

LABOPHARM INC.

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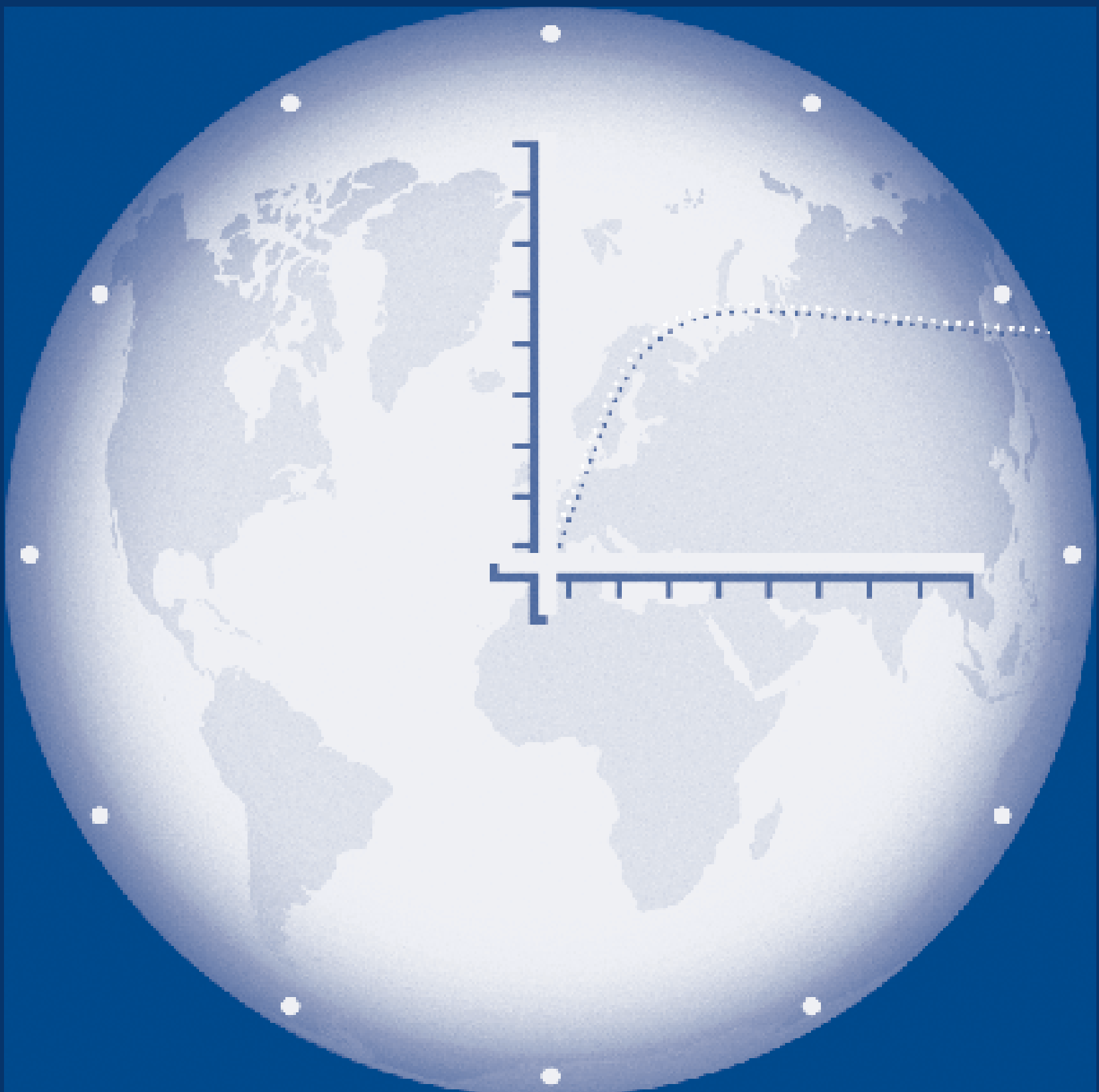
Labopharm Inc.

www.labopharm.com

• 2000 ANNUAL REPORT •

A1

SOLUTIONS TO DRUG DELIVERY PROBLEMS



CORPORATE PROFILE

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Labopharm is a dynamic specialty pharmaceutical company whose goal is to become a leading supplier of **controlled release systems** to the pharmaceutical industry worldwide. Its core platform technology, **Contramid**[®], can be applied to a wide range of medications in solid dosage form to improve their oral administration and performance.

Based in Laval, Quebec, **Labopharm** has a qualified staff and specialized facilities for the development of controlled release formulations. When necessary, it calls upon external resources such as clinical research organizations and manufacturers of final dosage forms. The Company's strategy is to build alliances with Canadian and international pharmaceutical companies for the manufacturing and marketing of products that utilize its technologies.

Labopharm has been a publicly traded company since June 1996; its shares are listed on the Toronto Stock Exchange under the ticker symbol **DDS**.



"I have the pleasure to be associated with Labopharm since 1996. In my opinion, the Company is based on solid and well protected technology, employs highly qualified and devoted individuals, and has a good chance for the future large scale success." *Vladimir Torchilin*

"I am delighted with the progress that has been made with Contramid. Recent developments confirm our collective belief that Contramid offers significant advantages in drug delivery. I anticipate continued success with a variety of drugs."

Joseph R. Robinson



"Labopharm's proprietary technology is based on sound scientific rationale. Consequently, it is strong with potential for further growth and commercial success." *Jindrich Kopecek*

HIGHLIGHTS OF FISCAL 2000

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1
Cerestar successfully manufactures commercial lots of Contramid®.

2
FDA and FCC Food Monograph compliance supports safety profile of Contramid.

3
New licensing agreement with international partner for oxybutynin, medication to counter urinary incontinence.

4
Solid, oral dosage form of Xopenex™ (levalbuterol HCl), for the treatment of asthma, under joint development with Sepracor Inc., proceeds to Phase II clinical trials.

5
Development work progresses well on once-a-day and twice-a-day formulations of tramadol, a leading analgesic for the alleviation of acute and chronic pain.

6
Company adopts dual development strategy, focusing on partnerships for life cycle management projects, and new chemical entities whilst also pursuing in-house development of existing products to shorten time to market and provide positive short-term financial results.

CORPORATE GOVERNANCE

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Labopharm believes that sound management is important for all of its shareholders. In accordance with the requirements of the Toronto Stock Exchange, the Board of Directors adopted internal corporate governance guidelines in January 1997. These guidelines were modified in July 1997. A policy on the use of insider information was also adopted by the Board in October of the same year. The overall structure and operating methods of the Board of Directors and its committees are discussed in the management proxy circular.

Message to Shareholders

Management Expresses Confidence in Company Progress

Many aspects of the Company's activity throughout the past year give Labopharm's management confidence that the Company is moving forward in a very positive manner. The progress of our clinical trial programmes, the success of our new manufacturing process, the strength of our intellectual property protection and exciting new applications for our technology allow us to view the Company's future with optimism.

We have seven clinical trial programmes in place, four in-house projects and three with clients. Our alliance with Cerestar has brought us a completely new manufacturing process which is reliable, reproducible and economical. With this new process, Contramid® falls under the umbrella of two very important regulatory monographs (U.S. and international) making it directly acceptable to health authorities and, in addition, this has given us an opportunity to file a "composition of matter" patent to further strengthen our intellectual property position.

Fundamental Research Enhances Technology: Research Targets Implants and Cancer Therapy

Labopharm has conducted a number of fundamental research programmes with very encouraging results.

We sponsored two recent animal studies in which mini-tablets of Contramid which contained an antibiotic were implanted in surgical wounds as a single dose. We were able to obtain therapeutic levels of antibiotic for 21 days in local tissue. This could be a very useful application in animal health.

Another programme, in conjunction with the Université de Montréal, is exploring a new polymeric micelles system to improve drug targeting in cancer therapy.

Additional Licensing Agreement and Important Management Appointment

In addition, we have licensed one of our in-house products, oxybutynin, a leading drug for the control of urinary incontinence, to an international company and are in discussion with several potential international partners with regard to the others.

Moreover, management has been strengthened by the recruitment of James R. Howard-Tripp, most recently, Senior Vice-President, Operations at Allelix Biopharmaceuticals and President and CEO of Allelix Neuroscience Inc., their U.S. subsidiary. Prior to that, Mr. Howard-Tripp was Vice-President of Business Development for a multinational company in Canada. His

Our alliance with Cerestar has brought us a completely new manufacturing process which is reliable, reproducible and economical.



DONALD BUXTON

PRESIDENT AND CHIEF EXECUTIVE OFFICER



experience in pharmaceuticals and in the international licensing arena will be invaluable to me personally and to Labopharm. Mr. Howard-Tripp will assume responsibility for business development and licensing while assisting me in corporate development and investor relations. He is currently a member of our Board and will continue to serve in this capacity.

Solid Progress on Clinical Trial Programmes

At the close of the third quarter of fiscal 2000, I advised you that we were planning to embark upon an ambitious programme of clinical trials in the fourth quarter, most of which involved in-house development projects. I am pleased to say that we were very successful in completing the trials on four in-house compounds to accelerate the licensing process with international partners. We have also made significant progress with client projects.

In clinical trial programmes, particularly ones designed to provide in vivo confirmation of laboratory results, there are many variables which can affect the way humans respond to a given medication, including patient idiosyncrasies, food, variable transit times in the gastrointestinal tract and individual drug reaction to variable pH conditions. In this particular series of studies we were

also adding another variable by using Contramid from the scaled up GMP batches produced by Cerestar, as opposed to ones which had been produced in small batches utilizing a different manufacturing process for our previous trials.

We were very pleased to find that with the trials on our four in-house compounds recently completed, the pharmacokinetic profiles were very close to the laboratory projections. This confirmed the flexibility of our technology because all the compounds had different physicochemical characteristics. It also demonstrated that the commercial batches of Contramid performed according to specifications in a totally reproducible fashion.

