1 mg (4 groups)	Oral, multiple dose	2005 to 2007

# Results from our previous trials

- Safety and tolerability
  - excellent results so far
- Efficacy
  - overall data support competitive efficacy
  - primary endpoint qualified
- Optimal Dose
  - initially unclear, now better understood
  - lower doses likely required
  - possible upside of better outcomes at lower doses
  - new trial will confirm

# Comparison with existing drugs

Drug	Gender demographics (male vs female)	Weight loss relative to placebo over 12 weeks (kg)
AOD9604 1mg	Roughly equal	2.0
AOD9604 1mg, females	100% females	2.7 ←
Xenical	80% female	1.8
Meridia (2000 study)	Roughly equal	2.8
Acomplia	"Mainly" female	3.0 ←



# Other major world drugs: 2004 global sales (US\$)

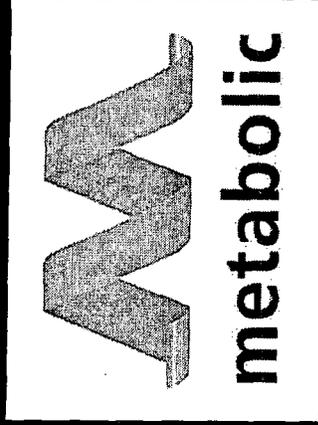
- Cholesterol lowering
  - Lipitor (Pfizer) \$10.9 b
  - Zocor (Merck) \$5.2 b
  - Pravachol (BMS) \$2.6 b
  - All drugs (13 in top 500) \$25.4 b
- Blood Pressure
  - Norvasc (Pfizer) \$4.5 b
  - Diovan (Novartis) \$3.1 b
  - Cozaar (Merck) \$2.8 b
  - All BP lowering (36 in top 500) \$25.5 b plus
- Obesity
  - Xenical (Roche) \$477 m
  - Meridia (Abbott) \$305 m
  - Acomplia (S-A), predicted >\$1 b
  - All (prescription) currently less than \$1b

# What's coming up?

- AOD9604 low dose STUDY started in Oct 2005, on schedule - (lower doses, more subjects, longer duration, diet program)
- AOD9604 recruitment progress updates - continual until recruitment complete
- ACV1 Phase 1 results to be announced in Nov 2005
- ACV1 Phase 2A starts H1 06 (subject to Phase 1 outcome)
- ACV1 Phase 2A ends H2 06
- AOD9604 low dose STUDY results to be announced early 2007
- Additional projects for clinical and preclinical pipelines under ongoing review

# The Metabolic Team

Arthur Emmett MBBS	Chairman of the Board	30 years in big pharma, incl SVP Global Medical and Public affairs for Novartis
Roland Scollay PhD, GAICD	CEO, Exec Director	25 years research management, 5 years Novartis executive, 7 years US biotech exec, experienced director
Chris Belyea PhD	CSO Exec Director	Founder and former CEO, 9 years biotech exec, registered patent attorney
Peter Dawson BBus, FICAA	CFO	30 years in commercial financial management, audit, CFO, M&A, turn around experience, public companies
Caroline Herd PhD	VP, Clinical Development	15 years as an experimental & clinical pharmacologist in industry and academia
3 Additional Directors	Independent NEDs	Experience in clinical drug development, global finance, commercial law



Thank you

Metabolic Pharmaceuticals Limited,  
Melbourne, Australia

# Low dose trial design: The “OPTIONS” study

- Randomised, double blind, placebo controlled
- 480 subjects to be recruited. 120 per group for ~90 completers at week 12
- Equal numbers of males and females, age 18-65
- BMI 30-45, waistline >102cm (males), >95cm (females)
- Primary end point weight loss at 12 weeks
- Treatment data collected for 24 weeks
- Placebo + 1mg, 0.5mg, 0.25mg
- Formal diet and exercise program (as per typical Phase 3 obesity trial design)
- 16 sites in Australia
- Powered to see ~1.8kg or better at 12 weeks
- Cost will be A\$8-10 million

