SUVODA

CASE STUDY:

Managing a Successful Phase 2/3 Direct-to-Patient Trial Using IRT

How Bellerophon Therapeutics is using IRT to successfully handle the multiple layers of complexity within a Direct-to-Patient trial

- Increased patient recruitment and retention
- Reduced frequency of site visits
- Reduced investigational product loss

Bellerophon THERAPEUTICS

About Suvoda

Suvoda is a global clinical trial technology company that specializes in highly complex, life-sustaining studies in therapeutic areas like oncology, central nervous system (CNS), and rare disease. Founded in 2013 by experts in eClinical technologies, Suvoda empowers clinical trial professionals to manage the most urgent moments in the most urgent trials through innovative trial design and advanced IRT, eConsent and eCOA solutions. Headquartered outside Philadelphia, Suvoda also maintains offices in Portland, Oregon; Barcelona, Spain; Bucharest, Romania; and Tokyo, Japan. The company consistently boasts customer satisfaction scores of 9 out of 10 and has been selected by trial sponsors and CROs to support more than 900 trials across 65 countries. To learn more, visit suvoda.com.

The Challenges

Even though Direct-to-Patient (DtP) has the potential to solve many common issues such as recruitment and retention, investigational product loss and reduced site visits, there are still additional complexities that present challenges.

Increased cost. This is often the biggest objection to the DtP model. With DtP, shipping costs will increase as material is being shipped individually to potentially hundreds of patients instead of several sites. In some cases, the product may be difficult to administer, so a home health service may have to be employed, which has additional cost implications for the sponsor.

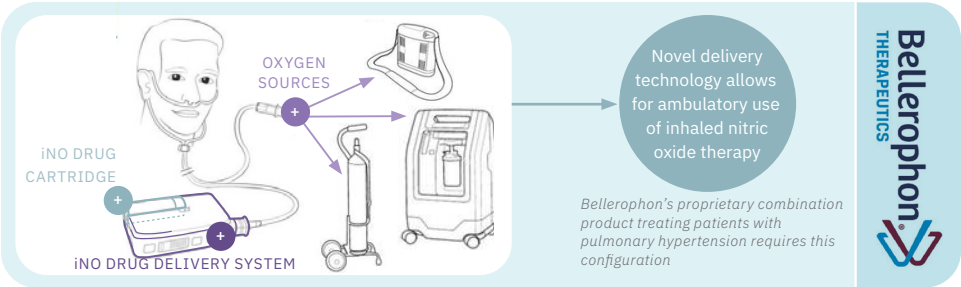
Reduced investigational product and patient oversight. While the site staff is ultimately responsible for drug accountability, sites are completely reliant on the depot or central pharmacy staff to make sure the correct supplies are provided to patients as well as accounted for at the end of a trial. By eliminating site visits, patients may not be as likely to call the site when they are having issues, which may lead to less patient feedback over time.

Protection of patient privacy. Adhering to the policies set forth by regulatory agencies, Institutional Review Boards (IRBs), and ethics committees is paramount. Delivering investigational product directly to a patient requires a name and address for each patient – which is clearly patient identifying information. If using a central depot, a consignee may need to be listed on proforma invoices to cross borders. It's important to work with a logistics provider that can control chain of custody while simultaneously protecting patient privacy.

Uncertain regulatory landscape. DtP is not yet heavily regulated, and therefore each trial is regulated on a case-by-case basis in most countries. This means regulatory documents may need to be submitted to each country that participates in the study.

Bellerophon's Clinical Study

Bellerophon began working with the DtP model in 2013 and is currently utilizing this trial design to assess the efficacy of their drug and device combination product in a Phase 2/3 trial for pulmonary hypertension associated with pulmonary fibrosis. Bellerophon's novel delivery system allows for the ambulatory use of inhaled nitric oxide (iNO) therapy. Their proprietary combination product consists of the INOpulse delivery system and the iNO drug cartridge, which contains a compressed gas – nitric oxide or matching placebo.

