

# Executive Summary

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In recent years, the pharmaceutical industry has been experiencing a shortage of new drugs reaching the market. One major factor contributing to this shortfall is the diminishing return from traditional drug discovery methods. The very limited number of targets addressed by drugs discovered through traditional methods suggests that these methods are “boxed in.” Companies have therefore turned to genomics- and proteomics-based drug discovery in order to increase the number of targets at their disposal.

The problem with the increased numbers of targets provided by genomics and proteomics is that researchers need to select the best drug targets, preferably early in the drug discovery process to reduce costly attrition rates. Target evaluation has thus become an increasingly important aspect of the drug discovery process. Little or nothing is known about the biological function or role in disease pathways of the vast majority of novel genomics- and proteomics-derived targets. This poses what is known as the target validation problem: The challenge of determining which of these targets are most worth pursuing. Skepticism about the target validation paradigm has increased and has led to the development of new and alternative strategies to improve or extend beyond that paradigm.

In this report, we review the following key target evaluation topics:

- The three stages of the evaluation process: target identification, target characterization, and target validation.
- Whole-pathway approaches to drug discovery.
- Approaches to developing therapies that address more than one molecular target.
- Targets and “druggability” for small- and large-molecule drugs.

- Biology-driven and technology-driven target evaluation and drug discovery and development strategies.
- Evaluation of drug targets for complex diseases with high unmet need.
- Strategies for connecting discovery with clinical outcomes.
- Targets and business issues in early-stage licensing deals and partnerships between big pharma and biotech companies or smaller pharmaceutical companies.