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INNOVATIVE ANALYTICS SOLUTIONS

Introducing KerusCloud 2023

Revolutionising clinical trial design with *in silico* studies using synthetic patient-level data.

KerusCloud®

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Improving Clinical Trial Success with New Approaches and Technologies

Huge patient-burden, time and costs are involved in developing new clinical treatments. This makes current trial failure rates untenable for the healthcare industry long-term. Whilst failure rates vary according to development phase and disease area, overall, over 90% of investigational treatments in clinic never reach the market [1] impacting return on R&D investment worldwide. Yet many failures could be avoidable due to flaws in study planning. Common flaws include the wrong choice of study design, improper dose selection, non-optimal or inappropriate efficacy assessment schedules, and unsuitable inclusion or exclusion (eligibility) criteria. These flaws can now be addressed prospectively by new technologies revolutionising the use of data to help design more effective and successful trials.

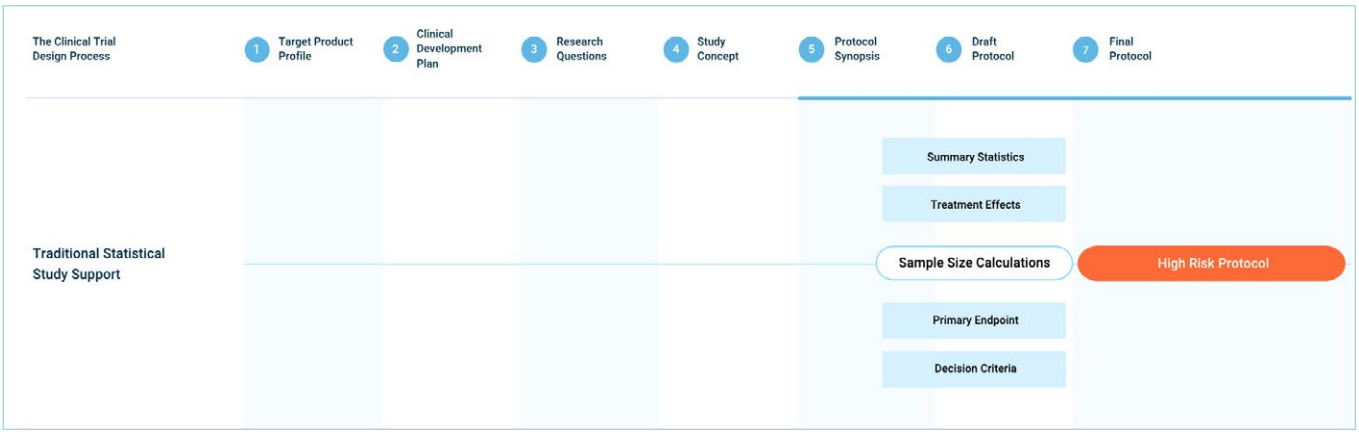
Regulators Recognise the Need for Transformation

The FDA and EMA are recognising the need to improve clinical development outcomes. In 2021 the **FDA** published their new areas of focus which highlighted complex innovative trial design, the use of biomarkers, model informed drug development and real-world evidence to support decision-making. Similarly, the **EMA's** strategic reflection to 2025 listed five core recommendations which could deliver the most significant change. These were innovation in clinical trials, real-world data in decision-making, reinforcing patient relevance in evidence generation, decision-making for innovative medicines and developments in precision medicine, biomarkers and omics. This increased focus by Regulators in these areas underlines the need for **better use of existing data, better understanding of patients and better study designs and decision-making.**

Traditional Approach to Designing Trials

Traditional statistics support for designing clinical studies (Figure 1) often starts late and can be limited to a sample size calculation or justification once most other decisions have already been made. This unintegrated approach to decision-making represents a missed opportunity to leverage data insights to de-risk clinical studies upfront by accounting for the uncertainties and complexity found in real studies. This over-simplistic approach can set up a study for failure with a **high-risk clinical protocol.**

