LSMP 1210
PROSEMINAR IN MANAGEMENT & THE LIFE SCIENCES

Freshman Year, Fall Semester 2024
Vagelos Life Sciences & Management Program

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Tina Horowitz
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Teaching Assistants:
[redacted]edu)

Class Meetings: **Time – Tuesday/Thursday, 10:15 am – 11:45 am**
Room – Colonial Penn Center Auditorium (3641 Locust Walk)

Office Hours: **Fridays by Zoom appointment (contact Tina Horowitz to schedule)**

Introduction and Course Objective:

This is the introductory course for the joint Wharton-College Life Sciences & Management (LSM) Program. Enrollment is limited to students admitted to that program; no other Wharton or College students are permitted to enroll. The objective of this seminar-type course is to introduce students to the multiple dimensions in which the life sciences, society, markets, and firms interact in market-based economic systems.

The course deals with three fundamental issues in the management of science:

- allocation of resources, public and private, to the discovery and development process

- organization and management of the 'twin towers' of innovation – research and discovery (R&D) and commercialization – the translation of discoveries into products/services
- prioritization and marketing of useful products and services

All three questions will be considered from a descriptive/behavioral viewpoint – how do they actually occur—and from a normative/social viewpoint – how should they ideally occur? The course will be led by Robert Burns from Wharton and Philip A. Rea from the Department of Biology, and will rely on both outside speakers and lectures/discussions with the course faculty. Written papers, participation in class discussion, and student presentations will form the basis for grading.

Course Sequencing:
The course has three major sections. The first section discusses the changing rates of discovery in the life sciences, the sources of creativity that lead to discovery, and whether the creative process can be managed. We then illustrate some of these themes in case studies of cardiovascular disease (CVD) and the discovery of statins. This section also sketches the history of the management of science. The second section of the course discusses the prospects and problems for the development and implementation of new discoveries in genomics and personalized medicine with an eye to cancer and cardiovascular disease. The third section of the course provides an overview of the life sciences sectors (pharmaceuticals, biotechnology, information technology, medical devices, and psychiatry), the major trends occurring within each, and the central issues that need to be confronted. Please note that the classes corresponding to each section may not be contiguous because many of the speakers who were so kind as to contribute to the course have very tight schedules that necessitated their speaking on days other than those that would have been ideal for the course sequence.

Assignments:
Students will be assessed on the basis of have two major assignments (a term paper and market scan) and four minor assignments (four one-two-pagers) as well as class attendance and participation.

1. Term paper on research translation: drugs or vaccines for antimicrobial resistant (AMR) infections (30 pts)
Though we are hopefully at the tailend, possibly the end, of the COVID-19 pandemic it would be folly if we were to let our guard down on the global pandemic front because we are in the midst of yet another, and one that will likely get much worse before it gets better. The 'other' pandemic to which we refer is antimicrobial resistance (AMR) which in 2019 was implicated in nearly 5 million deaths worldwide and is projected to cost the global economy US$100 trillion by 2050 (note that the running worldwide total for deaths from COVID-19 as of July 26, 2023 is about 7 million). And this is in the face of the fact that conventional drug and vaccine R&D is lagging behind in providing new agents targeting drug-resistant pathogens and that AMR has an impact on many aspects of medicine beyond bacterial infectious diseases in that it affects surgery, organ transplantation, and the treatments of many ailments and diseases including HIV, liver and kidney disease, cancer, and physical trauma.

What we are asking you to do is select a particular drug or vaccine that has been developed *de novo* or repurposed and is being explored with an eye to its deployment for AMR. In doing this we want you to consider the pros and cons of the drug or vaccine you select. Among the issues we would like you to address are:

- Development costs and timelines
- De-risking
- Barriers to repurposing if this is the approach for which you opt
- Patent and market exclusivity considerations
- Regulatory matters
- Measures of technical and commercial success

In engaging in this analysis be sure to define consumer need, balance the benefits and drawbacks of the potential product, and consider the impact the product might have on the stakeholders, for instance payers and physicians. Be careful to strike a good balance between scientific/clinical and business commercialization considerations, while at the same time incorporating some of the principles learned from course as a whole.

Your paper should be 10-15 double-spaced pages (12 pt font). The first draft is due on October 31st by 11:59 pm when we will provide comments on it and a preliminary assessment/grade. The final draft is due by November 29th at 11:59 pm.

