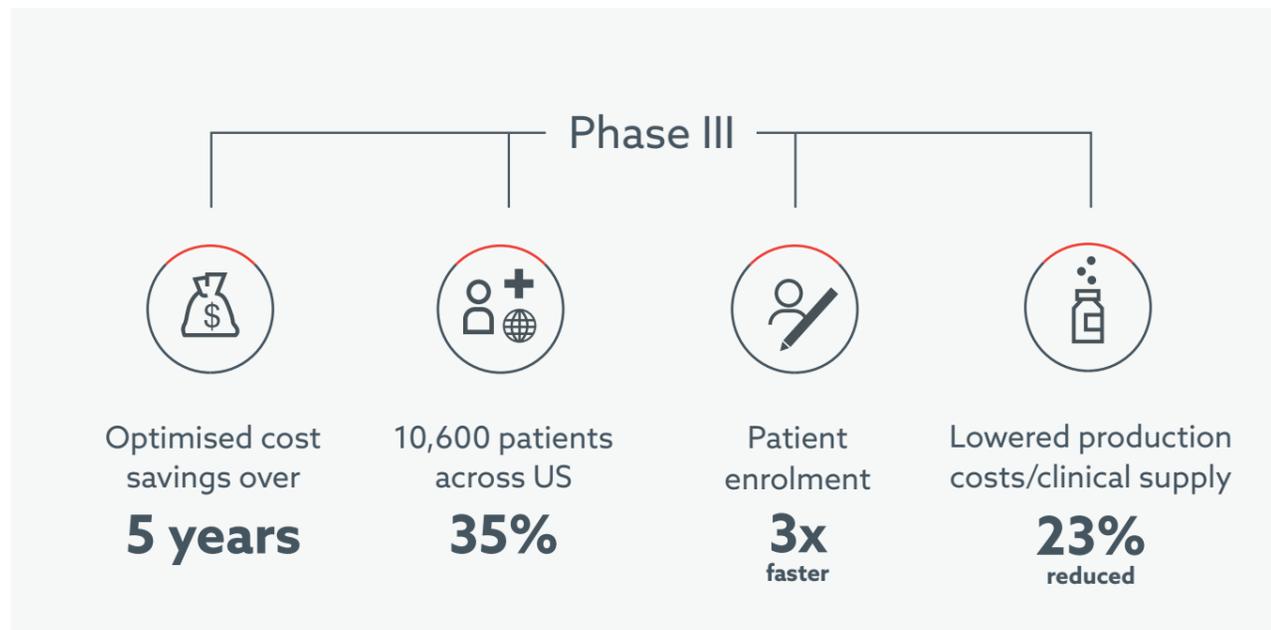


Almac's SupplyWise supports small biotech company with pivotal Phase III trial

Biotech company running a pivotal phase III study utilised the expertise of Almac's Supply Chain Management team to supplement their limited internal resources. Their oversight ensured continuity of drug supply when patient recruitment was x 3 times faster than anticipated.





BACKGROUND

A small, biotechnology company was planning a 5 year, phase III, randomised, double-blinded, placebo-controlled study. The study was conducted across multiple sites in the United States involving 10,600 patients.

This was a pivotal study for the client who initially contacted Almac for a better understanding of clinical trial supply management and to leverage our expertise to determine how much drug they would require. Following discussions with our Supply Chain Management (SCM) team, they felt they lacked the resources and expertise internally and contracted Almac to provide core supply chain management services. The Almac SCM team assisted with devising optimal and cost effective packaging, distribution and drug accountability strategies throughout the life of the study.

The business challenges

The SCM team overseeing the study faced a number of challenges:

The sponsor originally anticipated that the initial enrolment phase would be completed in 18-months, but due to an aggressive patient recruitment effort, patient enrolment greatly exceeded this expectation and was 3 x times faster than originally expected. This resulted in a significant increase in demand on bulk drug product manufacturing as well as primary and secondary kit production.

The increase also meant more frequent shipping and a higher volume of supply movement given the large number of sites involved (~300). The trial design, duration and higher risk patient population meant a higher degree of uncertainty in patient response. While the sponsor had some clinical study experience with the product and an anticipated drop-out rate, the different patient population presented an unknown.

