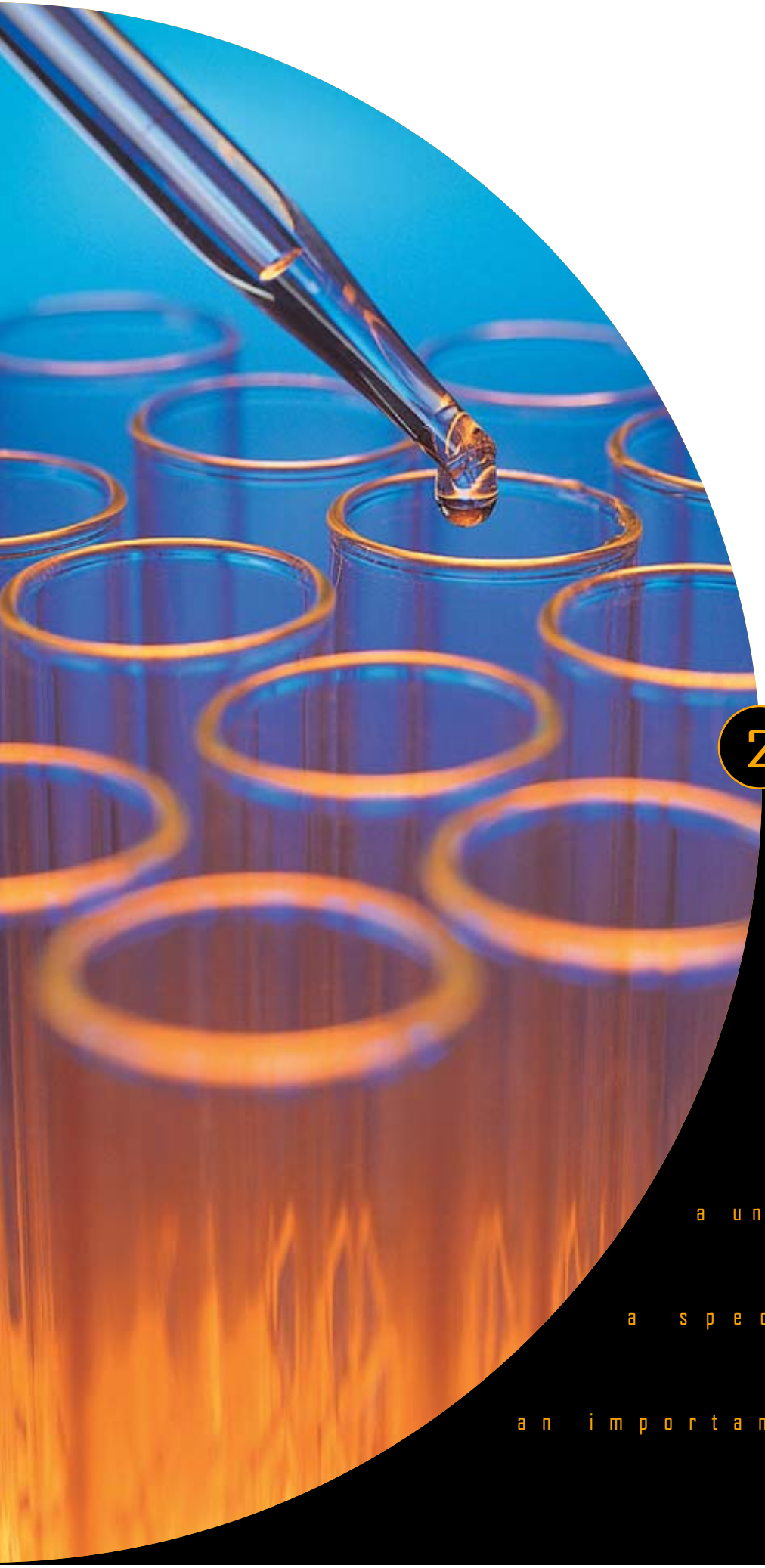


TRIMERIS

2000 annual report

a unique science

a special team

an important journey


a unique science
a special team
an important journey

a letter to the shareholders

2000 annual report

During the past year, our outstanding team of scientists, physicians, and business executives achieved significant milestones in the process of building a world-class biotechnology company and bringing our anti-HIV viral fusion inhibitor drug candidates closer to market.

Today, tens of thousands of patients worldwide are infected with strains of HIV that have become resistant to currently available therapies. Because Trimeris fusion inhibitor drugs function in a completely novel manner, they offer the potential to overcome this resistance and aid many of those in desperate need of new treatment options.

