WHITE PAPER

Phase-by-phase endpoint strategy guide for obesity and diabetes drug development

Supporting sponsors through each phase and endpoint

Jessica Emerson, M.S., Ph.D.
Vickas Patel, M.D., Ph.D.
Mark W. Tengowski, M.S., Ph.D.

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Introduction

Obesity and diabetes trials increasingly require sponsors to manage multiple, clinically connected endpoint areas at the same time: cardiovascular safety, glycemic control, participant experience, connected glucose monitoring and body composition analysis. As GLP-1–based therapies expand across obesity and adjacent cardiometabolic conditions, these endpoints are becoming more demanding and more interdependent.

However, these endpoints are still often planned and run across separate workstreams, vendors, systems and review processes. Fragmented data collection adds unnecessary complexity, reduces operational efficiency and can obscure clinically meaningful signals.

A therapy that reduces visceral fat, lowers blood pressure, improves glycemic time in range and supports meaningful patient-reported outcomes may tell a compelling cardiovascular-metabolic benefit story. However, that story is credible only when the underlying datasets are prospectively planned, consistently collected and reviewed on a coordinated participant-level timeline.

Recent FDA draft guidance for obesity and overweight drug development highlights the importance of cardiovascular safety evaluation, blood pressure monitoring, metabolic assessment and patient-focused outcomes.[1] It also indicates that additional cardiovascular evaluation may become important when safety signals emerge during development.

For sponsors, this reinforces the need to think beyond individual endpoint collection and toward an integrated endpoint strategy.

Supporting obesity, diabetes and GLP-1 development

Clario helps sponsors translate complex obesity, diabetes and GLP-1 endpoint requirements into coordinated, operationally feasible study designs. Our experience across cardiac safety; electronic clinical outcome assessment (eCOA) with integrated, connected blood glucose monitoring (BGM)/continuous glucose monitoring (CGM) devices; and centralized medical imaging supports cleaner data, faster signal interpretation and more coherent evidence packages.

By aligning endpoint strategy, device workflows, site training, participant support, data review and regulatory readiness planning, Clario helps sponsors reduce avoidable variability before it scales across global studies.

1,040+
diabetes and weight management trial opportunities

250+
GLP-1 opportunities supported

ALL
FDA and EMA-approved GLP-1 agonists supported*

*Accurate as of April 2026, based on FDA and EMA approvals

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Phase I: First-in-human and early safety

Phase I studies are designed to characterize safety, tolerability and pharmacokinetics in a controlled setting. As hybrid designs increasingly include overweight or obese participant cohorts, sponsors have an early opportunity to identify cardiovascular, glycemic, patient-reported and body composition signals before committing to larger participant trials.

Phase I is not only a safety checkpoint but also the foundation for endpoint selection, data linkage and operational feasibility.

What matters most in Phase I

Cardiac safety

The primary cardiac safety objective in Phase I is often QTc interval assessment under the ICH E14/S7B framework, using pharmacokinetically matched ECGs and concentration-QTc modeling.[2]

GLP-1 receptor agonists and other metabolic therapies can alter heart rate in ways that complicate standard QTc correction formulas. Applying individualized or supine heart rate correction early can reduce interpretive uncertainty, because clean drug-free baseline data become harder to collect in later-phase trials.

In hybrid Phase I cohorts that include overweight or obese participants, 24-hour ambulatory blood pressure monitoring, (ABPM) can provide an early view of hemodynamic drug effects that standard clinic blood pressure testing may miss.

eCOA with BGM/CGM connected devices

Integrated electronic patient-reported outcomes (ePRO) with Bluetooth-enabled BGM supports safety characterization and hypoglycemia event assessment. BGM helps confirm hypoglycemia events, while ePRO captures symptoms, fasting status, study drug timing, rescue actions and other participant-reported context.

CGM may be incorporated exploratorily in Phase I to characterize glucose trends across the dosing period. At this stage, CGM is often most useful for directional insight rather than confirmatory endpoint evidence.

Phase I can also be used to assess candidate participant experience instruments for initial signals and design features such as timing before they are deployed at scale.