# What does BMI mean?

- BMI = body mass index ("normal" is 20 - 25)
- Weight divided by height squared ( $\text{kg}/\text{m}^2$  or  $\text{lbs}/\text{inches}^2 \times 703$ )

Height	BMI 25	BMI 30	BMI 35	BMI 45
168 cm (5' 6")	71 kg (156 lbs)	85 kg (187 lbs)	99 kg (218 lbs)	127 kg (279 lbs)
173 cm (5' 8")	75 kg (165 lbs)	90 kg (198 lbs)	105 kg (231 lbs)	135 kg (297 lbs)
178 cm (5' 10")	79 kg (174 lbs)	95 kg (209 lbs)	111 kg (244 lbs)	143 kg (315 lbs)
183 cm (6' 0")	84 kg (185 lbs)	100 kg (220 lbs)	117 kg (257 lbs)	151 kg (332 lbs)



Australian Stock Exchange Limited  
ABN 98 008 624 691  
Exchange Centre  
Level 4, 20 Bridge Street  
Sydney NSW 2000

PO Box H224  
Australia Square  
NSW 1215

Telephone 61 2 9227 0334

Internet <http://www.asx.com.au>  
DX 10427 Stock Exchange Sydney

**FACSIMILE**

**Department: COMPANY ANNOUNCEMENTS OFFICE**

**DATE:** 16/11/2005

**TIME:** 11:36:13

**TO:** METABOLIC PHARMACEUTICALS LIMITED

**FAX NO:** 03-9860-5777

**FROM:** AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office

**SUBJECT:** CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

**MESSAGE:**

We confirm the receipt and release to the market of an announcement regarding:

Phase 1 Clinical Trial for Pain Drug - Positive Results

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16 November 2005

## **Metabolic's Phase 1 Clinical Trial Demonstrates Safety and Tolerability of Pain Drug**

***Metabolic Pharmaceutical's drug for the relief of neuropathic pain has successfully completed a Phase 1 human clinical trial and will now progress to Phase 2 human clinical trials in 2006.***

***The drug, called ACV1, offers a potentially novel way to deal with neuropathic (or nerve) pain, an area that is poorly covered by existing drugs. The current global market for neuropathic pain drugs is \$US2.5 billion annually, with this figure expected to double within five years.***

\* \* \*

Metabolic Pharmaceuticals today announced successful results of the Phase 1 single and multiple dose human clinical trial of its innovative neuropathic pain drug, ACV1, which will move into Phase 2a human trials in 2006 in patients suffering from neuropathic pain.

This Phase 1 study was the first time ACV1 has been administered to humans. The aim, when delivered by subcutaneous injection to healthy male volunteers, was to assess:

- Safety and tolerability (which was the primary endpoint);
- Pharmacokinetics of the drug (the appearance and disappearance of the drug in the body, particularly in the blood); and
- Pharmacodynamics of the drug (the physiological effects of the drug in the body).

The current global market for neuropathic pain drugs is in the order of US\$2.5 billion per annum, a number expected to at least double in the next five years. Presently this market is poorly served by existing drugs. ACV1's novel mechanism of action may offer an improved outcome.

Metabolic's CEO, Dr Roland Scollay, commented: "I am pleased to say that this study was performed on schedule and with successful outcomes. ACV1 was shown to have a very good tolerability profile in Phase 1 over the full dose range tested and this is a very pleasing result. All currently approved drugs used to provide relief in patients with neuropathic pain are substantially limited in their usefulness because the high doses that work well in animals are not well tolerated in humans due to side effects."

"It has always been our view that, based on animal data, ACV1 has significant potential as an analgesic drug. We have shown good efficacy in animal models with no observed adverse effects at many multiples of the effective dose. This safety study is the first step in confirming these expectations in humans."