In July 2000, the 48 week results from a phase II clinical trial of T-20—our lead fusion inhibitor compound—were presented at the 13th International AIDS Conference in Durban, South Africa. In this study, T-20 205, Trimeris, along with our partner, Hoffmann-La Roche, and academic collaborators demonstrated that ***T-20 in combination with other anti-HIV drugs was well-tolerated and may have contributed to lowering the level of HIV in patients who had previously failed an average of ten HIV medications.*** *This was a major accomplishment for Trimeris since these results—combined with data on over two hundred patients treated with T-20 in other clinical trials—supported a decision to proceed with the final stage of clinical testing. In Q4 2000, after seeking the advice of the United States Food and Drug Administration (FDA), and European regulatory authorities,* ***Trimeris and Roche initiated two large-scale, phase III pivotal trials of T-20—a drug that has received fast track designation by the FDA.***

In 2000, we also made significant progress in the development of our second HIV fusion inhibitor — T-1249. The first phase I/II clinical trial of T-1249 was conducted in 72 HIV-infected, treatment-experienced adults who received no other HIV therapy over the 14-day treatment period. The data from this study, T-1249 101, were reported in early 2001 and showed encouraging results. ***T-1249 was well tolerated and decreased HIV levels in a dose-dependent fashion.*** *Based on these results, we are continuing to explore higher doses and are excited about the potential clinical applications of T-1249.*

I am also pleased to report that during the past year substantial progress has been made in executing our commercial manufacturing plan for T-20. In August 2000, ***Trimeris and Roche jointly selected the Roche manufacturing facility in Boulder, Colorado as the primary site for large-scale production of T-20.*** *The construction of a new, state-of-the-art commercial manufacturing plant is now underway. We are highly confident that Roche Colorado will be able to successfully meet the global demand for T-20.*

In summary, 2000 was a year of successes for Trimeris as the company continued to grow and mature. There may be no better example of this continuous evolution than our ability to attract individuals with world-class talent and experience. The appointment of Lynn Smiley, M.D., former Vice President of HIV and Opportunistic Infections Clinical Development at Glaxo Wellcome to Senior Vice President of Clinical Research is a clear sign of our corporate vitality and strength.

When Tom Matthews and I founded Trimeris in 1993, we knew that bringing hope to patients in need was a worthy challenge—an important journey. With the remarkable results of 2000 firmly in hand, we are confident in our ability to achieve our corporate mission—to launch an entirely new class of antiviral drugs—the fusion inhibitors. When that vision is realized, every Trimeris stakeholder—our patients, physicians, investors, employees, and corporate partners—will reap the benefits. On behalf of the dedicated employees of Trimeris, I can assure you that we are well positioned, on-track, and committed to the task.

DANI P. BOLOGNESI, PH.D.
CHIEF EXECUTIVE OFFICER AND CHIEF SCIENTIFIC OFFICER

HIV Cell Fusion and Infection Process

The Need for New HIV Therapies Continues to Grow

The ultimate goal of anti-HIV drug therapy is to prevent the virus from reproducing and damaging the immune system. Although substantial progress has been made over the past fifteen years in the fight against HIV, a cure still eludes medical science. Today, physicians have more than a dozen antiretroviral agents in three different drug classes to manage the disease. Typically, drugs from two or three classes are prescribed in a variety of combinations known as HAART—Highly Active AntiRetroviral Treatment. While HAART has been shown to reduce the amount of HIV in the body (viral load) tens of thousands of patients encounter significant toxic problems with this therapy.

All currently approved anti-HIV drugs work by entering an HIV infected CD4+ T cell and blocking the function of a viral enzyme-either reverse transcriptase or protease. HIV needs both of these enzymes in order to reproduce. However, HIV can mutate and become resistant—rendering reverse transcriptase or protease inhibitor drugs ineffective. When this occurs, viral loads increase and dictate the need to switch the ineffective agent for another.

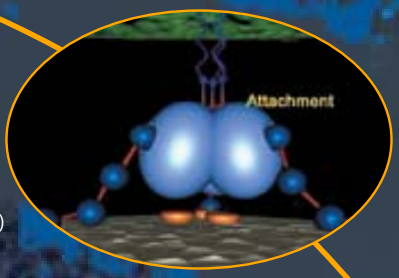
Unfortunately, when a virus becomes resistant to one drug in a class, other drugs in that class may become less effective. This phenomenon known as cross-resistance can further reduce the number of viable treatment options for patients. Finally, although HAART therapy can be effective in reducing viral loads, many patients cannot tolerate the toxic side effects over the long-term. Some side effects are serious and include abnormal fat metabolism, kidney stones, and heart disease. Other side effects such as—nausea, vomiting, and insomnia—are less serious, but still problematic for HIV patients on a lifetime of chronic drug therapy.

