

R&D Review

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This edition of the Novogen newsletter is a review of the Company's research and development activities. The substantial growth in this area of the Company's activity over the past 2 years is highlighted by the large number of clinical studies being conducted globally, the increasing amount of data being generated by those studies, an expanding product pipeline, and an expanding patent portfolio.

All of this effort continues to grow the intrinsic value of the Company's greatest financial asset – its intellectual property. This newsletter is intended to give shareholders an insight into the Company's intellectual property position so that they might better understand the growing value of that asset.

Pharmaceutical

Novogen and the Australian Federal Government (through its R&D START program) have made a substantial investment in the development of a new family of drugs based on the benzopyran (or isoflavonoid) ring structure. This opportunity stems from the Company's development over the last few years of an extensive library of novel drug candidates with a related chemical structure. Novogen now is the leader world-wide in this emerging field of drug development and is proposing to bring a range of drugs to market targeting some of the major causes of ill-health in our community.

Why isoflavonoid compounds?

Isoflavones are naturally-occurring plant compounds with a wide range of biological activities in humans. The potential of these compounds for drug development now has been recognised, with a number of drugs based on the isoflavonoid structure currently undergoing clinical evaluation. Where Novogen is distinctive is in having a major proprietary position in this field through international patents.

The inspiration for the Novogen program was the discovery announced in 1992¹ of the presence in human blood of a class of compounds formed within the human body from dietary isoflavones. Novogen acquired full rights to those compounds and set about exploring their biological

activities. It was found that the body's process of 'humanising' these plant isoflavonoids increased their biological potencies up to hundreds of times. This led Novogen scientists to propose that these compounds represented a previously undiscovered class of biological regulators in the human body with hormonal properties. The increased biological potency of these structurally modified isoflavones without comprising their inherent safety indicated a highly promising and rich source of drug discovery. This exciting concept is the basis of the Company's growing intellectual property.

What is this library of compounds?

The library is the result of a concerted effort over the past four years by a team of synthetic chemists working collaboratively between Novogen and Australian university chemistry departments. These scientists created modified versions (analogues) of these naturally-occurring 'humanised' isoflavonoids. The aim was to create new compounds with even greater biological potency or with different biological effects. That objective now has been reached through the identification of analogues with novel and strong drug-like actions. This library of compounds (code-named NV products) comprises the original 'humanised' isoflavonoid compounds plus new analogues.

What makes this library so promising?

A common feature of this family of compounds is their ability to regulate signal transduction processes. Signal transduction processes are the enzyme-mediated processes within cells that ensure that cells respond to the body's chemical messages and behave normally. In degenerative diseases such as cancer, cardiovascular disease, rheumatoid arthritis and inflammatory bowel disease, these signal transduction processes behave abnormally causing cells to proliferate when they shouldn't, to migrate when they shouldn't, and to survive beyond their programmed lifespan. It is now widely acknowledged that correcting these aberrant signal transduction mechanisms offers the best and safest means of treating degenerative diseases. Novogen believes that its library of isoflavonoids offers a significant opportunity to correct these aberrant mechanisms in a uniquely well tolerated way.

What drugs have emerged from this library?

Over the past 3 years, the library has been subjected to laboratory and animal screening studies both within Novogen and via collaborators world-wide in order to identify potential new drug candidates. Four therapeutic areas have been actively targeted – cancer, cardiovascular disease (atherosclerosis and hypertension), actinic (sunlight-induced skin) damage, and inflammatory disorders (rheumatoid arthritis and inflammatory bowel diseases such as ulcerative colitis). From these screening studies, four drug candidates have been selected for further development and these four drugs now form the basis of the Company's clinical trial program.

The library continues to grow as new analogues are created, and the library will continue to be screened for new drug opportunities. In due course it is proposed to expand the screening program to include other therapeutic areas such as neurology, immunology and osteoporosis. For the moment, however, the Company's efforts are focused on the current four therapeutic areas and four identified drug candidates.

Cancer program

Cancer cells escape from the body's control by either under or over expressing certain key signal transduction processes. Novogen has found a number of compounds in its isoflavonoid library that exert potent anti-cancer effects by regulating these signal transduction processes. Two compounds have been selected as the lead anti-cancer drug candidates – phenoxodiol and NV-50. Phenoxodiol has been selected because it displays broad anti-cancer activity against a wide range of human cancer types *in vitro*, while NV-50 has been specifically selected for its activity against breast cancer cells *in vitro*.

