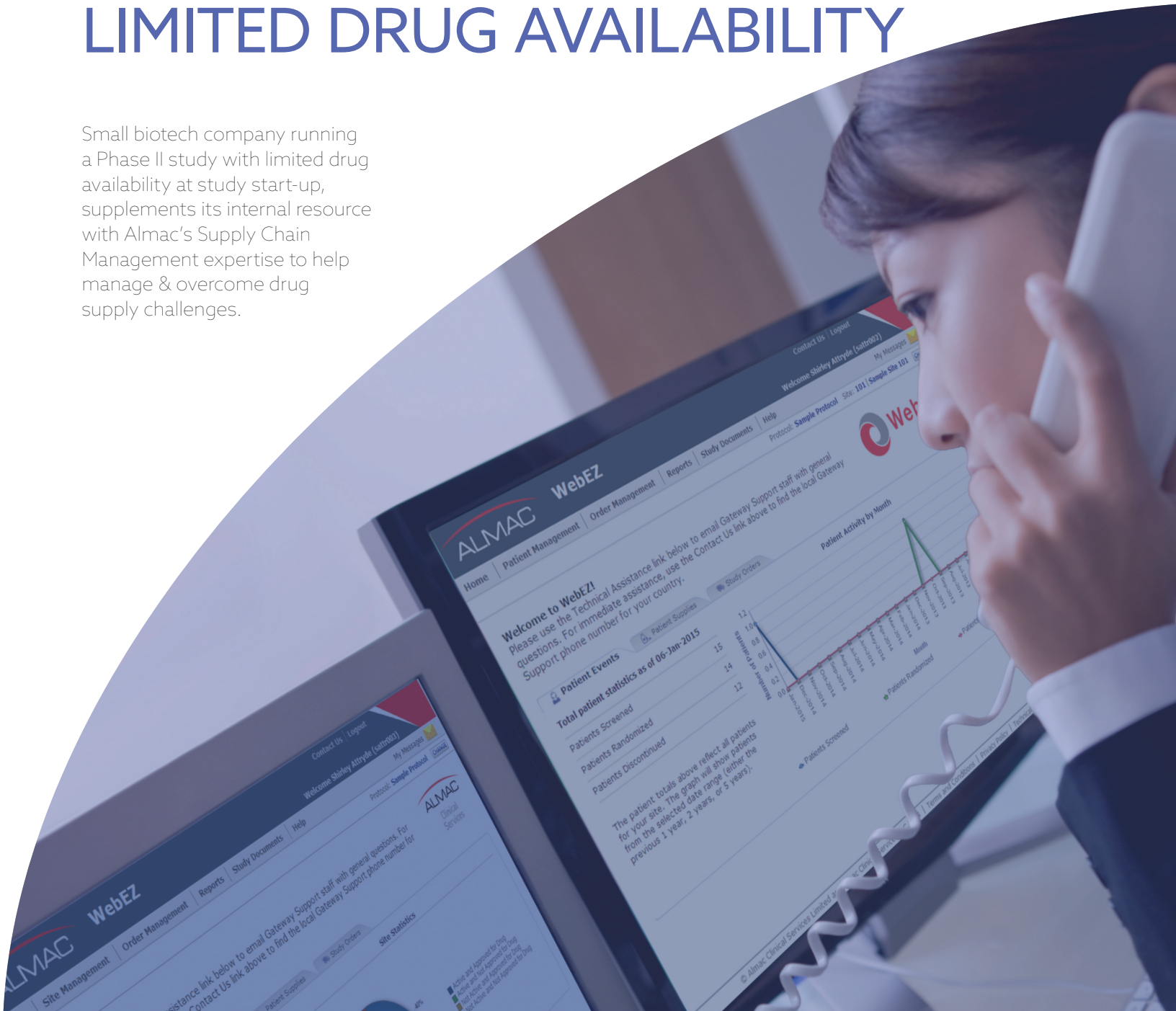
ALMAC

Partnering to Advance Human Health

CASE STUDY

SMALL BIOTECH COMPANY RUNNING A PHASE II STUDY WITH LIMITED DRUG AVAILABILITY

Small biotech company running a Phase II study with limited drug availability at study start-up, supplements its internal resource with Almac's Supply Chain Management expertise to help manage & overcome drug supply challenges.



BACKGROUND

Our client, a US-based biotech company with < 10 staff was conducting a phase II, multicenter, double-blinded, randomised, comparator controlled study to investigate the use of a new treatment for Ulcerative Colitis, a disease affecting a large population of middle-aged adults.

The study was conducted in the United States across 48 sites. The 120 study participants enroled were concurrently randomised to one of two treatments: the Investigational Medicinal Product (IMP) or comparator drug. The IMP and comparator were supplied in identical, single-use containers that patients could take home and self-administer once a day for six weeks. The sponsor's patient kit contained six weeks of treatment (42 single-use containers) plus seven additional doses to replace damaged or lost containers.