Problems with Current HIV Drug Regimens

- **Drug Resistance**
- **Drug Cross Resistance**
- **Toxic Side Effects**

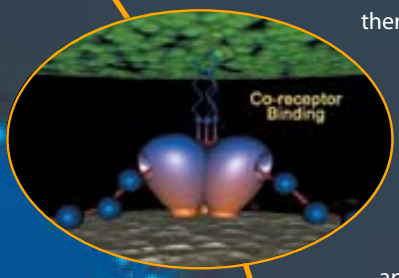
Attachment

HIV gp 120 protein (lt. blue) binds to CD4+ T cell via CD4 receptors (dk. blue) on cell membrane surface



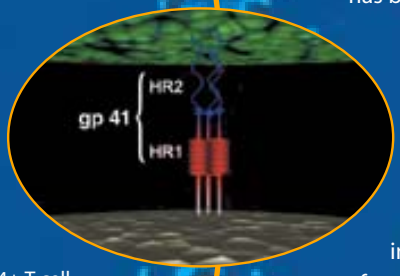
Co-Receptor Binding

HIV gp 120 protein binds to co-receptors on CD4+ T cell



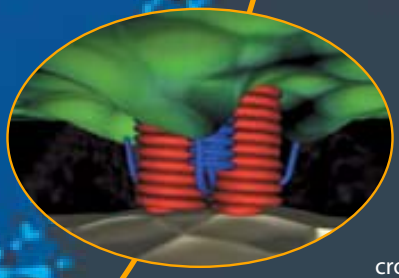
HIV Insertion

HIV gp 41 protein, composed of HR1 and HR2 subunits, "harpoons" CD4+ T cell



Fusion

HIV gp 41 protein folds on itself bringing HIV membrane and CD4+ T cell membrane together



Successful HIV Cell Infection

HIV genetic material transfers to CD4+ T cell

a unique science

FUSION INHIBITION

Blocking HIV Fusion Stops HIV Reproduction

HIV, like other viruses, is an infectious agent that lacks the ability to reproduce on its own. In order for HIV to reproduce, it must first invade a host CD4+ T cell—a critical component of the body's immune system. It then uses the cell's own machinery to make copies of itself. Viral replication typically results in the formation of hundreds of new viral particles and the death of the healthy CD4+ T cell.

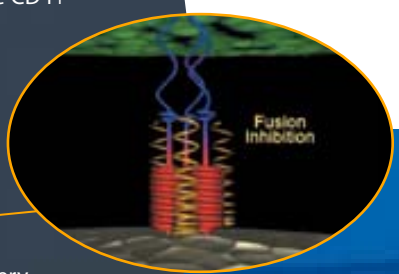
Scientists have determined that some viruses—including HIV—must undergo a complex process called fusion in order to enter the host cell and reproduce. During fusion, the outer membrane of the virus merges with the membrane of the CD4+ T cell. If HIV cannot undergo fusion, then it cannot reproduce itself and subsequently kill the vital CD4+ T cell.

Potential Benefits of Fusion Inhibitors

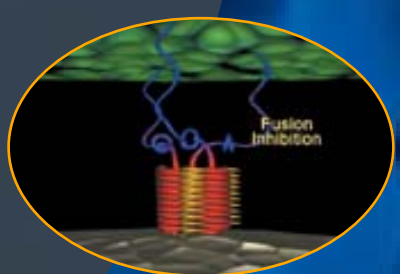
- **Novel Mechanism of Action**
- **Potent against Drug-Resistant HIV Strains**
- **Minimal Side Effects**
- **Simplified Dosing**

Fusion Inhibitors – Closing the Door on HIV

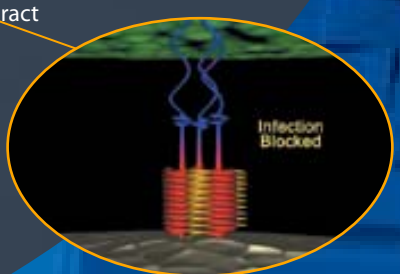
Trimeris researchers are leading the discovery and development of fusion inhibitors—drugs that block the viral fusion process and consequently HIV reproduction. Fusion inhibitors function in a way that is completely different from all currently approved anti-HIV drugs. This unique "mechanism of action" offers the potential for the class to be effective against resistant HIV strains. Unlike reverse transcriptase and protease inhibitors— which work inside a cell—fusion inhibitors function on the outside of a cell. By remaining outside and blocking HIV before it gains entry to the cell, fusion inhibitors are less likely to negatively interact with other drugs or interfere with important normal biochemical processes. This is a major advantage because it may decrease the likelihood of side effects, minimize drug-drug interactions, and simplify dosing.



