The MIT Program on the Pharmaceutical Industry
Announces a Special Executive Briefing on

The Future of the Pharmaceutical Industry

Integrating New Drug Discovery & Development Technology with Complex Biological Systems Research

Scientific and technological advances are making information about cellular mechanisms of disease available at an unprecedented rate. How is this information being converted into therapeutic knowledge? What are the implications for developing therapeutic solutions on a complex, biological, systems scale, for measuring drug effects and for predicting outcomes?

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Cambridge, Massachusetts

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The Program on the Pharmaceutical Industry
A UNIVERSITY-INDUSTRY-GOVERNMENT PARTNERSHIP
Massachusetts Institute of Technology | Sloan School of Management

ON THE STATE OF THE PHARMACEUTICAL INDUSTRY

> *"The knowledge base in molecular medicine is growing rapidly, and with the increased understanding of complex biological systems it affords, coupled with increasingly reliable computational models for predicting outcomes, society is approaching healthcare that* anticipates *disease states rather than simply ameliorates disease symptoms."*
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> *Technological Innovation in Pharmaceuticals*, Sarah C. Stallings, et al, Massachusetts Institute of Technology, Program on the Pharmaceutical Industry

Innovative new technologies are changing the face of pharmaceutical R&D by allowing researchers to more effectively identify, select and exploit therapeutic targets, design more efficient drug development models and more quickly analyze the economic efficacy of pharmaceuticals.

In this biennial program on the future of the pharmaceutical industry, senior faculty from MIT will be joined by researchers from Harvard and Stanford and by industry experts to explore the scope of these changes, the implications for the pharmaceutical industry, and the emergence of a new paradigm for drug discovery and development.

Scientific and technological advances have led to many important discoveries about cellular mechanisms of disease. You'll learn how these advances are allowing access to increasingly sophisticated data on the disposition of genetic information and how they are being integrated into the process of drug discovery and development.

Set in the context of pharmaceutical research currently underway for such hard-to-treat diseases as cancer, diabetes and depression, the program focuses on:

- technologies of the future and innovations in identifying, selecting and exploiting therapeutic targets that promise significant savings in time, cost and resource allocation
- developments in new, working, disease state models for clinical trials and the prospect they offer for improved productivity
- the use of modern IT to facilitate retrospective data analysis and allow more valid conclusions about treatment outcomes

Who Should Attend

This program has been designed for senior executives in organizations affiliated with the pharmaceutical/biotechnology industry, including: Chief Executive Officers; Presidents; Board Chairmen and Board Members; Executive Vice Presidents; Vice Presidents of Sales and Marketing, Manufacturing, Research and Development, Technology, Finance and Operations; Corporate Counsel; Strategic Planners, and other executives involved with scientific, technical or management issues critical to the long-term health of the industry.

AT THIS PROGRAM YOU WILL LEARN...

... about evolving pharmaceutical research technologies and the impacts they are having in:

- converting information from biomedical research into therapeutically relevant knowledge
- investigating complex biological systems, measuring drug effects and predicting outcomes
- selecting and exploiting an unprecedented new range of therapeutic targets
- the use of small molecule and protein microarrays to enable the high throughput study of protein function
- image informatics, a new cell imaging approach to drug discovery and target validation that provides new sources for targets not previously feasible
- decoding complex cell signaling pathways which play critical roles in the development of most human cancers
- microchemical systems for pharmaceutical manufacturing
- computer-aided trial design models to predict the probability distribution of clinical trial outcomes and maximize clinical trial strategies
- the development of proteasome inhibitors in cancer and the use of pharmacogenomics in their trials in an attempt to personalize the treatment with the proteasome inhibitor
- new approaches to the treatment of diabetes mellitus
- enabling the development of better metrics for cost effectiveness and drug effectiveness through the conversion, collection, management and analysis of retrospective data sets
- ameliorating the growing tension between pharmaceutical innovation and drug costs

About the MIT Program on the Pharmaceutical Industry

The MIT Program on the Pharmaceutical Industry (POPI) is a unique university-industry-government partnership based at MIT's Sloan School of Management. It was founded in 1991 to both perform multi-disciplinary research on the factors that drive, constrain and enhance the performance and competitiveness of the pharmaceutical/ biotechnology industry, and to educate future scientific and management leaders for the industry and for those organizations that supply it, regulate it or use its products. Among its research and educational accomplishments, POPI continues to track ongoing work in areas including drug development, pharmaceutical manufacturing and the pharmaceutical marketplace. It is supported by more than 30 faculty from the MIT Schools of Engineering, Science, and Humanities and Social Science, the MIT-Harvard Division of Health, Science and Technology and the MIT Sloan School of Management.

