**MATERIAL CHANGE REPORT UNDER**

***SECURITIES ACT* (BRITISH COLUMBIA) SECTION 85(1) FORM 53-901.F**
***SECURITIES ACT* (ALBERTA) SECTION 146 FORM 27**
***THE SECURITIES ACT* (SASKATCHEWAN) SECTION 84(1) FORM 25**
***THE SECURITIES ACT* (MANITOBA)**
***SECURITIES ACT* (ONTARIO) SECTION 75(2) FORM 27**
***SECURITIES ACT* (QUEBEC) SECTION 73**
***THE SECURITIES ACT* (NEWFOUNDLAND) SECTION 76(2) FORM 26A**
***SECURITIES ACT* (NOVA SCOTIA) SECTION 81(2) FORM 27**
***SECURITY FRAUDS PREVENTION ACT* (NEW BRUNSWICK)**
***SECURITIES ACT* (PRINCE EDWARD ISLAND)**

***Item 1. Reporting Issuer***

AnorMED Inc. ("AnorMED")
Suite 200, 20353 - 64th Avenue
Langley, British Columbia V2Y 1N5

***Item 2. Date of Material Change***

November 4, 2002

***Item 3. Press Release***

The press release was issued at Langley, B.C. on November 4, 2002 and disseminated via Canada NewsWire.

**Item 4. Summary of Material Change**

On November 4, 2002, AnorMED announced that it has been notified by its licensee, Shire Pharmaceuticals Group plc ("Shire"), that FOSRENOL™ has shown to be effective in reducing high phosphate levels associated with end stage renal disease, and also reduces the occurrence of hypercalcaemia, a side-effect which is increasingly linked to cardiovascular disease in these patients.

***Item 5. Full Description of Material Change***

AnorMED announced that FOSRENOL™ (lanthanum carbonate), a new phosphate binder for use in dialysis patients, licensed to Shire, has shown to be effective in reducing high phosphate levels associated with end stage renal disease, and also reduces the occurrence of hypercalcaemia, a side-effect which is increasingly linked to cardiovascular disease in these patients. In addition, new interim data from the US phase III clinical trials show the longer term efficacy and tolerability of FOSRENOL for up to two years.

Four posters[1,2,3,4,] on FOSRENOL, two of which feature data from phase III trials, are being presented today during the American Society of Nephrology 35th Annual Meeting and Scientific Exposition in Philadelphia, Pennsylvania, USA. These data on FOSRENOL have been submitted for regulatory review in the US, the EU and Canada, and development continues for Japan. *(Details of the studies are attached as an Appendix A hereto.)*

These results continue to support the potential of FOSRENOL as a new treatment option for patients with serious kidney disease. Data being presented at this meeting, and previously, clearly demonstrate that FOSRENOL, in addition to controlling the patient's phosphate levels, may also offer additional medical benefits compared to some currently available agents, such as calcium carbonate.

The two phase III studies[3,4] show that treatment with FOSRENOL (lanthanum carbonate) is not only effective in reducing high phosphate levels associated with end stage renal disease, but also reduces the occurrence of hypercalcaemia, a side-effect which is increasingly linked to cardiovascular disease. Interim data from a 1,200 patient long-term safety[3] study showed fewer serious adverse events and deaths in the FOSRENOL group. The study shows a statistically significant reduction in mortality in those patients receiving FOSRENOL compared with those receiving standard therapies. In the European study[4], calcium x phosphate product, known to be associated with increased mortality and morbidity in dialysis patients, was reduced to a greater extent by FOSRENOL treatment compared with calcium treatment. Data collection and analyses are ongoing.

According to the Canadian Institute for Health Information, over 14,000 Canadians underwent dialysis in 2000, with approximately 4,400 new patients beginning dialysis treatment in Canada each year. It is also estimated that there are approximately 280,000 kidney dialysis patients in the U.S., 225,000 in Europe, 190,000 in Japan and 90,000 in the Pacific Rim region.

One of the most serious and common side effects of kidney dialysis treatment is hyperphosphatemia, or an increase in the levels of phosphate in the blood. This increased phosphate, together with other biochemical disturbances such as hypercalcemia and hyperparathyroidism can result in a bone disorder known as renal osteodystrophy which causes pain and weakening of the bones. Recent clinical data also suggest that disturbance of calcium and phosphate levels may also be associated with the development of cardiovascular disease, which accounts for nearly 50% of all deaths in dialysis patients.

FOSRENOL is developed as a convenient chewable tablet, which unlike other treatments, can be taken without water. This is a significant advantage since dialysis patients must restrict their fluid intake. FOSRENOL binds in the stomach to phosphate derived from food; other existing treatments bind in the intestine, which is later in the digestive process. Once bound, the FOSRENOL/phosphate complex cannot pass through the gut lining into the blood stream and is eliminated from the body. As a consequence, overall phosphate absorption from the diet is decreased significantly. Shire has conducted an extensive clinical research program for FOSRENOL™ involving over 1700 patients, some of whom

have been treated for 36 months or more. This program has demonstrated that FOSRENOL™ is an effective phosphate binder with a proven safety profile. Further longer-term safety data continues to be collected. FOSRENOL™ has been submitted for regulatory review in Canada, the EU and USA, and development continues for Japan.