T-20 (yellow) Binds HIV gp 41 Protein



T-20 Blocks gp 41 Folding



HIV Cell Fusion and Infection Inhibited

First In Class, Late Stage Development

T-20 is the first member of the new class of viral fusion inhibitors to be developed by Trimeris. This molecule, a 36 amino acid peptide, has shown significant promise in phase I and II clinical testing. T-20 was tested in a phase II clinical trial—T-20 205—in advanced HIV patients who had previously failed on average 10 anti-HIV medications and entered the study with high viral load (median 4.8 $\log_{10}$ viral copies/mL) and low CD4 cell count (median 135 cells/mm^3). After 48 weeks, T-20, in combination with other anti-HIV drugs, may have contributed to a 56% (23/41) response rate in patients completing 48 weeks of treatment or 33% of the entire population who entered the study. The response rate for the T-20 205 study was defined as a 10-fold reduction in HIV viral load compared to baseline or viral load reductions below the limit of detection in HIV tests.

T-20 Highlights

- Fast Track Designation by FDA – Granted for products that may provide significant improvement for the treatment of serious or life threatening disease.

- Based on a survey of patients participating in the T-20 205 study, twice daily injections of T-20 did not substantially interfere with activities of daily living.

- Phase I/II clinical trial conducted in HIV-infected pediatric patients aged 3-12.

- Phase III, pivotal trial program — the final stage of pre-approval clinical testing— consisting of a North American study (T-20 301) and a European study (T-20 302) initiated in Q4 2000.

The Promise of Expanding HIV Treatment Options

T-1249 is the second fusion inhibitor in the Trimeris product development portfolio. This molecule, a 39 amino acid peptide, holds the promise of further expanding the treatment options for HIV patients. The history of HIV treatment has demonstrated that the existence of multiple drugs within the reverse transcriptase and protease inhibitor classes have allowed for a variety of drug combinations and improved patient treatment. Therefore, the availability of multiple products within the fusion inhibitor class may benefit patients by broadening the range of future treatment options.

A phase I/II clinical trial of T-1249 was conducted in 72 HIV-positive, treatment-experienced adults who received no other HIV therapy over the 14-day treatment period. In this study—T-1249-101—patients received T-1249 monotherapy for 14 days at doses ranging from 6.25 mg/day to 50 mg/day on a once or twice daily regimen. The results indicated that T-1249 was well tolerated over 14 days and confers dose-related suppression of HIV. On day 14, the median decrease in plasma HIV RNA levels from baseline ranged from 0.10 $\log_{10}$ reduction in viral copies/mL for the 6.25 mg/day dose to 1.4 $\log_{10}$ reduction in viral copies/mL for the 50 mg/day dose. These encouraging data provide the basis to continue the clinical development of T-1249.

- Fast Track Designation by the FDA
- Rationally designed in the laboratory to improve dosing
- Binds to a slightly different region of HIV gp41 protein than T-20
- Potent HIV suppression in laboratory tests
- May possess resistance profile distinct from currently approved anti-HIV drugs and T-20

Breaking New Ground in Pharmaceutical Manufacturing

Large-scale Chemical Synthesis of Therapeutic Peptides

With the impending launch of T-20, the Trimeris Roche alliance is clearly transforming the practice of clinical virology. However, the alliance is also creating a revolution in pharmaceutical manufacturing. Because of the large and growing number of HIV patients who are failing available medications, the worldwide demand for T-20 is expected to be significant. Meeting this demand will require the production of thousands of kilograms of the peptide. This scale of chemical production of peptide is unparalleled in the history of pharmaceutical manufacturing. By comparison, the annual production of currently available therapeutic peptides is less than 100 kilograms.

To satisfy this worldwide need, Trimeris and Roche scientists along with their engineering colleagues, are designing and building a new state-of-the-art manufacturing plant at the Roche Colorado facility in Boulder, Colorado. When completed in 2002, this facility will be capable of producing several metric tons of therapeutic peptides on an annual basis with—the ability to increase this capacity over time.

