A Second-Generation Process for the Small Molecule Drug Substance Intermediate for BDC-1001 and implementation in downstream bioconjugation

Diane Carrera
900 Chesapeake Drive Redwood City, CA 94063
Bolt Biotherapeutics
USA
dcarrera@boltbio.com

Immune-stimulating antibody conjugates (ISACs) represent a promising new therapeutic option for oncology. By harnessing mechanisms of the innate immune response, treatment with ISACs can lead to prolonged adaptive immune responses, effectively "teaching" the immune system to recognize and eliminate cancer cells. Bolt development compound BDC-1001 is currently progressing through a multi-arm Phase 1/2 clinical trial targeting HER2-expressing solid tumors and utilizes a novel small molecule linker-payload, A00104, to antagonize TLR 7/8 and initiate the ISAC mechanism of action. This presentation will describe a second-generation process for the synthesis of A00104 that significantly improves upon the first-generation process through the implementation of a new approach to a key linker-payload bond formation and application of solid-state principles to the isolation of the drug substance intermediate. We shall also demonstrate how improved process analytics enabled these improvements along with regulatory considerations and the approach for demonstrating comparability in the downstream bioconjugation.