COURSE COLOUR CODE: LAVENDER

MBIOTECH

MASTER OF BIOTECHNOLOGY PROGRAM

Elective Course

BTC 1860H

GAMBiT

GENERATIONS OF ADVANCED MEDICINE: BIOLOGICS IN THERAPY

Leigh Revers with Duncan Jones

Winter/Spring Term 2022

MASTER OF BIOTECHNOLOGY
UNIVERSITY OF TORONTO MISSISSAUGA

BTC 1860H – GAMBiT
Generations of Advanced Medicine: Biologics in Therapy

Course Outline (Winter/Spring 2022)

Class Location:	University College, UC-144 (Sessions 1-3); Faculty Club, 41 Willcocks Street (Sessions 4-9); Session 10, TBA.
Class Times:	Thursdays, 6:00-9:00 PM (exact timing and duration may vary).
Professors:	**Dr. Leigh Revers, M.A., D.Phil. & Duncan Jones, M.Sc., M.B.A.**
Office Hours:	By appointment.
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Leigh Revers is currently Associate Professor in the Department of Chemical & Physical Science and Director of the Master of Biotechnology (MBiotech) Program at the University of Toronto, Canada. He came to the program with an extensive background in biotechnology entrepreneurship, and he has over 25 years of experience working in the life sciences sector, both in world-class academic institutions and in industry. Trained as a chemist and molecular biologist in the Dyson Perrins Laboratory, he first came to Canada in 1996 as the recipient of a Leverhulme Scholarship to work with Professor Harry Schachter on developmental enzymes involved in human diseases at Toronto's Hospital for Sick Children. His research interests in complex carbohydrates as mediators of events at the cell-surface led to his interest in cancer. He joined Professor Jean Gariépy's research team in 1999 to work on novel biologic toxins capable of exploiting cancer-related carbohydrate signals. A long-held interest in entrepreneurship led in 2000 to his becoming a co-founder of **Molecular Templates Inc.** (MTI), a private biotechnology company focused on the development of novel toxin-based cancer therapeutics. In May 2006, he was appointed Assistant Director with the **MBiotech Program** at the University of Toronto. In 2007, Dr Revers co-founded a consulting practice, which provides specialist scientific and financial services to small and medium-sized enterprises in the life sciences. In 2009, he participated in a USD$2M Series A financing of MTI led by Santé Ventures, which saw the company relocate to Austin, Texas. Shortly afterwards, he co-founded a new Canadian company, **D5Pharma Inc.**, based out of the Sunnybrook Research Institute, which is presently focused on developing aptamer and other biomacromolecular technologies for diagnostic and therapeutic applications. Over the past eight years, he has spoken widely to healthcare professionals across Canada, and around the world, on the subject of biologics and biosimilars in the context of haematology, rheumatology and oncology. In September of 2017, his company MTI was listed on the NASDAQ (**MTEM**). Dr Revers holds Bachelor's, Master's, and Doctoral degrees in Physical Sciences from the University of Oxford in the United Kingdom.

Course Description

In this course, we focus exclusively on the dominant role of biologic therapies in modern medicine. In 2020, 6 of the top 10 drugs by revenue were molecules of biologic origin, namely those manufactured primarily by biosynthetic rather than chemical means, with annual sales of the top selling therapy, the anti-TNFα monoclonal antibody adalimumab, almost cresting the $20 billion mark. The lucrative preeminence of biologics is set to continue, bolstered by the introduction of innovative molecular delivery strategies, such as antibody-targeted conjugates, fragments and fusions, as well as by the robust staying power of market leaders. The latter phenomenon is an inevitable consequence of the higher-than-usual regulatory hurdles faced by conventional generic manufacturers seeking to make **biosimilars**: intended copies of off-patent biologics that, having undergone a strict comparability exercise, are approved by regulatory agencies such as the EMA and the FDA.

This course will survey this changing landscape within an historical framework and will highlight critical scientific and process parameters **unique** to biologics, that set them aside from conventional small-molecule medicines, including their molecular architecture and mechanisms of action, manufacturing considerations, analytical and functional lot release assays, and clinical trial design. We will explore some of the pitfalls by examining a roster of clinical case studies. The capacity of payers to afford these increasingly high-cost therapies in the face of current economic trends will be discussed.

The broad goals of the course are as follows:

1. A detailed understanding of the complexities associated with biologic drugs;
2. A broad familiarity with biologics manufacturing and its inherent variability;
3. A critical understanding of the aspects of biosimilarity; and
4. A familiarity with the clinical implications emerging from the use of biologics.

Industry Updates During Course

Students are expected to participate in a Twitter feed that highlights industry updates and changes in the regulatory environment related to this course using the hash-tag:

#GAMBiT_2022

IMPORTANT: You will be expected to contribute. Failure to post relevant tweets will trigger an automatic **ZERO** mark for *Participation* (see **Evaluation and Grades**, below).

