

## Financial Review

The profit after tax of £1.1 million for the second half of 2001 was a major achievement for Vernalis and enabled the Company to report a reduction in the full year loss of 53% compared to 2000.

Turnover increased by 372% due principally to the receipt of £10.3 million (\$15 million) in milestone income in the fourth quarter on FDA approval of frovatriptan. We maintained tight control over our operating costs, with administrative expenses and research and development costs both lower in the second half. Administrative expenditure excluding goodwill amortisation was 29% lower than in 2000, as we began to realise the full benefits of the rationalisation and integration programme.

The consolidated loss for the year after tax reduced by 53% to £9.9 million (2000: £21.2 million). The second half net profit of £1.1 million compares to a first half net loss of £11.0 million.

## Profit and Loss Account

Turnover for the year of £13.8 million (2000: £2.9 million) included total income of £10.9 million in relation to frovatriptan milestone payments following FDA approval and sales of bulk drug for the manufacture of launch stocks. It also included payments of £2.8 million from Roche under the collaboration on our obesity programme.

Research and development expenditure amounted to £20.4 million (2000: £18.6 million). Expenditure in the second half was £9.9 million compared to £10.5 million in the first half.

Expenditure on development projects increased 4% to £9.8 million (2000: £9.4 million). New clinical studies started during the year included frovatriptan Phase IV post-approval studies and a Phase I drug interaction study with VML 670.

Our expenditure on discovery research increased 15% to £10.6 million (2000: £9.2 million) reflecting increased activity on a number of projects, particularly our Parkinson's disease programme and our new project in diabetes.

Administrative expenses excluding goodwill amortisation decreased 29% to £3.2 million (2000: £4.5 million), predominantly due to the closure of our Guildford premises during 2000. Expenditure in the second half reduced to £1.5 million compared to £1.7 million in the first half.

The tax credit on loss on ordinary activities of £1.3 million (2000: £1.7 million) represents amounts that we expect to receive from the Inland Revenue under legislation on research and development tax credits for small and medium size companies introduced by the Government during 2000.

Interest receivable amounted to £0.8 million (2000: £1.4 million), reflecting lower interest rates and average cash and short term investment balances during the year.

Interest payable increased to £0.6 million (2000: £0.04 million), reflecting interest on a \$10 million loan which we drew down in two equal instalments in December 2000 and March 2001.

## **Balance Sheet**

Intangible fixed assets increased to £22.4 million (2000: £7.0 million) reflecting the capitalisation of payments conditionally due to GlaxoSmithKline (GSK) under the agreement of December 2000 to buy out royalties due to GSK on sales of frovatriptan. Conditional on US launch of the product, the Company is committed to make four annual payments to GSK of \$5 million, starting in 2002, with a fifth annual payment of \$5 million contingent on the achievement of cumulative sales from launch of \$300 million. Based on the Directors' expectation that these sales levels will be achieved, the full potential commitment of \$25 million has been recorded as an intangible asset in the balance sheet at 31 December 2001 and will be amortised on a straight line basis from the date of launch until 2014, being the date of frovatriptan's patent expiry in the US.

Tangible fixed assets increased to £2.4 million (2000: £2.3 million). Capital expenditure during the year of £1.1 million (2000: £1.0 million) included £0.6 million on laboratory equipment, £0.4 million on computer equipment and software, and a further £0.1 million on building improvements, fixtures and fittings. During 2001 we undertook a major programme to upgrade our IT capabilities and infrastructure. This exercise is now largely complete and we expect capital expenditure to run at a much lower level in 2002.

Cash and short term investments of £18.0 million at 31 December 2001 fell by £2.8 million during the year (31 December 2000: £20.8 million). The cash outflow from operating activities was £8.4 million (2000: £22.7 million). This was offset by net interest received of £0.8 million (2000: £1.7 million), net proceeds from the exercise of employee share options of £0.4 million (2000: £0.2 million), and receipts of £3.5 million from the second draw down under the Elan loan facility. The average yield achieved on investments during the year was approximately 5.3%.

Creditors falling due within one year increased by £11.0 million to £16.3 million (2000: £5.3 million). This is primarily due to reclassification of the Elan loan of £7.4 million from amounts due after one year. The conditional payments to GSK described above have also been included in creditors at year-end.