Medical imaging

Medical imaging in Phase I is typically selective rather than routine, because body composition, lean mass and bone mineral density (BMD) changes often require longer dosing periods to become meaningful. When included, dual x-ray absorptiometry (DXA) or magnetic resonance imaging (MRI) can establish baseline fat mass, lean mass, visceral adiposity and BMD for later interpretation. MRI-proton density fat fraction (PDFF) may be useful in short Phase Ib proof-of-mechanism studies when hepatic fat or ectopic fat reduction is mechanistically relevant, as liver fat changes may be detectable within weeks.

Phase I

Endpoint integration

A participant with a blood pressure change on ABPM and a concurrent BGM-confirmed hypoglycemia event may require integrated safety interpretation. Were the signals temporally related? Do symptoms, fasting status, dose timing or glucose trend data provide context? Those questions are answerable only when cardiac safety, eCOA with BGM/CGM and medical imaging data sit on a common participant timeline.

Sponsor decision checklist

- ☐ Have QTc and heart rate correction requirements been defined?
- ☐ Is ABPM needed for early hemodynamic signal detection?
- ☐ Are BGM/ePRO workflows designed for contemporaneous hypoglycemia capture?
- ☐ Should exploratory CGM be included to characterize glucose patterns?
- ☐ Are baseline body composition measurements needed to support Phase II/III interpretation?
- ☐ Are candidate participant experience instruments being tested for later use?

Phase II: Proof of concept and dose optimization

Phase II expands the program from early safety to dose response, preliminary efficacy, endpoint feasibility and participant-level signal interpretation. Participants are more likely to have cardiovascular disease, metabolic comorbidities, background medications, abnormal baseline ECGs and variable glucose patterns.

This makes standardized endpoint collection and expert interpretation essential. The endpoint decisions made in Phase II directly influence whether Phase III is adequately designed, appropriately powered, operationally feasible and scientifically coherent.

What matters most in Phase II

Cardiac safety

Frequent 12-lead ECG collection at protocol-defined intervals remains central in Phase II obesity and diabetes trials. In these populations, the risk is not only missed safety signals but also false-positive findings generated by automated ECG algorithms or local interpretations that may not account for non-standard morphologies, comorbid disease or participant-level variability.

Centralized ECG collection and cardiologist overread through a cardiac core laboratory can reduce false positives, protect participant safety and support consistent decision-making across sites.

Blood pressure is also an important endpoint in many obesity and diabetes programs, particularly when the investigational therapy may affect cardiovascular physiology or metabolic risk factors. FDA draft obesity guidance highlights the importance of blood pressure monitoring in obesity drug development,[1] and FDA pressor-effect guidance recommends systematic premarketing assessment of drug effects on blood pressure when relevant.[3]

A practical Phase II design may pair a pre-dose 24-hour ABPM baseline with a second assessment at pharmacodynamic steady state, often four to twelve weeks post-dose. Standardized technique, calibrated devices and automated ABPM upload reduce operational variability and improve endpoint sensitivity.

eCOA with BGM/CGM connected devices

In Phase II, hypoglycemia becomes a clinically meaningful safety endpoint. FDA diabetes endpoint guidance discusses hypoglycemia assessment, including clinically significant and severe events, as important safety outcomes in antidiabetic drug development.[4]

Integrated BGM and ePRO workflows help link glucose values with symptoms, rescue actions, timing, participant status and situational context. This reduces the interpretive gaps created when glucose readings, symptoms and event narratives sit in separate systems.

CGM is increasingly used as a supportive or secondary endpoint to capture glycemic patterns that point-in-time BGM may miss, including nocturnal hypoglycemia, post-prandial excursions, time in range, time below range and glucose variability. International consensus supports standardized CGM metrics in prospective clinical studies when implemented with appropriate data sufficiency and reporting standards.[5]

Participant experience also moves from feasibility to evidence generation in Phase II. Validated PRO instruments for weight-related function, treatment satisfaction, hunger and craving, gastrointestinal tolerability and quality of life can support dose selection and benefit-risk understanding.[6,7] Commonly

considered PRO instruments include the Columbia-Suicide Severity Rating Scale (C-SSRS), Patient Health Questionnaire (PHQ)-9, SF-36, Impact of Weight on Quality of Life (IWQOL)-Lite, Ask Suicide-Screening Questions (ASQ) and Three-Factor Eating Questionnaire (TFEQ).