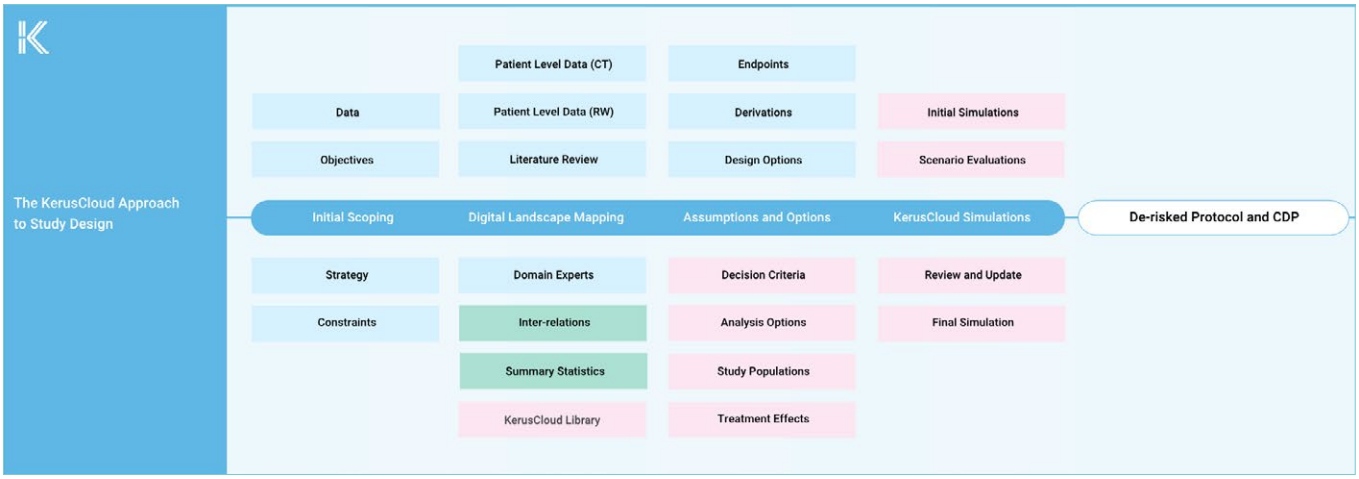
Figure 1. Traditional statistics support during the clinical trial design process.



A More Holistic Approach to Designing Trials

KerusCloud clinical trial simulation software offers a data-driven approach to trial planning and design (**Figure 2**), supporting end-to-end collaborative engagement on all crucial design decisions between clinical teams and statisticians. Its use ensures that the right data is collected in the right patients in the right way and provides quantitative insights that inform decision-making at all the key stages. This approach starts with early support in setting the overarching strategy with the target product profile and clinical development plan, help in identifying the important research questions and study concept, to finally drawing up a protocol synopsis and draft protocol to deliver a substantially **de-risked final protocol.**

Figure 2. End-to-end KerusCloud support during clinical trial design.



Leveraging Data Insights with KerusCloud to Deliver Evidence-Based Design

1. Building a data resource for a disease area or intervention of choice KerusCloud supports important decisions on development strategy by leveraging data insights to deliver robust and achievable plans. It uses a wide variety of data sources to inform and generate true-to-life *in silico* trials. Common data sources for KerusCloud include disease registries, historical trial data, the published literature and real-world data, as well as information from domain experts. Summary and patient-level data are collated into a data library by the Exploristics Data Strategy team centred around the disease area or intervention of choice and used to build a data model for a given project. This library can be updated allowing the project to stay responsive to emerging clinical developments, building a valuable and evolving knowledge resource that can be easily audited, reviewed and re-used.

2. Simulating life-like clinical trials to de-risk designs Data from the library is then used to build a bespoke data model. To do this, it is broken down into its key components (e.g., endpoints and risk factors) before being cleaned, standardised, curated and aligned. It is then transformed into a data model using Exploristics' Data Model Builder and loaded into KerusCloud. Here, it is used to create highly realistic patient-level synthetic datasets which accurately describe real data characteristics but avoid infringing patient privacy. These synthetic data can then be sampled to **build** virtual patient populations of interest which mimic the complexity and quirks of real subject-level patient data, such as non-random missingness and intercurrent events. Using these populations, it is possible to quickly **simulate** life-like clinical trials *in silico*, to test different 'what if' study scenarios or

study unknowns. KerusCloud quantifies the probability of success for scenarios comprised of both controllable and uncontrollable factors. This allows clinical teams to interrogate and **analyse** the impact on study success of different **study assumptions** and **options** such as **endpoints, derivations, design options, decision criteria, analysis options, study populations** and **treatment effects**. Users can visualise results using an interactive heatmap (**Figure 3**) and amend study parameters in an iterative way to balance benefits and risks to **optimise** the design within the project constraints. This fast, prospective approach delivers a **de-risked clinical protocol and development plan**, reducing unnecessary patient burden, time and costs associated with failed trials.