Therapeutic Peptides

Proteins are among the most important molecules found in nature. Peptides, which are small versions of proteins, are composed of molecular building blocks called amino acids—linked together in long chains. Trimeris is a world leader in the research, development, and manufacturing of therapeutic peptides to treat human disease.

PURIFICATION & ISOLATION PHASE (10 STEPS)

SOLUTION PHASE (8 STEPS)

Creating Competitive Advantage Through Rapid Process Development

Trimeris Invents the Future of Commercial Peptide Manufacturing

Several years ago it was considered impossible to contemplate the development of a therapeutic peptide--especially one as complex as T-20 —because the process of manufacturing the drug was simply uneconomical. Traditional methods of peptide synthesis—designed to make small quantities in the laboratory—are too wasteful, slow, and costly for commercial production. In addition, the highly specialized amino acids that serve as raw materials have never been produced in the quantities required for T-20. Trimeris scientists are successfully tackling all of the T-20 manufacturing challenges with rapid innovation in chemical process development.

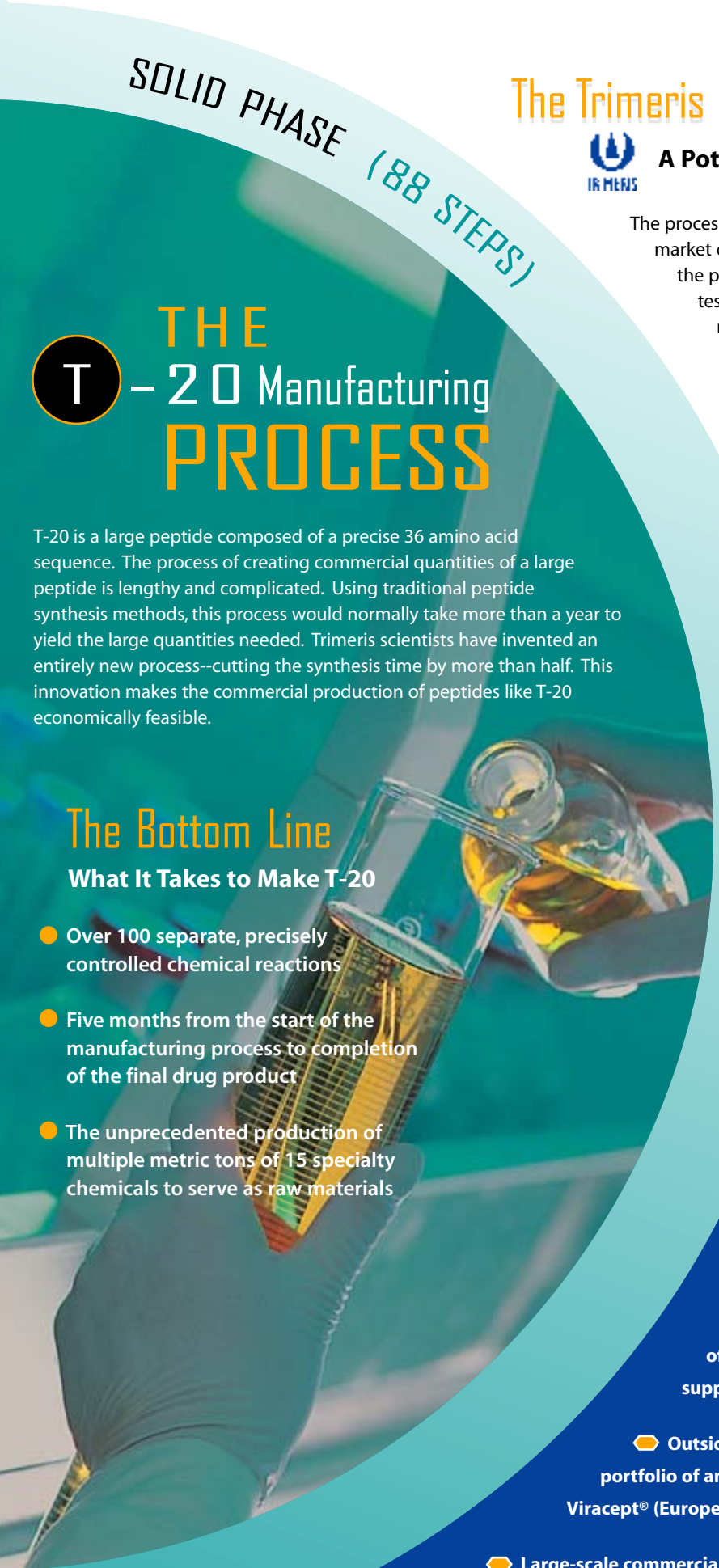
Trimeris Manufacturing Innovation

- Breakthrough High Efficiency Hybrid Solid/Solution Phase Synthesis Process
- Creation of a New Raw Material Supply Chain with Specialty Chemical Suppliers
- Unprecedented, Large-scale Chemical Production of a Complex Peptide