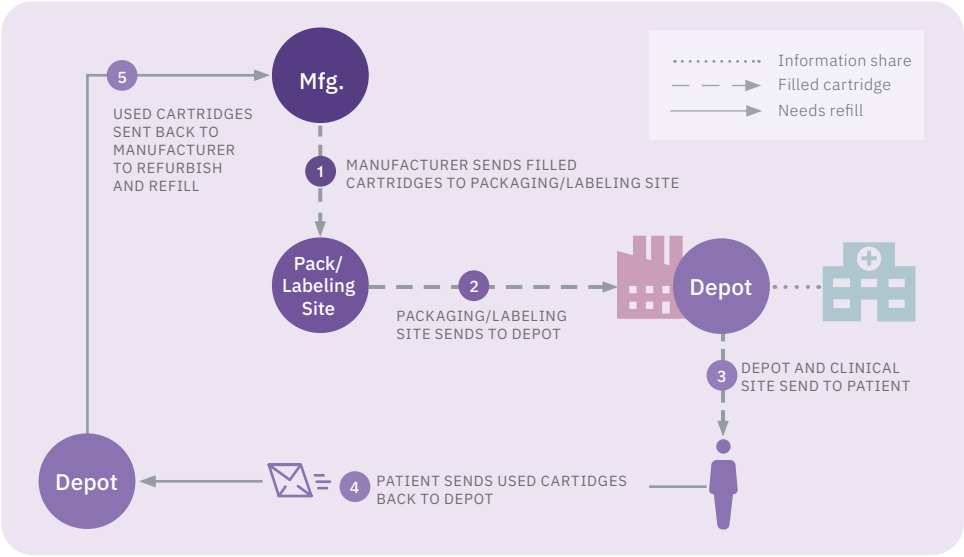


Due to the nature of the therapy and patient population, Bellerophon was an early adopter of the DtP model as part of their overall supply chain strategy. Unlike a traditional trial where supplies are destroyed, these need to be recycled for reuse.

The Solutions

Bellerophon was able to increase convenience for both site and patient by implementing a supply chain solution that allows for the delivery and collection of material directly at the patient's home. Site visits are reduced because patients no longer need to travel in order to get new supplies or return used materials. Once enrolled in the study, a courier simply arrives at the patient's home, delivers new material, and collects old material at a convenient time arranged by both parties.

The courier is also able to manage the preparation of all shipments in accordance with applicable regulations, benefiting both the site and subject. The amount of material in the field at any given time is reduced because sites do not need to retain excess supply for patients. By storing and processing most of the study materials in central depots, the Bellerophon team can more easily ensure that material is constantly flowing through a cyclical supply chain in which materials are efficiently recycled for reuse.



Cyclical supply chain: each INOpulse cartridge needs to be returned, refurbished, and refilled for use.

In order for this DtP model to be successful, it's crucial to find the correct IRT and logistics partners to help implement this strategy. Because drug supplies are managed and shipped from distribution facilities directly to patients' homes.

A dynamic IRT system is essential to accurately track the chain of custody, ensure patient blinding, and handle other logistical challenges.

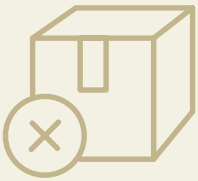
IRT Functionality for Direct-to-Patient Trials

Suvoda's IRT is built to solve complex clinical trial challenges so that study teams can continue to innovate their supply chain. In order to understand specific DtP functionalities for Bellerophon's study, it's important to understand and maintain the fundamentals of an IRT system, which include protecting the blind and ensuring consistency in drug assignment and logistics.

In a traditional trial design where patients are coming into sites, site users are interacting with the IRT system to enter screening information, register randomization, obtain drug assignments, and input drug accountability information. Patients never interact directly with the IRT system. However, in DtP studies, site users are very minimally needed for initial on-site visits and follow-up appointments. For this study – the site staff and study team are responsible for interfacing with IRT when the patients are receiving the shipments directly. The depot staff then perform all drug accountability on the cartridges and devices shipped back to the depot by the patients. With this in mind, some important considerations needed to be made when designing an IRT system to support Bellerophon's DtP study.

Ensure data and patient privacy. In a traditional trial, patient addresses are not needed within the supply chain process, so they are not stored within any IRT or depot system. In this study, all patient identifying information is stored solely by the depot. In order to manage DtP shipments effectively, IRT sends the patient ID to the depot as part of a drug order. The depot then pulls the appropriate patient address associated with the patient ID, prior to releasing a shipment. Therefore, only one computer system stores and retains that data, maximizing the security of the patient information.

Protect the blind. There are standard and robust practices built into Suvoda's IRT system to protect the blind in a double-blind trial. However, DtP shipping can introduce new unblinding scenarios that might not be protected by typical practices. For Bellerophon's study, there are additional precautions built into the IRT system for the following scenarios:



Shipment Cancellations

If a shipment is cancelled and the drug within the cancelled shipment is automatically reassigned to another patient, this could partially unblind a site user by revealing that both patients are on the same treatment. To mitigate this risk, the IRT marks drug from the cancelled shipment to a "temporarily unavailable" status automatically so it cannot be selected for subsequent shipments.

Ad-Hoc Shipments

To prevent unblinding when raising ad-hoc shipments, the site user enters a quantity for the blinded drug type description when submitting a DtP shipment request, and based on the patient ID, the IRT system automatically raises a shipment containing the appropriate drug types without revealing the patient's treatment to the site user.

Track shipments end-to-end. Drug dispensation and drug shipment are usually separate transactions within the IRT system. In a DtP trial these transactions become one and the same. For Bellerophon's study, whether a patient performs a visit at the clinical site or the drug is dispensed virtually, a DtP shipment is triggered in the IRT system. In managing these transactions more uniformly, drug assignment and drug shipment data are updated in tandem regardless of whether patients visited the site or not.

Manage accountability at the depot. While drug accountability is typically performed on-site when patients return any remaining supply, patients in Bellerophon's study are often returning drug directly back to the depot through the courier. IRT must allow depots to perform the accountability procedure that site staff would normally perform instead of accounting for these returns at the site. This ensures that accountability is performed where the drug is physically returned to maximize efficiency.

