APRECIA®
THE 3DP PHARMACEUTICAL COMPANY

Leveraging 3D-Printing Technologies In Clinical Trials To Accelerate Speed To Market

The clinical trial model for drug development requires a significant investment of time and money from pharmaceutical companies. A recent study estimates the cost of bringing a new drug to market at $2.6 billion.[1] When including post-approval R&D costs, that price tag increases to $2.87 billion. These numbers are already staggering, but when you consider that 90 percent of medicines fail in early-phase clinical trials, it becomes clear the industry is not getting back what it is putting into its drug development programs.[2] As drugs—and the clinical trials needed to ultimately commercialize them—continue to become more complex, they will also increase in cost. Therefore, it is more important than ever for pharmaceutical manufacturers to improve the speed and efficiency of their clinical trials.

In 2015, the use of 3D printing (3DP) for developing and formulating pharmaceutical dosage forms made news when the FDA approved the first prescription drug manufactured using the innovative technology. Yet, the enhanced precision used in 3DP to create successful fast-melting formulations does not just offer a way to improve the patient experience; it can also drive efficiencies in early drug development by allowing more flexibility with dosage size and strengths, leading to a more responsible use of precious and costly resources.

A Solution To Today's Early-Phase Formulation Challenges

Phases 1 and 2 of clinical trials focus on safety and efficacy, specifically determining what the recommended dose and toxicity profile should be for an investigational new drug. It is during these early phases that pharmaceutical manufacturers encounter major challenges in balancing the needs of the trial with cost and efficiency. Below are three areas where leveraging 3DP technologies during clinical trials can accelerate your time to market:

1. Reduces R&D Iterations Of Dosing Frequency And Size

A clinical trial design is based on a study plan developed by a researcher or manufacturer that outlines several details of the trial, including, but not limited to, dosage frequency and size. The plan may identify several dosage sizes that must be tested during Phase 1, of which batches need to be produced and ready. If, for example, a manufacturer determines it wants to test 50 mg, 100 mg, and 200 mg versions of a drug, it will need to be able to produce a batch for each of those dosages as needed. Because the patent clock begins ticking from the time a new chemical entity is filed, any delays can have a direct impact on your bottom line. Traditional manufacturing processes can take weeks to months to produce batches for a clinical trial, depending on the formulation and the number of dosage forms required. With 3DP, the design of the dosage form is preprogrammed using a digital print image. Once the powder blend and print fluid are identified, the process can be easily transferred from machine to machine, allowing for small batches to be created on the fly.

2. Provides Real-Time Formulation Support For Adaptive Clinical Trials

A growing trend in the pharmaceutical industry is the use of adaptive clinical trials, which allow for continual learning throughout the trial and the flexibility to make protocol amendments along the way. For example, a manufacturer may dose only two or three patients in an early phase, measure the concentrations, and then set the next doses in an escalating fashion based on those patients' results. Traditional tableting machines require a reset if parameters need to be changed. With 3DP, a manufacturer can quickly make dosing changes by simply adjusting the number of layers to be printed or the size of the tablet, facilitating the practice of adaptive trials.

Adaptive clinical trials also offer an opportunity to engage the patient voice, which the FDA has stressed as a critical part of product development and regulatory decision making.[3] Patient voice includes preferences on factors about the drug, such as taste. This information can be built into clinical trial endpoints and shared with payors or physicians during pre-commercialization. The agency recently developed guidance on patient-focused development, outlining the importance of the patient voice and suggesting drugmakers "meaningfully involve" it throughout the drug development process.

3. Produces Patient-Ready, In-Human Dosage Forms

The first in-human dosage forms developed during early clinical phases have little regard for taste or finished product. It is often just a powder blend mixed with water in a vessel and given to the patient to swallow as is, which, depending on consistency and flavor, can be extremely unpleasant. ZipDose (the formulation platform used to manufacture the first FDA-approved 3DP drug, Spritam) is a technology that uses an aqueous fluid to bind together multiple layers of powder, so the pill rapidly disintegrates on contact with liquid. This, combined with various taste-masking techniques, can eliminate the obstacles of early in-human dosage forms, easing

the patient experience and potentially improving compliance. 3DP also offers flexibility in terms of creating any size of tablet, which the FDA has recommended keeping as small as possible, as well as shape, whether it be oblong, circular, or oval.

Because of the high value and high stakes of drug development, the pharmaceutical industry has developed a reputation for being averse to change, and rightfully so. Many resources—and, more importantly, patient lives—are at stake if something goes wrong. Hence, bringing drugs to market safely and efficiently remains its primary goal. As we move toward a future where personalized medicine offers infinite possibilities for various therapeutic areas, 3DP paves the way for producing these smaller batches quickly and economically. This, and many other reasons, make it imperative to investigate opportunities for greater efficiency in the early stages of development that could increase time to market and bring lifesaving drugs to patients faster.

1. ScienceDirect, Innovation in the pharmaceutical industry: New estimates of R&D costs—https://www.sciencedirect.com/science/article/abs/pii/S0167629616000291
2. Forbes, The Cost Of Developing Drugs Is Insane. That Paper That Says Otherwise Is Insanely Bad—https://www.forbes.com/sites/matthewherper/2017/10/16/the-cost-of-developing-drugs-is-insane-a-paper-that-argued-otherwise-was-insanely-bad/#5167cdbe2d45
3. Regulatory Affairs Professionals Society, Patient Focused Drug Development: FDA Issues Guidance on Gathering Patient Input—https://www.raps.org/news-and-articles/news-articles/2018/6/patient-focused-drug-development-fda-issues-guida?feed=Regulatory-Focus