SOLID PHASE (88 STEPS)

THE T-20 Manufacturing PROCESS

T-20 is a large peptide composed of a precise 36 amino acid sequence. The process of creating commercial quantities of a large peptide is lengthy and complicated. Using traditional peptide synthesis methods, this process would normally take more than a year to yield the large quantities needed. Trimeris scientists have invented an entirely new process--cutting the synthesis time by more than half. This innovation makes the commercial production of peptides like T-20 economically feasible.



The Bottom Line

What It Takes to Make T-20

- **Over 100 separate, precisely controlled chemical reactions**
- **Five months from the start of the manufacturing process to completion of the final drug product**
- **The unprecedented production of multiple metric tons of 15 specialty chemicals to serve as raw materials**

The Trimeris Roche Strategic Alliance

A Potent Combination

The process of taking a new drug from the laboratory to the market on a global scale is a challenge for every company in the pharmaceutical industry. Typically, years of laboratory testing and clinical research in thousands of patients are required to produce enough evidence to demonstrate that a drug is both safe and effective. In order to expedite the global development, approval, and commercialization of T-20 and T-1249, Trimeris formed a strategic alliance with F. Hoffmann-La Roche, Ltd. Roche—a global leader in HIV diagnostics and therapeutics—brings its worldwide development expertise, marketing resources, and financial strength to the collaboration. In return, it receives exclusive marketing rights for the leading drug candidates in an important new class of anti-HIV agents. In the United States and Canada, Trimeris and Roche equally share development and marketing costs, as well as profits. Outside of North America, Trimeris receives royalties on sales of T-20 and T-1249. This business model allows Trimeris to retain a significant economic interest in the commercialization of the two lead fusion inhibitor drugs. In addition, Trimeris maintains a major role in strategic decision-making with its presence on joint Trimeris-Roche clinical research, manufacturing, and marketing teams.

The Roche Advantage

- **Global clinical development capabilities needed to obtain marketing approvals in all major pharmaceutical markets**
- **Highly trained and experienced team of HIV sales representatives and clinical support specialists**
- **Outside of the collaboration, Roche markets an existing portfolio of anti-HIV products - Fortovase®, Invirase®, Hivid®, Viracept® (Europe)**
- **Large-scale commercial manufacturing expertise and capacity**

TEAM TRIMERIS • WORLD-CLASS TALENT

Research and Development

The Trimeris Research and Development Teams are the world leaders in the discovery and development of antiviral drugs based on fusion inhibition. In addition to their groundbreaking work in HIV research, Trimeris scientists are applying fusion inhibitor technology to other viruses such as Respiratory Syncytial Virus (RSV), and Human Parainfluenza Virus (HPIV).

Molecular Screening Group
- Develops high throughput screening and other molecular tests for identifying new small molecule drug candidates

HIV Virology Group
- Characterizes the mechanism of action of peptide and small molecule inhibitors of HIV

Molecular Biology and Genotyping/Phenotyping Groups
- Analyzes the relationship between drug resistance and the genetic sequence of HIV to improve the potency of new drug candidates

Respiratory Virology Group
- Characterizes the mechanism of action of peptide and small molecule inhibitors of RSV and HPIV

Research Peptide Chemistry Group
- Develops and implements strategies for optimizing the efficient synthesis of therapeutic peptide drug candidates

Biophysical Chemistry Group
- Analyzes the structure/function relationship of viral fusion proteins to improve the design of new peptide and small molecule fusion inhibitors

Discovery Chemistry Group
- Designs and synthesizes small molecule inhibitors of viral fusion

Process Chemistry Group
- Discovers and develops new synthetic processes for optimizing the commercial production of peptides and small molecules

Analytical Science Group
- Develops and validates new methods of analytical and stability testing required by regulatory authorities to support the drug approval process

Pharmaceutical Science Group
- Discovers safe, effective, and stable formulations of new drug candidates

Clinical Research

The Trimeris Clinical Research Teams manage the complex clinical trial programs required to transition a drug candidate from the laboratory through the regulatory approval process required for marketing approval.