Four In-house Projects

Our primary in-house product in development is the once-a-day form of tramadol, a potent analgesic, currently in Phase I development which would be protected by our patent. It is considered more potent than codeine and just less than narcotics. There is currently no once-a-day formulation of this drug available. Worldwide sales of the current formulations are close to one billion US dollars and growing.

As the development of bio-equivalent drugs requires a shorter timeframe for regulatory approval, the Company is also developing a bio-equivalent twice-a-day formulation of tramadol for rapid entry into Europe.

Last year, Labopharm successfully completed a Phase I trial with a partner on a once-a-day formulation of betahistine, a drug for the treatment of Ménière's disease, a chronic distressing condition for which there is a limited range of treatment. The Company has since assumed 100% responsibility for the international development of this product and is ready to commence a multi-dose clinical trial. Discussions are already ongoing with international companies as possible partners.

The fourth in-house project is a 24-hour formulation of pseudoephedrine, a decongestant, in Phase I development. This has significant potential as a value-added product if combined with one of the anti-histamines which exist in a market that exceeds one billion US dollars.

On-going Client Projects

The Phase II study of the controlled-release oral form of Xopenex™, the anti-asthmatic drug being developed in cooperation with Sepracor was initiated last September. The patient enrolment and treatment phases are already complete and the analytical phase is expected to be completed in the second quarter of the current fiscal year.

We were very successful in completing the trials on four in-house compounds to accelerate the licensing process with international partners.

In January 2000, we signed an agreement with an international pharmaceutical company to pursue development of one of our in-house projects, a controlled-release formulation of oxybutynin, a leading drug for the control of urinary incontinence. This product is a pH-sensitive drug with variable absorption on a patient-to-patient basis. A pre-pilot pharmacokinetic (PK) study was conducted in February 2000 to fine-tune the formulation to overcome the inherent properties of the compound. This was achieved and a larger study will begin in the second quarter of the current fiscal year.

Labopharm is also ready to proceed with the clinical programme for a controlled-release version of Axcan Pharma's MODULON® which is indicated for the treatment of irritable bowel syndrome, a disease which affects 15% of the population. This study is expected to begin by June 2000.

Research

As indicated in our third quarter report, one of the fundamental research programmes funded by Labopharm through

the universities involved a rat study to determine the tolerance to subcutaneous insertion of Contramid® mini-tablets. This was followed by a preliminary study in rabbits to measure the release of an antibiotic, also contained in Contramid mini-tablets, which were implanted into surgical wounds next to bone and muscle. The objective was to measure the level of antibiotic in local and systemic circulation. Therapeutic levels were maintained in the local tissue for 21 days. Subsequently we extended the study to confirm the preliminary results and they were found to be identical.

We are currently in discussion with two animal health divisions of multinational pharmaceutical companies concerning the possible application of this technology in the animal health field.

The advantage of use in this sector is the relatively rapid development time frames compared with those required for human use. There is no such product on the market at present and the number of interventions where this procedure could prove useful exceeds 250,000 in the U.S. alone.

The second research project, which involves a different technology on which we are working with the Université de Montréal, although very early, is very exciting because it deals with the science of drug targeting. The objective, here, is to find a way to target a tumour with anti-cancer therapy without producing the typical toxic effects caused by circulating anti-cancer drugs. The current research using the new polymeric micelles, is preliminary but experiments using in vitro and in vivo

photodynamic therapy models, show a marked superiority over existing micelles models.

Intellectual Property

The new process for manufacturing Contramid has allowed us to create a product which is sufficiently novel in concept to permit the filing of a new "composition of matter" patent. This will further broaden the protection of our intellectual property which, in the view of our Scientific Advisory Board, is already among the strongest in the drug delivery field. We are also in the process of filing a patent covering the micelles research programme.

Business Development Strategy

The oral segment of the drug delivery market constitutes the most important in terms of dollars and it continues to grow at a fast pace. Product life cycle management is important to the pharmaceutical industry and the research-based companies try to modify the release profile of their maturing products to make it difficult to create generic equivalents.

This is the segment in which we concentrate. Labopharm can provide this value-added dimension which is good for the originator of the drug but also for our Company because royalty income will be higher and will continue longer for such products.

The progress we have made in terms of intellectual property, scale up of manufacturing and the provision of data supporting the safety profile of our technology, has been well

received by the industry and clearly indicates the maturing nature of our Company. We have many active files with the major pharmaceutical companies and although the process of decision making is complicated, we fully anticipate expanding our licensing arrangements within the next two quarters.

We have also decided to take some in-house initiatives with the development of our own products through the early stages of development in order to attract potential licensees more rapidly. This has already paid dividends in that once-a-day oxybutynin has already been licensed to an international company and we have several parties expressing an interest in licensing both the twice-a-day and once-a-day forms of tramadol. We certainly expect that the results of the initial studies with these two product forms will enhance our licensing opportunities.

Our strategy going forward is to continue working with the research based industry on life cycle management and new chemical entities and to add the dimension of early development of certain products in-house as our finances permit.

Organization and Human Resources

I cannot say enough about the tremendous achievements of our laboratory scientists during the past twelve months. Not only have they answered the challenge presented by the various formulations of in-house and client projects with alacrity, but they have tested and evaluated thirty to forty versions of Contramid as we went through the manufacturing and formulation process of the new Contramid developed with our partner Cerestar.

Their conscientiousness, professionalism and relentless pursuit of solutions should not be underestimated. The team was recently reinforced by the recruitment of Dr. Anh Thu Phan who, in her capacity as Process Development Manager, has suc-

cessfully conducted the scale up and manufacturing of several industrial lots of clinical supplies.

On the technical support side we have a valuable new addition in Dr. Tibor Kapusy who is the Project Manager coordinating the on-going studies on behalf of Labopharm and our clients. The benefits of his presence have already been felt.

James R. Howard-Tripp, who joined us just after the close of the year as Executive Vice-President, makes a remarkable addition to our management depth. His many years of experience in the industry will no doubt prove very valuable to the Company.

I would be remiss if I did not acknowledge the contribution of our Vice-President, Research and Development, Dr. Vincent Lenaerts for his overall management of the research and development programme, but specifically for his role in the re-formulation process of Contramid with Cerestar.

Jim McDonald, who served the Company exceptionally well for five years as Vice-President, Finance, Administration and Corporate Development, left Labopharm as an employee in January, but retained his connection with the Company as a Board member and consultant. I thank him personally for his contribution and look forward to his continued input in his new role.

It is essential that I also recognize the team spirit and devoted effort of the entire staff and the valuable support provided by our Board of Directors and the Scientific Advisory Board members throughout the year. To all I offer my sincere personal appreciation.

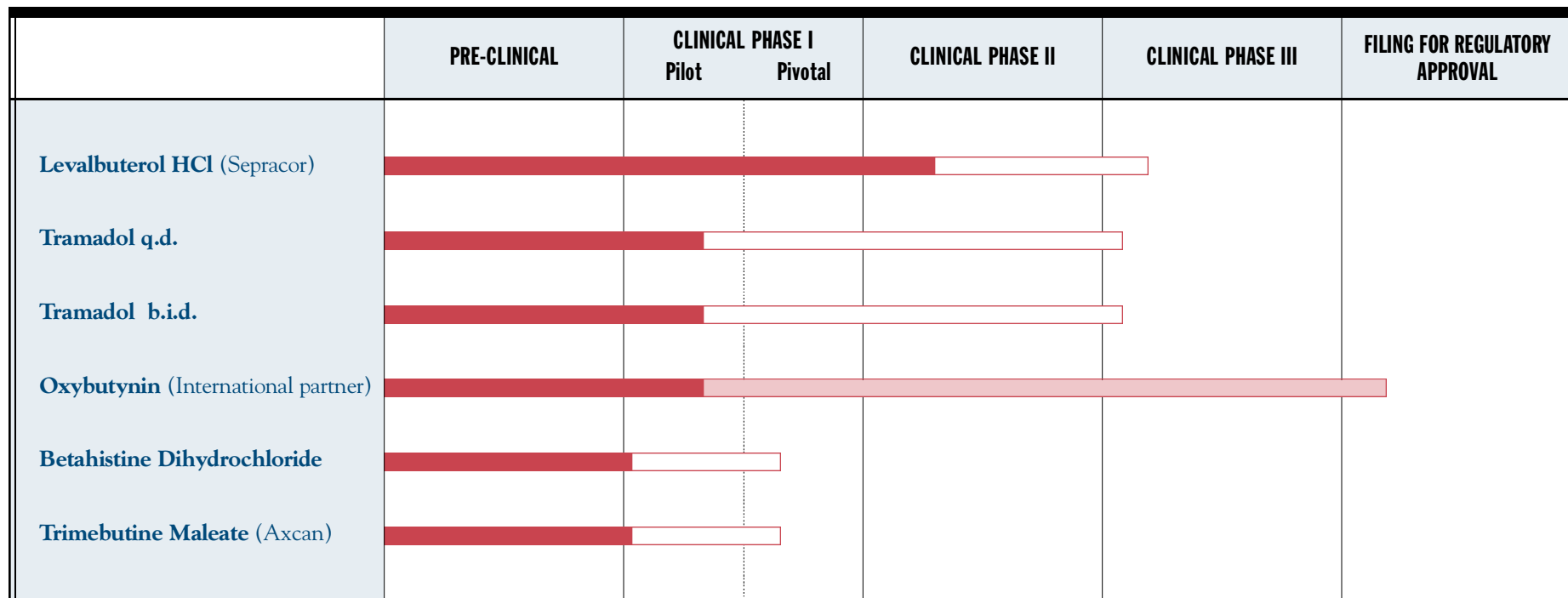


Donald Buxton
President and Chief Executive Officer

Laval, April 25, 2000

PROJECT ADVANCEMENT PLAN

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PROJECT STATUS: ■ February 28, 2000 □ February 28, 2001 ■ No need for Clinical Phases II and III for ANDA filing

Report on Activities



James R. Howard-Tripp

EXECUTIVE
VICE-PRESIDENT
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This past year has seen solid progress on many fronts. We have expanded our technology base through the commercial manufacture of Contramid®, and, at the same time, have developed a new application for our technology, in the form of implants, for use in animal health. We have also enhanced our intellectual property portfolio and signed a new licensing agreement for oxybutynin once-daily with an international partner. Our clinical trial programme has also progressed encouragingly with the initiation and conclusion of clinical trial studies with levalbuterol, oxybutynin, pseudoephedrine and two separate forms of tramadol. In terms of corporate strategy, we refined our long-term plans to include not only the development of new chemical entities (new products) as well as product life-cycle management with partners, but also the development of in-house programmes to deliver positive financial results in a shorter timeframe.