References:

1. "Administration of a novel phosphate binder, Fosrenol™, with food is associated with good tolerability and low systemic absorption". J. Stewart, N. Frazer. Poster presented at the annual meeting of the American Society of Nephrology, Philadelphia, USA, 1-4 November 2002.

2. "Fosrenol™ (lanthanum carbonate) is well tolerated in patients requiring hemodialysis: Results of a Phase I Clinical Trial". N. Frazer, M. Sack. Poster presented at the annual meeting of the American Society of Nephrology, Philadelphia, USA, 1-4 November 2002.

3. "Fosrenol™, a novel non-calcium, non-aluminium phosphate binder, has a good safety and efficacy profile in the long-term treatment of hyperphosphataemia in hemodialysis patients". WF Finn & MS Joy for the Fosrenol™ Study Group, Department of Medicine, University of North Carolina, Chapel Hill, NC, USA. Poster presented at the annual meeting of the American Society of Nephrology, Philadelphia, USA, 1-4 November 2002.

4. "The novel, non-aluminium, non-calcium phosphate binder, lanthanum carbonate (Fosrenol™ ), is an effective treatment for hyperphosphataemia and has a good safety profile". AJ Hutchison, Manchester Royal Infirmary, Manchester, UK. Poster presented at the annual meeting of the American Society of Nephrology, Philadelphia, USA, 1-4 November 2002.

Note: Certain of the statements contained herein contain forward-looking statements which involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of AnorMED, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. AnorMED does not expect to update forward-looking statements continually as conditions change. Investors are referred to the full discussion of risk factors associated with AnorMED's business contained in AnorMED's Annual Information Form filed with securities regulatory authorities dated August 16, 2002.

### *Item 6. Reliance on Section 85(2) of the Act*

Not applicable.

### *Item 7. Omitted Information*

No significant facts remain confidential and no information has been omitted in this report.

### *Item 8. Senior Officers*

**Name of Senior Officer**: Mr. W.J. (Bill) Adams
Chief Financial Officer

**Telephone Number**: (604) 530-1057

***Item 9. Statement of Senior Officer***

The foregoing accurately discloses the material change referred to herein.

DATED at Langley, British Columbia, this 8th day of November, 2002.

***"W.J. Adams"***

Signature

W.J. (Bill) Adams,
Chief Financial Officer

Name and Position of Signatory

## APPENDIX A

## Details of Studies

### Two-Year US Study

The two-year open-label randomised parallel group comparator trial was conducted at 96 sites across America. After screening and a three-week washout period, 600 patients were randomised to receive lanthanum, and 603 continued on their prestudy conventional phosphate binder. During the six-week dose titration phase, patients received a starting dose of lanthanum 750-1500mg/day at the discretion of the investigator, and could be titrated up to a maximum dose of 3000mg/day as necessary. Thereafter, patients received maintenance therapy for a further 24 months.

Interim analysis showed that control of serum phosphorous levels were comparable between the two groups over one year. At this time point, the mean serum phosphate level was 6.3 $\pm$ 1.7 mg/dL in lanthanum-treated patients compared with 6.3 $\pm$ 1.9mg/dL in patients receiving standard therapies. At week 104, there was no significant difference between the lanthanum and conventional groups in the proportion of patients whose pre-dialysis serum phosphorous levels were adequately controlled ($\leq$5.9mg/dL) ($p = 0.13-0.55$). Treatment-emergent adverse events were more common in the conventional treatment group than in the lanthanum treatment group (92.3% vs 90.9%).

To date, interim data from this long term safety study enrolling over 1,200 patients show a statistically significant reduction in mortality in favour of FOSRENOL compared with those receiving standard therapies.

### European Study

Separately, a six-month, randomised multi-centre open-label active comparator controlled trial carried out in 67 centres from the UK, Germany, Belgium and the Netherlands was presented by Dr Alastair Hutchison, consultant nephrologist and Clinical Director of the Renal Unit at The Royal Infirmary, Manchester, UK. Patients were randomised to either lanthanum (375-3000mg/day, n = 510) or calcium carbonate (1500-9000mg/day, n = 257) during a five-week titration period, and remained on maintenance therapy for a further 20 weeks. Analysis showed that lanthanum treatment was associated with greater decreases in calcium x phosphate product (used to assess treatment efficacy) at both week 9 ($p = 0.009$ vs calcium) and week 25 ($p=0.061$ vs calcium).

Lanthanum was associated with a significantly lower risk of hypercalcaemic episodes than calcium carbonate – almost 40% of patients on calcium compared with only 6% of lanthanum-treated patients ($p = 0.001$) had high serum calcium levels above the normal limit during the study. In addition, hypercalcaemia was reported as an adverse event substantially more frequently with calcium carbonate (20.2%) than with lanthanum (0.4%). Metastatic and vascular calcification, resulting from hypercalcaemia, has well-recognised cardiovascular risks, and significantly contributes to overall morbidity and mortality in dialysis patients. Other adverse events were similar in the two groups.