Phenoxodiol

Background

Phenoxodiol has proven in pre-clinical studies to be an effective inhibitor of 3 key enzymes involved in important signal transduction processes – *topoisomerase 2* (an enzyme that promotes the ability of a cell to divide); *EGF-protein tyrosine kinase* (an enzyme that promotes the response of epithelial cells such as prostate and bowel cancer cells to growth factor); *sphingosine kinase* (an enzyme that promotes the ability of a cell to survive). The potent effect of phenoxodiol on sphingosine kinase is particularly important as this enzyme has only recently been recognised as a key contributor to the cancer process and is now identified as a priority target for anti-cancer drug development.²

By targeting such a wide range of key enzymes, phenoxodiol offers a unique opportunity to attack cancer cells on a broad front. The ability of phenoxodiol to knock out these three enzymes, and sphingosine kinase in particular, helps explain the observations in laboratory and animal studies that phenoxodiol blocks cancer cells from dividing and causes them to undergo natural death (apoptosis).³

Clinical status

Phenoxodiol has been prepared both as an intravenous formulation and an oral formulation. The clinical focus to date has been on the intravenous formulation with trials with the oral formulation about to start.

Phenoxodiol (intravenous form) has undergone two Phase Ia studies and currently is engaged in three Phase I/II studies.

Phase Ia

Two studies were conducted in small groups of cancer patients in mid-2000 in Australia. These studies were to establish that it was possible to achieve phenoxodiol levels in blood that were thought to be therapeutically relevant, and that the drug was well tolerated intravenously.

Phase Ib studies

These three studies all involve patients with late-stage malignant cancers whose cancers are refractory (unresponsive) to standard therapies. Phenoxodiol is the only anti-cancer therapy being used in these patients. The studies are open to patients with any form of solid cancer with the exception of breast cancer (see NV-50 below). These are dose-escalating studies, which means that patients are recruited onto progressively higher doses, with each patient remaining on the same dose throughout.

The objectives are at this stage of clinical development (a) to characterise the drug's toxicity, (b) to determine the maximum dose that can be tolerated, and (c) to look for evidence of the types of cancers that might be sensitive to phenoxodiol. Patients have their cancer status reviewed every 6 weeks including assessment of tumour mass by radiology. Therapy can be extended beyond 6 weeks provided that there is no drug-associated toxicity, and that there is no disease progression.

Study #NV06-0022. This study commenced at St George Hospital, Sydney, in late-2000 and is employing a low intensity treatment regime of single weekly injections. The doses being tested are 1, 2, 5, 10, 15, 20, 25 and 30 mg/kg. To date, 12 patients have been treated and the current dosage level is 20 mg/kg. A number of patients have had their therapy extended past 6 weeks, with the longest duration of therapy being 8 months. Completion of the formal part of this study is anticipated in Q3 2001.

Study #NV06-0023. This study is being conducted at the Sydney Cancer Centre, Royal Prince Alfred Hospital, Sydney, and commenced in March 2001. This study is employing a more intensive treatment regime with phenoxodiol being given by continuous intravenous infusion for 7 days followed by 7 days with no therapy.

This cycle is repeated until either toxicity or disease progression occurs. The doses being tested are 1, 5, 10, 16, 25, 33 and 40 mg/kg/day. To date, 10 patients have entered the study and the current dosage level is 16 mg/kg/day. No drug-associated toxicity has been encountered. Completion of this study is anticipated in Q4 2001.

Study #NV06-0024. This study is being conducted at The Cleveland Clinic, Cleveland, Ohio. It has been able to commence because of the granting by the US FDA to phenoxodiol of Investigational New Drug (IND) status in January this year. This study is a repeat of Study #NV06-0023 and is intended to provide expanded patient numbers and to ensure a variety of different cancer types. The first patient commenced treatment in July 2001. Completion of this study is anticipated in Q1 2002.

The results of studies #NV06-0022 and #NV06-0023 are to be made public later this year at scientific conferences. Until that time, the company is prevented under US FDA regulations to make any statement about the progress of clinical studies that may imply a therapeutic benefit for drugs under study.