Kit design considerations

Upon review of the clinical protocol, the SCM team realised that a common pack design would be key to meeting the high volume of supply that this study was going to require. However, the varied duration of visit lengths throughout the run-in, randomisation and maintenance phases presented some challenges to developing the kit strategy. After thorough consideration, the SCM team proposed the following supply strategies:

- For the lead-in phase, which consisted of 14 days of dosing (7 days on active and 7 days on placebo), the patient supply was packaged in 7-ct bottles. Due to the uncertainty in the pace of enrolment and a high number of sites, a 100% overage of the 7-ct lead-in bottles were prepared. This provided assurance that ample supply would be available, but because of the low bottle count this came at little cost to overall supply.
- While there was variation in visit lengths in the randomisation and maintenance phases, spanning 8 weeks to 26 weeks, the SCM team identified the potential to employ a common pack design of 140-ct bottles and use the Interactive Response Technology (IRT) to assign the appropriate number of bottles based on the visit length. In addition, to assist with site and patient compliance, 3x kits of 140-ct bottles were packed and labelled to better facilitate the dispensation of kits required for the longest duration visits. The use of a common bulk drug supply (140ct bottles) simplified primary and secondary production planning and lowered production costs.

Clinical supply forecasting

The original enrolment expectation was 18-months, but as the study start grew closer, the sponsor became concerned with that estimate based on recruitment efforts. Utilising Almac's proprietary clinical supply forecasting solution - SupplyWise™, the Supply Chain Manager prepared multiple forecast scenarios by altering variables such as patient

enrolment, site start-up, patient drop-out rates, site seeding levels and overage factors. The reporting features available in SupplyWise™ allowed for a side-by-side assessment of the forecast demand for each scenario. The creation of multiple scenarios with varied patient enrolment completion periods ranging from 6 to 18 months allowed for a robust assessment of the impact on demand and, after evaluation of the reports, the sponsor settled on the 8-month forecast as the baseline scenario and planning around that model was initiated.

The Almac solution

SCM Oversight - monitoring of actual events vs. projected

As anticipated, enrolment got off to a very quick start. The SCM maintained close oversight of the enrolment and tracked the actual supply use to the projected demand. After the first couple of months, it was evident that enrolment and supply use was outpacing the 8-month projection scenario and was more aligned with the 6-month forecast scenario. Fortunately, adjusting the supply strategy to this scenario in response to the actual recruitment rate was not a significant challenge because this scenario was evaluated early on and the sponsor had already planned for that contingency with their drug product manufacturer. Once the sponsor decided to update the active forecast to the 6-month demand scenario, the SCM continued to monitor actual vs. forecast supply use and updated forecast projections with actual enrolment data on a monthly basis. Implementing the clinical forecast into the overall supply plan enabled the Almac SCM and sponsor team to see that the projected demand stayed in line with expectations to ensure the bulk production schedule was still in alignment with the customer's desire to never fall below 3-months of on-hand inventory. Another key to the forecast maintenance was ensuring the drop-out rate was in line with the projections originally predicted by the sponsor. A lower than expected drop out rate could have had significant downstream impact on demand in the maintenance phase. When there was a variance in the initial projected drop-out rate, the close oversight of the SCM ensured they were able to modify the forecast accordingly which reduced the supplies needed by 23%.

Patient Visit Projections - Scenario Comparison

The SCM utilised SupplyWise™ - Almac's clinical forecasting solution to enable a side-by-side assessment of the forecast demand for each scenario.



Due to the large number of sites and rapid enrolment rate, the sponsor was also concerned about the frequency of shipments and especially sensitive to the possibility of stock outs. To address this concern, the Almac SCM developed 4 different supply strategies that were designed to satisfy 4 different screening and lead enrolment levels. The screening and lead enrolment levels at the sites were then monitored on a weekly basis and when site activity reached the pre-defined level, the sites were adjusted to a higher supply strategy. Likewise, when site activity declined and screening and lead-in levels fell, the strategy would be downgraded to reduce on-hand quantity. These adjustments to the IRT system ensured adequate supply levels were maintained while also reducing the frequency of shipments.

- Development of site stocking strategies based on screening and enrolment levels and weekly monitoring of site activity provided a means for ensuring sites were assigned to the appropriate supply strategy based on their patient levels. The strategy proved highly effective at both reducing the frequency of shipping and avoiding site stock out events due to inadequate supply levels.

The Almac solution

SCM Oversight - monitoring of actual events vs. projected

- The kit design recommendations that Almac made for the lead-in, randomisation and maintenance phases coupled with the development and assessment of multiple clinical supply forecasts enabled planning for the sponsor's desired forecast scenario and also assured that adequate supply would be available to meet the projected demand for each of these phases of the study.
- Monitoring actual patient enrolment and supply demand and comparing to the original projection based on the 8-month forecast scenario allowed for confirmation that the 6-month forecast scenario was more appropriate and facilitated a quick decision by the sponsor to adjust their strategy to fit the 6-month enrolment projection. At the same time, long term monitoring of patient retention rates and adjusting the forecast to account for the differences resulted in a 23% reduction of the long term maintenance kits that would need to be produced.

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