Medical imaging

Phase II is where imaging can become a direct measure of drug effect, particularly when body composition, regional adiposity, hepatic fat, lean mass or bone safety are important to the program narrative. DXA is the cornerstone for total and regional fat mass, lean mass and BMD assessment, while MRI provides greater precision for regional and organ-specific fat depots, including visceral, hepatic, pancreatic and intramuscular fat.

MRI-PDFF can serve as an early translational biomarker for hepatic fat reduction and may support proof-of-concept and dose-selection decisions. A ≥30% relative reduction is commonly used as a response threshold, although absolute change from baseline should also be considered.[8] Lean mass should be monitored alongside fat loss when clinically relevant, particularly in older adults or other sarcopenia-prone populations.

Phase II

Endpoint integration

A reduction in visceral fat on DXA or MRI, lower blood pressure on ABPM, improved CGM time in range and favorable participant-reported function can create a coherent cardiovascular-metabolic benefit narrative. No single endpoint can establish that story alone. It depends on cardiac safety, eCOA with BGM/CGM connected devices and medical imaging being planned, collected, reviewed and interpreted together.

Sponsor decision checklist

- ☐ Which endpoints will carry forward into Phase III?
- ☐ Is ABPM needed to support blood pressure interpretation?
- ☐ Do you have an adequate number of 12-lead ECGs at the appropriate time points?
- ☐ Are BGM, CGM and ePRO data linkable at participant level?
- ☐ Are PRO instruments fit for purpose for the target indication and population?
- ☐ Is lean mass being monitored alongside fat loss?
- ☐ Are imaging endpoints exploratory, supportive or central to the regulatory narrative?

Phase III: Confirmatory evidence and regulatory submission

Phase III tests whether endpoint strategy can scale. Sponsors must preserve endpoint precision, participant-level context and inspection readiness across large populations, global sites, multiple languages and long study durations. At this stage, site execution becomes part of endpoint quality. Standardized training, clear escalation pathways, device accountability, centralized review and proactive data monitoring help reduce protocol deviations and missing or unusable data.

What matters most in Phase III

Cardiac safety

Regular 12-lead ECG monitoring continues at protocol-defined intervals at global scale. Centralized reading helps ensure that safety findings are interpreted using a consistent expert standard across countries, sites and time points.

Phase III should also be designed with cardiovascular outcome trial (CVOT) readiness in mind when the mechanism, population, prior signals or regulatory strategy suggests that cardiovascular outcome assessment may become important. FDA draft obesity guidance indicates that cardiovascular safety signals observed earlier in development may require additional cardiovascular evaluation.[1]

CVOTs require independent Clinical Events Committee processes for event identification, source document management and formal adjudication of major adverse cardiac events, including cardiovascular death, non-fatal myocardial infarction and non-fatal stroke. Sponsors that proactively build CVOT-ready data architecture can avoid the delays and complexity of retrofitting adjudication workflows after a signal emerges.

eCOA with BGM/CGM connected devices

Phase III eCOA, BGM and CGM generate safety and efficacy evidence for regulatory review. FDA diabetes guidance continues to position HbA1c as a central efficacy endpoint in antidiabetic drug trials, while hypoglycemia remains a key safety outcome requiring standardized collection.[4] EMA diabetes guidance similarly emphasizes rigorous glycemic endpoint characterization and hypoglycemia assessment in pivotal diabetes trials.[9]

At-home ePRO with BGM integration automates data transfer and in-the-moment participant reporting on glucose readings for safety reporting. CGM supports efficacy endpoints defined around time in range, nocturnal hypoglycemia and glucose variability and is typically collected during specific protocol-defined periods.[5]

PROs carry the participant voice into the benefit-risk package and can support labeling discussions when appropriately designed.FDA PRO and PFDD guidances emphasize validated instruments, fit-for-purpose assessments and documentation sufficient to support regulatory interpretation.[1,6,7]

Inspection-ready eCOA and BGM/CGM data require audit trails, 21 CFR Part 11 controls, multilingual deployment, reminders and alerts for at-home data collection, participant training and data review processes that can withstand global scale for real-time data oversight of compliance, missingness and data quality.

