ASX Announcement

metabolic

ASX code: MBP

Metabolic's obesity drug - Phase 2B clinical trial results

- **Trial results do not support commercial viability of obesity project: programme is terminated**
- **Metabolic will focus on development of its high potential pipeline, which includes pain, osteoporosis and the Oral Peptide Delivery Platform**
- **Current cash position ~$24 million, sufficient to fund all activities in the medium term**

Melbourne, 21 February, 2007. Metabolic Pharmaceuticals Limited (ASX: MBP) announced today that the Phase 2B trial results for its drug, *AOD9604*, do not support the commercial viability of the drug as a treatment for obesity. Development of the drug for this condition is terminated.

Trial results showed that weight loss compared to placebo at the primary and secondary endpoints of 12 or 24 weeks of treatment, was too low to reach statistical significance. The design of the obesity trial included Phase 3 conditions, such as a broader population of subjects (536 in total) and a formal diet and exercise programme. Under these additional conditions the *AOD9604* treatment did not demonstrate the weight loss required to support commercial outcomes.

The Company will focus on its other projects, including *ACV1* for neuropathic pain (currently in Phase 2 trials) and *AOD9604* for osteoporosis, as well as extending the application of its *Oral Peptide Delivery Platform* to other high value drugs.

Dr Arthur Emmett, Chairman of Metabolic said "It is the nature of our industry that not all clinical stage drugs progress from Phase 2 to Phase 3 trials. That is why the Board of Directors has long emphasised the building of a strong and diverse pipeline. We will progress our programmes for the treatment of neuropathic pain and osteoporosis, and are continuing with preclinical development of the *Oral Peptide Delivery Platform*. These products are aimed at addressing unmet needs in multi-billion dollar markets".

Metabolic CEO, Dr Roland Scollay, said "We set out to conduct a high quality trial that would be predictive of a Phase 3 result and provide data to establish the commercial viability, or otherwise of the drug, prior to committing to the significant expense of a full Phase 3 trial. These objectives were achieved. The important thing for Metabolic now is that we maintain our focus on advancing the development of our other programmes, all of which have the potential to generate significant value for shareholders".

Weight loss at the primary and secondary endpoints of 12 or 24 weeks of treatment, after allowing for the effects of the diet and exercise programme, was less than 1 kg in all dose groups. There was a subgroup, predetermined in the trial design, which did show weight loss at the levels seen in the previous trial (see appendix), but the overall population did not respond consistently. Given the high levels of weight loss seen in the placebo group (diet and exercise but no drug), it may be that the drug effects were overwhelmed by the effective weight loss programme, a programme which was consistent with that outlined in the relevant FDA guidelines. The safety and tolerability of *AOD9604* was excellent with no evidence of any difference from placebo.

The result of the *OPTIONS Study* has been announced ahead of schedule due to the clear and definitive outcomes which required less internal analysis than expected by the Company.

Detailed information regarding the trial design and results can be seen in the Appendix.

Pipeline

ACV1 for Neuropathic Pain currently in Phase 2A clinical trials

The neuropathic pain programme will continue to be a major activity, with the first of two Phase 2A clinical trials on *ACV1* in progress and results due in mid 2007. The second Phase 2A clinical trial is due to commence in March 2007. *ACV1* has shown strong effects in animals and a clean safety and tolerability profile in a human Phase 1 trial. Neuropathic pain is a large and growing market (US$2.7 billion in 2005).

AOD9604 for Osteoporosis

In animal studies, *AOD9604* has shown beneficial effects in the prevention and treatment of osteoporosis. Ongoing animal studies for the osteoporosis programme are expected to be completed during the second half of 2007. Further development will be considered in light of the study results and a costing analysis.

Oral Peptide Delivery Platform

Metabolic's *Oral Peptide Delivery Platform* achieved proof-of-concept in 2006, following animal studies testing a newly created oral variant of Metabolic's pain drug (*ACV1*) which displayed high levels of oral availability for the drug which was previously only effective by injection. The Company is currently designing and testing oral variants of a range of high-value peptide drugs, and will report progress over 2007.

New opportunities

Metabolic will continue its active search for new opportunities to add to the existing pipeline.

Resources

Current cash position of ~$24 million

The Company has sufficient funds to continue all its planned activities in the medium term. Projections show that as at June 2007, Metabolic will have cash reserves sufficient to progress existing projects to significant milestones, including *ACV1* neuropathic pain trials and the advancement of the *Oral Peptide Delivery Platform.*

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Appendix 1: The OPTIONS Study trial design