The next steps

The Phase I/II clinical trial program is following a strategy of progressively increasing intensity of treatment. As a general rule, sustained, intensive anti-cancer therapy is recognised as providing the best possible anti-cancer effect. Currently available anti-cancer drugs cannot in general be used this way because of their toxicity which limits their use to high dosages over short periods. Animal studies have indicated that phenoxodiol is well tolerated when used intensively and continuously over a period of 28 days both orally and intravenously. The purpose of the next stage of the studies is to ascertain whether that same situation is possible in humans.

On this basis, phenoxodiol now is in a position to graduate to the most intense level of therapy possible, that being continuous, high dosage treatment for long periods

of time. This will be done with both the intravenous and the oral forms in order to provide an indication of the preferred dosage form.

A Phase II clinical trial of phenoxodiol given continuously by oral administration for 28 days has been approved to begin in an Australian hospital and is planned to commence in August 2001. Also, expansion of the current 7-day continuous intravenous infusion treatment regime with phenoxodiol to 28-day or greater continuous intravenous infusion is planned for Q3 2001.

The current Phase I/II program is projected to complete in mid-2002 and is expected to provide information on the most appropriate tumour types and the most appropriate treatment regime to pursue with phenoxodiol. Novogen anticipates that it then will be in a position to commence Phase IIb or Phase II/III studies at that time. Those studies are expected to be with one or two designated cancer types.

Phase II/III clinical studies to commence in 2002

NV-50

NV-50 is a derivative of phenoxodiol, specifically created to enhance the anti-cancer effect of phenoxodiol on breast cancer. In pre-clinical studies, in addition to the inhibition of signal transduction mechanisms in breast cancer cells displayed by phenoxodiol, NV-50 also has shown potent anti-estrogenic effects, blocking α -estrogen receptors and depriving breast cancer cells of growth stimulation by estrogen in the body.

NV-50 currently is completing pre-clinical studies and is expected to be in a position to enter clinical studies in early 2002.

Phase I clinical studies to commence in 2002

Cardiovascular diseases program

Most cardiovascular disease can be traced to abnormal signal transduction behaviour in cells making up the wall of blood vessels. Hypertension (high blood pressure) and atherosclerosis (thickening of artery walls) are the two most prominent cardiovascular diseases associated with abnormal signal transduction behaviour. Despite considerable medical research into this field, hypertension and atherosclerosis remain the major causes of death (through heart attack and stroke) in our community.

To date, available cardiovascular drugs have focused on individual therapies for hypertension (ACE inhibitors) and atherosclerosis (statins). The Novogen goal is to co-treat hypertension and atherosclerosis as a single disease with a single drug, and also to treat the underlying pathologies in an effective and comprehensive manner. In a recent major advance in this field, Novogen in collaboration with a number of prominent research institutions, has discovered a number of compounds from its isoflavonoid library that have displayed in pre-clinical studies a potential ability to switch off the underlying pathologies leading to hypertension and atherosclerosis. The first of these studies was recently

published⁴, and concluded that these isoflavonoid compounds have opened the door to the development of a new generation of cardiovascular drugs.

Pre-clinical studies to date have indicated that these drugs may induce significant improvements in central and peripheral blood vessel reactivity, significant reductions in cholesterol deposition in arteries, improved HDL ("good cholesterol") levels, reduced atherogenic plaques and reduced cholesterol oxidation. These effects have been shown to translate into improved control of blood pressure and atherosclerosis in animal studies. These highly promising results suggest the potential use of such drugs in both the prevention and treatment of hypertension, heart disease and stroke.

Pre-clinical studies are continuing with a number of drug candidates (of which NV-04 is the prime candidate). Human trials are expected to commence in 2002.

