LSMP 121
PROSEMINAR IN MANAGEMENT & THE LIFE SCIENCES

Freshman Year, Fall Semester 2019
Vagelos Life Sciences & Management Program

Lawton Robert Burns, Ph.D., M.B.A.
Health Care Management Department
The Wharton School
Room 203 Colonial Penn Center
Office Hours: Thursdays, 12:00 – 2:00
Phone: 215.898.3711
E-mail: burnsl@wharton.upenn.edu

Philip A. Rea, D.Phil.
Department of Biology
School of Arts & Sciences
110 Stephen A. Levin Building, Suite 101
433 South University Avenue
Phone: 215.573.1429
E-mail: parea@sas.upenn.edu

Administrative Assistant:
Tina Horowitz
Room 304 Colonial Penn Center
Phone: 215.898.4268
E-mail: horowitt@wharton.upenn.edu

Teaching Assistants:
Karlos Bledsoe kbledsoe614@gmail.com
John Brock brockj@wharton.upenn.edu
James Buxton buxtonj@wharton.upenn.edu
Frank Fengqi Cai frankcai@wharton.upenn.edu
Cody Carpenter codycar@wharton.upenn.edu
Jillian Dunne jdunne@wharton.upenn.edu
Haley Fitzpatrick haleyf@wharton.upenn.edu
Gabrielle Manoff manoffg@wharton.upenn.edu

Class Meetings: **Tuesday/Thursday, 10:30 AM – 11:50 PM**
Classroom: Colonial Penn Center Auditorium

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:

(1) allocation of resources, public and private, to the discovery and development process
(2) organization and management of the 'twin towers' of innovation –
research and discovery (R&D)
commercialization – the translation of discoveries into products/services
(3) 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 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:

(1) A paper critically examining the translation process for new beneficial life sciences products and what government, firms, investigators, investors, and universities have done or are doing well or ought to do differently in the context of some aspect of genomics and consumer need. The first draft, which will be commented on by the faculty and returned to the students for preparation of the final draft, is due on October 29th by 5 P.M. The final draft is due on December 6th at 5 P.M.

(2) An oral briefing to be presented at the end of the semester together with written background material 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 be grouped into six teams. The teaching assistants – second-year MBA students in Wharton's healthcare management program who have science backgrounds – will serve as team advisors.

There will also be two very short ('one-pager') writing assignments 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 personalized diagnostics and strategic planning in life sciences firms. Due dates for the two papers are September 12th and October 24th. See the syllabus for those dates for more details.

Readings

Reading assignments for this course will be taken from:

(a) Burns. *The Business of Healthcare Innovation* 2nd Edition, (Cambridge University, 2012) which is available for purchase at the bookstore.
(b) Rea, Pauly, and Burns. *Managing Discovery* (Cambridge University, 2018) which is available for purchase at the bookstore.
(c) The remainder of your readings can be found in three different places on *Canvas*. You can access *Canvas* directly through the following link: https://canvas.upenn.edu. You will need your Wharton ID and password to log in.

Files: Slide decks, notes, assignment instructions, syllabi, and other instructor-provided resources.
Course Materials @ Penn Libraries: Newspaper and journal articles, book chapters, and videos placed on electronic course reserves and provided through Penn Libraries. Providing materials through electronic course reserves helps to reduce costs for students.
Study.Net Materials: Copyright-protected case studies, book chapters, and simulations. Study.Net materials are marked with an * on the syllabus.

COURSE OUTLINE

August 27: 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*: Chapter 2.

Burns. *The Business of Health Care Innovation*: Chapter 8.

USFDA. *2017 New Drug Therapy Approvals (2018)*.

August 29 Economic and managerial perspectives on innovation in the life sciences

Readings

Rea et al. *Managing Discovery*: Chapter 15.

Burns. *The Business of Health Care Innovation*: Chapter 3

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

September 3: Statins - Part I (Rea)

Readings

Rea et al. *Managing Discovery*: Chapter 4

September 5 Statins - Part II (Rea)

Readings

Rea et al. *Managing Discovery*: Chapter 5

September 10: Translational research in genomics and personal genome sequencing (Marc S. Williams, M.D., Director, Geisinger Genomics Institute, Danville, PA)

Readings

Williams. "Early Lessons from the implementation of genomic medicine programs." In *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*: Chapter 10

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 Medicine*. (August 2, 2018).

Khoury and Evans. "A public health perspective on a national precision medicine 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).