Clinical Studies Management Group
- Designs and manages the clinical trials needed to test the safety and efficacy of a drug

Clinical Pharmacology Group
- Analyzes the biological properties and characteristics of a drug as well as the blood levels seen in man

Biostatistics Group
- Develops conclusions regarding a drug's efficacy and safety based on statistical analyses of clinical trial data

Clinical Virology Group
- Analyzes the antiviral efficacy of a drug and characterizes the drug resistance profiles which may emerge during treatment

44% of Trimeris employees hold Masters or Doctoral degrees in fields including:

- **Medicine**
- **Microbiology**
- **Virology**
- **Chemistry**
- **Biophysics**
- **Business**
- **Biostatistics**
- **Biochemistry**
- **Law**

Business

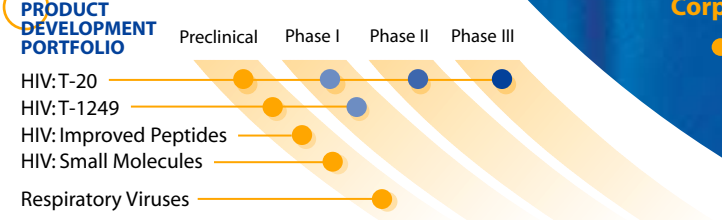
The Trimeris Business Teams strive to maximize the return on capital generated by corporate investments in research and development.

Marketing Group
- In partnership with Hoffmann-La Roche, jointly develops key strategies to maximize the market opportunity for T-20 and T-1249

Corporate Development Group
- Leverages the core Trimeris viral fusion inhibitor and small molecule technology platforms through licensing and acquisition with corporate partners

Finance and Administration Groups
- Manages the short and long-term capital needs of Trimeris to ensure future growth of shareholder value

PRODUCT DEVELOPMENT PORTFOLIO



Corporate and Stockholder Information

BOARD OF DIRECTORS

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Chief Executive Officer, Chief Scientific Officer, Trimeris Inc.

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Retired President and Chief Executive Officer, Witco Corporation

J. Richard Crout, M.D.
President Crout Consulting

Jeffrey M. Lipton
Chairman of the Board of Directors
President and Chief Executive Officer, Nova Chemicals Corporation

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Chief Financial Officer, General Counsel

Timothy J. Creech
Corporate Secretary, Director, Finance and Administration

M. Nixon Ellis, Ph.D.
Chief Business Officer, Executive Vice President

SENIOR MANAGEMENT

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Senior Vice President, Development

Dennis M. Lambert, Ph.D.
Vice President, Biological and Molecular Sciences

Thomas J. Matthews, Ph.D.
Senior Vice President, Research and Development

Elinor M. Munsch
Vice President, Human Resources

Carol A. Ohmstede, Ph.D.
Vice President, Corporate Alliances and Project Planning

Michael A. Recny, Ph.D.
Vice President, Corporate Development

M. Lynn Smiley, M.D.
Senior Vice President, Clinical Research

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Professor of Medicine, Director of AIDS Clinical Trials Unit/Retrovirus Laboratory, Harvard Medical School

Eric Hunter, Ph.D.
Professor of Microbiology, Director, Center for AIDS Research, University of Alabama-Birmingham

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Professor of Medicine and Microbiology and Immunology, Director, Lineberger Comprehensive Cancer Center, University of North Carolina-Chapel Hill

Jerome J. Schentag, Pharm.D.
Professor of Pharmacy and Pharmaceutics, Director, Clinical Pharmacokinetics Laboratory, Director, Center for Clinical Pharmacy Research, School of Pharmacy, State University of New York-Buffalo

Judith M. White, Ph.D.
Professor of Cell Biology and Microbiology, University of Virginia

Richard J. Whitley, M.D.
Loeb Eminent Scholar Chair in Pediatrics, Professor of Pediatrics, Microbiology and Medicine, University of Alabama-Birmingham

ANNUAL SHAREHOLDERS MEETING

The Trimeris Annual Shareholders Meeting will be held on June 27, 2001 at 2 p.m. at the North Carolina Biotechnology Center, 15 Alexander Drive, Research Triangle Park, North Carolina. All shareholders are cordially invited to attend.