Phase I clinical studies to commence in 2002

Anti-Inflammatory program

NV-07

NV-07 has been identified as a novel and potentially important anti-inflammatory drug. It's novelty relates to its ability to control inflammation in a similar manner to the standard anti-inflammatory agents, corticosteroids, but unlike corticosteroids, NV-07 stimulates (rather than depresses) the immune system and has no known side-effects. NV-07 currently is engaged in two distinct areas of study – actinic skin damage and inflammatory bowel disease.

a) Actinic skin damage

NV-07 has shown exciting and significant results in pre-clinical trials where it has demonstrated an ability to reverse damage to skin caused from exposure to ultraviolet light or harmful chemicals. In pre-clinical studies, this therapeutic effect was obtained when NV-07 was applied to the skin after the damage was inflicted, suggesting that NV-07 has specific potential application as an after-sun skin repair lotion to undo the major damage caused to human skin as a result of sun exposure. The specific benefits were a reduction in the degree of sun-burn, reduced actinic

damage (wrinkling, thickening of skin), increased immune responsiveness in skin, and reduced skin cancer development. These outcomes are unique and point to a major opportunity for NV-07 in the therapeutic dermatologic field.

A Phase I clinical trial program is current with NV-07 being tested in human subjects for its ability to protect skin against both acute and chronic damage from sunlight. This is with a view to the commercialization of NV-07 as a novel dermatologic ingredient.

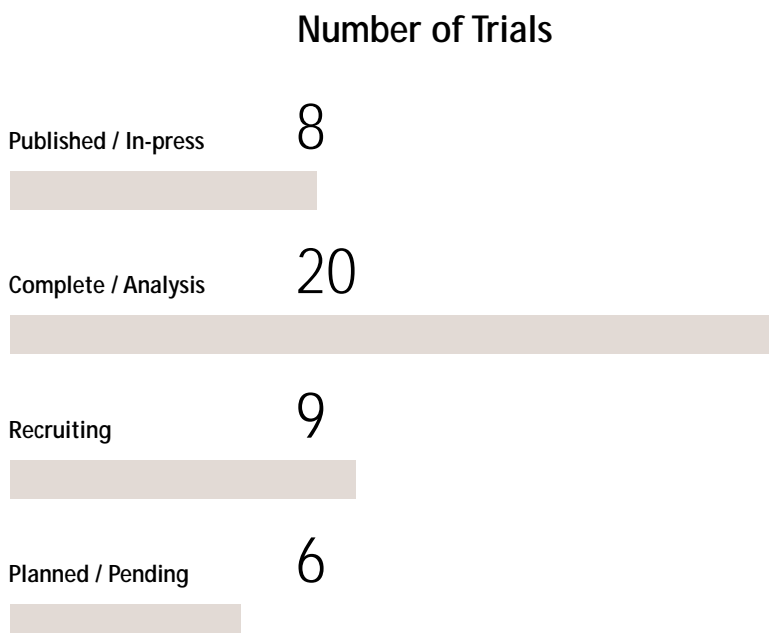
Phase II clinical studies to commence in 2002

b) Inflammatory bowel disease

Further development work is being undertaken to develop its use as a prescription systemic anti-inflammatory drug. The mechanisms of action of NV-07 suggest that it is a highly promising therapy for inflammatory bowel disease and rheumatoid arthritis. Pre-clinical tests are continuing in order to better understand its novel mechanisms of action and its level of effectiveness in the treatment of inflammatory disease in animals.

Phase I clinical studies to commence in 2002

Consumer Health Products



Novogen continues to invest considerable funds and energy in R&D in support of its consumer health products. The purpose of this considerable R&D program is to provide the clinical evidence necessary to support product marketing, to reassure consumers and doctors as to the products' safety, and to explore the full relevance of isoflavones to human health. The extensive number of clinical studies being funded by Novogen demonstrates why the Company has become the world leader in this important area of human health.

In the case of women's health, a notable feature of the R&D program is the expansion of the potential actions of isoflavones beyond that of acute menopausal symptoms. As important as acute symptoms such as hot flushes and mood swings are to women as they enter menopause, the more serious health consequences of menopause are increased risks of heart disease, osteoporosis and senile dementia. Another feature of women's health is in the area of breast disease, where diseases such as fibrocystic breast disease and breast cancer remain serious community concerns. Current therapies poorly address all of these important areas of community health and Novogen believes that its isoflavone consumer health products have the potential to make an important contribution in those areas by helping a growing number of 'baby boomers' maintain cardiovascular and breast health as well as mental alertness as they age.