Evaluation and Grades

Grading will be based on case study reports submitted by students, and on in-class presentations. Participation is also a component.

1. **In Class Case Discussions 40%**
2. **Case Reports 50%**
3. **Participation 10%**

1) **In Class Case Discussions (6 equally weighted)** — SESSIONS 4-9, IN-CLASS

Students will be asked to discuss their opinions of the cases in class (see Schedule of Activities), and, on each occasion, must adopt **ONE** of up to three distinct industry perspectives, **EITHER**—

a) The stance of an innovator company; **OR**

b) The stance of a biosimilars manufacturer; **OR**

c) The stance of a government regulatory body.

Students will then prepare their positions ahead of time, based on the assigned case readings, which will be made available to the class via Blackboard exactly one week before the relevant case discussion. Hence, all students will have the same preparation time. Students will then come to class and present their stances on the case in a debating format. Presentation aids of all kinds are permitted. Marks are earned by all students attending based on the instructor's and TA's grading, which will take into account the **articulacy**, **relevance** and **insightfulness** of the arguments.

2) **Case Reports (6 equally weighted)** — SESSIONS 4-9, SUBMITTED BEFORE CLASS

All students must prepare a TWO-PAGE executive summary of the case readings (made available each week, exactly one week prior), which must be submitted in person and through Quercus **BEFORE** each class begins. All *Case Reports* must fulfill **ALL** of the following criteria to be acceptable—

a) **MUST** be bounded by a margin of at least 2 centimetres;

b) **MUST** be rendered electronically at US letter-size; AND

c) **MUST** be set in 11-point Arial font **ONLY**. No other fonts; italics and bold are accepted.

Discussion between students before class is **discouraged**, as each student is expected to bring their unique insight to bear on the problem.

3) **Participation (10%)** — WEEKLY, IN-CLASS

Participation is determined by the instructor based on individual contributions to case debates, and on attendance. Attendance is monitored at the beginning of each class and all participants must have arrived by 10 minutes after class has begun (1 mark per attendance for a maximum of 10 marks: one for each of the cases, and one for the finale).

SCHEDULE OF ACTIVITIES

Session	Topic	Readings	Cases & Activities
1 13-Jan	**Introduction**	Revers, L. & Furczon, E. (2010) *Can. J. Pharm.* **143**(3):92-97 & **143**(4):184-191.	Surveying the landscape of biologics in therapy. An industry gambit?
2 20-Jan	**Manufacturing Challenges in the Production of Biologics**	1. Kozlowski, S. & Swann, P. (2006) *Adv. Drug Delivery Rev.* **58**:707-722. 2. Schiestl, M., *et al.* (2011) *Nat. Biotechol.* **29**(4):310-312.	Host cell selection, master cell banking, scalability & variability, process change sensitivity, comparability exercises, quality by design, functional assays, acceptance criteria.
3 27-Jan	**Biosimilars: A New Paradigm for Pharmaceutical Facsimiles**	GUIDANCE FOR SPONSORS: Information and Submission Requirements for Subsequent Entry Biologics (SEBs), Health Canada; https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/brgtherap/applic-demande/guides/seb-pbu/seb-pbu-2016-eng.pdf	Size & complexity, post-translational variability, Hatch-Waxman Act vs. BPCIA, similarity vs. comparability, clinical endpoint selection, interchangeability & substitutability.
4 3-Feb	**Case Study**	*To be announced on 27-Jan.*	*See below for possible topics.*
5 10-Feb	**Case Study**	*To be announced on 3-Feb.*	*See below for possible topics.*
6 17-Feb	**Case Study**	*To be announced on 17-Feb.*	*See below for possible topics.*
7 3-Mar	**Case Study**	*To be announced on 24-Feb.*	*See below for possible topics.*
8 10-Mar	**Case Study**	*To be announced on 3-Mar.*	*See below for possible topics.*
9 17-Mar	**Case Study**	*To be announced on 10-Mar.*	*See below for possible topics.*
10 7-Apr	**Finale**	*Students select their own topics.*	Trends, new technologies and possible futures.

Sample Case Topics:

1) *The Fall and Rise of Antibody-Drug Conjugates: Mylotarg® vs. Kadcyla™.*
2) *The Crying Game: Lessons Learned from TGN1412.*
3) *Not Everyone's Cup of Tea: ERBITUX® and Anaphylaxis in Patient Sub-Populations.*
4) *Evergreen—A Star is Reborn: A New Lease on Life for AMGEN's Enbrel.*
5) *The Proof of the Pudding is in the Formulation: EPO Biosimilars & PRCA.*
6) *Checkpoint Charlie: Targeting Undercover Cancer Cells with Pembrolizumab, Nivolumab and More.*
7) *Go CAR-T! Entering a New Race.*
8) *Brodalumab and the Black Box.*