Number of subjects:	536 subjects enrolled, approximately equal numbers of men and women
Key subject selection criteria:	▪ BMI (Body Mass Index) 30-45 kg/m^2; ▪ Age 18-65 years; and ▪ A waist circumference of more than 102 cm for males and 95 cm for females, in otherwise healthy subjects.
Rationale:	A previous Phase 2B trial involved no formal diet and exercise programme. In that trial all five dose groups of *AOD9604* produced average weight loss greater than placebo after 12 weeks of treatment. The response was bimodal for both genders with the best dose group at 1mg, which fell short of significance (p=0.1, p=0.05 required) on the primary analysis but reached significance in the female subgroup. This *OPTIONS Study* was designed to explore doses at and below 1mg and to seek to confirm the prior observations with a formal diet and exercise programme more similar to Phase 3 conditions in line with relevant FDA guidelines.
Blinding status:	Double-blind
Placebo controlled:	Yes
Treatment route:	Oral (tablets)
Study design:	A four-week run-in period commencing at enrolment (week -4) involved the start of a dietician-supervised diet and exercise programme, with all subjects receiving placebo in a single-blinded manner. At week 0 the subjects entered the double-blind period and were randomised to one of the once daily dose levels of *AOD9604* or placebo. At week 24 the treatment and the diet and exercise programme ended. At week 28 the subjects were given final assessments and exited the study.
Dose groups:	0, 0.25, 0.5 and 1 mg (the 0 group was the placebo group)
Primary endpoints:	▪ Statistically significant weight loss after 12 weeks of treatment for any one of three daily AOD9604 oral doses of 0.25 mg, 0.5 mg and 1 mg compared to placebo; and ▪ Safety and tolerability. The trial was powered for an 80% chance of achieving significance on the primary endpoint if the weight loss compared to placebo was 1.8 kg.
Secondary endpoints:	▪ Weight loss over 24 weeks of treatment; ▪ Comparison of the effects of the three different dose levels; ▪ Waistline reduction over 24 weeks of treatment; ▪ Body fat reduction assessed by whole body DEXA scans; and ▪ Improvement in risk factors such as glucose control and lipid profiles over 24 weeks of treatment.
Trial sites:	16 clinical trial sites throughout Australia
Contract Research Organisation:	Kendle Pty Limited

Appendix 2: Results of the OPTIONS Study

Subject demographics:

56% female (one-third post-menopausal), 44% male

Average height 170 cm

Average weight 106 kg

All dose groups similar

Subjects attending each visit:

Dose Group	0mg	0.25mg	0.50mg	1.0mg
Week 0 (randomisation)	125	127	125	125
Week 12 (primary endpoint)	106	103	101	98
Week 24 (end of treatment)	92	90	90	85

No significant difference between groups.

Primary endpoint – weight loss outcome and comment:

Not met.

A plot of weight change over the course of the study for the full analysis set is provided on the following page.

Pre-defined subgroups for secondary analysis were stratified into gender, initial BMI (<35 or >=35 kg/m^2), and weight loss response to the 4 weeks of diet and exercise before randomization (<2 kg or >=2 kg).

Examination of the subgroups shows that females with low response to the diet and exercise before randomisation show similar effect sizes to those reported in the previous trial.

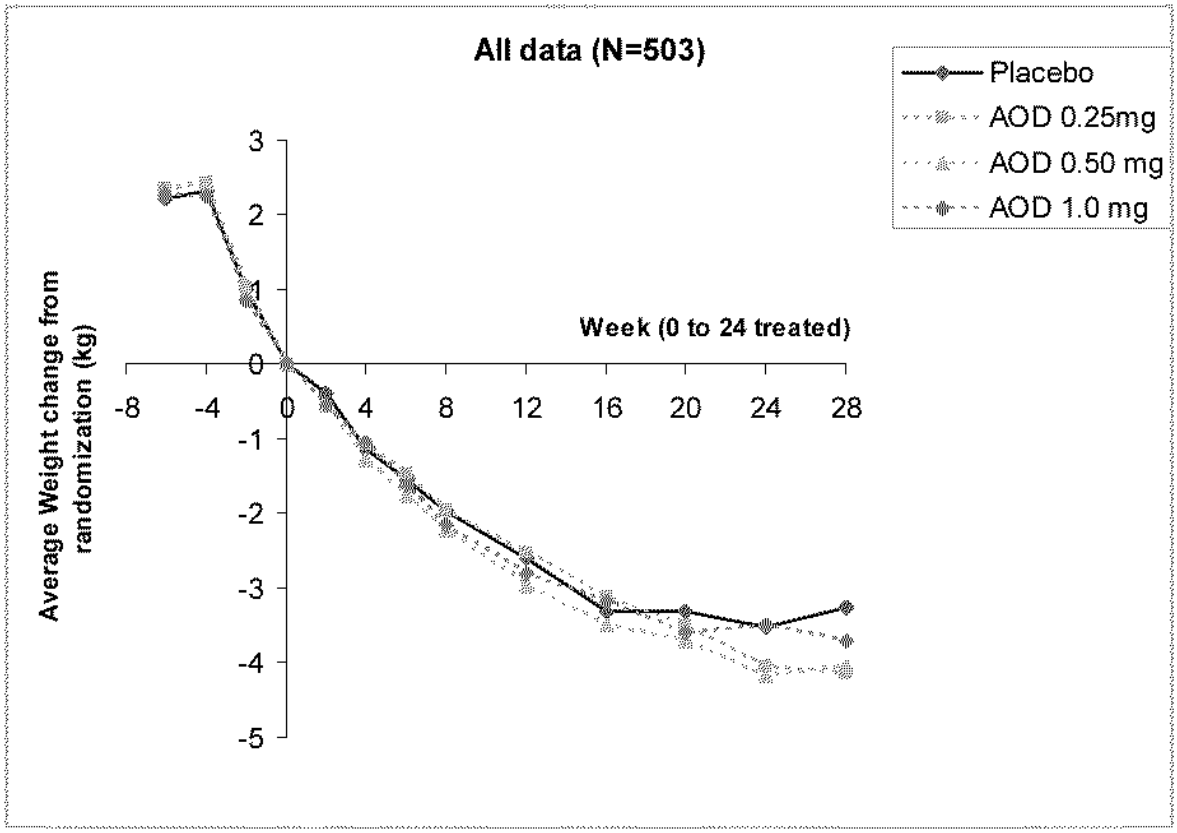
Our conclusion is that *AOD9604* does not combine or synergise with successful use of an ongoing diet and exercise programme, but may show some effect with moderate weight loss effort in females.