2. Market Scan (20 pts)

Students will present an oral briefing at the end of the semester together with written background material (i.e., a PowerPoint deck) on a "market scan" that identifies a product or area in which scientific discoveries might match consumer demands/needs, and which outlines a translational strategy. For the background research and presentations, students will self-select and form six teams of four individuals. The student teams need to identify their topic and inform the instructors of both the topic and team composition by October 24th. The teaching assistants – second-year MBA students in Wharton's healthcare management program who have science backgrounds – will serve as team advisors. Market scans will be presented in the last two class sessions (December 3rd and 5th).

3. Short Essays (40 pts)

There will also be four short writing assignments ('one-two-pagers'), each worth 10 pts, which will form the basis for formulating ideas, researching small sections of the literature and/or enlarging on some of the ideas discussed in class. The topics will cover strategic planning in life sciences firms (due September 11th at 11:59 pm), a repurposed drug for the treatment of cardiovascular disease (due October 8th at 11:59 pm), an explanation of the rising price for insulin (due October 25th at 11:59 pm), and the magic (or not) of Casgevy™ (due November 12th at 11:59 pm).

4. Attendance and Participation (10 pts)

Students will be awarded a maximum of 10 pts for class attendance and participation.

Readings:

Reading assignments for this course will be taken from:

1. Burns. *The U.S. Healthcare Ecosystem* (McGraw-Hill, 2021), available at bookstore.
2. Rea, Pauly, and Burns. *Managing Discovery* (Cambridge University, 2018), available at bookstore.
3. Burns. *The Business of Healthcare Innovation* 3rd Edition, (Cambridge University, 2020), available at bookstore – This text, which provides more in-depth coverage of the technology sectors, is optional.

   The remainder of your readings can be found in three different places on *Canvas*: under "Files" in the "Readings" folder, "Course Materials @Penn Libraries" or "Study.Net Materials". You can access *Canvas* directly through the https://canvas.upenn.edu link using your PennKey and password.

Files – is a folder in which the course Syllabus ("Syllabus"), most of the readings ("Readings"), the slide decks for the classes ("Slides"), notes, assignment instructions, and other resources provided by the instructors are posted.

Course Materials @ Penn Libraries – is a collection of newspaper and journal articles, book chapters, and videos placed on electronic course reserves and provided through Penn Libraries. The provision of materials through electronic course reserves helps reduce student costs.

Study.Net materials – is a collection of copyright-protected case studies, book chapters, and simulations. Study.Net materials are marked with an [*] on the syllabus.

A note on the teaching assistants (TAs):

We are very fortunate in having eight TAs for this course, all of whom have science backgrounds and are MBA students in Wharton's Health Care Management Program. Please note, however, that they have been recruited to assist in the grading and evaluation of the term papers, and provide advice on the market scans, but not to assist or provide advice on the four one-two-pager assignments.

COURSE OUTLINE

August 27

Introduction to the course and general introductions.
The twin towers of innovation and R&D trends in pharmaceutical discovery (Burns)

Readings

Rea et al. *Managing Discovery* (2018): Chapter 2.

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 20.

USFDA. *New Drug Therapy Approvals 2020* (January 2021). Available at: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2020

August 29

Economic and managerial perspectives on innovation in the life sciences (Burns)

Readings

Rea et al. *Managing Discovery* (2018): Chapter 15.

Gertner, *The Idea Factory* (Read pp. 101-104, 150-155, 260-265, 342-360). [*]

September 3

CVD – What you need to know (and would perhaps prefer not to know) about it (Rea)

Readings

Andersson et al. "70-year legacy of the Framingham Heart Study," *Nat Rev Cardiol* 16 (2019): 687-697

Libby et al. "Atherosclerosis," *Nat Rev Dis Primers* 5 (2019): 1-18

September 5

Regenerative medicine (Saar Gill, M.D., Ph.D. Associate Professor of Medicine, Perelman School of Medicine, University of Pennsylvania)

Readings

Chalsani et al. "Cost and access implications of defining CAR-T therapy as a drug," *JAMA Health Forum* (2020) 1(7).

Gustafson et al. "Emerging frontiers in immuno- and gene therapy for cancer," *Cytotherapy* (2023) 25: 20-32.

Sharma et al. "Nomenclature for cellular and genetic therapies: A Need for standardization," *Transplant Cell Ther* (2022) 28: 795-801.

Qiu et al. "Regenerative medicine regulatory politics: A systematic review and international comparison," *Health Policy* 124 (2020): 701-713.

