Success in fragment and structure-based drug discovery relies on effective use of a range of biophysical methods. The initial stages of a project rely on production of suitable reagents and assays which can be used with confidence, initially for screening and hit identification. Improving the properties of hit compounds requires a model of how the compound is binding to the target to guide optimization, to be followed by rapid and robust methods for profiling the resulting compounds.

I will summarize experiences in target enablement, hit identification and compound optimization from several drug discovery projects on several different proteins at Vernalis, with a particular focus on the biophysical methods used. The techniques include thermal shift analysis, ITC, SPR, ligand-observed and protein-observed NMR and high throughput crystallography.