Expansion of the Technology Base

Commercialization—This year saw the realization of a major milestone: the scale-up and first commercial manufacture of Contramid lots by Cerestar, a division of the multinational company Eridania Béghin-Say.

The ability to reliably produce commercial supplies of a product is always of critical importance. In scaling up from bench-top to full commercial production, problems are often encountered which may make commercialization difficult and/or uneconomical. Cerestar has now manufactured three different lots of full commercial size, with no deviation from specification. Batch-to-batch variation, stability, performance under manufacturing conditions as well as in clinical trials, have proven most gratifying.

In developing a new method of production, Contramid, as manufactured by Cerestar, fully complies with regulatory monographs from the FDA and the Food Chemicals Codex. This means Contramid will be acceptable to the Health Authorities from a safety perspective. We believe we are now positioned to fully commercialize our lead products through partnerships with large pharmaceutical companies.

Seven Clinical Trial Programmes

Development of New Technology—As technologically advanced as Contramid is, it is essential we continue to expand the capabilities of the system and to develop new and exciting applications. Delivery of drugs through surgical implants is one such opportunity.

In the treatment of infections which may arise as a result of surgery, it is necessary that high concentrations of an effective antibiotic reach the site of infection, i.e. the localised tissue. This means high systemic levels of the drug, often with concomitant side effects and high costs. If one could deliver the antibiotic to the site of infection, during surgery, and contain it only in the local tissue, it would not only offer convenience but permit the avoidance of toxicity and side effects of systemic circulation. Labopharm researchers, together with our academic collaborators, have developed a slow-release, implantable Contramid “minitablet” into which a variety of drugs may be incorporated.

The initial study, to test safety, involved histological examination following subcutaneous implantation of Contramid minitablets in an animal model. The results were excellent. A second animal study was then conducted in which small Contramid tablets, containing an antibiotic in a slow release form, were inserted into surgical wounds alongside bone and muscle tissue, the objective being to measure the levels of antibiotic in both local tissue and systemic circulation. Results, again, were excellent. The release of the antibiotic was controlled, and therapeutic levels were maintained in the local tissue for 21 days while there was virtually no drug detected in the systemic circulation.

Early application may be in animal health, especially veterinary care, in the prevention of infection associated with post-surgical orthopaedic care and in the treatment of post-traumatic infections. The ease of administration would represent a tremendous advantage over the current approach which requires the animal owner to give an oral antibiotic to his/her companion animal 2-3 times a day for several weeks. In addition, the cost of the treatment could be substantially reduced. In North America, there are over 250,000 surgical interventions per year of the kind that could benefit from this technology. This has attracted the interest of the large animal health-care

groups and discussions are in progress regarding the potential commercialization of this technology.

Intellectual Property Portfolio—The patent portfolio is always the lifeblood of an innovative company, and it is essential to build and strengthen it.

This year our portfolio has been strengthened in several important ways: the issuance of a U.S. patent for resistance of Contramid tablets to degradation by digestive enzymes, as well as full resumption of all intellectual property rights to Contramid from Rougier.

The portfolio is being expanded by the filing of new patent applications with respect to composition of matter of Contramid and its use in implants. Composition of matter patents reflect the strongest patent protection since they cover a given chemical structure and its applications. They are only very rarely encountered in the drug delivery sector. Innovative aspects of our research into micelles as part of our collaboration with the Université de Montréal will also serve to expand our patent portfolio.

Scientists Honoured—Of particular relevance to the quality of our science, the 1999 “Joseph-Armand-Bombardier Prize for technical innovation which has been successfully commercialized,” was awarded to the scientists who made the initial discovery leading to the controlled release technology, Contramid. Dr. Vincent Lenaerts, who is a co-founder of Labopharm and the Vice-President, Research and Development, was pivotal in the discovery of Contramid by the university team at the Université de Montréal, where he was Professor of Pharmacy.

Oxybutynin license

A licensing agreement, with a U.S.-based pharmaceutical company for the development and marketing of oxybutynin, a leading drug for the treatment of urinary incontinence, was signed during the fourth quarter.

The company will pay Labopharm for formulation and clinical development through to product registration. In addition, milestone payments will be due throughout the development phase, with royalties on U.S. sales and profit-sharing on international sales.



Vincent Lenaerts

VICE-PRESIDENT,
RESEARCH AND DEVELOPMENT
...

Clinical trials

R-Albuterol

Collaboration with Sepracor.

Indication: Asthma

Global market: US\$1.4 billion+

In 1997, Labopharm entered into a licensing and co-development agreement with Sepracor Inc. for the development of solid, oral dosage forms of Xopenex™ (levalbuterol HCl). Xopenex™ is the therapeutically active isomer of racemic albuterol.

Racemic albuterol, an equal mixture of (R) and (S) isomers is currently marketed by several companies and is the world's leading bronchodilator for asthma, with worldwide sales of \$1.4 billion in 1997 for all forms of the medication. This new oral formulation, Xopenex™ with Contramid, will be indicated for the treatment of asthma and other chronic respiratory diseases.

Phase II trials for Xopenex™ with Contramid started in Canada on September 19, 1999. The clinical work is now complete and the analysis of levalbuterol in the plasma samples is on-going. Interim results should be available in the second quarter of 2000.

Tramadol

Indication: Treatment of moderate to severe pain

Global market: Estimated at US\$900 million+ for the year 2000 (US: \$450 million, Europe: \$450 million). No once-a-day formulation yet in the market.

Once-a-day Formulation

Labopharm is developing a Contramid-based formulation of tramadol for once-a-day use. Tramadol hydrochloride is a centrally acting analgesic that reduces pain by two demonstrated mechanisms: one is the binding of tramadol to μ -opioid receptors, and the second is weak inhibition of the action of the neurotransmitters, norepinephrine and serotonin. Since chronic pain involves several biochemical pathways, tramadol offers a unique advantage over most other existing analgesics.

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“Labopharm Inc. has developed an innovative technology for oral drug delivery based on an approved natural product. This truly new concept is very versatile and can be used for various types of modulated drug release such as constant, delayed and pulsive release and has shown great potential in clinical trials.” *Robert Gurny*



“I had the privilege of evaluating the Contramid® technology during the early round of Labopharm financing and I then felt very strongly, as I still do, that this technology will become a dominant technology in the sustained oral delivery arena. But, a promising technology without the intelligent and dedicated work of many people is not sufficient to create a successful company, and in this regard, Labopharm has been most fortunate to be able to attract a first class management and research team.” *Jorge Heller*

The Story of Contramid

Dr. Vincent Lenaerts

Labopharm's core platform technology, known as Contramid®, is a controlled release system for the oral administration of solid dosage forms. Contramid, in white powder form, is obtained by the chemical cross-linking and gelatinization of a starch consisting mainly of amylose. During production, amylose is treated with a cross-linking agent to obtain a three-dimensional structure. When used as an excipient or combined with other excipients and compressed with an active drug substance into a solid dosage form, Contramid allows for the controlled release of the active drug over an adjustable period of time.

Once the Contramid dosage form is in the stomach, gastric fluids turn its surface to gel and the resulting semipermeable membrane stabilizes rapidly. This self-forming membrane ensures that a regular release of the active ingredients is contained in the dosage form. In traditional tablets without controlled release, blood levels of the drug rise quickly after ingestion, reach a peak and then drop fairly rapidly, thus resulting in frequent dosing.

It has long been known that a drug's effects may vary according to the concentration of the active ingredient in the bloodstream or other sites of action. Too low a concentration can often mean reduced efficacy, while too high a concentration increases the risk of side effects. For any drug, there is a range in which the desirable and undesirable effects are optimized. This is known as the "therapeutic window." By controlling the release of the active ingredients, we can maintain the concentration within this window and prolong the therapeutic effect over 12 or 24 hours. By definition, this means the drug is more effective, has a better safety profile, and for example, can be taken more conveniently such as once a day instead of three times a day, a fact that significantly increases patient compliance. Patient compliance is affected by a number of drug related factors such as dosage

regimen, palatability, route of administration, speed of onset of effect and level of side effects. According to a 1993 U.S. journal from "Annals of Pharmacotherapy," the overall cost of non-compliance is 10 percent of total U.S. healthcare costs, or \$100 billion, and results in a 30-50 percent failure of prescriptions to produce desired results.

Labopharm's research to date indicates that Contramid makes it possible to reproduce blood concentration profiles obtained with leading competing technologies which are more complex and costly to manufacture. In addition, Contramid allows for more flexible adjustment in the rate of release of active ingredients.

Presently there are three classes of delivery systems consisting of osmotic pumps, multi-particulate systems (coated beads) and hydrophilic matrices. Of the three, Contramid's performance is comparable to that of osmotic systems which offer an ideal constant release rate. However, osmotic pumps, which consist of a semipermeable polymer membrane fitted with an orifice, involve a complex manufacturing process. Secondly, Contramid was shown to be an improvement over matrix systems in terms of both in vivo performance and variability. Lastly, coated beads usually give PK profiles similar to those of matrices, but their manufacturing is more complex.

Unlike osmotic systems and other complex technologies such as coated beads, Contramid is easy to manufacture and at a cost that makes it one of the most economical controlled release systems available. Another advantage in using Contramid is that it is generally possible to integrate a high proportion of active ingredient in the final dosage form. Tablets can therefore be manufactured in an acceptable size, which is not always the case with other technologies. Moreover, Contramid's controlled release properties have a very limited dependence on manufacturing variables which readily facilitates scale-up.

