1.3 DRUG DEVELOPMENT PROCESS: AN OUTLINE

The stages through which a drug discovery/development project proceeds from inception to marketing and beyond are illustrated in Figure 1.2 and described briefly in the following text. The discovery and development process can be described by a number of individual steps, but is also a continuous and iterative process not necessarily performed in a strict stepwise process. From this outline, the complexity of the task of finding new therapeutic agents is evident:

- Target discovery comprises identification and validation of disease-modifying targets. Two major strategies are used for target identification and validation: (1) the molecular approach, with focus on the cells or cell components implicated in the disease and the use of clinical samples and cell models, and (2) the systems approach based on target discovery through the study of diseases in whole organisms.
- Before or after identification of target disease, establishment of a multidisciplinary research team, selection of a promising approach, and decision on a sufficient budget. Initiation of chemistry normally involves synthesis based on available chemicals, in-house chemical libraries, or collection of natural product sources. Start of pharmacology includes suitable screening methods and choice of receptor or enzymatic assays.
- Confirmation of potential utility of initial class(es) of compounds in animals, focusing on potency, selectivity, and apparent toxicity.
- Analog syntheses of the most active compounds, planned after careful examination of literature and patents. More elaborated pharmacology in order to elucidate the mode of action, efficacy, acute and chronic toxicity, and genotoxicity. Studies of ADME characteristics. Planning of large-scale synthesis and initiation of formulation studies. Application for patent protection.

These first project phases which typically last 4–5 years, are followed by highly time- and resource-demanding clinical, regulatory, and marketing phases which normally last 6–10 years:

- Very-large-scale synthesis in parallel or before clinical studies
- Phase I clinical studies which include safety, dosage, and blood level studies on healthy volunteers
- Phase II clinical studies focusing on efficacy and side effects on delimited groups of patients
- Phase III clinical studies which involve studies of range of efficacy and long-term and rare side effects on large patient groups
- Regulatory review
- Marketing and phase IV clinical studies focusing on long-term safety
- Distribution, advertisement, and education of marketing and information personnel

After these project stages from initiation to successful therapeutic application after approval, the patent protection expires, normally after 17–25 years, and generic competition becomes a reality.

This outline of a drug discovery and development process illustrates that, it takes many years to introduce a new therapeutic agent, and it must be kept in mind that most projects are terminated before marketing, even at advanced stages of clinical studies. The later a project fails the more expensive, and many efforts are done in order to consider as many potential failure problems as early as possible in the process. Especially forward translation of preclinical data to possible clinical outcome and back translation of clinical data to "humanized" preclinical data of more predictive value are important issues in the desire to avoid late failures.

Some of the aspects of drug discovery phase are described in more detail in the following sections.