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Technological Innovation and Complex Biological Systems: An Overview

Pharmaceutical development is changing as understanding of the molecular mechanisms of disease and the knowledge of complex biology increases. In this presentation, you'll learn how the process of discovering and developing innovative pharmaceuticals is evolving, and how advancing technological capabilities are driving a drug discovery paradigm shift. What is the potential for pharmaceutical innovation given current scientific advances? How are increasing amounts of data providing researchers with a window on increasingly complex systems? Where do the key opportunities for pharmaceutical development reside?

I. Technology of the Future: Innovations in Identifying, Selecting and Exploiting Therapeutic Targets

New research tools for identifying and following therapeutic leads are moving pharmaceutical R&D toward a more network health systems view. In this section of the program, we will examine pharmaceutical research innovations that promise significant savings in time, cost and resource allocation, including:

1. Protein Microarrays and Functional Genomics: Multiplexing Analysis Strategy for Target Selection

Microarray research at the Harvard Center for Genomics Research (CGR) is taking the study of protein function to a new level by helping researchers get closer to understanding the function of the cell. How they're enabling the high throughput study of protein function using:

Small Molecule Microarrays to screen large libraries of compounds very efficiently and to identify new binding partners for any protein of interest

Protein Microarrays to identify protein-protein interactions and targets of biologically active small molecules and to screen libraries for binding specificity

2. Image Informatics for Drug Discovery and Target Identification

Drug discovery focused on complex cellular processes is often limited by the difficulty of devising suitable assays. New image processing and data handling technologies are being developed to extract quantitative information from biological images. Cellular responses that are not amenable to current in vitro screening methods, such as regulated nuclear import of transcriptional regulators, can be targeted successfully by small molecules using this "screening by imaging " approach. How this quantitative imaging data serves as a basis for a new approach for drug discovery and target validation, providing:

- New sources for targets not feasible previously
- A way to design cell-based tests to validate target hits

3. Genome-Wide Prediction of Signaling Pathways

Mutations in signaling pathways that respond to DNA damage play critical roles in the development of most human cancers. How are these signaling pathways assembled? What are the key molecules involved? Traditional attempts to decode this communication function have been slowed by the need to study them iteratively, one interaction at a time. At MIT, researchers are using bioinformatics technology for predicting protein-protein interactions on a wide scale that allows them to:

- Predict the cell pathway context for proteins of known sequence but unknown function
- Predict additional targets within a cell pathway of pharmaceutical interest

Learn about the implications of this research for the design of specific chemical inhibitors that may be of therapeutic benefit in the treatment of cancer and inflammatory diseases.

4. Integrated Chemical and Biological Microsystems for Discovery and Process Development

Miniaturization techniques are revolutionizing the drug discovery process through implementing faster, smaller, integrated analytical and synthesis tools. Development of microchemical systems for pharmaceutical manufacturing offers additional opportunities for increased throughput, reduced costs, safer environmentally-benign processing and integration of monitoring and control. In this session, we will discuss design, fabrication and application issues in the development of microchemical systems for typical unit operations in pharmaceutical manufacturing.

II. From Molecule to Disease State: Innovative Models for Drug Development

From better target selection to more effective drugs, innovations in drug modeling and development offer pharmaceutical companies the prospect of improved productivity and more effective resource allocation. This session will examine developments in new working disease state models for clinical trials and the impacts they are having on the discovery, preclinical and clinical stages of drug development.