The extensive clinical trial program revolving around the Company's three core products – Promensil™, Rimostil™, Trinovin™ – is best considered in terms of the following therapeutic objectives.

1. Isoflavones in the Management of Menopause

A supplement⁵ to the prestigious Journal of the British Menopause Society was published in March 2001 containing the proceedings of an educational symposium held in London in September last year on the benefits of red clover isoflavones in the management of menopause and the maintenance of bone and heart health. A number of papers delivered by international experts in the field of isoflavones and women's health were reproduced in the supplement and distributed internationally to women's health professionals. In an introduction to the volume, the eminent British gynecologist and Chairman of the British Menopause Society, Dr Malcolm Whitehead, stated that women are turning away from prescription HRT because of fear of side-effects and are turning increasingly towards alternative therapies. This publication represents a milestone in international acceptance of the health benefits of Novogen red clover supplements.

2. Promensil and Acute Symptoms of Menopause

Two preliminary studies were conducted with Promensil in this area between 1996-8. Those two studies broke new ground in being the first controlled studies of a standardised dietary isoflavone supplement conducted anywhere in the world in any therapeutic area and provided important information on appropriate design of clinical studies involving dietary isoflavones. Since then, Novogen has conducted a number of other, larger studies in the area of acute menopausal symptoms.

A study in The Netherlands at the Free University, Amsterdam, has now been completed and has produced a successful result in the management of acute menopause symptoms in women taking Promensil. The full findings will be presented at the annual meeting of the North American Menopause Society in October this year. Briefly, this study demonstrated that treatment with Promensil resulted in a statistically significant reduction in hot flushes from baseline in the treated group compared to the placebo group. This concurs with the finding of a South American double-blind, placebo-controlled study conducted independently of Novogen that showed a significant reduction in the incidence of hot flushes in the Promensil group versus the placebo group.

An open trial of Promensil has just been completed in Oxford, UK, and the results were reported in June at the British Menopause Society meeting in Birmingham.⁵ This study demonstrated that in postmenopausal women, with a minimum of 5 flushes per day, one Promensil tablet daily resulted in a significant reduction in hot flushes at weeks 4, 8 and 12 (33.15%, 45.5% and 58.5% reduction respectively).

Comment: Promensil has been evaluated in over 1000 women in formal clinical studies for its effects on a range of menopausal symptoms such as hot flushes. The overall summary is that Promensil provides significant and worthwhile symptomatic relief in the majority of the approximately 75% of women who either cannot or will not or should not take HRT because of prescription estrogen side-effects such as increased risk of stroke, and breast and uterine cancer.

3. Promensil and Breast Health

Breast diseases associated with hormone dysfunction remain major community problems, with 1 in 4 women suffering fibrocystic breast disease (cyclic mastalgia)⁶ and

1 in 10 having a lifetime risk of breast cancer⁷. Estrogen therapies such as HRT increase the risk of both diseases. Anti-estrogen therapies remain the treatments of choice for both conditions, despite only limited success and the presence of unwanted side-effects.

Novogen believes that isoflavones could play an important role in hormone-associated breast diseases in helping women maintain normal breast health throughout their lives. This belief is based on Novogen laboratory studies showing that the isoflavones in red clover although estrogenic, are selectively estrogenic, providing a strong estrogen effect on arteries and bone, but very little estrogenic effect on the type of estrogen receptor found on breast tissue. This raises the possibility of red clover isoflavones having a protective anti-estrogenic effect on breast tissue. This theory was supported by a study conducted recently at Sir Charles Gairdner Hospital, Perth, Australia, and supported by Novogen, showing a four-fold lower incidence of breast cancer in women with high isoflavone intake.⁷

Novogen has conducted a number of studies over the past 2 years to further test this theory. In a follow-up interventional study conducted at Sir Charles Gairdner Hospital, 18 pre-menopausal women with severe cyclic mastalgia were treated with either Promensil or a placebo for 3 months. The results of this study have recently been accepted for publication in the international journal "The Breast"⁶ and the full details must await that publication, however, the results in summary showed that Promensil produced a significant reduction in breast pain over that of placebo, suggestive of a strong anti-estrogenic effect.