Elan has an option, expiring during 2002, to pay Vernalis a reduced royalty on frovatriptan sales in return for agreeing to forgive the full amount of the loan including accrued interest. Our current expectation is that this option will be exercised. Subsequent to the balance sheet date the companies agreed to extend the repayment date for the loan, in the event that the option is not exercised, to May 2003.

Of the total conditional payments of \$25 million to GSK described above, an amount of £3.4 million (\$5 million) has been included in creditors falling due within one year in respect of the first annual payment, and a further £13.7 million (\$20 million) has been included in creditors falling due after one year, relating to the four subsequent annual payments. Creditors due after one year increased by £10.5 million to £14.1 million (2000: £3.6 million), reflecting the accounting treatment of the payments to GSK, offset by the reclassification of the Elan loan.

## **Headcount**

Headcount levels have remained stable during 2001. At the end of the year Vernalis employed 133 permanent staff (2000: 126) of which 103 (2000: 105) were employed in research and development.

## **Financial Outlook**

The milestone income following FDA approval of frovatriptan and the funding from the new agreements with Roche signed in early 2002 have significantly improved the near-term financial outlook for the Company. In the medium-term our funding requirements will continue to be influenced by the performance of frovatriptan in the market place. Our current expectation is that the product will be launched in the US and the first European markets in the second quarter of 2002.

Looking forward, we also anticipate the potential to generate income from earlier stage programmes in our portfolio. In January 2002 the announcement of the selection of the first candidate drug from our Parkinson's disease programme attracted attention from multi-national and regional pharmaceutical companies interested in forming a collaboration with us.

Furthermore, we expect the two new deals with Roche in obesity and diabetes to have a very positive impact on the Company's financial prospects. In addition to committed research funding over the next two years, we have the potential to receive substantial milestone payments from these programmes when candidate drugs progress through development, as well as very competitive royalties on future sales. Funding and potential milestone income from the Company's commercial collaborations now exceeds \$150 million in addition to the potential royalty revenues.

In addition, we continue to make the business more efficient by eliminating non-essential expenditure, and we have also taken steps to focus our research and development resources on the key programmes. Taken together these measures have enabled us to achieve ongoing cost reductions.

## **Portfolio Review**

### **Migraine (Frova<sup>TM</sup> / Migard<sup>R</sup>)**

We have made very significant progress in the last year and regulatory approval has now been achieved in the US and throughout the European Union (EU). In November 2001 FDA granted approval to market Frova<sup>TM</sup> in the US for the acute treatment of migraine. In January 2002 we received notification of regulatory approval for Migard<sup>R</sup> in 14 EU countries, having already received approval in France, which acted as the reference member state for the EU mutual recognition process.

Our licensees for frovatriptan, Elan for North America and Menarini for Europe, are now well advanced with preparations for launch in their respective territories. Elan has announced its intention to appoint a co-promotion partner and to launch the drug early in the second quarter. We anticipate that Menarini will commence the roll out into the initial European markets during second quarter 2002.

We expect our marketing partners to focus on the potential advantages from frovatriptan's prolonged presence in the bloodstream compared to other drugs in its class, particularly for patients with long duration migraines. The Vernalis clinical team is now conducting a number of new studies designed to further exploit this distinctive feature of the drug and to expand its clinical profile.

The first of the new studies, which is now complete, was designed to investigate the use of frovatriptan early in a migraine attack when patients' symptoms were still only mild. Preliminary results indicate that in the majority of cases, the symptoms had either completely resolved or had not progressed beyond the mild stage two hours after taking the drug. Importantly, the incidence of headache recurrence in a 24 hour period following dosing was very low, which is consistent with the experience of patients who have taken frovatriptan in earlier trials. We expect results from this study to be published later this year.

Patient recruitment has now been completed in a 400 patient, multi-centre study in the US which will investigate the prevention of migraine attacks in women with menstrually associated migraine. It is estimated that 30% or more of female migraine sufferers often experience attacks during their menstrual period. This study is designed to show that frovatriptan is an effective preventative treatment for this form of migraine. We expect to have preliminary results from this study by the end of this year.

## **Sexual Dysfunction – VML 670**

Approximately 60% of the estimated 150 million people receiving medication for depression are treated with selective serotonin re-uptake inhibitors (SSRIs), and it is estimated that around 30-40% of these patients, both male and female, experience some form of sexual dysfunction as a side effect of the treatment.