Irvine et al. "The future of engineered immune cell therapies," *Science* 378 (2022): 853-858.

September 10 Beyond CART: CAART technology for autoimmune disease therapy (Mike Milone, M.D., Ph.D., Associate Professor of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania)

Readings

Rea et al. *Managing Discovery* (2018): Chapter 14.

June et al. "CAR T cell immunotherapy for human cancer," *Science* 359 (2018): 1361-1365.

Ellebrecht et al. "Reengineering chimeric antigen receptor T cells for targeted therapy of autoimmune disease," *Science* 353 (2016): 179-184.

Ellebrecht et al. "On the mark: genetically engineered immunotherapies for autoimmunity," *Curr Opin Immunol* (2019) 61: 69-73.

September 12 Translational research in genomics in the age of personalized medicine (Sheri Schully, Ph.D., National Institutes of Health, Deputy Chief Medical and Scientific Officer of the *All of Us* Research Program)

Readings

Khoury et al. "A collaborative translational research framework for evaluating and implementing the appropriate use of human genome sequencing to improve health," *PLoS Med* (August 2, 2018).

Collins and Varmus. "A New Initiative on Precision Medicine." *NEJM* 372 (2015): 793-795.

Denny et al. "The 'All of Us' Research Program" *NEJM* 381 (2019): 668-676.

Ramirez et al. "The All of Us Research Program: Data quality, utility, and diversity" *Patterns* 3 (2022): 100570

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 4.

September 17 AI for antibiotic discovery (César de la Fuente-Nunez, Presidential Assistant Professor, University of Pennsylvania)

Readings

Wan et al. "Deep-learning-enabled antibiotic discovery through molecular de-extinction," *Nature Biomed. Eng.* (2024): https://doi.org/10.1038/s41551-024-01201-x

Santos-Júnior et al. "Discovery of antimicrobial peptides in the global microbiome with machine learning," *Cell* 187 (2024): 3761-3778.

September 19 Translational science in the era of precision medicine (Garret FitzGerald, M.D., McNeil Professor in Translational Medicine and Therapeutics, Associate Dean for Translational Research, Perelman School of Medicine, University of Pennsylvania)

Readings

Melamud et al. "The promise and reality of therapeutic discovery from large cohorts," *J Clin Invest* 130 (2020): 575-581.

FitzGerald et al. "The future of humans as model organisms" *Science* 361 (2018): 552-553.

Fitzgerald. "Anecdotes from ITMAT: Building capacity for translational science," *Clinical Pharmacology & Therapeutics* 94 (2013): 291-296.

Cappola and Fitzgerald. "Confluence, not conflict of interest: Name change necessary," *JAMA* 314 (2015): 1791-1792.

September 24 Medical innovation and health disparities (James Guevara, M.D., Professor of Pediatrics and Epidemiology, Vice-Chair for Diversity, Equity, & Inclusion, Lead Diversity Search Advisor, Perelman School of Medicine, University of Pennsylvania)

Readings

Perez-Stable et al. "Definitions, principles, and concepts for minority health and health disparities research," In: *The Science of Health Disparities Research*, Dankwa-Mullan et al. (Eds) (Wiley, 2021).

Reitsma et al. "Quantifying and benchmarking disparities in COVID-19 vaccination rates by race and ethnicity," *JAMA Network Open* 4 (2021): e2130343.

Walker et al. "Reduction of racial/ethnic disparities in vaccination coverage, 1995-2011," *Morbidity and Mortality Weekly Report* 63 (2014): 7-12.

September 26 The statins: cholesterol's 'penicillins' (Rea)

Readings

Rea et al. *Managing Discovery* (2018): Chapters 4 and 5.

October 1 Genetic testing for cancer susceptibility: an evolving landscape (Payal Shah, M.D., Assistant Professor of Medicine, Perelman Center for Advanced Medicine, and Jackie Cappadocia, M.S., L.C.G.C., Perelman Center for Advanced Medicine)

Readings

Shah. "Polygenic risk scores for breast cancer – Can they deliver on the promise of precision medicine?" *JAMA Network Open* 4(8) (2021). Available at: https://pubmed.ncbi.nlm.nih.gov/34347063/

Bedrick et al. "Creating breast and gynecologic cancer guidelines for transgender patients with BRCA mutations." *Obstet Gynecol* 138 (2021): 911-917.

Tandy-Connor et al. "False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for

appropriate patient care," *Genetics in Medicine* 20(12) (2018): 1515-1521.

