## **Innovation in the Synthesis of Complex Pharmaceutical Agents**

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Modern pharmaceuticals are both increasingly complex<sup>1</sup> and increasingly diverse. Today's clinical candidates often contain challenging stereochemistry, unique molecular architectures, and uncommon heterocyclic frameworks; they range from small molecules to natural products, peptides, oligonucleotides, antibody-drug conjugates and other modalities. Developing safe, scalable and sustainable routes to molecules, in the context of increasingly short development timelines, requires an approach focused on maximizing impact through innovative chemical solutions – so called 'disruptive innovations'.<sup>2</sup> However, increases in molecular complexity bring new challenges to the decision making process, complicating our ability to identify the synthetic strategies which will produce the most sustainable outcomes. These decisions can be aided by predictive decision making tools, cognizant of potential environmental impact, and recent advances have begun to establish such methodologies.<sup>3</sup>

This presentation will cover the synthetic strategies and chemical innovations developed to address several clinical candidates from the Bristol-Myers Squibb portfolio. Our approach<sup>2</sup> has led to the invention of several new synthetic approaches,<sup>4</sup> new chemical methods,<sup>5-8</sup> and new concepts in predictive data analytics.<sup>3</sup>

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