Adaptive Manufacturing: A New Paradigm to Improve Efficiency and Effectiveness in Early Oncology Development
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Purpose
The efficient conduct of early clinical trials in oncology patients can be challenged by problematic recruitment rates, protracted study durations and the need for drug products to be tailored to individual subject requirements. Example scenarios include:

• Dose escalation algorithms in the First-in-Human/Patient (FIH/P) study
• Evaluation of improved formulations to address sub-optimal pharmacokinetics (PK)
• Conduct of the regulatory ADME mass balance study

Conventional drug product manufacturing and supply chains are not effectively configured to address these growing challenges given the increasing industry focus on oncology research and early development.

Methods
Translational Pharmaceutics™ is a new platform in which drug products are manufactured in “real time” in response to patient recruitment timelines. It also allows formulation compositions to be adjusted in ‘real time’ in response to emerging data.

Through the integration of pharmaceutical development, GMP manufacturing and patient supply activities, customized drug product formulations can be supplied to specialist clinics globally within 2-3 weeks from patient notification.

Case Study 1: A flexible CMC program was designed to support a Phase I dose escalation study in oncology patients. A manufacturing space was established around the immediate release (IR) tablet which included two dose strengths and the option to vary batch size. The manufacturing space was utilised in the clinical study for flexible resupply based on on-going recruitment rates and emerging data.

Case Study 2: 14C intravenous drug product was manufactured and supplied to support a clinical ADME study in oncology patients at a specialist clinic in Europe, with an expected duration of up to 18 months. QP released intravenous drug product was supplied on a ‘per patient’ basis within 2 weeks from notification.

Results
Adaptive CMC and supply programs undertaken for these studies reduced the timelines to get to clinic, reduced stability requirements needed to support the study, increased the efficiency of drug substance consumption and allowed ‘in study’ adjustments to be made to the drug product.

Conclusion
Translational Pharmaceutics enables an adaptive manufacturing approach to be utilised to support a range of early development studies and can deliver reductions in timelines, drug substance and cost.