REPORT, continued from Page A6

Tramadol is highly prescribed in Europe and the US for the alleviation of acute and chronic pain, and has sales of close to US\$1 billion. The Company is in discussion with potential partners in Europe and the U.S., and expects to have a distribution agreement signed before the drug is ready to go to market. There is no once-a-day product currently on the market, despite attempts by several companies, the difficulty lying in the narrow therapeutic index of this compound (i.e. the plasma levels where pharmacological activity and untoward side effects are obtained, are not very far apart.)

A pilot PK study has just successfully been completed. Our formulation is characterized by a quick onset of action and an excellent control of plasma levels within the therapeutic limits for 24 hours. The pivotal development program is to start in the second quarter, and it is believed we can be in a position to file an NDA within 24-30 months.

Twice-a-day (b.i.d.) Formulation

Although in Europe there are twice-a-day formulations of tramadol, this is not so in the U.S. Development of a twice-a-day formulation of tramadol, has the advantages of a more rapid development timeline, lower development costs and the ability to reach market sooner. The Company is therefore developing a b.i.d. formulation in parallel to the once-a-day dosage.

A pilot pharmacokinetic study has successfully been completed, and a full development plan is in preparation to take the greatest possible advantage of this opportunity.

Pseudoephedrine 24-hour

Indication: Seasonal allergies
Global market: US\$1 billion+

The Company is developing a version of pseudoephedrine 240 mg to be bio-equivalent with an existing formulation. The controlled release pseudoephedrine will then be combined with an immediate release antihistamine for the symptomatic treatment of seasonal allergies. The Labopharm formulation will have a marked advantage over existing leading products in that the size of the tablet will be substantially smaller, thereby improving patient acceptability.

The current leading products in the market have sales well in excess of US\$1 billion.

Betahistine

Indication: Ménière's Disease, vertigo

In 1997, the Company signed an agreement which called for the development of a once-a-day version of betahistine for Ménière's Disease. In March 2000, Labopharm reassumed all rights to develop the product for the global market, with full ownership of existing clinical data. Labopharm will continue development of this product for the entire international market, and is currently in discussion with potential international partners.

Ménière's Disease is a disorder characterized by recurrent dizziness (vertigo), possible hearing loss and ringing in the ears (tinnitus). It is associated with dilation of the membranous labyrinth (endolymphatic hydrops) in the ear.

A pilot pharmacokinetic study has successfully been completed with our once-a-day

formulation. This produced a very smooth and well controlled plasma profile instead of the peaks and troughs obtained with the existing three-times-a-day immediate release dosage form.

Oxybutynin

Indication: Urinary incontinence

In the fourth quarter, Labopharm signed an agreement with an international pharmaceutical company to develop a controlled-release formulation of oxybutynin, a leading drug for the control of urinary incontinence. Oxybutynin, being both poorly soluble and pH-sensitive, required adaptation of the Contramid® system, and a pilot pharmacokinetic study was performed to evaluate the efficacy of this adapted system. The results, as predicted, were satisfactory and we are now moving to larger scale studies which should start in the third quarter of 2000. Under the agreement, Labopharm will receive development funding, milestone payments and royalties on sales to certain markets including the United States. In other markets, including Europe, a profit-sharing formula has been determined and the companies are in the process of identifying partners in the relevant local markets.

Trimebutine

Indication: Irritable bowel syndrome

In 1999, Labopharm and Axcan Pharma signed an agreement to develop a controlled-release formulation of the currently marketed product, MODULON® (trimebutine maleate), which is indicated

for the treatment of irritable bowel syndrome. The new formulation is expected to reduce daily dosage requirements from three to four times a day, to once-a-day and, as a result, enhance patient compliance. The Company is ready to start the clinical study programme in the second quarter of 2000.

Conclusion

The development of sophisticated controlled-release, drug delivery systems has taken on vital importance for pharmaceutical companies. Fully 50% of new chemical entities do not become marketable drugs purely because they cannot be delivered appropriately.

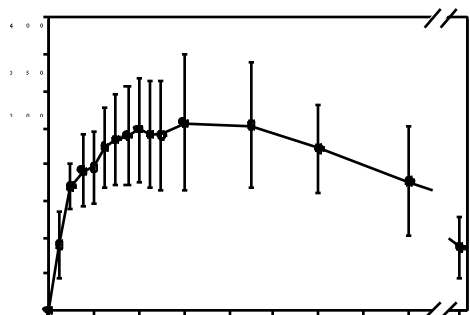
It has long been known that a drug's effects vary according to the concentration of the active ingredient in the bloodstream or other sites of action. Too low a concentration can often mean reduced efficacy, while too high a concentration increases the risk of side effects. For any drug, there is a range in which the desirable and undesirable effects are optimized.

Controlled release formulations make drugs more effective, provide them with a better safety profile and increase patient compliance due to a more convenient dosing schedule.

Over the past year, Labopharm's Contramid technology has demonstrated repeated success in helping solve drug delivery challenges for both new chemical entities and existing products. The Company's major priority is now to establish licensing agreements with appropriate international partners.

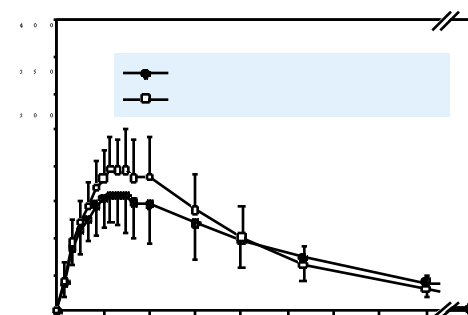
Contramid-Tramadol 200 mg once-a-day PK Study

Single dose, fasted healthy subjects (means \pm s.d., n=14)



Contramid-Tramadol vs. Tramal Long 100 mg Bioequivalence

Single dose, fasted subjects (means \pm s.d., n=14)



Tramadol: A Unique Analgesic Agent for Acute and Chronic Pain

Walter F. Kean M D (Glas) FRCP (Edin & C) Clinical Professor in Medicine

Tramadol has been used in Germany for the management of acute and chronic pain since the late 1970s and more recently, has gained wide acceptance across Europe and in the U.S. This growing interest in tramadol by clinicians and researchers is because of its unique mode of action on opioid receptors and inhibition of serotonin and noradrenaline activity.

Tramadol hydrochloride is a centrally acting analgesic which reduces pain by a central analgesic action. Animal studies have demonstrated two mechanisms: one is the binding of tramadol and its main M1 (O-demethylated) metabolite to μ -opioid receptors and the second is weak inhibition of the action (reuptake) of the neurotransmitters, norepinephrine and serotonin. These two mechanisms appear to contribute independently but synergistically to the reduction of pain. After oral ingestion, pain relief in humans occurs within one hour and reaches a peak in approximately two to three hours.

Since chronic pain often involves several biochemical pathways, tramadol offers a unique advantage over many other existing analgesics for the management of persistent pain. In the U.S., tramadol is available in tablets which contain 50 mg of tramadol hydrochloride and in Europe there are additional dosage forms of 100 mg and 200 mg sustained release tablets given twice per day.

Pharmacokinetics

Like many analgesic medications, the chemical structure of tramadol is an enantiomer or left and right handed three dimensional structure. Tramadol is well

absorbed after oral intake, it is 20% bound to plasma proteins, and is well distributed in the tissues. Administration with food does not significantly affect its rate or extent of absorption.

Tramadol is extensively metabolized by a number of pathways, and it, along with its M1 metabolite, are mainly excreted in the urine, with plasma half-lives of 6.3 and 7.4 hours respectively.

The dose of tramadol should be reduced in patients with impaired renal function, and/or reduced hepatic function.

Healthy elderly subjects, aged 65 to 75 years, have been observed to have plasma tramadol concentrations and elimination half-lives similar to healthy individuals less than 65 years of age. However adjustment of the daily dose is recommended for patients older than 75 years since the maximum serum concentrations are slightly elevated and the elimination half-life is slightly prolonged compared to subjects 65 to 75 years of age.

Adverse Reactions and Precautions

In double blind and open research studies of chronic malignant pain, the toxicity profile is favourable for tramadol when compared to acetaminophen with codeine 30 mg and aspirin with codeine 30 mg.

Clinical Drug Use

Tramadol is an effective analgesic for relief of moderate to severe pain in acute and chronic conditions. It is a useful adjunct and alternative to existing analgesics and

non steroidal anti-inflammatory drugs (NSAIDs) since the analgesic mode of action resembles the narcotics. Tramadol has a less serious side effect potential than the standard narcotics, and there is significantly less risk of drug abuse and addiction. In addition Tramadol does not suppress respiratory function under normal conditions, and has shown a low incidence of cardiac depression and significantly less dizziness and drowsiness than morphine. Tramadol is not an NSAID and thus does not have an increased risk of serious gastrointestinal injury.

Acute Pain

Tramadol is used in single oral doses of 50, 75, 100, 150 and 200 mg in patients with acute pain following surgical procedures, including post thoracotomy pain, and post heart surgery pain. In these single-dose models of post surgical pain, 150 mg provided analgesia generally comparable to the combination of acetaminophen 650 mg with propoxyphene napsylate 100 mg.

In single-dose models of pain following oral surgery (extraction of impacted molars), pain relief was demonstrated in some patients at doses of 50 mg and 75 mg. A dose of 100 mg of tramadol tended to provide analgesia superior to codeine sulphate 60 mg.

Chronic and Persistent Pain

Tramadol has been extensively studied in chronic pain states such as low back pain, arthritis and malignancy. In three long-term controlled trials involving a total of 820 patients (530 patients on tramadol), subjects with a variety of chronic painful conditions were studied over one to three months. Average daily doses of tramadol 250 mg, in divided doses, were generally comparable to five doses of acetaminophen 300 mg with codeine phosphate 30 mg

(Tylenol#3) daily, five doses of aspirin 325 mg with codeine phosphate 30 mg daily, or two to three doses of acetaminophen 500 mg with oxycodone hydrochloride 5 mg daily.