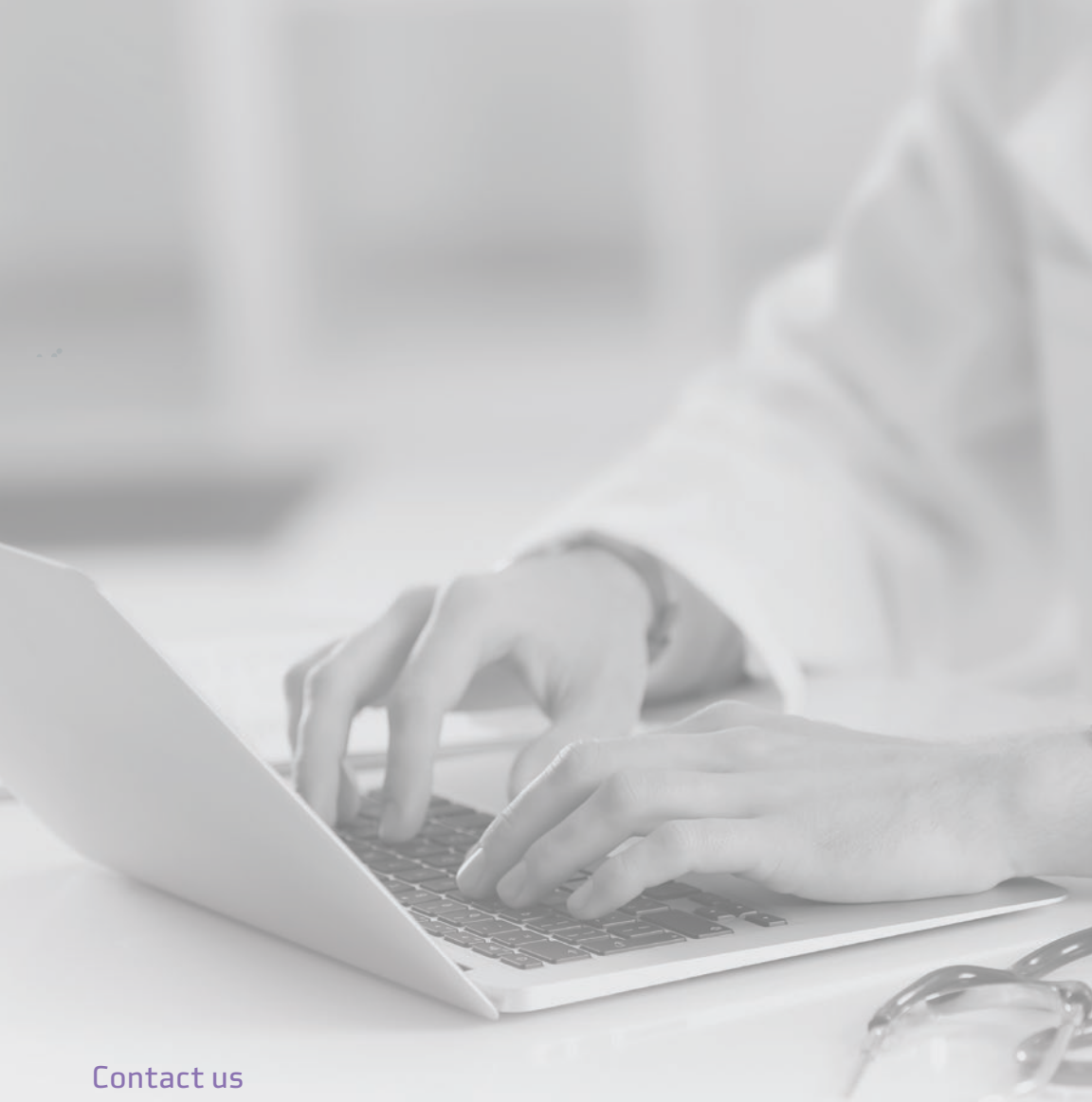
> Your vendors have to be enthusiastic about this. They have to be willing to think outside the box, but also maintain the fundamentals, in order to make this work to help the patients. Because ultimately that's what we're really trying to do — improve the lives of patients.
>
> **— Lisa Killi**
> Director of Clinical Supplies Management, *Bellerophon*

The Takeaway

DtP presents a number of challenges while creating an opportunity for more patient-centric trials that can result in higher recruitment rates with the right planning and technology in place. However, it is still largely uncharted territory. eClinical systems must be equipped to handle a variety of regulatory and study-specific idiosyncrasies and unknowns. An IRT that can do that while creating efficiencies within patient and clinical supply logistics is an invaluable asset to a study team pioneering newer and less familiar trial territory.

By adding simple functionality into the IRT system, Direct-to-Patient trials can become easier to run and therefore allow study teams to truly focus on their patients.

Clinical trials will only continue to become more complex and patient-centric as the clinical and cultural landscape evolves. Sponsors jumping into the DtP arena are paving the way towards a better future for everyone, and as an eClinical technology provider, Suvoda is committed to providing steadfast partnership, and the software and services necessary to create sustainable improvements for clinical teams.



Contact us

Speak with an IRT expert about your specific business needs.
Email us at salesinfo@suvoda.com or call one of our locations below.

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