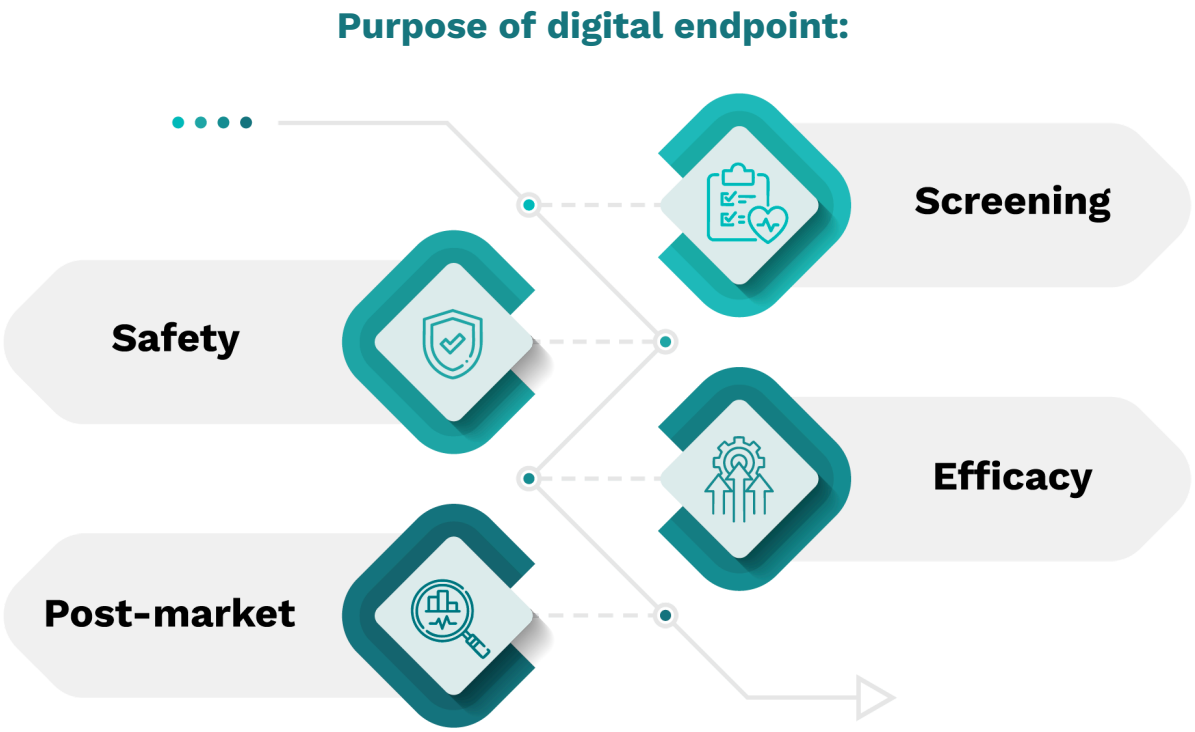
Digital Endpoints Value Framework

Your first step in leveraging digital endpoints is identifying their value across each phase of a clinical trial. Use this value framework to define key drivers at every stage and outline the conditions needed to maximize their impact.

Start at any stage to identify value drivers, measure impact, and maximize success.



Screening

Enroll the right participants through objective, real-world measures

Trial phases used: Phase I, II, III: Remote pre-screening to identify eligible participants and enrich the target population based on real-world behaviors/ symptoms

Value of digital endpoints (vs. traditional endpoints)	**Conditions that must be met** to realize the value of digital endpoints
✔ Faster recruitment leads to reduced recruitment costs and trial delays due to efficient, remote identification of eligible participants ✔ Increased access to representative patient populations due to decentralized recruitment ✔ Better identification of target population due to increased sensitivity enabled by frequent, objective, and continuous measurement	• Digital measures are valid for inclusion/exclusion criteria • Seamless integration with recruitment workflows • High participant adherence during screening For digital endpoints at all stages, the following must be met: • High participant adherence to device use and the V3+ framework

Case studies and evidence

- Multimodal digital health technologies (DHTs) allow for more efficient and less costly recruitment and reduced patient burden with decentralized clinical trials
- Estimating the benefits of digital and plasma-based pre-screening in Alzheimer's Disease trial recruitment

