preclinical information database must be predicated on minimizing clinical risk. The preclinical database strictly serves to predict (1) drug absorption and disposition and (2) the physiological outcome from exposure to that drug and its metabolites. This is very simply accomplished by conducting a series of studies that will form a foundation for efficient clinical development.

Figure 3 represents a temporal schematic of issues that are commonly addressed throughout the preclinical development program. In this example, the drug candidate might treat a chronic illness in a diverse patient population. A drug intended for acute or intermittent use or a drug intended for a narrower patient population might have fewer issues to consider and thus fewer studies in the program.

Figure 3 also illustrates that understanding the similarities and differences between nonhuman and human physiological systems is vital to obtain quality information from the program. Virtually every study and every decision to be made on the development of a drug candidate will be predicated on the assumption that preclinical models are a predictor of human exposure.

Shapiro addressed the issue of animal models that mimic human disease states and his thoughts can apply to the broader scope of this text (1). Quantitative validity of an animal model may have less value than the productive generativity of a model. While it is unlikely that anyone will ever validate a nonhuman model in a true or absolute sense, the nonhuman model will generate a body of evidence and confidence that the drug

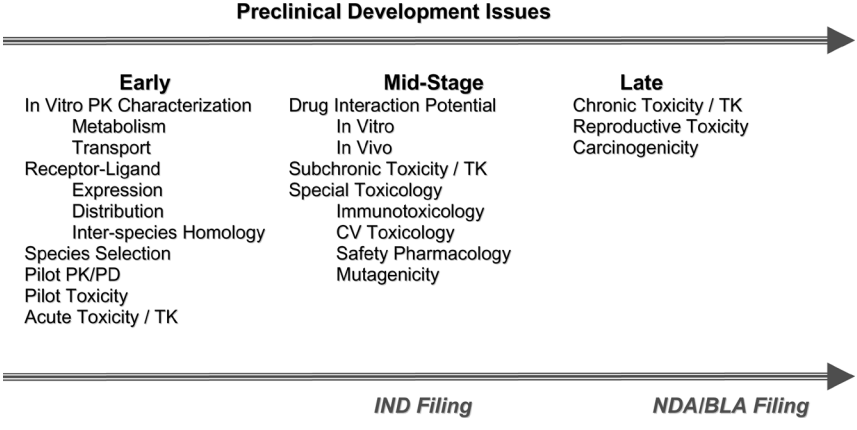

Figure 3 Preclinical development programs begin prior to IND-enabling work and extend through the clinical development stage. Each program is unique, is dependent on the intended therapeutic use, the potential patient population and historical reference. The following program might be acceptable for treatment of a chronic illness in a diverse population.