LSMP 121
PROSEMINAR IN MANAGEMENT & THE LIFE SCIENCES

Freshman Year, Fall Semester 2020
Vagelos Program in Life Sciences & Management

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Class Meetings: **Tuesday/Thursday, 10:30 am – 11:50 am**
Classroom: Online

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 led by 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 a case study of 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, and medical devices), 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 have two major assignments and four minor assignments. These are:

1. Term paper on research translation: drug repurposing.
For this paper we are asking you to critically analyze the translation process for a recently repurposed drug or one that is being considered for repurposing. Also known as drug repositioning or indication expansion, drug repurposing involves the establishment of new uses for drugs that are already known, including approved, discontinued, shelved or experimental drugs. Although this strategy is not a new one, it has attracted a lot of attention in the last decade. Indeed, about one-third of recent approvals have come from repurposed drugs which collectively account for roughly 25% of the pharmaceutical industry's annual revenue.

One of the most famous examples of drug repurposing is Viagra™ (sildenafil, Pfizer). Originally discovered and developed as an antihypertensive in the mid-1990s, Viagra was serendipitously shown in its Phase I clinical trials to have beneficial effects on erectile dysfunction (ED). On the basis of this finding and in the light of its limited efficacy in treating the very thing it was targeted to treat, hypertension and angina, it was studied and approved for the treatment of ED in 1998. Since then, Viagra™ has generated over $35 billion globally with peak sales in the order of $2 billion in 2012.

What we are asking you to do for this assignment is select a particular repurposed drug or one

that is being explored with an eye to repurposing and consider the pros and cons of this approach *versus* the discovery and development of a drug *de novo*. Among the issues we would like you to address are:

- Development costs and timelines
- De-risking
- Barriers to repurposing
- Patent and market exclusivity considerations
- Regulatory matters
- Measures of technical and commercial success

In engaging in this analysis be sure to define the 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 balance between scientific/clinical and business commercialization considerations, while at the same time incorporating some of the principles learned from the course as a whole.

For a comprehensive treatment of drug repurposing see: Pushpakom et al. (2019) Drug repurposing: progress, challenges and recommendations. *Nature Reviews* | *Drug Discovery*, 18: 41-58.

Your paper should amount to between 10-15 double-spaced pages (12 pt font). The first draft is due on November 2nd by 11:59 pm when we will give you comments on it and a preliminary assessment/grade. The final draft is due by December 10th at 11:59 pm.

2. Market scan

Students will present an oral briefing at the end of the semester together with written background material (i.e. a PowerPoint slide 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 people each. Student teams need to identify their topic and inform the instructors of both the topic and team composition by November 3rd at 11:59 pm. 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 8th and 10th).

3. Short essays

There will also be four short writing assignments ('one-two-pagers') 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 10th at 11:59 pm), development of a COVID-19 vaccine (due October 1st at 11:59 pm), an explanation of the rising price for Epi-Pens (due October 22nd at 11:59 pm), and a discussion of the inequities in the prevalence and treatment of COVID-19 patients (due November 17th at 11:59 pm.

Readings

Reading assignments for this course will be taken from:

1. Burns. *The Business of Healthcare Innovation* 3rd Edition, (Cambridge University, 2020) which is available for purchase from Amazon.
2. Rea, Pauly, and Burns. *Managing Discovery in the Life Sciences* (Cambridge University, 2018) which is available for purchase from Amazon.

   The remainder of your readings can be found in three different places on *Canvas*: under "Files" in the "Reading"' folder, "Course Materials @Penn Libraries" or "Study.Net Materials". You can access *Canvas* directly through the following link: https://canvas.upenn.edu 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, ad videos placed on electronic course reserves and provided through Penn Libraries. The provision of materials through electronic course reserves helps reduce costs for students.

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.

COURSE OUTLINE

September 1

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

Readings

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

Burns. *The Business of Health Care Innovation* (2020): Chapter 1.

USFDA. 2017 New Drug Therapy Approvals (2018).

September 3

Economic and managerial perspectives on innovation in the life sciences

Readings

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

Gertner, *The Idea Factory* (Read pp. 101-104, 150-155, 260-263, 343-360). [*]

September 8

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

Readings

Melamud et al. "The promise and reality of therapeutic discovery from large cohorts," *Journal of Clinical Investigation* 130(2) (2020): 575-581.

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

Cappola and FitzGerald. "Confluence, not conflict of interest: Name change necessary," *JAMA* 314(17) (2015): 1791-1792.