First One-Page Paper Due: September 12th

Without going into great detail (which would be unfair to you at this stage and not possible in ‘one page’), focus your first one-pager on personalized diagnostics by providing a brief account of a recent development in molecular diagnostics, its potential impact, and some of the challenges it has or may have to face if it is to be implemented comprehensively. Either choose a particular molecular diagnostic or a particular disease to which personalized diagnostics might be applied. The type of written piece we have in mind is something along the lines of a *New York Times* (or better still *Financial Times*) OpEd-type column. In addressing this matter consider some but not necessarily all of the following: what exactly do we mean by personalized and molecular diagnostics; what are the kinds of scientific and technological innovations that have and are continuing to make this possible; who might benefit from these developments, and who might not, and in what way; would you be correct in having concerns about the possibility of widespread disease ‘orphanization’ by stratification, and if so what would these concerns be; in a perfect world, what types of molecular diagnoses would you like to see come to the fore in the years to come, and why?

No one has readymade answers to these questions but you should back up your conclusions 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 wish to make.

The primary objective here is to get you started in your thinking on 21st century 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 1.5 pages, excluding bibliography, using a minimum of a Times 12 pt font, single spacing.

September 17 Genetic testing for cancer susceptibility: an evolving landscape (Payal Shah, M.D., Assistant Professor of Medicine, Perelman Center for Advanced 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).

September 19 Overview of health care system (Burns)

Readings

Burns. *The Business of Healthcare Innovation:* Chaper 1.

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

September 24 Issues in translational 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

Fitzgerald. "Anecdotes from ITMAT: Building capacity for translational science," *Clinical Pharmacology & Therapeutics* 94(3) (2013): 291-296.

Fitzgerald. "Evolution in translational science: Whither the CTSAs?" *Science Translational Medicine* 7(284) (2015): 1-3.

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 26 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.

October 1 Beyond CART: CAART technology for autoimmune disease therapy (Aimee Payne, M.D., Ph.D., Associate Professor of Dermatology, Perelman School of Medicine)

Readings

Rea et al. *Managing Discovery*: 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 3 Cancer genomics applications (Brian Keith, Ph.D., Director of Education, Abramson Family Cancer Research Institute, Perelman School of Medicine)

Readings

Vogelstein et al. “Cancer genome landscapes,” *Science* 339 (2013): 1546-1551.

Visit *Inside Cancer* (especially watch “Hallmarks of Cancer”): http://www.insidecancer.org

October 8 Promises and challenges for utilizing cancer genomics to improve patient outcomes: Focus on childhood cancers (John Maris, M.D., Division of Oncology, Children’s Hospital of Philadelphia).

Readings

Schnepp et al. “Improving patient outcomes with cancer genomics,” *JAMA* 314(9) (September 1, 2015): 881-883.

Maris. “Defining why cancer develops in children,” *NEJM* 373 (December 10, 2015): 2373-2375.

Mody et al. “Integrative clinical sequencing in the management of refractory or relapsed cancer in youth,” *JAMA* 314(9): 913-925.

Zhang et al. “Germline mutations in predisposition genes in pediatric cancer,” *NEJM* 373(24) (December 10, 2015): 2336-2346.

October 10 **Fall Break – no class**

October 15 Life sciences venture investing: Oncoceutics, a case study. Take a ride with the founders of a biotechnology company that is developing a novel drug for brain cancer as they discuss the tortuous path from discovery in the lab to clinical trials in people to the challenges of managing the regulatory environment. Hear about the factors that led them to chose this opportunity, see how they wrestled with decisions on key topics like trial design, IP strategy and fundraising, and have the opportunity to engage in an interactive discussion of the constant need to balance upside and risks. (Lee Schalop, M.D. and Wolfgang Oster, M.D., Ph.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).

October 17 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.[*]

October 22 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."

October 24 Overview of health care insurance (Burns)

Readings

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

Second One-Page Paper Due: October 24th

Readings:

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

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

Assignment : consider the following:

- 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. 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 1.5 pages, excluding bibliography, using a minimum of a Times 12 pt font, single spacing.

October 29
October 31 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.

November 5 Overview of the pharmaceutical sector (David Blumberg, Former Principal, U.S. Pharmaceuticals and Life Sciences Advisory, KPMG LLP)

Readings

Burns. *The Business of Healthcare Innovation*: Chapter 2.

November 7 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*: Chapter 6.

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 12 Regenerative medicine (Jon Epstein, MD, Executive Vice-Dean and Chief Scientific Officer, Perelman School of Medicine,)

Readings

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

Lanza and Rosenthal. "The stem cell challenge," *Scientific American* (June 2004).

Minkel. "Potent alternative," *Scientific American* (February 2008).

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

https://stemcells.nih.gov/

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

November 14 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 4.

November 19 Biotech venture capital and new company creation (Jason Rhodes, M.B.A., Partner, Atlas Venture)

Readings

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 21 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 Rules. Congressional Research Service. (January 2014).

November 26 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*: 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/.

November 28 **Happy Thanksgiving – no class**

December 3 Market Scan Presentations

December 5 Market Scan Presentations