Medicinal Chemistry: An Overview

Course Outline

Lecture	Date	Topic
1	2015/12/17	General Aspects of Medicinal Chemistry
2	2016/01/07	General Biochemistry
3	2016/01/21	Principles of Chemical Synthesis
4	2016/02/04	Chemical Synthesis of Small and Complex Molecules
5	2016/02/18	Chemical Synthesis of Peptides
6	2016/04/07	Strategies for Discovering Lead Compounds
7	2016/04/17	Structure-Activity Relationships
8	2016/04/25	Spatial Organization, Receptor Mapping, and Molecular Modeling
9	2016/05/02	Pharmacokinetic Properties
10	2016/05/09	Legal and Economic Aspects of Drug Development

The Sale of a Drug

The end of the medical art is health and that of economics is wealth.

Aristoles (Ethics)

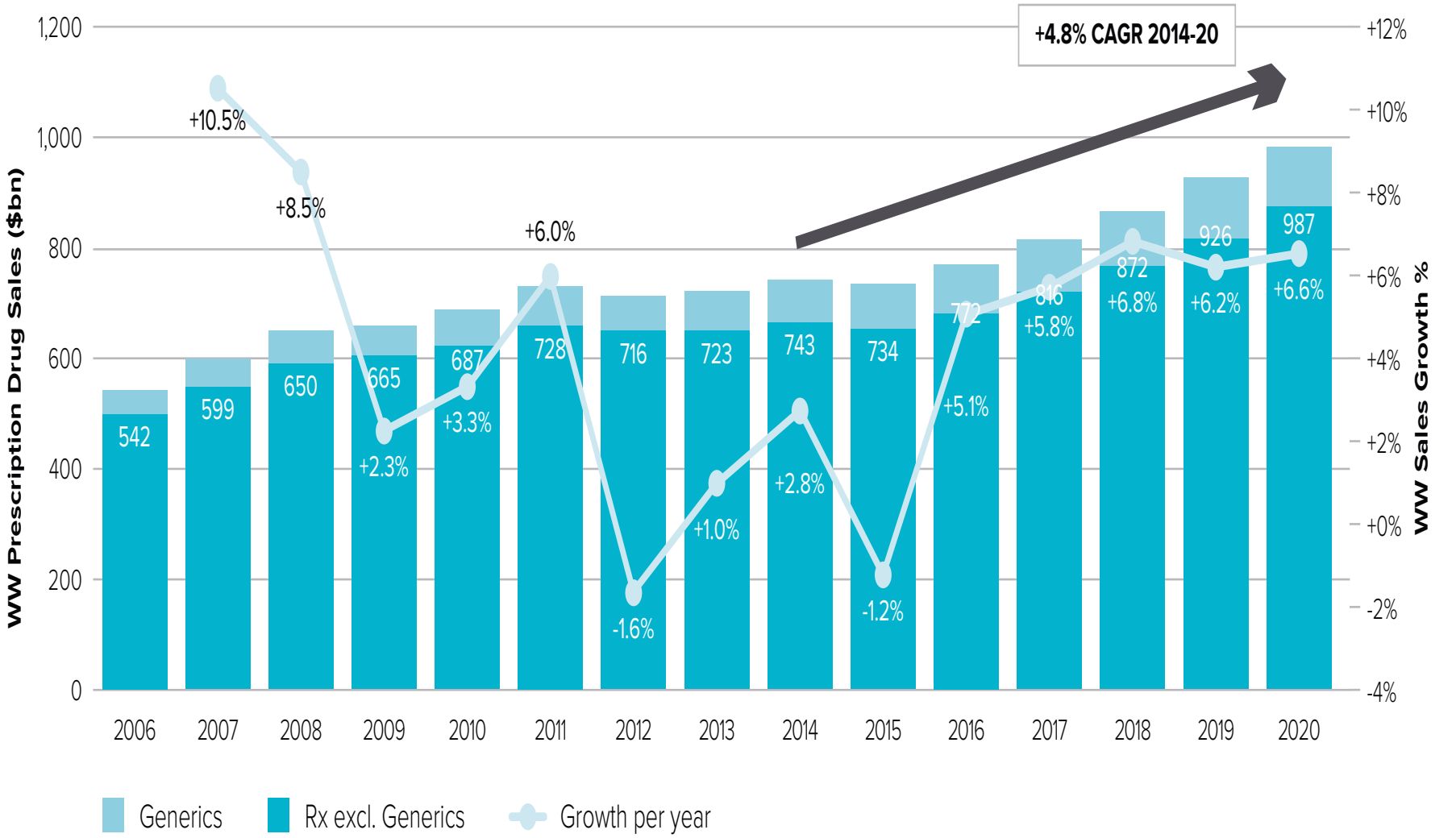
Despite its obvious academic and intellectual importance, medicinal chemistry is richly funded because it promises cure or alleviation of diseases. Medicines are judged by their results.