FitzGerald. "Measure for measure: Biomarker standards and transparency," *Science Translational Medicine* 8(343) (2016): 1-2.

September 10 Overview of health care system (Burns)

Readings

Burns and Liu. "China's healthcare industry: A system perspective." Chapter 1 in Burns and Liu, *China's Healthcare System and Reform* (Cambridge, 2017.)[*].

First One-Two-Pager Due: September 10th

Role of Strategic Planning in Amgen's Early Success

Readings:

HBS Case: "Amgen, Inc: Planning the unplannable." [*]

Gordon Binder. *Science Lessons* (2008): Chapters 3 and 4

For this assignment considering the following questions based on the two readings listed above:

- What is planning like at Amgen?
- Do senior managers and scientists see it the same way?
- Is one of them wrong? Are they both wrong?
- Does planning serve any useful function at Amgen?
- What does the case teach you about strategic planning in general?

There is no one right answer to these questions, but you should back up your conclusions as best you can with insights gleaned from class lectures and readings, as well as any other sources you wish to consult. The primary objective here is to get you started in your thinking on how managers in life sciences companies like Amgen plan for the future when the science they are engaged in is so unpredictable.

Please keep your text to 1-2 pages, excluding bibliography, using a minimum of Times 12 pt font, and single spacing.

September 15 Translational research in genomics and personal genome sequencing (Marc S. Williams, M.D., Director, Geisinger Genomics Institute, Danville, PA)

Readings

Buchanan et al. "Clinical outcomes of a genomic screening program for actionable genetic conditions," *Genetics in Medicine* (2020)

Williams. "Early Lessons from the implementation of genomic medicine programs," *Annual Review of Genomics and Human Genetics* (2019).

Williams et al. "Patient-centered precision health in a learning health care system: Geisinger's genomic medicine experience," *Health Affairs* (May 2018).

Dewey et al. "Distribution and clinical impact of functional variants in 50,726 whole-exome sequences from the DiscovEHR study," *Science* (December 23, 2016).

Rea et al. *Managing Discovery* (2018): Chapter 10

September 17 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 Medicine*. (August 2, 2018).

Khoury and Evans. "A public health perspective on a national precisionmedicine cohort: Balancing long-term knowledge generation with early health benefit," *JAMA* 313(21) (2015): 2117-2118.

Stark et al. "Integrating genomics into healthcare: A global responsibility," *American Journal of Human Genetics* (January 3, 2019).

Birney et al. "Genomics in healthcare: GA4GH looks to 2022," *GA4GH Connect* (October 2017).

September 22 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, Memorial Sloan Kettering Cancer Center)

Readings

Hyman et al. "Precision medicine at Memorial Sloan Kettering Cancer Center: Clinical next-generation sequencing enabling next-generation

targeted therapy trials," *Drug Discovery Today* 20(12) (2015): 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* 338(6104) (October 12, 2012): 21 and *Supplementary Materials*.

Zehir et al. "Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients," *Nature Medicine* 23(6) (2017): 703-713.

September 24 Cancer genomics applications (Brian Keith, Ph.D., Dean, Biomedical Studies, Wistar Institute)

Readings

Vogelstein et al. "Cancer genome landscapes," *Science* 339 (2013): 1546-1551. [Please read the entire article, but don't worry about the gene names/acronyms and details in the section "Signaling pathways"]

Rozenblatt-Rosen et al. "The human tumor atlas network: Charting tumor transitions across space and time at single-cell resolution," *Cell* 181 (April 16, 2020): 236-249. [Please read only the first few sections of the article up to "How to build a tumor atlas" on p. 240]

September 29 Promises and challenges for utilizing cancer genomics to improve patient outcomes: Focus on childhood cancers (John Maris, M.D., Giulio D'Angio Chair in Neuroblastoma Research, Professor of Pediatrics Division of Oncology, Children's Hospital of Philadelphia)

Readings

Matthay et al. "Neuroblastoma," *Nature Reviews* | *Disease Primers* 2(2016): 1-21.

Bosse et al. "Identification of GPC2 as an oncoprotein and candidate immunotherapeutic target in high-risk neuroblastoma," *Cancer Cell* 32 (2017): 295-309.

October 1 Genetic testing for cancer susceptibility: an evolving landscape (Payal Shah, M.D., Assistant Professor of Medicine, and Danielle McKenna, M.S., LCGC, Genetic Counselor, Perelman Center for Advanced Medicine)

Readings

Domchek et al. "Multiplex genetic testing for cancer susceptibility: Out on the hire wire without a net?," *Journal of Clinical Oncology* 31(10) (2013): 1267-1270.