In a study of 60 patients (44 men, 16 women; average age 61.4 years) with advanced malignancy tramadol 300 mg/day had a similar analgesic effect to the opioid, buprenorphine. The improvement with Tramadol was significant in 1 hour and more marked. Tramadol improved sleep and had an overall better efficacy, better patient acceptability, and less side effects than buprenorphine.

Conclusions

Tramadol has been used in Europe since the late 1970s. In the last few years there has been a marked increase in its clinical use in Europe and the U.S. because of its unique biochemical action and its position as an analgesic capable of controlling moderate to severe, acute and chronic pain. Tramadol has proved most useful in pain management since it occupies a position between the NSAIDs and the narcotics.

Key References

- 1 Tramadol; Data on file Ortho-McNeil Pharmaceutical Inc. www.rxlist.com
- 2 Lewis KS, Han NH Tramadol: a new centrally acting analgesic. *Am J Health Syst Pharm* 1997; 15; 54 (6): 643-52.

Walter F. Kean is a Clinical Professor in Medicine and Head of Service of Rheumatology at McMaster University Medical Centre, Hamilton, Ontario, Canada. His research interests are in the pharmacokinetics of analgesic agents, and the clinical management of acute and chronic musculo-skeletal pain.

Incidence of Asthma on the Rise

According to the Centers for Disease Control and Prevention, asthma affects more than 17 million people in the U.S. and approximately 5 million of them are children. While many diseases have diminished through medical advances, the incidence and morbidity associated with asthma have increased. In fact, the number of people afflicted with the disease has more than doubled in the last ten years, and asthma-related deaths have increased by 117 percent since 1979 according to reports by the American Lung Association. It is estimated that by the year 2000, asthma-related costs will exceed \$14.5 billion per year. At present, worldwide sales for prescription asthma drugs exceed \$5 billion annually with half of this amount being spent on bronchodilators, including both inhalers and oral dosage forms.

Asthma is defined as a chronic, often progressive disease for which there is no cure, only control. The disease is characterized by temporary obstruction of airflow that leads to breathing difficulty, coughing, inflammation of the airways, and an increased sensitivity to a variety of triggers that can cause breathing difficulty. Attacks can range from slight breathing difficulties to life-threatening respiratory failure. Bronchodilators, which open up the passageways of the lungs, give rapid, symptomatic relief to asthmatics. The active ingredient in these drugs is usually racemic albuterol, the most widely-used bronchodilator on the market today. In 1995, almost 40 million prescriptions were written for racemic albuterol in the U.S. alone, with annual sales totalling \$1.2 billion in 1998.

Labopharm and its partner, Sepracor are currently working on developing a controlled release version of an oral dosage bronchodilator of levalbuterol, trade-named Xopenex™. Recently, the inhalation version of Xopenex™ for use with a nebulizer was approved by the FDA for the prevention and treatment of bronchospasm in adults and adolescents 12 years and older, with reversible obstructive airway disease, such as asthma.

Patients who stand to benefit from an orally-dosed bronchodilator are those who experience chronic obstructive pulmonary disease (COPD) and asthmatics — primarily children and elderly patients—who have difficulties using inhalers. In addition, the product may be attractive for those patients who do not use existing solid oral forms due to tolerability issues.

Irritable Bowel Syndrome — a Common Disorder

Irritable bowel syndrome (IBS) is considered to be one of the most common gastrointestinal disorders that leads to cramp-like pain, gassiness, bloating, and changes in bowel habits. IBS tends to be a chronic problem and is estimated to affect about 15 percent of the adult population. Of the sufferers, only 20 percent are likely to seek medical attention because their symptoms are acute. Women are affected twice as often as men, and the symptoms typically occur early in life, with half of the patients indicating symptoms before the age of 30.

The symptoms, which can cause grave discomfort, and range from inconvenience to deep personal distress, are known to be a leading cause of worker absenteeism, second only to the common cold. Technically, IBS is defined as being a syndrome, or group of symptoms, and not a disease. Similarly, doctors call it a functional disorder because there is no sign of disease when the colon is examined.

Although IBS does cause a great deal of discomfort and distress, it does not cause permanent harm to the intestines and does not lead to intestinal bleeding of the bowel or to a serious disease such as cancer. As a result, treatments are directed towards relief of symptoms.

Labopharm and its partner, Axcan Pharma, are currently developing a controlled release formulation of MODULON®, the trade-name for trimebutine, which is a drug that is currently used to modulate intestinal activity by providing symptomatic relief of lower abdominal pain, flatulence, diarrhea or constipation in patients.

The present drug contains 300 mg of trimebutine, the active ingredient in MODULON® and the new formulation aims to reduce the number of daily doses taken, enhance patient compliance and improve the therapeutic index.

Management's Discussion and Analysis



James R. Howard-Tripp

EXECUTIVE VICE-PRESIDENT

Overview

Established in 1990, and operational since 1995, Labopharm specializes in controlled-release drug delivery technologies and the development of pharmaceutical products incorporating its proprietary technologies. To this end, the Company is developing and improving its existing technologies, including Contramid® and looking to acquire complementary technologies. The Company's strategy is to form strategic alliances or licensing agreements with national or international pharmaceutical companies that already have the necessary resources and distribution networks to market and sell pharmaceutical products incorporating the Company's proprietary technologies.

In December 1994, Labopharm acquired all rights relating to cross-linked amylose technology held by the Université du Québec à Montréal and the Université de Montréal. These rights were acquired in return for a cash amount, Class A shares, an option to buy common shares and royalties on the revenues the Company derives from the technology. Since that time, the Company has independently researched and developed proprietary technologies, one of which culminated in the issuance of a U.S. patent in March 1999.

In the latter part of the fiscal year under review, Labopharm strategically undertook pilot pharmacokinetic studies on four in-house projects reformulating already marketed drugs in order to accelerate the licensing process to international pharmaceutical companies.

Partnership Projects

In June 1997, Labopharm concluded a licensing and co-development agreement with Sepracor Inc., of Massachusetts, for the development of solid oral dosage forms of levalbuterol, trade-named Xopenex™, as a treatment for asthma and other chronic respiratory diseases. During the fiscal year under review, the Phase I study was

successfully completed and a Phase II clinical study was initiated.

In February 1999, Labopharm announced the signing of a letter of intent to work with Axcan Pharma to develop a controlled-release formulation of the currently marketed product, MODULON®, which is indicated for the treatment of irritable bowel syndrome, a disease present in 15% of the population. The new formulation is expected to reduce the daily dosage requirements and to enhance patient compliance. Phase I clinical trials are expected to begin by June 2000.

In January 2000, Labopharm signed an agreement with an international pharmaceutical company to continue to develop one of its in-house projects, a controlled-release formulation of oxybutynin, a leading drug for the control of urinary incontinence. A pilot pharmacokinetic (PK) study was initiated in February 2000 and a larger scale study will follow shortly.

Under the agreement, Labopharm will receive development funding, milestone payments and royalties on sales to certain markets including the United States. In other markets, notably Europe, a profit sharing formula has been determined and marketing partners will be identified.

An agreement was signed in 1997 with a multinational pharmaceutical company to develop new controlled-release formulations for a currently marketed drug to reduce the side effects of the product and to improve its daily dosing schedule. The multinational partner decided not to pursue the drug's development due to a change in corporate priorities, despite the fact that Labopharm had successfully modified the release profile of the drug. Although this programme was discontinued, it allowed Labopharm to develop a proprietary controlled-release technology for drugs with pH dependent solubility, an extremely difficult feat to achieve.

Another agreement signed in 1997 with the French pharmaceutical company, Les Laboratoires du Dr. E. Bouchara, was recently discontinued. Labopharm has taken back the full control of the development and the licensing programme for all international markets.

In-house Projects

The Company is also developing four in-house projects to accelerate the licensing process with international partners.

Labopharm's primary in-house product in development is the once-a-day form of tramadol, a potent analgesic, currently in Phase I development. It is considered more potent than codeine and just less so than narcotics. There is currently no once-a-day formulation of this drug available. Worldwide sales of the current formulations are close to one billion US dollars and growing.

As the development of bio-equivalent drugs requires a shorter timeframe for regulatory approval, the Company is also developing a bio-equivalent twice-a-day formulation of tramadol for rapid entry into Europe.

Last year, Labopharm successfully completed a Phase I trial on a once-a-day formulation of betahistine, a drug for the treatment of Ménière's disease, a chronic distressing condition for which there is a limited range of treatment. The Company is continuing the development of this product and discussions are already ongoing with international companies as possible partners.

The fourth in-house project is a 24-hour formulation of pseudoephedrine, a decongestant, in Phase I development. This has significant potential as a value-added product if combined with one of the anti-histamines which exist in a market that exceeds one billion U.S. dollars.

Manufacturing Agreement

Labopharm formally entered into an agreement with Cerestar in November 1998, to exclusively manufacture Contramid. Cerestar is a major global operating company in the starch and starch derivatives industry and part of the worldwide agrifoods conglomerate, Eridania Béghin-Say. As the leader in the European market and the fifth largest producer in North America, Cerestar is regularly audited by pharmaceutical companies and has extensive experience in producing Drug Master Files. Cerestar has now scaled up the production process and has produced three separate GMP batches exceeding one ton each.

Later, in April 1999, Labopharm signed a binding Memorandum of Understanding with its former supplier of Contramid, a company previously known as Rougier. Under its terms, Labopharm acquired rights to intellectual property including a Drug Master File, patent filings and related manufacturing "know-how" in

exchange for \$1,000,000 in cash, the issuance of 300,000 common shares and 200,000 common share purchase warrants. The companies mutually released and discharged each other from any future legal actions or claims.

Additional Intellectual Property

In March 1999, the Company received a new patent from the U.S. Patent Office. This additional patent will expand and solidify Labopharm's position on the current range of controlled release platforms offered with Contramid.