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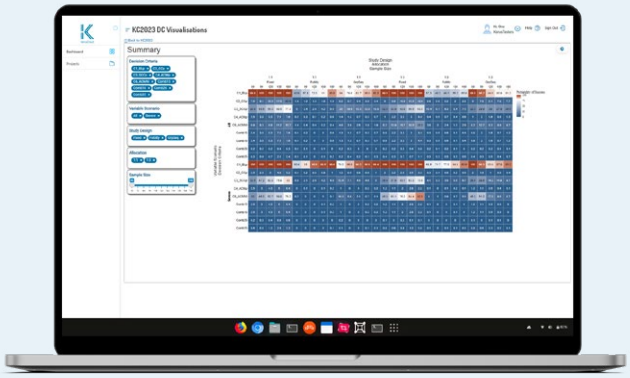
Figure 3. Scenario outcomes are easily visualised using a heatmap. Click below to explore this further in the KerusCloud Playground.

Visit Playground



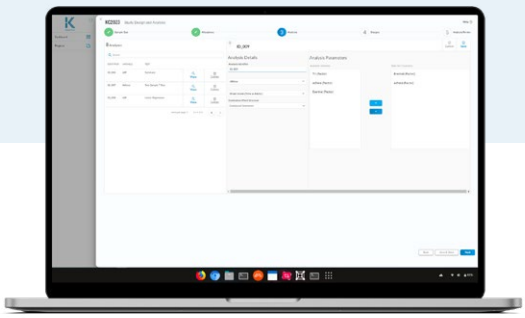
For Spring 2023 KerusCloud now also features:

- **Bayesian posterior probabilities**
  for greater flexibility in defining study success criteria.
- **Repeated measures**
  across multiple time points.
- **Enhanced estimand strategies**
  to ensure proper handling of intercurrent events and address Regulatory guideline, ICH E9 as recommended by the FDA and the EMA.
- **Estimands in the Context of Repeated Measures**
  so estimand conditions can be created and defined using repeated measures variables.
- **Visualisation of Virtual Population QC**
  so quality control (QC) checks can be run and visualised for virtual populations.
- **Live Notifications**
  of new features or scheduled maintenance for more effective planning and platform use.
- **KerusCredit Ledger**
  so KerusCredit usage for a project can be viewed and tracked.

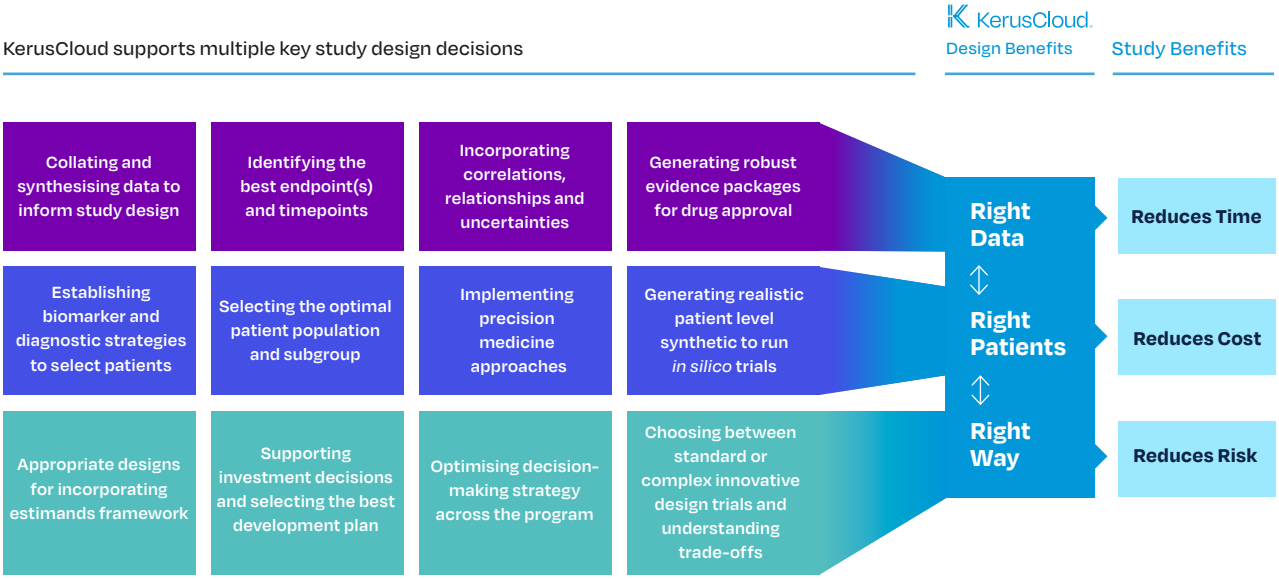
Transforming Development Success with KerusCloud