Safety

Continuous, real-time monitoring of early safety signals

Trial phases used:

- Phase I & II: Early detection of adverse events
- Phase IV: Long-term safety surveillance

Value of digital endpoints (vs. traditional endpoints)	**Conditions that must be met** to realize the value of digital endpoints
✔ Near real-time safety monitoring ✔ Comprehensive and earlier detection of adverse events (subtle, cumulative, or transient events) ✔ Enhanced participant protection and improved adverse event resolution due to earlier detection and intervention ✔ Improved patient experience of monitoring at home as compared to in-clinic	• Identify appropriate safety signals • Establish feasibility and validity of this signal to be collected remotely using digital health technologies (DHTs) • Clear safety thresholds and event notifications • A triage protocol to review safety signals and weed out false positives • Robust data monitoring infrastructure For digital endpoints at all stages, the following must be met: • High participant adherence to device use and the V3+ framework

Case studies and evidence

- Next-generation implementation of chimeric antigen receptor T-cell therapy using digital health
- Smart devices to measure and monitor QT intervals

Efficacy

Measure of treatment efficacy and benefit

Trial phases used:

- Phase I: Disease extension cohorts
- Phase II POC: Early efficacy proof in smaller populations
- Phase III: Confirmatory evidence of efficacy
- Phase IV: Real-world insights

Value of digital endpoints (vs. traditional endpoints)	**Conditions that must be met** to realize the value of digital endpoints
✔ Higher frequency, continuous, and ecologically valid measurement of treatment effects ✔ Earlier go/no-go decisions due to improved data-driven decision-making ✔ Reduced recall bias through objective, passive, and real-time data collection ✔ Improved ability to detect treatment effects via more frequent, more precise, and/or less variable objective measures ✔ Remotely collected, objective measures of additional treatment benefits ✔ Reduced sample size due to improved ability to detect treatment effect ✔ Reduced trial time due to the ability to detect treatment effects sooner	• Efficacy requirement is pre-specified in the protocol and statistical analysis plan • Regulatory alignment on endpoint relevance and use for phase III studies For digital endpoints at all stages, the following must be met: • High participant adherence to device use and the V3+ framework

Case studies and evidence

- Impacts on study design when implementing digital measures in Parkinson's disease-modifying therapy trials
- Quantifying the Benefits of Digital Biomarkers and Technology-Based Study Endpoints in Clinical Trials: Project Moneyball
- Ponsegromab for the treatment of cancer cachexia

- Estimating the benefits of digital and plasma-based pre-screening in Alzheimer's Disease trial recruitment
- Advancing digital biomarkers to accelerate Parkinson's disease drug development
- Enhancing clinical insights: De-risking traditional outcome measures in Bellerophon Therapeutics REBUILD study
- Value of novel digital endpoints in late-stage trials
- Simulator of study power for Parkinson's Disease trials
- Multimodal digital measures demonstrate greater responsiveness and sensitivity to disease progression and treatment effects than traditional clinical scales
- Driving innovation in Huntington's Disease by tracking progression through at-home digital measurements
- Advancing nano-rare disease treatment with Syde technology in clinical trials
- Accelerated trial setup & operations: A case study in Cystic Fibrosis to illustrate the ROI of improved data availability

Post-market

Monitor ongoing safety, effectiveness, and potential for label expansion in real-world use

Trial phases used: Phase IV: Real-world evidence generation for safety, effectiveness, and new insights

Value of digital endpoints (vs. traditional endpoints)	**Conditions that must be met** to realize the value of digital endpoints
✔ Potential for additional label claims through the collection of more comprehensive and continuous data allowing sponsors to investigate additional therapeutic benefits on measures meaningful to patients ✔ Informs post-market recommendations, such as off-label use and new indications ✔ Informs market access and reimbursement by generating objective, real-world data	• Long-term participant retention and digital health technology adherence • Integration with healthcare data systems (EHRs, registries) • Scalable infrastructure for global data collection • Ongoing regulatory engagement to align real-world evidence use For digital endpoints at all stages, the following must be met: • High participant adherence to device use and the V3+ framework

Case studies and evidence

- Developing a novel measurement of sleep in rheumatoid arthritis: Study proposal for approach and considerations