Ford. "Totally unexpected: Nonsyndromic *CDH1* mutations and hereditary diffuse gastric cancer syndrome," *JCO Precision Oncology* (March 29, 2017).

October 3 **Fall Break – no class**

October 8 Overview of information technology and impact on health care (William Hanson, M.D., Chief Information Officer, University of Pennsylvania Health System)

Readings

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 24.

Sahni and Carrus. "Artificial intelligence in U.S. health care delivery," *NEJM* 389 (2023): 348-358.

Dorsey and Topol. "State of telehealth," *NEJM* 375 (2016): 154-161.

Mandl and Kohane. "Escaping the EHR trap – The future of health IT," *NEJM* 366 (2012): 2240-2242.

Office of the National Coordinator for Health Information Technology. *Federal Health IT Strategic Plan 2015-2020* (Washington, DC: ONC).

Schulte and Fry. "Death by 1,000 clicks: Where electronic health records went wrong," *Fortune* (2019). https://khn.org/news/death-by-a-thousand-clicks/.

October 10 Digital health across the value chain (David Gluckman, Lazard)

Readings

TBA

October 15 Developing immunotherapies for children with cancer (John M. Maris, M.D., Giulio D'Angio Endowed Chair, Professor of Pediatrics, Division of Oncology, CHOP)

Readings

Bosse et al. "Identification of GPC2 as an oncoprotein and candidate immunotherapeutic target in high-risk neuroblastoma," *Cancer Cell* 11 (2017): 295-309.

Yarmarkovich et al. "Cross-HLA targeting of intracellular oncoproteins with peptide-centric CARs," *Nature* 599 (2021): 477-484.

October 17 Precision therapies for children with cancer (Yael P. Mossé, M.D., Patricia Brophy Endowed Chair, Professor of Pediatrics, Division of Oncology, CHOP)

Readings

Infarinato et al. "The ALK/ROS1 inhibitor PF-06463922 overcomes primary

resistance to crizotinib in ALK-driven neuroblastoma," *Cancer Discov* 6 (2016): 96-107.

Goldsmith et al. "Lorlatinib with or without chemotherapy in ALK-driven refractory/relapsed neuroblastoma: phase 1 trial results," *Nature Medicine* 29 (2023): 1092–1102.

October 22 Overview of the pharmaceutical sector (David Blumberg, VP Global Commercial Compliance, Teva Pharmaceuticals)

Readings

Burns. *The Business of Healthcare Innovation* (2020): Chapter 2.

October 24 Overview of biotechnology sector (Eric Schmidt, Ph.D., Senior Managing Director and Biotechnology Analyst, Cantor Fitzgerald)

Readings

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 22.

Burns. *The Business of Healthcare Innovation* (2020): Chapter 4.

October 29 Pricing and market access 101 (Volker Janssen, Ph.D., Senior Partner, Simon-Kucher & Partners)

Readings

Schoonveld. "Market access and pricing strategy implementation." In: *The Price of Global Health*, 2nd edition: 277-341.[*]

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapters 15, 17-19.

October 31 Overview of the healthcare ecosystem (Burns)

Readings

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapters 1-3.

November 5 Biotech venture capital and new company creation (Jason Rhodes, M.B.A., Partner, Atlas Venture, Cambridge, MA)

Readings

Burns. *The Business of Healthcare Innovation* (2020): Chapter 4.

Kuratko and Brown. "Emerging life sciences ventures: The quest for legitimacy," *Business Horizons* 53 (2010): 211-220.

Booth. "If I were a big pharma head of R&D…" *Life Sci VC.* http://lifescivc.com/2013/08/if-i-were-a-big-pharma-head-of-rd/

Booth. "Lessons learned: Reflections on early-stage biotech venture investing."

http://lifescivc.com/2013/02/lessons-learned-reflections-on-early-stage-biotech-venture-investing/

Hansen. "Versanis Takeout Takes Lilly Beyond Incretins in Obesity," *Biocentury* (2023).

Hansen. "Takeda Lands Anchor Immunology Asset in $4B TYK2 Deal with Nimbus," *Biocentury* (2022).

"Rectify Pharmaceuticals Launches with $100M Series A Financing from Atlas Venture," https://www.businesswire.com/news/home/20211014005236/en/Rectify-Pharmaceuticals-Launches-with-100-Million-Series-A-Financing-from-Atlas-Venture-Omega-Funds-Forbion-and-Longwood-Fund

November 7 Overview of medical device sector: Emerging trends and markets (Mark Turco, M.D., CEO, JC Medical and President Vascular Intervention, Genesis MedTech)

Readings

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 23.