1. New Working Disease State Models for Computer-Aided Trial Design

Economic pressures on the pharmaceutical industry mandate a major change in the way drugs are developed. Technology is providing tools for effecting change at all stages, including clinical development, where clinical-aided trial design (CATD) and clinical trial simulation are helping to change the face of contemporary drug development practice. In this presentation, you will learn about CATD methodologies for eliminating bottlenecks in the drug development pipeline by increasing project team knowledge about patient variability, time, dose range, response rate and safety more rapidly, thus improving decision making in regard to alternative treatment, trial and development strategies. You will also learn about procedures for clinical trial simulation (running a set of virtual clinical trials on the computer before the actual clinical trial is performed) that provide a clear, documented, consistent, scientific and quantitative rationale for selecting trial strategies.

2. New Working Models for Clinical Trials of Complex, Therapeutically Difficult Diseases

A. Advances in Molecular Oncology: New Pathways to Personalized Medicine

Millennium Pharmaceuticals is currently in Phase II trials with the first proteasome-inhibitor drug. The proteasome is a protein complex that regulates the life span and activation of other proteins, most notably cell cycle regulatory proteins (p53, p21/wafl, and p27Kipl), the activation of which in turn regulates some cell adhesion molecules involved in cancer metastasis and angiogenesis. You'll learn how pharmacogenomics information (genetic information about how patients respond to the drug) is being applied in their trials in an effort to personalize the treatment with the proteasome inhibitor (i.e., target it only to those patients who will benefit from its use).

You'll also learn about proprietary genetic biomarkers Millennium has uncovered for predicting individual response of ovarian cancer patients to the current first-line therapy.

B. Advances in Technology and the Treatment of Diabetes Mellitus

Driven by advances in technology, the diabetes pharmacopeia has expanded rapidly in the past two decades, but the translation of these new drugs into effective treatment programs has been slowed by the shortage of well trained physicians, by managed care organizations that regulate formularies, and by a lack of consumer and patient education. A similar situation is occurring on the device side. New devices for blood glucose monitoring and insulin pumps and advances in islet cell transplantation have overtaken the healthcare system's ability to use them effectively.This presentation will look at the rationale for continuing to develop new

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therapies and diagnostics for diabetes within the context of the current epidemic of diabetes and obesity. It will also explore how the current healthcare environment has stressed patients and providers and has inhibited the more rapid deployment of new therapies.

III. Innovations in Outcomes Research

In this segment, senior researchers and industry experts examine the effects of cost effectiveness policies on innovation and competitiveness in the pharmaceutical industry. They also explore the use of information technologies to facilitate hard-to-use techniques for collecting, converting and managing large insurance and clinical trial data sets and drawing valid conclusions about treatment outcomes. How IT is changing researchers' ability to use retrospective data analysis, remove selection bias from treatment analysis outcomes, and connect their conclusions to real-world medical practices. How this is affecting the tension over drug cost.

1. Analyzing the Efficacy of Medical Practices for Depression: Using IT to Facilitate the Use of Retrospective Data Analysis

Recently published reports from a multisite randomized clinical trial demonstrate that the combination of an antidepressant pharmaceutical and a particular form of psychotherapy achieved almost twice the remission rate than either modality alone in the treatment of acute phase chronic depression. Moreover, treatments involving the antidepressant, by itself or in combination with the psychotherapy resulted in more rapid response than the psychotherapy alone. Combination and psychotherapy alone treatments, however, are typically more costly than drug therapy alone. In this presentation, you will learn how data from the 12-week acute phase of the trial, as well as from a medical claims database encompassing 1.4 million lives, were used in a modern IT technology-enabled retrospective analysis to attribute cost-effectiveness to the three treatment alternatives. The cost comparisons employed alternative measures of outcomes (e.g., days of partial remission, days of full remission and quality-adjusted life years), direct treatment costs, indirect costs (including opportunity costs of patient time) and other economic aspects.

2. Removing Selection Bias From Treatment Analysis Outcomes

This presentation provides key insights for researchers involved in the design or conduct of economic or clinical outcomes using retrospective data, observational data from non-randomized studies, or data from randomized clinical trials. It focuses on specification issues in the estimation of outcomes models in these areas, including: (1) the use of episodes to establish time-sequence of events and how this information can be used in model specification, (2) the role of a structural equations approach in the specification of outcomes models, and (3) testing and adjusting for several types of specification errors (e.g., endogeneity, sample selection bias, omitted variables, multicollinearity, incorrect functional form). A model of cost outcomes associated with depression will be used to illustrate the use of episodes in model specification, the structural equation approach to model specification and model specification tests.