By supporting clinical teams to make the right study design decisions so that the **right data is collected in the right patients in the right way** (**Figure 4**), KerusCloud addresses some of Pharma's key challenges as well new areas of Regulatory focus to transform clinical development success. Integrating KerusCloud into an agile, collaborative data-driven approach to clinical protocol planning:

- **Reduces patient-burden, and the development risks and costs** that impact R&D ROI.
- **Provides more robust evidence packages** to meet regulatory hurdles.
- **Delivers faster, more efficient development** bringing treatments to market more quickly.
- **Supports precision medicine approaches** to address growing demand for more targeted medicines.
- **Leverages available and emerging data** more efficiently without infringing on patient privacy.
- **Navigates teams through large quantities of data** to inform better development decision-making.



KerusCloud supports multiple key study design decisions

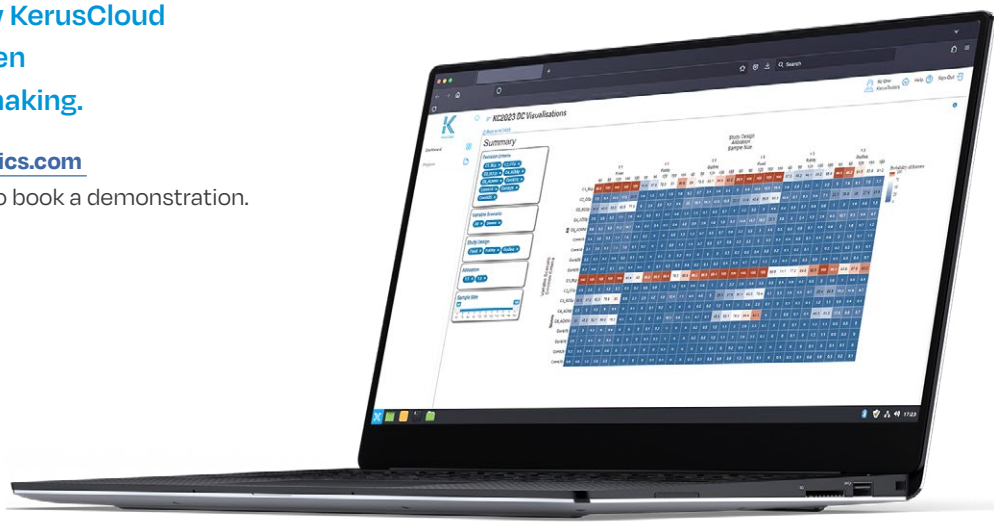


Six Reasons to Join the Clinical Trial Design Revolution Today

- **Most clinical trials currently risk failure** as they don't adequately consider sources of uncertainty.
- **Many trial failures could be prevented with better planning and design** using *in silico* trials.
- **Regulators indicate that trial designs should harness more data sources** to improve development.
- **Simulation of plausible 'what if' study scenarios ensures that clinical teams have a better understanding of the impacts of uncertainty and assumptions** on a given study.
- **Embedding *in silico* study design strategies as good practise de-risks clinical studies upfront** avoiding unnecessary failure due to poor design.
- **A more holistic and collaborative approach to clinical planning and study design a** guided by statisticians from the outset will improve evidence-based decision-making and study success.

Find out more about how KerusCloud delivers better data-driven development decision-making.

Contact **abbas.shivji@exploristics.com** today for more information or to book a demonstration.



References:

[1] Thomas DW et al. 2016 Clinical development success rates 2006-2015. Biotechnology Innovation Organization, Washington DC. June 2016

Further reading: https://exploristics.com/insights-white-papers/ ; https://exploristics.com/case-studies/