Case study

ActiGraph

Enhancing clinical insights: De-risking traditional outcome measures in Bellerophon Therapeutics REBUILD study

About ActiGraph

ActiGraph provides end-to-end digital health technology (DHT) solutions by integrating and operationalizing the best hardware, software, and algorithms. This generates reliable evidence and delivers the right treatments to patients faster.

The opportunity

- While traditional clinical outcome assessments (COAs) and endpoints like oxygen saturation (SpO_2) and 6-minute walk distance (6MWD) provide valuable insights, they may not fully capture the scope of a treatment's effectiveness.
- Digital endpoints, such as those measuring physical activity (PA) using wearable technology, offer a complementary assessment by providing continuous, objective, real-world data as a direct measure of the patient's health and functioning.
- This can revolutionize measuring efficacy, offering stronger evidence for regulatory approvals and support for advancing to later trial phases.

The challenge

- Bellerophon Therapeutics faced a significant challenge in its Phase 2b clinical trial. While clinically positive, traditional COA endpoints like SpO_2 and 6MWD did not achieve statistical significance.
- This lack of strong statistical evidence hindered the progression to a Phase 3 clinical trial, placing the entire development program at risk if they could not demonstrate treatment efficacy.

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The approach

- To address this challenge, Bellerophon incorporated ActiGraph's DHT into their study as an exploratory endpoint, focusing on changes in study participants' PA—specifically, the analysis centered on the change in Moderate to Vigorous PA (MVPA) from baseline.
- The DHT allowed for continuous monitoring and provided a more patient-centered and objective assessment of treatment efficacy. MVPA showed clinically and statistically significant improvements with the treatment, offering a stronger and more convincing measure of efficacy than traditional endpoints.

The impact

- ✔ The digital endpoint (MVPA) provided the necessary statistical significance and gained FDA endorsement as the sole primary endpoint for Bellerophon's follow-up Phase 3 pivotal trial. This milestone marked the first time an FDA-endorsed primary endpoint in a pivotal trial was based on wearable data and saved the clinical development program.
- ✔ The substantial effect size from the Phase 2 data prompted FDA approval to reduce the sample size of the Phase 3 trial from 300 to 140, speeding completion by 18 months and reducing costs. ActiGraph's PA digital endpoints saved the program and enabled more efficient, patient-centered confirmatory studies.

> "The approval of a digital measure as a primary endpoint in a Phase 3 pivotal trial marks a major milestone for the industry. This achievement highlights Bellerophon's commitment to identifying a clinically meaningful, patient-centric outcome and the FDA's openness to collaborating with the industry to advance trial design. It's a pivotal step forward, demonstrating the possibilities that digital transformation brings to clinical research."

— Christine Guo, PhD
Chief Scientific Officer, ActiGraph

This case study was based on data gathered from the following study: **A Study to Assess Pulsed Inhaled Nitric Oxide in Subjects With Pulmonary Fibrosis at Risk for Pulmonary Hypertension (REBUILD)**.