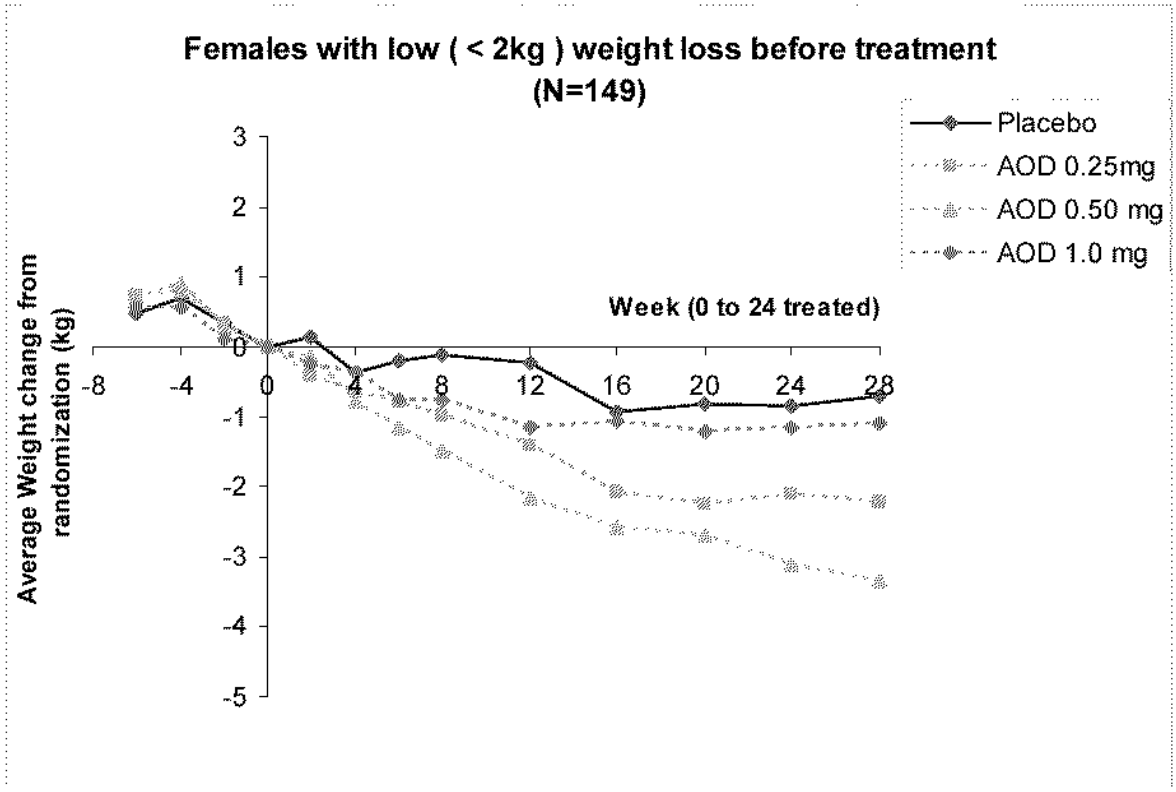
Primary endpoint – safety:

Preliminary analysis shows no evidence of any difference between placebo and any of the *AOD9604* treatment groups on safety or tolerability.

Secondary endpoints:

No relevant findings.


All data (N=503)
Placebo
AOD 0.25mg
AOD 0.50 mg
AOD 1.0 mg
Average Weight change from randomization (kg)
Week (0 to 24 treated)
3
2
1
0
-1
-2
-3
-4
-5
-8
-4
0
4
8
12
16
20
24
28


Females with low (< 2kg) weight loss before treatment (N=149)
Placebo
AOD 0.25mg
AOD 0.50 mg
AOD 1.0 mg
Average Weight change from randomization (kg)
Week (0 to 24 treated)
3
2
1
0
-1
-2
-3
-4
-5
-8
-4
0
4
8
12
16
20
24
28