Customer Story

F-STAR THERAPEUTICS

Challenge

Standard biological experimentation methods today fall short of scientists' needs in the increasingly data-rich environment of early-phase biopharmaceutical development. Biologists need alternatives to deliver more precise outcomes, more reproducibly and on a shorter time scale.

A paradigm shift in cancer therapy

Statistical approaches to experimentation open the door to the exploration of novel biology and much-needed innovation in advanced-stage cancer

The search for new ways to prevent, diagnose and treat cancer is one of the largest branches of pharmaceutical research and development worldwide, with immuno-therapies quickly becoming one of the more exciting areas of development in modern oncology. F-star Therapeutics, a clinical-stage biopharmaceutical company based in Cambridge, UK, and Cambridge, MA, is working to advance first and best-in-class immunotherapies for patients with late-stage cancer.

Central to F-star's efforts is its proprietary Modular Antibody Technology, a platform that introduces two additional antigen-binding sites into an antibody's constant region. This "plug-and-play" engine acts as a building block for a variety of drug formats and opens the door to discovery of novel bispecific and monospecific product opportunities. It's an approach that uses the body's natural immune response to target inoperable cancer cells and prolong the survival of patients with advanced disease.

Though still early in the development life cycle, F-star's pipeline of immuno-oncology programs shows promise, and the company has secured partnerships with industry leaders AbbVie, Merck KGaA and Denali Therapeutics, among others. Some therapies are already in the clinical stage of development; if successful, F-star's innovation has the potential to shift the entire cancer therapy paradigm.

Having exhausted other solutions to a development challenge, scientists turn to design of experiments

To translate F-star's groundbreaking molecules into patient-ready therapies requires significant scaling and is dependent on researchers creating robust bioprocesses to ensure the product is manufactured at optimal stability and safety. Central to this effort are those like Jon Armer who, as Formulation Lead Senior Scientist, spends his time digging into the data to evaluate any factors that might affect batch outcomes from both a quality and yield perspective.

Armer partners with F-star scientists at every stage of the pipeline from early development through the early clinical phase. Each stage has its own data challenges, from collecting the right data to ensuring that what is collected is usable and will produce meaningful results. Scientists in the pre-clinical space, Armer says, are used to wide margins of error and lack exposure to the sophisticated statistical techniques more commonly used in later phase research where precision is essential. With only limited uptake of statistical methods in early phase work, biologists may be reticent to branch outside of typical approaches.

Not so many years ago, Armer says, he himself was in this very position. While working on a development project, his team experienced sudden and unexpected issues. "We did all the standard analyses," he recalled. "We checked all the raw material. We went back to auditing the people who supplied us the chemicals for the buffers. We started redeveloping the formulation, the presentation and [our processes]."

Unable to identify the source of the problem – and therefore unable to fix it – Armer began exploring design of experiments (DOE) approaches to evaluate differences between batches, eventually tying his issues to a trace element that wasn't routinely monitored. "There was a big flag on the data saying, there's something here you need to look into," he recalls. Without the ability to analyze the data at a higher level, he wouldn't have even considered this possibility.

Reduced experimentation times and reproducibility seed DOE across the organization

Despite not yet being seen as a standard practice in the biotech world, DOE is a powerful and focused statistical approach that offers precision and the ability to handle multiple factors at a time – not to mention reproducibility and the time savings that ultimately bring therapies to market faster. Though DOE may require more time up front, Armer explains, "once you've done it, you're not doing repeats. You don't have inconclusive data that you've got to figure out. It's moving away from the more academic mindset towards a more engineering mindset."

Through his collaborations with scientists across F-star, Armer has seeded interest in multivariate approaches among his colleagues; he isn't just analyzing data for them and handing it back, but working alongside them to show more effective ways to exploit the data they have than with one-factor-at-a-time analysis. As they are exposed to – and become more invested in – DOE, he says, they see real-time benefits, thus leading the entire organization toward a more effective standard going forward.

