

INTRODUCTION: DRUG DISCOVERY IN THE 21st CENTURY

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1 INTRODUCTION

The discovery, development, and registration of a pharmaceutical is an immensely expensive operation and represents a rather unique challenge. For every 9000 to 10,000 compounds specifically synthesized or isolated as potential therapeutics, one (on average) will actually reach the market. This process is illustrated diagrammatically in Figure 1. Each successive stage in the process is more expensive, making it of great interest to identify as early as possible those agents that are likely not to go the entire distance, allowing a concentration of effort on the compounds that have the highest probability of reaching the market. Compounds “drop out” of the process primarily for three reasons:

1. Toxicity or (lack of) tolerance
2. (Lack of) efficacy
3. (Lack of) bioavailability of the active moiety in humans

Early identification of poor or noncompetitive candidates in each of these three categories is thus extremely important [1], forming the basis for the use of screening in pharmaceutical discovery and development. How much and which resources to invest in screening and each successive step in support of the development of a potential drug are matters of strategy and phasing that are detailed later in this Introduction. In vitro methods are increasingly