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800-633-4236

LEGAL COUNSEL

Wilmer Cutler & Pickering
2445 M Street, N.W.
Washington, D.C. 20037

FINANCIAL AND OTHER INFORMATION

A copy of the Company's Annual Report filed with the Securities and Exchange Commission on Form 10-K is available to stockholders without charge. To obtain a copy contact:

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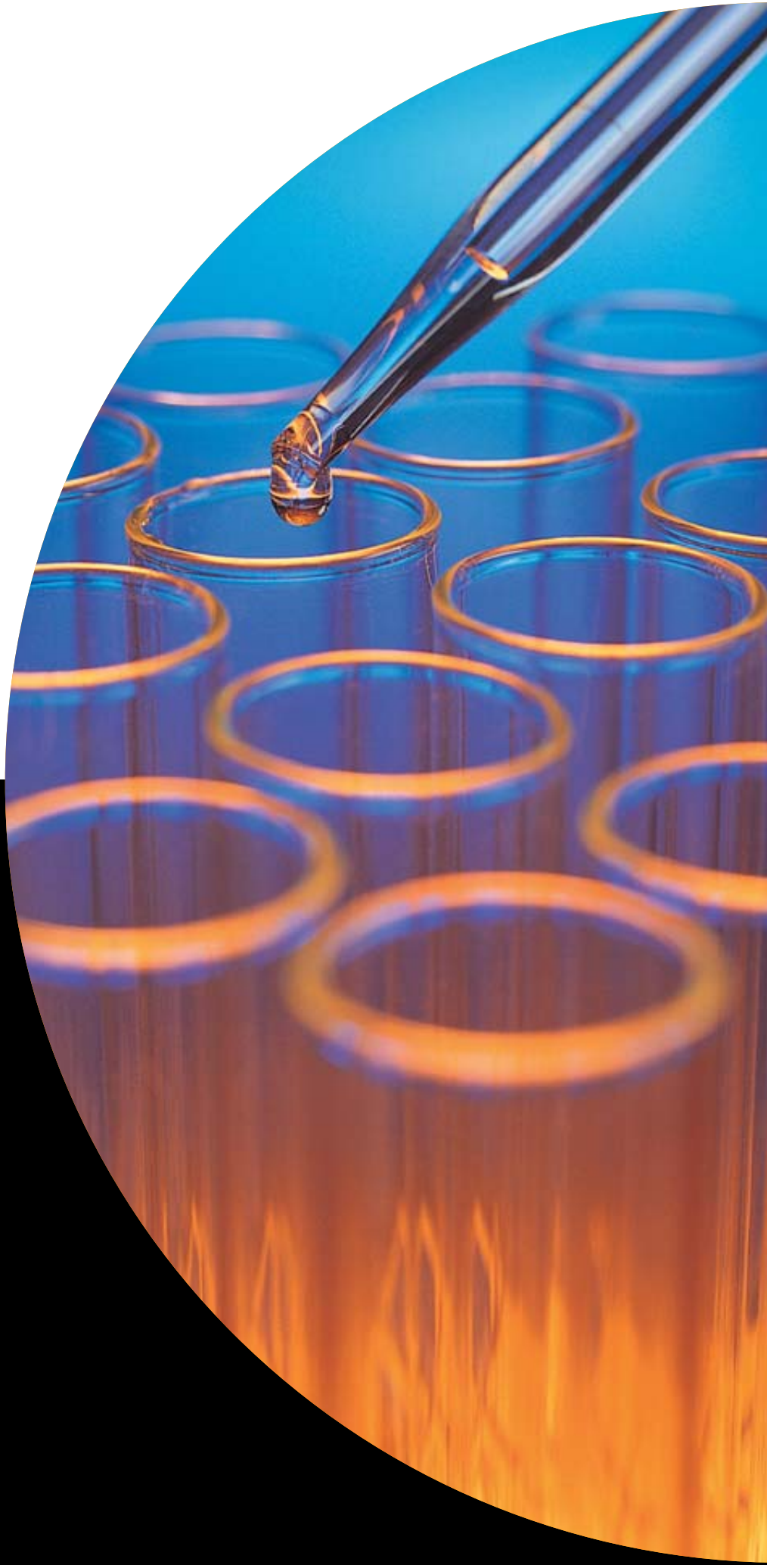
Website: www.trimeris.com

Except for any historical information presented herein, matters presented in this annual report are forward-looking statements that involve risks and uncertainties. The results of the Company's previous clinical trials are not necessarily indicative of future clinical trials, and future results could differ materially from the results presented herein. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors"section included in the Company's Form 10-K for the year ended December 31, 2000 filed with the Securities and Exchange Commission on April 2, 2001.

TRIMERIS

2000 annual report



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