of compound candidate efficacy. In some cases, such as changes in viral load or $CD4^+$ lymphocytes in HIV infection, biomarkers are biochemically assessed. There are, however, physiological outcomes, such as blood pressure reduction (cardiovascular disease) or sleep induction (insomnia) that can serve as outcome biomarkers. In many cases, there is an overlap between mechanism biomarkers and outcome biomarkers. It is also important to be aware that outcome biomarkers can also be used to screen out candidate compounds that have undesired side effects. A candidate compound designed to treat a migraine headache that also induces sleep or sedation may have limited commercial utility. The early application of an outcome biomarker to detect potential problems can be very effective in limiting the forward momentum of flawed candidate compounds.

Toxicity biomarkers are similar to outcome biomarkers, but as their name implies, these biomarkers are associated with negative outcomes. Data developed through the application of a toxicity biomarker are generally perceived to be strong indication that the candidate compound has a serious flaw that must be considered before moving forward with further development efforts. QT prolongation and hERG channel blockade, for example, are well known physiological and biochemical toxicity biomarkers associated with torsade des pointes and sudden cardiac death[20] that are employed in almost every drug discovery and development program. Toxicity biomarkers that are associated with other forms of toxicity such as liver or kidney issues are also available, and their application early in a program via *in vitro* methods can provide an opportunity for a program to use medicinal chemistry tools to design out the toxicity. Identifying these kinds of issues prior to initiating advanced animal studies or human trials can be a very effective method of conserving resources and limiting patient exposure to potentially harmful candidate compounds.

Pharmacogenomic biomarkers are primarily used in clinical settings, and their main purpose is to provide an improved understanding of the target patient population, especially with regard to predicting which patients are likely to respond. Consider, for example a candidate compound that targets a specific variation of a biomolecule or physiological state, such as a mutation that activates or eliminates a specific gene. Identifying patients with this particular mutation would increase the likelihood of demonstrating utility in a clinical trial. At the same time, patient without the desired trait (e.g., genetic mutation) would not be admitted into the clinical trials, as it would already be apparent that they would be unlikely to benefit from exposure to the candidate compound. In this manner, patient risk is limited, clinical trial sizes are diminished, and overall program costs are lowered.

Diagnostic biomarkers are also used primarily in the clinical setting, but can also be used in animal models where appropriate. This class of biomarkers can be used to identify patients that are at risk for developing