VML 670 is a potent and selective 5-HT<sub>1A</sub> receptor agonist that we are developing as a treatment for sexual dysfunction experienced by patients taking SSRIs. We believe that VML 670 has the potential to restore normal sexual function in these patients, based on our understanding of the role of 5-HT<sub>1A</sub> receptors in modulating sexual activity.

We have now successfully completed a series of Phase I safety studies in human volunteers. Phase II patient trials are scheduled to commence in the second quarter of 2002.

## **Obesity – VR 1065**

Obesity is now recognised as a global epidemic and the incidence is increasing markedly both in developed and developing countries. It has been shown to substantially increase the risk of developing type 2 diabetes, coronary heart disease, hypertension, osteoarthritis and cancer. It is estimated that more than 250 million people worldwide are clinically obese. In the US, obesity affects around 35% of the population and more than 50% are overweight. The UK has one of the highest rates of obesity in Europe at around 18% of the population.

The important role played by the 5-HT<sub>2C</sub> receptor in controlling eating and satiety was a ground breaking discovery by Vernalis scientists in 1997. In many obese people, this control mechanism does not appear to work effectively and leads to excess food consumption, which the body stores as fat. Compounds that activate this receptor can help to promote the feeling of satiety and control the urge to eat to excess. Our programme is focused on developing novel and highly selective 5-HT<sub>2C</sub> receptor agonists as drugs to improve weight loss.

We made excellent progress during 2001 in our existing collaboration with Roche and received a third milestone payment in June following selection of VR 1065 as the first candidate drug. Roche has subsequently conducted a pre-clinical development programme with VR 1065 and anticipates commencing clinical trials in human volunteers early in the second quarter of 2002.

Based on the considerable success of this programme, we announced a second collaboration with Roche in obesity in February 2002 with the objective of taking further candidate drugs into clinical development. This new agreement provides additional research funding and increased milestones and royalties to reflect the potential market value of successful products in the field of obesity. Under both arrangements, Roche will fully fund the development of candidate drugs arising from this new collaboration.

## **Parkinson's Disease - VER-11135**

We made tremendous advances on this project last year and in January 2002 were able to announce the selection of VER-11135 our first candidate drug. This compound has now entered pre-clinical development with the objective of commencing Phase I clinical studies in the first half of 2003.

Most conventional therapies for Parkinson's disease are based on dopamine replacement. Although generally effective in the short term, these treatments can have severe, or even disabling, side effects and their effectiveness tends to decrease over time. In addition, current therapies that target dopamine do not slow down or stop progression of Parkinson's disease.

The neurotransmitter adenosine plays an important role in motor co-ordination and movement control. The adenosine A2A receptor is found in high density in the part of the brain responsible for motor function, where it appears to direct the activity of other neurotransmitter mechanisms that are dysfunctional in Parkinson's disease. We believe this may provide a novel approach to treat the symptoms of Parkinson's disease and to slow or stop its progression. This hypothesis is supported by data that Vernalis and other companies have generated on this class of compound. We have identified novel chemical classes of A2A receptor antagonists including compounds that have been shown to be effective in models of Parkinson's disease.

There is increasing evidence that A2A antagonists may also offer benefits to patients with other CNS disorders including depression and Alzheimer's disease.

### **Diabetes – Novel Targets**

Type 2 diabetes comprises a group of diseases characterised by high uncontrolled levels of blood sugar. Diabetes is associated with serious medical conditions including coronary heart disease, kidney failure, stroke, high blood pressure, blindness, nervous system disorders and disruption of blood supply to limbs, ultimately leading to amputation.

In the US alone it is estimated that type 2 diabetes affects approximately 14 million individuals and this is projected to increase by 40% by 2020. Diabetes can lead to multiple organ damage and it is estimated that 65% of diabetics die as a result of heart attack or stroke. There is mounting evidence that type 2 diabetes, which is often described as "adult-onset" diabetes, is now beginning to appear in adolescent and teenage children, probably as a result of the increasing prevalence of obesity in the young.

Our new strategic alliance with Roche is an important new deal for Vernalis with significant commercial potential. The agreement pools intellectual property and resources to discover, develop and commercialise new candidate drugs for the treatment of diabetes that target novel mechanisms of action for control of blood sugar levels.

In addition to the research funding over the next two years, we have the prospect of substantial milestone payments as well as very competitive royalties on future worldwide sales. Overall this represents potentially our largest commercial deal to date.