The new process developed with Cerestar allowed the Company to recently file a composition of matter patent for which it has exclusive use in pharmaceutical products.

Potential New Applications for Contramid Technology

Labopharm has conducted a number of new research programmes in cooperation with universities that point towards new applications for Contramid technology.

The use of Contramid could be very valuable in the prevention of infection in post-surgical orthopedic care in animals and in the treatment of post-traumatic infections. Two recent animal studies which the Company had sponsored and which were conducted in an academic veterinary clinic, produced very promising results. Mini-tablets of Contramid which contained an antibiotic were implanted in surgical wounds. The release of the antibiotic was controlled and therapeutic levels were maintained in the local tissue for 21 days.

Labopharm is also sponsoring university research aimed at developing a new polymeric micelles system to improve cancer chemotherapy. Results of preliminary experiments using in vitro and in vivo photodynamic therapy models demonstrate a marked superiority of this system over existing micelles.

Operating Revenue

Operating revenue for the fiscal year ended February 28, 2000, amounted to \$1,902,652 compared to \$1,301,985 the preceding year, for an increase of 46%. Revenues from research and development contracts totalled \$1,520,190, an increase of \$1,060,905 compared to the previous

The use of Contramid could be very valuable in the prevention of infection in post-surgical orthopedic care in animals and in the treatment of post-traumatic infections.

Management's Discussion and Analysis

year, primarily as a result of the three clinical studies undertaken during the fiscal year on projects with our partners. Investment income was \$382,462 compared to \$842,700 during the previous year. This reduction is due to the lower amount of cash and temporary investments compared to the previous year.

Research and Development Expenses

The Company incurred research and development expenses of \$3,938,377, before investment tax credits, during the last fiscal year compared to \$3,532,764 in the previous year, representing an 11% increase. Tax credits for research and development totalled \$651,008 or the equivalent of 16.5% of research and development expenses, compared to \$223,826 for the previous year.

Research and development expenses, net of investment tax credits, therefore totalled \$3,287,369 for the year compared to \$3,308,938 in the previous period. This stabilization is primarily explained by the financial contribution of our multinational partner in Phase II of the clinical study.

Galenic laboratory expenses increased by 37% to \$1,853,920 due to increased activity on projects and clinical studies. Clinical research expenses totalled \$1,183,338 compared to \$1,251,004 for the same period last year. Labopharm also devoted \$201,529 to external research compared to \$242,265 in the previous fiscal year. Several university projects were completed and new ones, such as the animal health studies, were introduced.

Selling and Administrative Expenses

Selling and administrative expenses amounted to \$2,312,778 in fiscal 2000 compared to \$2,915,217 for fiscal 1999, a decrease of 21% due to cost cutting in the Finance, Administration, Business Development and Corporate Affairs Departments.

Finance Charges

Finance charges were \$54,295 during fiscal 2000 compared to \$35,868 for fiscal 1999. The increase in finance charges is due to the payment of interest on reassessment of tax credits.

Net Loss

The net loss from operating activities, before discontinued operations and unusual item, amounted to \$3,751,790 compared to \$4,958,038 for the preceding fiscal year primarily due to the increase in R&D contract revenues and reduction in selling and administration expenses.

The net loss for fiscal 2000 was \$3,649,916 compared to \$6,463,392 for the preceding year. These numbers include for fiscal 2000 a net gain of \$59,375 related to discontinued operations

due to the sale of Analex in 1998, and \$194,646 for the preceding year.

Last fiscal year-end also includes non-recurring expenses such as our settlement with Rougier for \$1.7 million. Without these amounts, we would compare a net loss of \$3,751,790 for the fiscal year ended February 28, 2000, with \$4,958,038 for the previous year, which is more representative of the on-going situation.

Cash Position and Funding Sources

Since its creation, Labopharm has financed its activities by issuing equity, by the use of term loans, as well as by funds derived from operations. On December 21, 1994, the Company completed a private placement and realized net proceeds of \$5,136,141. In October 1995, the Company received \$660,000 from the government of Quebec as a tax credit to increase capitalization of small and medium-sized businesses. On June 25, 1996, the Company completed an initial public offering that resulted in net proceeds of \$20,989,257.

With regard to the Statement of cash flows, funds applied to operations amounted to \$6,371,776 in fiscal 2000, compared to \$3,480,571 in fiscal 1999. In fiscal year 2000, accounts receivable rose by \$1 million due to new research contracts. At the same time, the Company's accounts payable declined by \$2.3 million including last year's settlement with our former Contramid® supplier. Thus, net operating expenses for fiscal 2000 represent \$3,071,776 of the \$6,371,776.

Capital expenditures were \$484,965 for fiscal 2000 compared to \$420,272 for fiscal 1999. Capital expenditures for fiscal 2000 were principally related to the acquisition of laboratory and computer equipment.

At the close of fiscal 2000, long-term debt was zero compared with \$21,612 at the close of fiscal 1999. The long-term debt for fiscal 1999 is related to obligations arising from capital leases.

Overall, these transactions resulted in a decrease of liquidity in the amount of \$7,034,797 for fiscal 2000. Cash and temporary investments totalled \$5,476,012 at the end of fiscal 2000, compared to \$12,510,809 at the end of the previous fiscal year. The burn rate for the year 2000-2001 is projected at \$4,000,000 and we estimate our cash position to be sufficient for more than a year.

Risks and Uncertainties

The field of drug delivery systems is still a relatively new and rapidly expanding market, that brings therapeutic benefits to patients and offers great commercial potential for pharmaceutical companies.

Labopharm's success in this market will depend, in the short- and medium-term, on the applicability of its Contramid technology and its competitiveness with other

available technologies. The Company is of the opinion that Contramid can be applied successfully to a wide variety of active ingredients. Even though no product incorporating Contramid has yet been fully developed and marketed, Labopharm's results to date with different active ingredients have been promising. Contramid's performance in the studies done to date has been shown to be equivalent to the most advanced competing technologies, while remaining among the most economical. Nevertheless, there has been rapid and considerable evolution of technology within the drug delivery system industry and the competitive advantages of new systems developed by competitors could surpass those of Contramid.

Labopharm places great importance on the protection of its intellectual property and has a portfolio of patents and patent applications that it intends to enforce. However, nothing guarantees that these patents are valid, even if they are reputed to be, or that its patent applications will be approved, or that the

Company will be successful in defending them.

Labopharm's success also depends, in large measure, on its ability to conclude licensing, development, manufacturing and marketing agreements for products using its drug delivery systems with other pharmaceutical companies. This type of agreement or alliance is common in the pharmaceutical industry, and we are pleased with the way in which Labopharm's technology has been received in the industry. To date, the Company has signed five agreements with pharmaceutical companies, with three of these agreements remaining in effect. There is no assurance that partners will not withdraw from agreements at a later date or that projects will successfully reach the market.

The development of pharmaceutical products is a process that requires large investments and can take years to complete. Projects can be abandoned along the way or regulatory authorities can refuse to approve new products. With respect to projects it has itself initiated, the Company attempts to minimize risk through the judicious selection of product candidates and by focusing on improving products that have already been approved.

With respect to manufacturing Contramid, the Company has an exclusive manufacturing agreement with Cerestar, a well-known European manufacturer of starch and starch derivatives. Scaled up batches were manufactured and made available during the summer of the year under review. Cerestar is qualified to provide the scaled up quantities required to satisfy Phase III and commercial needs.

Labopharm expects to generate significant revenues from the licensing agreements and alliances it has concluded and will continue to conclude with pharmaceutical companies. Conditions of these

agreements could vary greatly depending on a number of factors. The principal forms of revenue will be milestone payments, which are lump-sum payments made at key stages of product development, as well as royalties on product sales.

Until it begins to receive royalties and milestone payments according to the terms of its strategic alliances, the Company foresees continued losses, primarily as a result of its research and development activities. Over the last three fiscal years, Labopharm's drug delivery systems' activities have accumulated net losses of approximately \$16 million.

Labopharm's management believes that current liquidity, funds from operations and funds available through its line of credit are sufficient to allow it to respond to the Company's liquidity needs for the next 16 months. During the next fiscal year, liquidity is expected to diminish by approximately \$4 million.

The Company will also need supplementary, medium-term capital. The amount and the time needed will depend on a number of factors, notably the costs associated with research and development activities and the activities necessary to obtain regulatory approvals. The Company will maintain its efforts to raise capital under reasonable terms and conditions. However, it is uncertain that the Company will be able to raise all the funds it needs at the necessary time.

The price of Labopharm's common shares is subject to fluctuation. Factors such as the conclusion of strategic alliances, research results and clinical studies, questions regarding patents and any number of other factors could considerably influence the price of Labopharm's common shares.

Impact of the Year 2000 on Labopharm's Computer Systems

The Company experienced no problems due to the impact of the year 2000 on its computer systems. The Company mandated its working group to make the Year 2000 plan effective by May 30, 1999. All computer and laboratory equipment was tested and changes were made according to supplier specifications. Labopharm nevertheless remains vigilant on this issue.

MANAGEMENT'S REPORT

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The accompanying financial statements of Labopharm Inc. are the responsibility of the management and have been approved by Labopharm's Board of Directors.

These financial statements were prepared by management in accordance with generally accepted Canadian accounting principles. They include some amounts that are based on estimates and judgments. The financial information contained elsewhere in the annual report is consistent with that in the financial statements.

To ensure the accuracy and objectivity of the information contained in the financial statements, Labopharm's management maintains a system of internal accounting controls. Management believes this system gives a reasonable degree of assurance that the financial documents are reliable and provide an adequate basis for the financial statements, and that the Company's assets are properly accounted for and safeguarded.

The Board of Directors carries out its responsibility for the financial statements in this annual report primarily through its audit committee. The audit committee is formed of outside directors who review the Company's annual financial statements as well as the management's analysis and the operating results and recommend their approval by the Board. Mallette Maheu, General Partnership, the external auditors designated by the shareholders, periodically meet with the audit committee to discuss auditing, the reporting of financial information and other related subjects.