Burns. *The Business of Health Care Innovation* (2020): Chapters 5 and 6.

Henning Rud Andersen. "How transcatheter aortic valve implantation (TAVI) was born: The struggle for a new invention," *Front Cardiovasc Med* 8 (2021): 1-21.

Gottlieb. "Advancing policies to promote safe, effective MedTech innovation," *FDA Voice* (2017). https://www.fda.gov/news-events/fda-voices-perspectives-fda-leadership-and-experts/advancing-policies-promote-safe-effective-medtech-innovation

Holmes et al. "The medical device development ecosystem: Current regulatory state and challenges for future development a review," *Cardiovasc Revasc Med* (2023) https://doi.org/10.1016/j.carrev.2023.09.005

November 12 Defining the actionable cancer genome (David B. Solit, M.D., Geoffrey Beene Chair in Cancer Research; Director, Marie-Josée and Henry R. Kravis Center for Molecular Oncology, and Chief of the Molecular Medicine Service, Memorial Sloan Kettering Cancer Center)

Readings

Chakravarty and Solit. "Clinical cancer genomic profiling," *Nature Rev Genet* 22 (2021): 483-501.

Hyman et al. "Precision medicine at Memorial Sloan Kettering Cancer Center: Clinical next-generation sequencing enabling next-generation targeted therapy trials," *Drug Discovery Today* (2015) 20: 1422-1428.

Koboldt, et al. "The next-generation sequencing revolution and its impact on genomics," *Leading Edge Review* (September 2013).

Iyer et al. “Genome sequencing identifies a basis for everolimus sensitivity,” *Science* (2012) 338: 21 and *Supplementary Materials*.

Zehir et al. “Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients,” *Nature Med* (2017) 23: 703-713.

November 14 Overview of pharmaceutical development (Vlad Hogenhuis, M.D., M.B.A., President and CEO, Chimera Bioengineering, San Francisco)

Readings

Ng. *Drugs: From Discovery to Approval*. Chapters 7 and 8.

Burns. *The U.S. Healthcare Ecosystem* (2021): Chapter 21.

November 19 Opportunities in psychosis research and the potential to alter ‘reality’. (Jerome Taylor, M.D., Assistant Professor of Psychiatry, CHOP and Perelman School of Medicine, University of Pennsylvania)

Readings

https://nami.org/About-Mental-Illness/Mental-Health-Conditions/Anxiety-Disorders

https://nami.org/About-Mental-Illness/Mental-Health-Conditions/Psychosis

https://www.nami.org/About-Mental-Illness/Mental-Health-Conditions/Schizophrenia

November 21 Spark Therapeutics (Jeff Marrazzo, M.B.A., M.P.A., Co-Founder and Former CEO, Spark Therapeutics)

Readings

HBS Case. *Spark Therapeutics: Pioneering Gene Therapy* (9-818-059) [*]

November 26 Translating the hope of AI in medicine to reality: the promise, the challenges, and the cautionary tale (Kevin B. Johnson, M.D., M.S., David L. Cohen University PIK Professor of Biomedical Informatics, Computer/Information Science, Pediatrics, and Science Communication, University of Pennsylvania)

Readings

Umeton et al. “GPT-4 in a cancer center – institute-wide deployment challenges and lessons learned,” *NEJM* (2024) 1: https://ai.nejm.org/doi/full/10.1056/AIcs2300191

Clark et al. “TechQuity is an imperative for health and technology business: let's work together to achieve it,” *J Am Med Inform Assoc* (2021) 28: 2013-2016. https://pubmed.ncbi.nlm.nih.gov/34157112/

Lindsell et al. “Action-informed artificial intelligence – matching the algorithm to the problem. *JAMA* (2020) 2;323(21):2141-2142. https://jamanetwork.com/journals/jama/article-abstract/2765667

Zehir et al. “Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients,” *Nature Med* (2017) 23: 703-713.

Adams et al. “Artificial intelligence in health, health care, and biomedical science: an AI code of conduct principles and commitments discussion draft,” https://nam.edu/artificial-intelligence-in-health-health-care-and-biomedical-science-an-ai-code-of-conduct-principles-and-commitments-discussion-draft/

November 28 **Happy Thanksgiving – no class**

December 3 Market Scan Presentations

December 5 Market Scan Presentations