Rank	Product	Generic Name	Company	Pharmcological Class (Use)	2014 Worldwide Product Sales ($m)
1	Humira	Adalimumab	AbbVie + Eisai	Tumor necrosis factor alpha (TNFα) inhibitor (anti-rheumatoid)	12,890
2	Sovaldi	Sofosbuvir	Gilead Sciences	Hepatitis C nucleoside NS5B polymerase inhibitor (antiviral)	10,283
3	Enbrel	Etanercept	Amgen + Pfizer + Takeda	Tumor necrosis factor alpha (TNFα) inhibitor (anti-rheumatoid)	8,915

EvaluatePharma 2015

Worldwide (WW) Total Prescription Drug Sales (2006–2020)

Source: EvaluatePharma® 22 May 2015



Manufacture of Drugs

The production of drugs is based on the synthesis of a large number of chemicals in high purity (>99.9%). Hence, if the drug is under patent, the manufacturer has complete control on the price of the drug.
To ensure high purity at every stage, a code of good manufacturing practice (GMP) must be followed.

Plant design: large pharmaceutical companies will operate several large different plants.

Choice of chemicals: use of chemicals that reduce the number of synthetic steps as well as those that enable selective reactions.

Green chemistry: use of environmentally-benign chemicals.

Downstream processing: solvent extraction, filtration, leaching, adsorption, crystallization, freeze drying, centrifugation, ion exchange, preparative chromatography, and sterilization.

Formulation and packaging: depending on the product, most companies formulate and package their products in controlled environment.

Outsourcing: using other companies for all or part of the industry's work.

Social and Economic Factors

Pattern and cost of innovation: given the large sums of money involved, only the large multinationals can play the "game" of drug development.

Orphan drugs: these are compounds used for treating a disease or condition that affects less than 200,000 people. The "Orphan Drugs Act," passed in 1983 (USA) and 1999 (Europe) has encouraged the development such drugs. Examples of orphan drugs include: 1) Pulmozyme (dornase alpha) for the treatment of thick mucous secretion associated with cystic fibrosis. 2) alglucerase (imiglucerase, Cerezyme) for the treatment of Gaucher's disease.

Parallel trade: higher drug prices for richer countries.

Cost containment measures: measures by government to reduce expenditure on health care.

Pharmacoeconomics: cost-effectiveness study by companies.

Patents.

Patent

A patent provides exclusive right to an inventor for a limited term for them to recoup the cost of their invention. For this right, the inventor must disclose their invention in a way that it can be repeated by a person of average skill.

General points of a patent

1) Patent development is teamwork.

2) The patent term is relatively short.

3) Patents are territorial.

4) Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement.

Patentable Inventions

1) New and useful medicinal molecules.

2) Novel medical use of an old molecule.

3) New drug-discovery target or screening method.

4) New mode of administration.

5) Novel manufacturing processes.

6) New forms of a known molecule:
   salts, esters, amides; crystals or amorphous forms; hydrates or solvates; particle size or shape; separated isomers; and pro-drugs.

7) Formulations and formulation processes.

8) Product packaging.

9) Diagnostic tools.

Patent Law: Basics

Requirements:

1) Novelty
2) Inventive step
3) Utility or industrial application
4) Sufficient Description

Exclusions:

Scientific discoveries and products of nature: USA excludes purified naturally DNA sequences while the European Patent Office (EPO) includes them if they have useful purposes. India does not grant patents for new forms of a known compound that does not improve efficacy.

Patent Specification:

This includes: a description of the invention, the claims, relevant drawings and an abstract.

First filing, priority date, and international arrangements.

Patent prosecution: the negotiation process between the patentee and the patent office.

Patent Law: Basics

Queries to patent validity: given their lack of relevant expertise, examiners do not have the depth and breath of knowledge and experience to accurately access a patent.

Protection term: 20 years from the filing date of the application provided the maintenance fees are paid.

Patent extension/restoration and supplementary protection certificates: only patents that claim a drug product, a method of manufacturing or using the product can be extended.

Patent infringement and patent enforcement: a patent is a restricted right. Showing the evidence for patent infringement is not always simple, and linguistics play a major role in the interpretation patents. However, the disclosures of patents can be used freely for experimental purposes.

Employees' inventions: generally, the inventions belongs to the employer.

The Medicinal Chemist and Patents

Notify the patent department as soon as possible.

Unambiguous definition of patent boundaries.

Clear documentation of events as they occur.

Provide all information in the drafting and prosecution of the patent application.

Important role in opposition and court proceedings.

Summary

Drug development require large sums of money that are protected by complex patent laws. While the medicinal chemist is neither a financial expert nor a lawyer, nevertheless, they need a basic understanding of the economic and legal aspects involved in bringing medicines to the market.