Donald Buxton
President and
Chief Executive Officer



James R. Howard-Tripp
Executive Vice-President

Laval, April 25, 2000

AUDITORS' REPORT

To the Shareholders of Labopharm Inc.

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We have audited the balance sheets of LABOPHARM INC. as at February 28, 2000 and 1999 and the statements of income, deficit and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with Canadian generally accepted auditing standards. Those standards require that we plan and perform and audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

In our opinion, these financial statements present fairly, in all material respects, the financial position of the Company as at February 28, 2000 and 1999 and the results of its operations and its cash flows for the years then ended in accordance with Canadian generally accepted accounting principles.



Mallette Maheu, associated with Arthur Andersen
General Partnership
Chartered Accountants

Montreal, March 22, 2000

Statement of Income

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Years ended February 28	2000	1999
Operating revenue		
Research and development contracts	\$ 1,520,190	\$ 459,285
Investment income	382,462	842,700
	1,902,652	1,301,985
Operating expenses (Note 4)		
Research and development expenses (Note 5)	3,287,369	3,308,938
Selling and administrative expenses	2,312,778	2,915,217
Finance charges	54,295	35,868
	5,654,442	6,260,023
Loss before other item and discontinued operations	(3,751,790)	(4,958,038)
Costs related to an agreement with a former supplier (Note 9)	42,499	(1,700,000)
Loss before discontinued operations	(3,709,291)	(6,658,038)
Discontinued operations (Note 15)		
Gain from discontinued operations	59,375	194,646
Net loss	\$ (3,649,916)	\$ (6,463,392)
Loss before discontinued operations per share	\$ (0.1860)	\$ (0.3379)
Net loss per share	\$ (0.1830)	\$ (0.3280)

Statement of Deficit

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Years ended February 28	2000	1999
Balance at beginning	\$ (19,678,331)	\$ (13,214,939)
Net loss	(3,649,916)	(6,463,392)
Balance at end	\$ (23,328,247)	\$ (19,678,331)

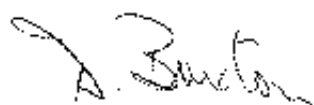
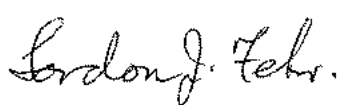
Balance Sheet

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February 28	2000	1999
Assets		
Current assets		
Cash	\$ 248,716	\$ 517,503
Temporary investments	5,227,296	11,993,306
Accounts receivable	1,071,429	126,815
Tax credits receivable on research and development (Note 5)	631,539	201,622
Prepaid expenses	17,188	4,779
	7,196,168	12,844,025
Capital assets (Note 6)	2,092,244	1,962,686
Deferred income taxes	176,154	176,154
	\$ 9,464,566	\$ 14,982,865
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities	\$ 963,052	\$ 3,271,379
Current portion of obligations under capital leases (Note 8)	21,612	190,056
	984,664	3,461,435
Obligations under capital leases (Note 8)	-	21,612
	984,664	3,483,047
Shareholder's equity		
Capital stock (Note 9)	31,808,149	31,178,149
Deficit	(23,328,247)	(19,678,331)
	8,479,902	11,499,818
	\$ 9,464,566	\$ 14,982,865

Commitments (Note 11)

On behalf of the Board of Directors


Donald Buxton
Director

Gordon J. Fehr
Director

Cash Flows

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Years ended February 28	2000	1999
Operating activities		
Loss before discontinued operations	\$ (3,709,291)	\$ (6,658,038)
Items not affecting cash:		
Amortization	337,104	321,527
Loss on disposal and write-off of capital assets	6,303	130,320
	(3,365,884)	(6,206,191)
Net change in non-cash operating working capital items	(3,065,267)	2,842,555
	(6,431,151)	(3,363,636)
Gain from discontinued operations (Note 15)	59,375	194,646
Items not affecting cash:		
Amortization	-	28,261
Gain on disposal of assets and liabilities of the subsidiary (Note 15)	-	(622,535)
	59,375	(399,628)
Net change in non-cash operating working capital items related to discontinued operations	-	282,693
	59,375	(116,935)
	(6,371,776)	(3,480,571)
Investing activities		
Proceeds from disposal of the subsidiary	-	800,000
Acquisition of temporary investments	(1,015,672)	(3,471,008)
Proceeds of temporary investments	7,781,682	6,372,829
Acquisition of capital assets	(484,965)	(420,272)
Leasehold improvements allowance receivable	-	197,675
Proceeds from disposal of capital assets	12,000	1,846
Discontinued operations investing activities	-	(5,780)
	6,293,045	3,475,290
Financing activities		
Variation in bank loan	-	581,354
Reimbursement of capital lease obligations	(190,056)	(263,626)
Proceeds from issuance of capital stock	-	41,400
Financing activities related to discontinued operations	-	(23,837)
	(190,056)	335,291
Increase (decrease) in cash and cash equivalents	(268,787)	330,010
Cash at beginning	517,503	187,493
Cash at end	\$ 248,716	\$ 517,503
Cash flows include the following element:		
Interest paid	\$ 54,295	\$ 35,868

Notes to Financial Statements

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February 28, 2000 and 1999

1. STATUTES OF INCORPORATION AND NATURE OF ACTIVITIES

The Company, incorporated under the *Companies Act* (Québec), is engaged in controlled release systems and specializes in the development of pharmaceutical products utilizing its own drug delivery technologies.

The Company's strategy is to form strategic alliances or licensing agreements with national or international pharmaceutical companies that already have the necessary resources to support the development and to market and sell the pharmaceutical products which incorporate the Company's proprietary technology. The future profitability of the Company is dependent upon such factors as the success of the clinical trials, the approval by regulatory authorities of products developed by the Company, and the ability of Labopharm to obtain the necessary financing to complete its projects through licensing and research agreements.

2. SIGNIFICANT ACCOUNTING POLICIES

Temporary investments

Bonds are stated at the lower of unamortized cost or market value. Premium or discount is amortized over the remaining term of the bonds.

Property, plant and equipment

Property, plant and equipment are carried at cost less any tax credit on research and development.

Assets acquired under capital leases are carried at cost, being the present value of the minimum lease payments after deduction of executory costs.

Amortization of property, plant and equipment and assets acquired under capital leases is calculated over their useful life using the following methods and rates:

	Methods	Rates
Laboratory equipment	Diminishing balance	20%
Computer hardware	Diminishing balance	30%
Software	Diminishing balance	30%
Furniture	Diminishing balance	20%
Leasehold improvements	Straight-line	3 years

Intangible assets

Intangible assets are valued at cost.

Intellectual property rights are amortized using the straight-line method at the rate of 5% which approximates the service lives of the related assets.

Patents will be amortized over periods of 17 to 20 years beginning on the date they are used in commercial activities.

Research and development expenses

Research expenses are charged to operations less related tax credits. Development costs net of related tax credits are charged to operations as incurred unless a development project meets generally accepted accounting criteria for deferral and amortization. As at February 28, 2000, no development costs have been deferred.

Use of estimates

The presentation of financial statements in accordance with Canadian generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingencies at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Stock-based compensation plans

The Company has a stock-base compensation plan, which is described in Note 10. No compensation expense is recognized for this plan when stock or stock options are issued to employees.

3. CHANGE IN ACCOUNTING POLICY

The Company adopted retroactively the recommendations of the Canadian Institute of Chartered Accountants concerning the cash flow statement. The prior year figures have been restated. The changes relate primarily to the components of cash and cash equivalents and to the presentation of non-cash transactions.

4. INFORMATION RELATING TO THE STATEMENT OF INCOME

	2000	1999
The following items are included in the operating expenses:		
Amortization-capital assets	\$ 337,104	\$ 321,527
Interest on long-term debt	\$ 8,495	\$ 29,579
Other interest	\$ 45,800	\$ 6,289

Research and development expenses are presented net of tax credits of \$651,008 for the year ended February 28, 2000 and of \$223,826 for the year ended February 28, 1999.

5. RESEARCH AND DEVELOPMENT TAX CREDITS

Certain research and development tax credits accounted for are related to tax returns not yet assessed by the taxation authorities.

6. CAPITAL ASSETS

	2000		1999	
	Cost	Accumulated amortization	Cost	Accumulated amortization
Property, plant and equipment:				
Laboratory equipment	\$853,055	\$299,446	\$494,426	\$113,324
Computer hardware and software	262,698	148,519	137,460	40,690
Furniture	220,547	96,216	184,270	47,986
Leasehold improvements	234,035	173,113	177,327	84,297
	1,570,335	717,294	993,483	286,297
Net value	853,041		707,186	
Capital lease				
Laboratory equipment	367,382	175,757	549,053	219,255
Computer hardware and software	67,201	46,056	160,060	96,827
Furniture	43,645	21,858	76,151	32,575
Leasehold improvements	-	-	34,076	34,076
	478,228	243,671	819,340	382,733
Net value	234,557		436,607	
Intangible assets:				
Intellectual property rights	500,000	125,000	500,000	100,000
Patents	629,646	-	418,893	-
	1,129,646	125,000	918,893	100,000
Net value	1,004,646		818,893	
Net value	\$2,092,244		\$1,962,686	

7. BANK INDEBTEDNESS

The Company has available a credit line of \$500,000 secured by a movable hypothec on the universality of claims and bearing interest at prime rate. As at February 28, 1999 and 2000, there is no credit balance on the credit line.