Critical to the uptake of DOE at F-star is JMP® software. A lower threshold of statistical expertise is required to get started with JMP than with other software, without sacrificing

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>
> –Jon Armer, Formulation Lead Senior Scientist

sophisticated statistical capabilities, making it uniquely suited for research applications that deal with a high volume of data and multiple variables that all must be assessed in detail.

Visual capabilities in JMP® smooth the transition to a statistical approach to experimentation

To sift through the complexities of multiple parameters involved in modeling a new formulation, particularly for scientists with less statistical expertise, Armer explains that a highly visual and user-friendly tool is critical. The DOE platform in JMP enables users to visualize the design space and quickly see interactions between factors.

And Armer says it's easy to forget the wider context and implications when experimenting with numerous variables and needing to focus on the details of each to ensure you're collecting consistent and quality data. "You may think you've found something, but you'll get nowhere," he explains. "So being able to take a step back and look at [the data] impartially helps." Using the DOE platform in JMP, scientists drive at the "why" behind each aspect of an experiment, homing in on those factors that actually have an impact on the experiment's outcome.

"As scientists and engineers, we're really good at collecting data, but not so great at using it," Armer says. "One of the things I liked when I first started using DOE, in JMP specifically, was that it forced you to think about your experiment – why am I testing this? Do I need to? Having that framework as you're working through the experiment and analysis really helps."

The strong visual capabilities of JMP also make it easy to explore the data and observe trends, gaps, mistakes and potential correlations. "The Graph Builder in particular is just fantastic for this. And everyone I've shown it to has stopped using Excel and Prism and they now use Graph Builder. They save so much time."

From one day to one hour, reducing analysis time with definitive screening designs

With so many factors having a potential effect on the formulation of pharmaceuticals, scientists like Armer must account for the potential confounding of data and detect nonlinear responses to fully understand what is going on in experiments. Using a definitive screening design (DSD), Armer can study the effects of multiple factors in a small experiment – it's a powerful way of determining which components have the biggest effect, with data visualizations in JMP providing an easy and visual way of exploring massive amounts of data.

"If I'm doing a standard size grid using definitive screening and graph building options on top of that, I can analyze [my data] in an hour and know what I'm doing next. Without JMP and design of experiments, you'd be looking at about a day," he says – a remarkable time saving that also minimizes user error with automated graph building and data formatting. "The thought of going through that with a table is not something I ever want to go back to."

Communicating results to a broader audience

Scientists aren't the only important audience for these data. Presentations to company leadership require clear and dynamic visualizations that translate complex data into a decision-making tool for audiences without specific domain expertise. With the dynamic interface of JMP, Armer adapts his analyses on the fly to respond to questions from executives.

"I've always got the window open because there's always the question, 'Well what if we change this?' You're literally three or four clicks and you've done it." In particular, Armer says he finds the Profiler to be a handy feature for these types of presentations with its ability to update, in real time, the responses as different factors are adjusted on the screen. Not only does it let you look at and adjust data quickly, you also see effects that otherwise may be missed by looking at a static graph, he explains.

Bringing tools to new industries

Although multifactor experimentation approaches like DOE have been slow to catch on in the biopharmaceutical development sector, the immense time and cost savings of its DOE platform make JMP a valuable untapped resource. But convincing decision makers to invest in new tools and approaches that haven't been used before can be a hard sell, Armer says. Instead, he starts by just helping his colleagues to solve problems by showing them the tangible benefits to their day-to-day work.

Inevitably, more and more people are exposed to useful tools like the Profiler in JMP and begin asking questions. "I've been able to demonstrate to leaders effectively that [JMP] is something that has a huge benefit," Armer says. Not only does it benefit the researchers themselves; more importantly, it gets critical treatments into the hands of patients faster.

Solution

Formulation scientists have turned to JMP, a user-friendly software that allows researchers to quickly implement new statistical approaches to experimentation like design of experiments (DOE).

Results

Scientists say DOE in JMP has condensed what used to take one day into just one hour. Effective and powerful data analysis is saving time, and therefore also shortening drug development cycles. These innovations have the potential to get a critically needed cancer therapy into the hands of patients and doctors sooner.

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