Medical imaging

In Phase III, imaging can provide objective, quantitative evidence of treatment effect on body composition and safety. Longitudinal DXA and MRI may help sponsors characterize fat mass, lean mass, regional adiposity, hepatic fat and organ-specific fat changes.

For longer-duration studies, BMD monitoring may be an important safety consideration, particularly in populations vulnerable to bone loss or fracture risk, such as older adults and post-menopausal women.

Centralized image review, protocol harmonization, quality control and expert reader oversight are essential. Multi-site imaging variability can otherwise obscure true treatment effects or create avoidable regulatory questions at submission.

Phase III

Endpoint integration

In a Phase III CVOT, a MACE event may raise adjudication questions that span multiple endpoint areas. Was the event temporally linked to a hypoglycemia episode? Were there concurrent blood pressure changes? Did the participant have a documented lean mass trajectory? Were symptoms, function and rescue actions captured close to the event? These questions are answerable only when cardiac safety, ePROs, eCOA with BGM/CGM connected devices and medical imaging data are collected to a common quality standard with complete participant-level linkage.

Sponsor decision checklist

- ☐ Are endpoint workflows scalable across countries, languages, and sites?
- ☐ Are cardiac events and glucose events linkable for adjudication?
- ☐ Do you have an adequate number of 12-lead ECGs at the appropriate time points?
- ☐ Are PRO instruments fit for purpose and deployed consistently at global scale?
- ☐ Are BGM/CGM integrations scalable, and are the data available for real-time oversight of compliance?
- ☐ Are imaging protocols standardized across all sites?
- ☐ Is the dataset inspection-ready from acquisition through submission?
- ☐ Is CVOT-ready architecture in place if a cardiovascular signal emerges?

Beyond approval: Post-market commitments and long-term safety surveillance

Regulatory approval does not end endpoint responsibility. Depending on the therapy's mechanism, observed safety profile, regulatory feedback and target population, sponsors may need to support post-approval CVOT commitments, long-term BMD monitoring, blood pressure surveillance, ECG pharmacovigilance, registry studies, observational programs or real-world patient-experience research.

Sponsors who maintain endpoint continuity across development and post-market phases benefit from consistent data standards, protocol knowledge, validated patient experience instruments, device workflows, imaging methods and adjudication history. This turns ongoing surveillance into an extension of the development program rather than a new operational build.

Conclusion

Cardiovascular safety, glycemic control, participant experience, connected glucose monitoring and body composition are not independent workstreams. They are interconnected dimensions of a single evidence story.

Sponsors who manage these endpoints together generate cleaner data, respond to safety signals faster and build regulatory packages that are easier to interpret. Coordinated endpoint planning also reduces site burden by standardizing workflows, training, device logistics, participant support, data review expectations and escalation pathways before global scale magnifies variability.

Clario brings scientific depth, global operational infrastructure and regulatory experience across cardiac safety, eCOA with BGM/CGM connected devices and medical imaging. The value is not only execution within each domain but also the ability to align endpoint strategy, timing, data standards, participant-level linkage, site execution and review processes from first participant to final submission.

