modified. It becomes particularly important in human evaluations to understand the mechanism of elimination since it is common for manufacturing changes to occur in the clinical or commercial setting. Here, the preclinical database provides invaluable insight into potential changes in human efficacy or safety.

Antigenicity remains a unique and often troublesome property of these molecules. While antigenicity can result in simple binding complexes, they can also neutralize the pharmacologic activity of the molecule and may cross-react with endogenous or similar molecules. These latter responses can result in profound and chronic toxicity. Understanding the outcome of induced antibodies on the PK/PD of large molecules in preclinical models provides an understanding of safety that cannot be studied in humans.

While the issues of large molecule drug development are unique from small molecules, those issues can be challenging and complex. Nevertheless, biotechnology has proven itself as a realm of therapeutic intervention that can treat some of our most daunting and destructive diseases. Indeed, our understanding of these diseases, the mechanisms by which we can modulate disease pathways and the technology around development science will continue to fuel the success of biotechnology.

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