The sponsor of the trial had limited internal clinical supply expertise and had initially outlined a manufacturing, packaging and labelling schedule for clinical trial material that was closely aligned with the study start date and site ramp-up period with full release of initial batches expected just days prior to the first patient screened (FPS) target date. Realising the clinical trial material challenges, the sponsor reached out to Almac's Supply Chain Management (SCM) team to develop an understanding of the clinical protocol requirements and drug supply variables.

CHALLENGES FACED

The SCM overseeing the study faced a number of challenges, considering initial discussions commenced seven weeks from the planned date for FPS.

- Limited drug availability and the proposed kit design complicated their ability to enrol and meet patient needs based on enrolment projections.
- They expected to manage the drug supply challenges with a customised and costly Interactive Response Technology (IRT) system requiring complex programming that could not be completed prior to the expected FPS date.
- The sponsor's manufacturing capacity was limited- this resulted in small batch sizes for both the IMP and comparator supply. The full clinical trial material need was satisfied through numerous production runs with new batches delivered on a bi-weekly basis throughout the first three months of the study. Based on this production plan, the ability to satisfy site and patient needs during the first month of study conduct was tenuous.

Due to limited availability of drugs throughout the start-up phase, the sponsor did not plan to seed investigator sites with clinical trial material. The strategy was to delay site supply shipment until a patient was screened and then send one kit based on the predicted treatment group in which the patient was randomised. If the patient was not randomised, the site would keep the kit until a new patient was screened. When a new patient was screened, the treatment group assignment would again be predicted and a new kit of the appropriate treatment type would be shipped if necessary.

This scenario presented multiple challenges:

- The study used a centralised randomisation scheme. If more than one subject was in screening at any given time there would be no certainty as to which treatment group would be assigned next, presenting a significant risk that the appropriate treatment type would not be available to assign at randomisation.
- The potential for unblinding increased due to the fact that a new kit shipped to the site (whether due to the inability to

"Our company selected Almac after an extensive comparison of comparable vendors. Almac's staff worked closely with our personnel and demonstrated a high level of energy, enthusiasm, and ownership of our clinical study. Rather than seeming like a typical uninvolved, relatively distant vendor, the Almac team become almost an extension of our company, and we sensed that 'our' clinical study was 'their' clinical study as well."

Vice President of Product Development

assign a kit on site or the kit being inappropriate for the next assignment) could differ in design from existing kits on-site.

- The supply forecast at the initial stages was not sufficient to satisfy the projected patient demand due to the plan to provide patients with supply needed for the treatment duration at randomisation.

ALMAC APPROACH

Based on these components the Almac's SCM team formulated a new kit design and drug assignment schedule that would overcome the drug supply vs. demand challenges.

The sponsor's kit design was composed of seven weekly kits that were to be consolidated into one large patient kit and assigned at randomisation (day zero). Upon review of the clinical trial material packaging, kit design, protocol and patient visit schedule, the SCM quickly realised that initial demand on supply could be reduced by splitting up the consolidated patient kit, uniquely numbering each weekly kit, and reducing the number of weekly kits assigned at the randomisation visit.

Instead of assigning seven weekly kits at randomisation, kits would be assigned over a 21-day period with two kits assigned at day zero (one kit for the first seven days of treatment and one kit for replacement purposes), two kits assigned at day seven, and three kits assigned at day 21. This design resulted in a number of benefits:

- **Flexibility** for the sponsor on the delivery and release of new batches of clinical trial material and significantly reduced potential for a depot stock-out.
- Ability to seed sites with enough supply to **eliminate the unblinding risk** and a treatment specific site stock-out scenario – to further maintain control of clinical supplies, the seven-day period between screening and randomisation was an advantage as only sites that screened patients would be seeded.
- **Eliminated need for a customised IRT system** due to a simplified design – it became possible to use Almac's configurable solution - aXcess™ that saved the client **$100k** while enabling them to meet their study timelines.
- Allowed the set-up of a more **efficient** and **simplified** drug shipment strategy.

To maximise the flexibility of available clinical trial material during start-up, on-hand site inventories were minimised by reducing values for trigger/resupply and projection windows. Once the depot inventory levels reached a comfortable surplus, the trigger/resupply and projection windows were adjusted to reduce the number of shipments and to optimise shipment efficiency.

RESULTS

The strategy developed by Almac did not lead to a greater burden on sites or require any changes to the protocol as it fit within the context of the protocol visit schedule. The SCM team assisted the sponsor partner in developing solutions to multiple clinical trial material concerns and as a result of the SCM's recommendations:

- An aggressive study start date was met.
- Drug wastage was minimised as the sponsor was able to make more efficient use of available clinical trial materials, preventing potential stock-outs and unblinding scenarios.
- The simplified study design eliminated the need for a customised IRT system and instead Almac's configurable, IRT system - aXcess™ with a shorter, development lead time could be used which met the client's study timelines saving them $100k.

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