A second, larger study recently concluded at Cambridge University, UK.⁸ That study enrolled 175 women aged up to 65 years who were confirmed by mammography as having dense breast tissue. Such women have a 6 times increased risk of breast cancer. HRT increases breast density and anti-estrogen drugs reduce it. In a double-blind, placebo-controlled study, the women were given either Promensil or a placebo for 12 months and the effect on their breast density evaluated. Promensil produced a significant reduction in breast density in women aged 56-65 years of age, supporting the theory that Promensil is anti-estrogenic in the breast.

A third study conducted at University College London⁹ looked at the effect of Promensil (versus placebo) on levels of a chemical known as insulin-like growth factor (IGF-1) in the breast tissue of young women. IGF-1 levels normally rise in conjunction with ovulation and an increased IGF-1 level is associated with increased risk of breast cancer. Promensil reduced the IGF-1 rise at the time of ovulation, one further piece of evidence pointing to a protective effect of Promensil on the breast.

Two other studies are current in the UK evaluating the effect of Promensil prospectively on the incidence of breast cancer surrogate markers and cancer incidence in women at high risk of breast cancer.

Comments: All the evidence collected to date from the use of Promensil indicates that the product has an anti-estrogenic effect on breast tissue. The epidemiological study by Dr Ingram in Perth suggested a protective link between dietary isoflavones and breast cancer, and the three studies conducted by Novogen demonstrating an anti-estrogenic effect provides a plausible explanation for that observation. Ongoing research with Novogen red clover isoflavones continues to support their role in maintaining breast health.

4. Promensil and Bone Health

The study mentioned earlier conducted at Cambridge University involving women with dense breast tissue, also examined the effect of Promensil (versus placebo) on bone density. The early findings involving 107 women were presented to a scientific conference in Canada in 2000.¹⁰ Over a 12 month period, participants were monitored for the effects of Promensil on changes in bone mineral content (BMC) and bone mineral density (BMD), as well as rates of bone formation and bone loss. In pre- and peri-menopausal women the decrease in spine BMD and BMC was significantly less in the Promensil group than in the placebo group. In fact loss of BMD was almost halved by Promensil treatment. Following notification of these findings to the Australian regulatory authorities, enhanced claims were recently allowed for the marketing of Promensil in Australia. The product can now be sold for the maintenance of bone health in menopausal women in addition to its current status as a therapy for relieving the symptoms of menopause.

Comments: Although bone loss leading to osteoporosis and fractures is well recognised as a problem associated with menopause and advancing age, it is less well understood that this bone loss starts in the years before the onset of menopause. The effect of Promensil in halving the rate of bone loss from the spine of pre-menopausal and peri-menopausal women points to a potent biological effect of isoflavones in this area, and indicates a means by which pre-menopausal women can help maintain normal bone health as they enter the menopause.

5. Promensil and Cardiovascular Health

Previous reports have demonstrated a range of beneficial effects of Promensil on cardiovascular health, including increased vasodilation (associated with reduced risk of hypertension)¹¹ and increased levels of the 'good' cholesterol, HDL, profile in women.¹²

In a recently published double-blind, placebo-controlled study conducted at The Royal Hospital for Women, Sydney,¹³ a statistically significant increase in plasma HDL or "good" cholesterol of 18.1% was observed in patients in the Promensil group. In a recent double-blind, placebo-controlled study conducted more recently at University College London⁹, a one month supplementation of Promensil (two tablets daily) boosted HDL levels by 10 per cent.

Comments: Increased vascular rigidity and declining HDL levels are known effects of falling estrogen levels after menopause and are key factors in the increased risk of heart disease and stroke after menopause. Long-term HRT use recently was shown to increase the risk of cardiovascular disease in women. The benefits of Promensil on vascular wall reactivity and HDL levels is consistent with the known estrogenic effects of Promensil isoflavones on the estrogen receptors in non-reproductive tissues such as the artery wall and support the role of Promensil in helping women maintain cardiovascular health at this time of their lives.