Integrated capabilities summary

A single partner across every phase and endpoint

Phase	Cardiac safety	eCOA with BGM/CGM connected devices	Medical imaging
Phase I	▪ QTc strategy ▪ ICH E14/S7B alignment ▪ Concentration-QTc modeling ▪ Heart rate correction ▪ ABPM in hybrid cohorts	▪ BGM-based safety data ▪ Electronic diary ▪ Near-real-time review ▪ Exploratory CGM ▪ PRO feasibility testing ▪ Participant onboarding	▪ Baseline DXA/MRI ▪ Visceral fat and lean mass reference measurements ▪ Body composition risk stratification
Phase II	▪ Central ECG overread ▪ 24-hour ABPM ▪ Standardized BP collection ▪ Cardiac core lab review	▪ Level 2/3 hypoglycemia data via integrated BGM + ePRO ▪ Supportive CGM for time in range and variability ▪ Fit-for-purpose PROs ▪ Compliance support	▪ DXA fat/lean/BMD ▪ Regional fat including VAT, SAT, liver and pancreas ▪ MRI precision imaging ▪ Lean mass monitoring
Phase III	▪ Global ECG monitoring ▪ CVOT readiness ▪ MACE adjudication ▪ CEC management ▪ Cardiac safety review	▪ Confirmatory BGM/CGM ▪ Validated PROs ▪ PFDD alignment ▪ Multilingual deployment ▪ 21 CFR Part 11 readiness ▪ Inspection-ready workflows	▪ Confirmatory DXA/MRI ▪ BMD safety monitoring ▪ Organ-specific fat ▪ Centralized imaging QC ▪ Expert reader oversight
Beyond approval	▪ Post-market CVOT support ▪ Blood pressure surveillance ▪ ECG pharmacovigilance	▪ Real-world PRO/eCOA ▪ Long-term patient experience data ▪ Connected glucose monitoring workflows	▪ Long-term BMD monitoring ▪ Body composition surveillance ▪ Visceral fat and regional fat assessment

Discuss your program with Clario.

Clario's cross-functional teams support endpoint strategy, protocol design, operational planning and global delivery across all phases of obesity and diabetes development. Whether you are designing an early-phase GLP-1 study, preparing for Phase III scale or planning long-term safety monitoring, Clario can help align cardiac safety, eCOA with integrated BGM/CGM and medical imaging into a coordinated evidence strategy.

Contact your Clario representative at clario.com

References

1. "Obesity and Overweight: Developing Drugs and Biological Products for Weight Reduction. Draft Guidance for Industry." U.S. Food and Drug Administration, January 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/obesity-and-overweight-developing-drugs-and-biological-products-weight-reduction (Accessed 28 May 2026).
2. "E14 and S7B Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential: Questions and Answers." U.S. Food and Drug Administration, August 2022, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e14-and-s7b-clinical-and-nonclinical-evaluation-qtqtc-interval-prolongation-and-proarrhythmic (Accessed 28 May 2026).
3. "Assessment of Pressor Effects of Drugs Guidance for Industry." U.S. Food and Drug Administration, February 2022, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/assessment-pressor-effects-drugs-guidance-industry (Accessed 28 May 2026).
4. "Diabetes Mellitus: Efficacy Endpoints for Clinical Trials Investigating Antidiabetic Drugs and Biological Products." U.S. Food and Drug Administration, May 2023, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diabetes-mellitus-efficacy-endpoints-clinical-trials-investigating-antidiabetic-drugs-and-biological (Accessed 28 May 2026).
5. Battelino, Tadej et al. "Continuous glucose monitoring and metrics for clinical trials: an international consensus statement." *The lancet. Diabetes & endocrinology* vol. 11,1 (2023): 42-57. doi:10.1016/S2213-8587(22)00319-9
6. "Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments." U.S. Food and Drug Administration, October 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-selecting-developing-or-modifying-fit-purpose-clinical-outcome (Accessed 28 May 2026).
7. "Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims." U.S. Food and Drug Administration, December 2009, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims (Accessed 28 May 2026).
8. Stine, Jonathan G et al. "Change in MRI-PDFF and Histologic Response in Patients With Nonalcoholic Steatohepatitis: A Systematic Review and Meta-Analysis." *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association* vol. 19,11 (2021): 2274-2283.e5. doi:10.1016/j.cgh.2020.08.061
9. "Clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus. Revision 2." European Medicines Agency, January 2024, https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-or-prevention-diabetes-mellitus-scientific-guideline (Accessed 28 May 2026).

About Clario

Clario is a leading provider of endpoint data solutions to the clinical trials industry, generating high-quality clinical evidence for life sciences companies. We offer comprehensive evidence-generation solutions that combine medical imaging, eCOA, precision motion, cardiac and respiratory endpoints.

For more than 50 years, Clario has delivered deep scientific expertise and broad endpoint technologies to help transform lives around the world. Our endpoint data solutions have been deployed over 30,000 times to support clinical trials in more than 100 countries. Our global team of science, technology, and operational experts have supported over 70% of all FDA drug approvals since 2015.