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,” *Precision Oncology* (2017).

Second One-Two-Pager Due: October 1st

COVID-19 vaccine: is our priority speed or safety?

Without going into great detail (which would be unfair to you at this stage and not possible in a ‘one-two page’ document), focus your second one-pager on COVID-19 vaccines, specifically the pros and cons of their speedy development and widespread administration, possibility at the expense of safety, *versus* the pros and cons of ensuring their safety before deployment possibly at the expense of delaying their widespread administration. As good a place as any to start when thinking about this is a brief video-cast with the same title made earlier this year by Dr. Art Caplan – COVID-19 vaccine: is our priority speed or safety? Please note that in drawing your attention to this video-cast we are not necessarily expecting you to agree with everything or even anything that Dr. Caplan says; rather we are using it as a device to get you thinking.

The type of written piece we have in mind is something along the lines of a New York Times OpEd-type column. Of course, no one has a ready-made answer to this question, but you should back up your conclusions/ opinions as best you can with logic, empirical evidence and/or information gleaned from other sources. We encourage you to use any source you see fit such as the primary biomedical literature and/or conversations with investigators, for instance those expert in the field, or others who are able to reinforce and/or shed a new light on the points you make.

The primary objective here is to get you started in your thinking about current (very current!) biomedical issues; real issues that must somehow be addressed. Writing of a particularly high quality and clarity as if for the educated layperson that catches the attention of the reader without compromising the “truth” or overstating or understating the case is what we’re looking for.

Please keep your text to 1-2 pages, excluding bibliography, using a minimum of Times 12 pt font, and single spacing.

October 6 Overview of health care insurance (Burns)

Readings

Kongstvedt. *Essentials of Managed Health Care* (Sixth Edition): Chapters 1 and 2

October 8 Beyond CART: CAART technology for autoimmune disease therapy (Mike Milone, M.D., Ph.D., Associate Professor of Pathology, Associate Director, Toxicology Laboratory, Center for Cellular Immunotherapies, Perelman School of Medicine)

Readings

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

June et al. "CAR T cell immunotherapy for human cancer," *Science* 359 (23 March 2018): 1361-1365.

Lee and Payne. "Advances in targeting CAR-T therapy for immune-mediated diseases," *Cell & Gene Therapy Insights* (27 March 2018): 255-265.

Mukherjee. "The promise and price of cellular Therapies," *The New Yorker* (July 15, 2019).

October 13
October 15 Overview of pharmaceutical development and delivery process. (Robert Willenbucher, M.D., M.B.A., Head of Cell Therapy and Jannsen Incubator)

Readings

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

October 20 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: 277-315.[*]

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.

Third One-Two-Pager Due: October 22nd

What explains the rising price of Epi-Pens?

Reading:

1. EpiPen ERISA Litigation (2018)
2. Pharmacy Benefit Managers (2018) As Drug Prices Soar, Policymakers Take Aim

This complaint suggests that pharmacy benefit managers (PBMs) are largely responsible for the dramatic hike in prices for EpiPens by virtue of inducing (or colluding with) the pharmaceutical manufacturer of EpiPen™ to raise prices. Your analysis, in attempting to explain the rising price of Epi-Pens, should:

- Sketch out the causal logic of the complaint
- Critically evaluate this causal logic
- Examine what other factors might explain EpiPen™ price hikes and what types of insurance coverage lead patients to be exposed to these price hikes

Please keep your text to 1-2 pages, excluding bibliography, using a minimum of Times 12 pt font, and single spacing.

October 27 The statins: cholesterol's 'penicillins' – Part I (Rea)

Readings

Rea et al. *Managing Discovery* (2018): Chapter 4

October 29 Life sciences venture investing: Oncoceutics, a case study (Lee Schalop, M.D., Oncoceutics, Inc., Philadelphia)

Readings

Frechtling et al. *The CTSA National Evaluation Final Report*. (Westat, April 2012).

Booth. "Foundings matter: Thiel's law applied to biotech," *Biotech Financing* (June 11, 2013).

Price. "Overhauling translational thinking," (2013).

November 3 The statins: cholesterol's 'penicillins' – Part II (Rea)

Readings

Rea et al. *Managing Discovery* (2018): Chapter 5

November 5 Overview of FDA regulation (Monica Ferrante, D.P.A., VP Regulatory, Quality and Clinical Studies, Aspire Bariatric, Inc.)