February 28, 2000 and 1999

8. CAPITAL LEASE OBLIGATIONS

	2000	1999
Laboratory equipment and other capital assets lease contract, repayable in monthly instalments of \$13,522 including interest calculated at 8.98% with transfer of ownership at maturity on July 31, 1999	\$ -	\$ 67,610
Laboratory equipment, computer hardware and other capital assets lease contract, repayable in monthly instalments of \$10,912 including interest calculated at 7.82% with transfer of ownership at maturity on April 30, 2000	21,824	152,768
	21,824	220,378
Interest included in instalments	212	8,710
	21,612	211,668
Current portion	21,612	190,056
	\$ -	\$ 21,612

9. CAPITAL STOCK

	2000	1999
Authorized		
Unlimited number of preferred shares, non-participating, non-voting, without par value		
Unlimited number of common shares, without par value		
Issued		
20,016,681 common shares		
(1999 - 19,716,681)	\$31,808,149	\$31,178,149

Issuance

During the year ended February 28, 1999, the Company provided a provision of \$1,700,000 for negotiating an agreement with the former manufacturing supplier of Contramid®. During the current year an agreement was concluded, which is a consideration of an issuance of 300,000 common shares at a price of \$2.10 per share and an amount of \$1,000,000 in cash.

Furthermore, the Company has issued 200,000 warrants, to the supplier, which can be exercised at the average market price of the last five days, expiring on May 2004.

10. STOCK-BASED COMPENSATION PLANS**Stock option plan**

In May, 1995, Labopharm Inc. established a stock option plan for directors, executive officers, employees and consultants of the Company, which was modified in March and June 1996. The maximum number of common shares that are issuable under the plan will not exceed 2,856,578 shares including the 891,000 options granted prior to the public offering, and the maximum number of common shares that may be optioned in favour of any individual will not exceed 5% of the number of outstanding common shares.

The price at which the common shares may be purchased will not be lower than the average of the closing prices of the common shares on the Toronto Stock Exchange for the five preceding days. Any options issued will be non-transferrable.

All of the options that may be granted under the Plan are exercisable according to a schedule up to a maximum period of 10 years following the grant date thereof. The outstanding options as at February 28, 2000 may be exercised not later than July 2004.

The changes in the number of stock options granted are as follows:

	2000	1999
Balance at beginning	1,904,300	1,497,100
Granted	348,000	683,000
Exercised	-	(41,400)
Cancelled	(16,750)	(234,400)
Balance at end	2,235,550	1,904,300
Options eligible to be exercised	1,304,300	936,700

During the year, no option was exercised (1999 - 41,400 options were exercised for \$41,400 in cash).

The following table summarizes information about fixed stock options outstanding at February 28, 2000:

Range of exercise price	Number of options outstanding at February 28, 2000	Weighted-average remaining contractual life	Weighted-average exercise price	Options eligible to be exercised at February 28, 2000	Weighted-average exercise price
\$1 to 3	768,050	2.4 years	\$1.92	288,300	\$1.92
\$3 to 6	968,500	2.8 years	\$4.26	517,000	\$4.26
\$6 to 9	499,000	1.3 years	\$6.62	499,000	\$6.62
\$1 to 9	2,235,550	2.3 years	\$3.98	1,304,300	\$3.98

In addition, the Université de Montréal and Université du Québec à Montréal were granted an option to purchase 160,000 common shares at the price of \$6.25. Such option will expire on June 25, 2001.

During the month of March 2000, the Company granted 200,000 options to a newly appointed officer. These options can be exercised at a price of \$2.52 per option.

11. COMMITMENTS

The Company rents premises under operating leases. The aggregate minimum rental commitment amounts to \$533,698 excluding a property tax escalator clause. The aggregate minimum rental commitments for the next four years are as follows:

2001 - \$182,800
2002 - \$161,517
2003 - \$143,967
2004 - \$ 45,414

Furthermore, a first rank chattel mortgage without delivery has been granted for an amount of \$100,000 to the lessor on all present and future movable assets located in the rented space.

12. RELATED PARTY TRANSACTIONS

The principal transactions undertaken with a shareholder company during the year were as follows:

	2000	1999
Fees	\$50,000	\$50,000

These transactions are carried out in the normal course of operations and are measured at the exchange amount.

February 28, 2000 and 1999

13. INCOME TAXES AND TAX BENEFITS

The spread between the income taxes presented in the income statement and those that would be calculated using the basic income tax rates in effect, is primarily caused by the fact that most tax benefits resulting from loss carry forward, as well as deferred income tax debits related to research expenses not deducted, have not been accounted for.

The fiscal losses available to reduce future income taxes payable, amount to \$13,830,516 and \$12,412,766 at the federal and provincial levels, respectively. The expiration dates of the loss carry forwards are as follows:

	Federal	Provincial
2002 -	\$ 299,898	\$ -
2003 -	\$1,854,365	\$1,623,317
2004 -	\$1,838,927	\$1,607,644
2005 -	\$3,633,666	\$3,846,237
2006 -	\$3,900,953	\$3,480,160
2007 -	\$2,302,707	\$1,855,408

The balance of scientific research expenses, that could possibly reduce future income taxes, amounts to \$4,923,874 and \$9,035,236 at the federal and provincial levels respectively. The Company can take advantage of tax benefits resulting from carry forward of these expenses over an undetermined period.

The balance of the income tax credits related to scientific research applicable against future federal income taxes amounts to \$1,467,600. The Company can take advantage of tax benefits resulting from the carry forward of these credits until the following years:

2005 -	\$ 38,527
2007 -	\$217,818
2008 -	\$345,129
2009 -	\$368,893
2010 -	\$497,233

The capital losses that could possibly reduce future income taxes are \$2,532,529. The Company can take advantage of these losses resulting from carry forward over an undetermined period.

Other timing differences which can be carried forward to offset net income for tax purposes amount to \$402,146.

The eventual tax benefit has not been recognized, except on losses of \$447,780 and \$715,336 at the federal and provincial levels, respectively.

14. FAIR VALUE OF FINANCIAL INSTRUMENTS

Given their short-term maturity, the fair value of cash, accounts receivable and accounts payable approximate the carrying value.

Temporary investments include bonds issued by governments and public companies. These bonds primarily mature over the next two years with an average weighted yield of 4.80%. The market value of securities held as at February 28, 2000 is \$5,192,131 (1999 - \$12,002,171).

The fair value of the obligations under capital leases approximates the carrying value given the short-term maturity or the interest rates.

15. DISCONTINUED OPERATIONS

On January 31, 1998, the Company announced its intention to dispose of its subsidiary Analex Inc. operating an analytical test laboratory in the fields of pharmaceutical and food industries, and adopted a formal plan of disposal.

On April 16, 1998, the subsidiary has been disposed of for an amount of \$800,000 in cash. The assets and liabilities related to discontinued operations include:

Non-cash assets	
Accounts receivable	\$ 573,701
Inventory	106,027
Prepaid expenses	32,034
Capital assets	1,360,192
	<u>2,071,954</u>
Non-cash liabilities	
Accounts payable	659,308
Long-term debt	653,827
	<u>1,313,135</u>
Non-cash net assets disposed	758,819
Liability cash item disposed	
Bank loan	581,354
Net assets disposed	<u>\$ 177,465</u>

The gain resulting in 1999 from the disposal of the subsidiary amounting to \$194,646 is summarized as follows:

Proceeds on disposal	\$800,000
Net assets disposed	<u>177,465</u>
Gain on disposal of assets and liabilities	622,535
Costs of disposal	<u>220,000</u>
	402,535
Operating loss from measurement date to disposal date (including amortization of \$28,261)	<u>207,889</u>
Gain from discontinued operations	<u>\$194,646</u>

The sales figure for the subsidiary for the seven week period ended April 16, 1998 is \$480,146.

The financial statements for the year ended February 28, 1999 include all Labopharm Inc. accounts and those of its subsidiary.

CORPORATE PROFILE



Labopharm is a dynamic specialty pharmaceutical company whose goal is to become a leading supplier of controlled release systems to the pharmaceutical industry worldwide. Its core platform technology, **Contramid®**, can be applied to a wide range of medications in solid dosage form to improve their oral administration and performance.

Based in Laval, Quebec, Labopharm has a qualified staff and specialized facilities for the development of controlled release formulations. When necessary, it calls upon external resources such as clinical research organizations and manufacturers of final dosage forms. The Company's strategy is to build alliances with Canadian and international pharmaceutical companies for the manufacturing and marketing of products that utilize its technologies.

Labopharm has been a publicly traded company since June 1996; its shares are listed on the Toronto Stock Exchange under the ticker symbol **DDS**.

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Chairman of the Board, Labopharm Inc.
President, BioCapital Inc.

Donald Buxton ⁽¹⁾
Vice Chairman of the Board
President and Chief Executive Officer
Labopharm Inc.

Jean-Denis Dubois ⁽³⁾
Director Investments,
Health and Biotechnology
Fonds de Solidarité FTQ

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Corporate Director
Former Chairman and President
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James R. Howard-Tripp ⁽³⁾
Executive Vice-President
Labopharm Inc.

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President and Chief Executive Officer
Stiefel Canada Inc.

Jim McDonald ⁽⁴⁾
Executive Vice-President
Corporate Development
Nexia Biotechnologies Inc.

Frédéric Porte ⁽¹⁾
President
Mediprass Management Inc.

Percy Skuy ⁽²⁾
Corporate Director
Former President
Johnson & Johnson Corporation Affiliate

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President and Chief Executive Officer

M^{me} Lisane Dostie
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Corporate Affairs and Secretary

James R. Howard-Tripp
Executive Vice-President
(Since March 7, 2000)

Vincent Lenaerts
Vice-President
Research and Development

Jim McDonald
Vice-President
Finances, Administration
and Corporate Development
(Until January 6, 2000)

General Information

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Annual Meeting

July 5, 2000, 10 a.m.
Omni Hotel, Montreal
Room Été

Investor Relations

Donald Buxton
President and Chief Executive Officer

James R. Howard-Tripp
Executive Vice-President

Stock Exchange Listing

Toronto Stock Exchange
Trading Symbol: DDS

Transfer Agent

General Trust of Canada

Auditors

Mallette Maheu

1. Member of the Executive Committee
2. Member of the Human Resources Committee
3. Member of the Audit Committee
4. Mr. McDonald joined the Board of Directors
on January 6, 2000.

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