6. Rimostil and the Post-Menopausal Woman

Rimostil is a red clover isoflavone product specially formulated to meet the bone and cardiovascular needs of the post-menopausal woman. A report on a study conducted on the bone and heart benefits of Rimostil has been published in the most recent issue of "Menopause", the official journal of the North American Menopause Society.¹⁴ This reports a single-blind trial of 50 post-menopausal at Sydney's Royal North Shore Hospital. The women were recruited onto the study with an initial placebo "run-in" phase in which they were given tablets containing no isoflavone. Then they were given active Rimostil tablets for 6 months, followed by an additional 2-month wash-out phase back on placebo. The study revealed a 4% increase in bone density and a 21% increase in HDL cholesterol levels in blood at the end of the treatment phase compared to the baseline levels established during the placebo run-in phase. The researchers concluded that this could translate into a substantial reduction in the risk of cardiovascular disease. A larger study at the same hospital involving women being treated with Rimostil over a 2-year period is current in order to extend the understanding of the effects of red clover isoflavones on bone health.

Comments: The effects on bone density and HDL levels observed in this study could be expected to have a significant impact on the incidence of heart disease and hip fracture in women. The levels of the responses achieved are equal to or better than currently used drugs. Confirmation of these results over a 2-year period in the current study would make Rimostil a highly attractive alternative to drugs such as HRT and SERMs currently used to control osteoporosis.

7. P-07 and Premenstrual Syndrome

Novogen researchers have been working towards a new product for the management of premenstrual syndrome (PMS) in younger women. This new product is based on an anti-estrogenic formulation of red clover isoflavones (P-07). One of the hallmark symptoms associated with PMS is cyclical breast pain, and the demonstrated benefit of Promensil in this condition points to the potential benefit of isoflavones in the broader symptoms of PMS.

The safety of P-07 was tested recently in a double-blind study at the Cedars Sinai Hospital in Los Angeles. Women experiencing endometrial hyperplasia were treated with P-07 or placebo and the effect of treatment on the endometrium measured. The findings, which are to appear shortly in "Menopause", report that P-07 produced no proliferative effects on the endometrium.

A new study has been commissioned to evaluate P-07 over a broader range of PMS symptoms and is to be conducted at John Radcliffe Hospital, Oxford, UK.

8. Trinovin and Prostate Health in Men

Trinovin has been formulated to deal specifically with the changes that occur in the prostate in men from middle-age.

In an open study conducted at the University of Chicago, USA, men between the ages of 50 and 75 with moderate prostate enlargement showed a 23.3% improvement in International Prostate Symptoms Scores (IPSS) and a 27.8% decrease in nocturia (getting up at night to urinate) and a 17% benefit to quality of life scores over a 3-month period of treatment.

To deal with any concerns consumers might have over the use of isoflavone supplements on male fertility, a safety study involving 45 men was conducted in a placebo-controlled clinical trial at the Monash University Institute for Reproduction and Development (Melbourne, Australia). No differences between Trinovin and placebo groups were found in semen volume, semen concentration or quality, or in male sex hormone profiles.

In studies performed in mice, the same institution reported at last year's International Congress for Endocrinology the results of a study examining the effect of Trinovin dietary isoflavones on prostate growth in intact male mice. The results demonstrated that prostate (but not testis) size was significantly reduced over 4 weeks of an isoflavone supplemented diet and histological examination revealed an increase in apoptotic cells. These findings have now been accepted for publication in "The Journal of Reproduction and Fertility" and support the claim that Trinovin can assist not only in reducing prostate size but also in regulating the orderly progression of cell turnover.

9. Studies in Progress

Promensil

- a) Effects on uterine blood flow and endometrial thickness (Kings College Hospital, London, UK)
- b) Effects on breast cancer incidence in women at risk (University College London, UK)
- c) Effects on breast cancer incidence in a prospective controlled study (Royal Marsden Hospital, London, UK)

Rimostil

- a) Effects on clotting factors (Baker Medical Research Institute, Melbourne, Australia)
- b) Cardiovascular effects of biochanin and formononetin (Baker Medical Research Institute, Melbourne, Australia)
- c) Effects on lipid profile in diabetic women (Royal North Shore Hospital, Sydney, Australia)
- d) Effects on menopause symptoms (University of New York, USA)
- e) Long term bone density (Royal North Shore Hospital, Sydney, Australia)

Trinovin

- a) Anti-cancer effects in men with prostate cancer (Monash Medical Centre, Melbourne, Australia)

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- a) Effects on lipid profile in men (Royal Prince Alfred Hospital, Sydney, Australia)

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