3. Caveats of Randomized Clinical Trials for Economic Analysis: Dealing With Tensions Over Drug Costs

Randomized clinical trials (RCTs) constitute the preferred source of effectiveness data for economic analysis. However, RCT data do not necessarily address the needs of non-regulatory bodies (e.g., pricing and reimbursement agencies, and managed care organizations) trying to gauge the full impact of new technologies on actual practice. The focus of this talk is to compare and contrast the emerging needs of these "economic" decision-makers with the data available from RCT evidence. Taking as a departure point requirements for economic data from various international health care systems, we will discuss the limitations of traditional clinical trial designs and suggest the impact of new data needs on clinical research programs.

PROGRAM FACULTY

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Registration:

Please complete and return entire page to Alison Dibner, Center for Management Research (conference administration office), 55 William Street, Wellesley, MA 02481, or call Ms. Dibner at (781) 239-1111. You may also fax this page to (781) 239-1546. Confirmation of receipt will be made by mail.
The registration fee is $1450. It includes luncheons, reception, and complete program materials. It does not include hotel accommodations.

- **Accommodations**: We have reserved a block of rooms at a hotel convenient to the program site. Information on how you may arrange for accommodations will be sent to you approximately 8 weeks prior to the session.
- **Certificates**: Certificates of Participation will be awarded to all those attending the Program.
- **Attendance Limitations & Liability**: Attendance will be reserved on a first-come, first-served basis. If a session is canceled, MIT's liability is limited to the registration fee.

Return this form to: Ms. Alison Dibner
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55 William Street, Wellesley MA 02481
or call (781) 239-1111; FAX: (781)-239-1546

[ ] Please register me for the December 13-14, 2001 MIT executive briefing on **The Future of the Pharmaceutical Industry**

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Team Registration: Others attending with me include:
Name_____Title_____
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Name_____Title_____
(please note if addresses of those on team differ)

[ ] Check enclosed. (Please make payable to CMR/POPI.). U.S. dollars only.
[ ] Please bill me. Payment is requested prior to session.
[ ] Confirming earlier registration by phone.
[ ] I cannot attend the program on the date listed but would like to be notified of future executive programs offered by the MIT Program on the Pharmaceutical Industry.

MIT PHARM ’01: INTERNET

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Program on the Pharmaceutical Industry

MIT

Stan N. Finkelstein
Co-Director

Innovative new technologies
in drug discovery and development
are at the forefront of a new era
in basic pharmaceutical research.

What are the scientific, clinical and entrepreneurial implications of these new approaches to selecting and exploiting therapeutic targets?

In MIT's biennial briefing on **The Future of the Pharmaceutical Industry**, to be held December 13-14, 2001, in Cambridge, Massachusetts, researchers from MIT will examine these issues, along with the impact of advances in biology and biochemistry on drug discovery and development. Aided by industry experts and scientists from Harvard and Stanford Universities, they will explore innovations that are beginning to move pharmaceutical R&D from iterative experiments focusing on individual disease targets toward a network systems view of the molecular mechanisms of disease.

You'll learn how new biological tools, techniques and computing are being used to improve small molecule discovery, as well as about pharmaceutical research innovations that promise significant savings in time, cost and resource allocation, including:

- small molecule and protein microarray technologies that enable high throughput study of protein function
- new imaging and data handling technologies for drug discovery and target validation
- microchemical systems for pharmaceutical manufacturing
- developments in new working disease state models for clinical trials, including computer-aided trial design and trials of complex, therapeutically difficult diseases
- innovations in outcomes research and the use of information technologies to enable retrospective data analysis, to remove selection bias in order to draw more valid conclusions from treatment analysis outcomes, and to link conclusions to real-world medical practices.

I urge you to review the enclosed prospectus, then to contact Alison Dibner, program coordinator, at (781) 239-1111 to reserve your place at this important briefing. We look forward to seeing you in Cambridge.

Sincerely,

Stan N. Finkelstein, M.D.
Conference Co-Chairman

Anthony J. Sinskey
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