Development of a Second Generation Process for Belvarafenib, a pan-RAF Inhibitor

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This lecture will describe the discovery and development of a proposed late stage and commercial route to pan-RAF inhibitor belvarafenib, a small molecule treatment for solid tumors. Key features of this route include a novel heterocyclic starting material synthesis and a catalytic nitro group hydrogenation. Significant development work was required to successfully develop and implement a production scale synthesis of the heterocyclic starting material. A regulatory strategy for the control of genotoxic and potentially genotoxic impurities in this route will also be discussed.