Further, Dr Scollay said that "given the level of interest in ACV1 received from overseas pharmaceutical companies and specialty biotechs and its high value potential, we look forward with considerable excitement to its further human clinical development."

## **Key Findings**

- There was no evidence of drug-related adverse effects with ACV1, at any of the dose levels used in either the single or multiple dose components of the study, except for transient and mild local skin reactions around the injection site. These skin reactions are common with injected drugs and, at the level observed in this trial, will not present a problem for ongoing development of the drug.
- The pharmacokinetic information from the study showed that the drug distributed throughout the bloodstream in line with a time profile predicted from animal studies.
- The drug caused no numbing of normal sensation or blunting of normally painful stimuli in these healthy subjects - a desirable outcome. This result is consistent with the accumulated animal data on ACV1, which indicate that the drug specifically reverses the *abnormal* sensitivity (manifested as "burning or aching") in pain sensing nerves called C-fibers experienced in the injured nerve ("neuropathic") state.

See Appendix for Phase 1 trial details.

## **Next Steps**

Protocols for the Phase 2a trial are currently being designed, in consultation with experts in Australia and the US. The trial will be held in Australia and is planned to commence in 2006 as soon as the drug supplies are produced and ethics committee approvals obtained. All the required animal toxicity and safety studies have been completed.

Given the high value potential of ACV1 and in order to accelerate its further development, Metabolic will be reviewing the various options available for financing Phase 2 clinical trials.

## **Neuropathic pain**

Neuropathic pain is generated from damaged nerves. The damage may be mechanical or result from diseases such as diabetes, from viral infections such as herpes or HIV, or from the side effects of toxic drugs such as those used to treat cancer. Neuropathic pain affects 1-3% of the population and the number is growing. In many cases the pain is severe, long lasting and debilitating and current drugs only provide relief to about half of the affected individuals. The current global market for neuropathic pain drugs is about US\$2.5 billion per annum and this is expected to grow to about US\$5.5 billion by 2010.

\* \* \*

## Appendix – ACV1 Phase 1 Trial Details

<b>Name</b>	METACV101
<b>Investigational Product</b>	ACV1: 16 amino acid peptide, nAChR antagonist
<b>Type</b>	Phase 1 single and multiple ascending dose
<b>Blinding</b>	Double blind
<b>Controls</b>	Placebo (vehicle)
<b>Drug Administration</b>	
<i>Route</i>	Subcutaneous injection
<i>Frequency</i>	Single dose Multiple dose: once per day for 7 days
<i>Dose levels</i>	Single dose: 0.005, 0.015, 0.05, 0.1, 0.2, 0.4 mg/kg Multiple dose: 0.1, 0.2, 0.4 mg/kg per day
<b>Number of Subjects Enrolled</b>	45 (all completed)
<b>Subject Selection Criteria</b>	Healthy males aged 18 to 49 years
<b>Subjects Recruited</b>	Age range 18 to 45 years
<b>Trial Location</b>	CMAX Clinical Study Facility, Adelaide, Australia
<b>Primary Endpoint</b>	
<i>Safety and tolerability</i>	No evidence of drug-related adverse effects at any dose except for transient and mild injection site reactions
<b>Secondary Endpoints</b>	
<i>Pharmacokinetics</i>	Linear over the dose range Profile as predicted from animal studies
<i>Pharmacodynamics</i>	No effect on threshold of normal sensation No effect on threshold of normally painful stimulus

### **About Metabolic**

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### **Background information on the drug development process**

The steps required before a drug candidate is commercialised include:

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2. Pre-clinical testing, laboratory and chemical process development and formulation studies;
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5. Marketing and sales

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Of short duration.

#### **Phase 2**

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- to determine tolerance and optimal dosage (2B).

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Trials undertaken to further evaluate dosage and clinical efficacy and to further test for safety in an expanded patient population in clinical study sites throughout major target markets (e.g. USA, Europe and Australia).

---

#### **Contact Information**

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