Readings

Ferrante. "Evolution of public health regulation."

November 10 Regenerative medicine (Jon Epstein, M.D., Executive Vice-Dean and Chief Scientific Officer, Perelman School of Medicine)

Readings

https://stemcells.nih.gov/

Khademhosseini et al. "Progress in tissue engineering," *Scientific American* (May 2009).

Lambers and Kume. "Navigating the labyrinth of cardiac regeneration," *Developmental Dynamics* (2016): 751-761.

Epstein. "A time to press reset and regenerate cardiac stem cell biology," *JAMA Cardiology* 4(2) (2019): 95-96. doi: 10.1001/jamacardio.2018.4435

Hill. "When the CAR targets scar,"*NEJM* 381(25) (2019): 2475-2476.

Epstein. "Teasing the immune system to repair the heart," *NEJM* 382(17) (2020): 1660-1662.

November 12 Biotech venture capital and new company creation (Jason Rhodes, M.B.A., Partner, Atlas Venture)

Readings

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

Generation Bio. "Atlas venture launches generation bio." https://generationbio.com/atlas-venture-launches-generation-bio/

Generation Bio. "Generation bio announces $100 million series B financing to advance GeneWave™ platform for re-dosable gene therapy." https://generationbio.com/generation-bio-announces-100-million-series-b-financing-to-advance-genewavetm-platform-for-re-dosable-gene-therapy/

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/

Life Sci VC. "VC-backed biotech IPOs: Valuations and virtuous cycles."

http://lifescivc.com/2014/08/vc-backed-biotech-ipos-valuations-and-virtuous-cycles/

Fleming. "The decline of venture capital investment in early-stage life sciences poses a challenge to continued innovation, " *Health Affairs* (February 2015)

November 17 COVID-19 and its impact on minority populations (Dr. Natasha Chida, M.D., M.S.P.H, Assistant Professor Infectious Diseases, Johns Hopkins University)

Readings

https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

Chowkwanyun and Reed. "Racial health disparities and Covid-19 – caution and context," *NEJM* 383 (July 16, 2020): 201-203.

Fourth One-Two-Pager Due: November 17th

COVID-19 pandemic and inequities in the U.S. health system

The COVID pandemic has made apparent certain inequities in the U.S. healthcare system. Explain what these inequities are, how they manifest themselves, and how they might be addressed.

As was the case for the second one-two-pager, the type of written piece we have in mind is something along the lines of a New York Times OpEd-type column. Of course, no one has a ready-made answer to this question, but you should back up your conclusions/opinions as best you can with either logic, empirical evidence and/or information gleaned from other sources. We encourage you to use any source you see fit such as the primary biomedical literature and/or conversations with investigators, for instance those expert in the field, or others who are able to reinforce and/or shed a new light on the points you make.

Please keep your text to 1-2 pages, excluding bibliography, using a minimum of a Times 12 pt font, single spacing.

November 19 Overview of medical device sector. Emerging trends and markets. (Mark Turco, M.D., Chief Innovation Officer, Penn Center for Innovation)

Readings

Burns. *The Business of Health Care Innovation* (2020): Chapter 5.

Ernst & Young. *As Change Accelerates, How can Medtechs Move Ahead and Stay There? Pulse of the Industry 2017* (2017).

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

November 24 Overview of biotechnology sector. (Eric Schmidt, Ph.D., Chief Financial Officer, Allogene)

Readings

Deloitte. *2019 Global Life Sciences Outlook* (2019).

Burns. *The Business of Healthcare Innovation*: Chapter 3.

November 26 **Happy Thanksgiving – no class**

December 1 Overview of information technology and impact on health care. (William Hanson, M.D., Chief Information Officer, University of Pennsylvania Health System)

Readings

Burns. *The Business of Healthcare Innovation* (2020): Chapter 7.

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

Mandl and Kohane. "Escaping the EHR trap – The future of health IT," *New England Journal of Medicine* 366 (June 14, 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* (March 8, 2019). https://khn.org/news/death-by-a-thousand-clicks/.

December 3 Intellectual property and patent issues in the life sciences. (Marc Segal, M.S., J.D., Ballard Spahr LLP)

Readings

Holman. "AbbVie hopes to maintain Humira exclusivity through secondary patents and regulatory barriers to entry." *Biotechnology Law Report* 36(1) (2017), 9-16.

Gene Patents: A Brief Overview of Intellectual Property Issues. Congressional Research Service. (January 2014).

December 8 Market Scan Presentations

December 10 Market Scan Presentations