CERTARA

Phoenix WinNonlin

The Gold-Standard in Pharmacokinetic, Pharmacodynamic and Non-compartmental Analysis

Phoenix® WinNonlin® is the industry standard for the analysis of pharmacokinetic and pharmacodynamics data. The integrated tools for data processing, non-compartmental analysis (NCA), PK/PD modeling, post-analysis statistics, table creation, and graphics create an all-in-one collaboration workbench for analysts, reviewers, medical writers, and quality assurance team members. The intuitive graphical user interface allows users to spend less time learning the software and managing data and more time to model, interpret, and understand the data. The result? Efficient drug development decisions with more confidence.

Proven Software with a Vast Global Footprint

Phoenix WinNonlin has a proven 30-year history of providing trusted PK/PD analysis results. It is used by over 6,000 scientists in 60 countries at nearly 2,000 institutions, including the top 50 global pharmaceutical companies. Regulatory agencies, including 11 divisions of the US Food and Drug Administration (FDA), Japan Pharmaceutical and Medical Device Agency (PMDA), China Food and Drug Administration (CFDA), and the UK Medicines and Healthcare Products Regulatory Agency (MHRA), use Phoenix WinNonlin for analysis and to evaluate drug submissions.

The WinNonlin NCA Engine Can Do It All

The Most Comprehensive Set of Analysis Tools for any Non-clinical or Clinical PK/PD Study

From early non-clinical research to large clinical trials, the NCA engine, individual PK/PD modeling engine, and statistical analysis tools can be used for a wide-range of studies and analyses:

- Single, multiple or steady-state dosing
- Sparse sampling studies
- Drug concentration data in plasma or urine, or pharmacodynamics data
- Formulation comparison
- Toxicokinetics

- First-in-human
- Single and multiple ascending dose
- Drug-drug interaction
- Bioequivalence
- Mass balance

New in Phoenix WinNonlin

- New Ratios and Differences tool provides automated calculation of NCA ratios
- Additional descriptive statistics
- More flexible charting and plotting capabilities
- Additional new NCA parameters for plasma and urine
- User-defined NCA parameters
- Setting of criteria for the terminal slope calculation in NCA
- Enhanced fully-integrated Phoenix WinNonlin Validation Suite for fast automated software validation in under 30 minutes

Example of Lambda Z Rules for Best Fit Option: Before and After Setting "Start Time Not Before"

Statistical Tools Help Answer Critical Questions

Did the new formulation meet bioequivalence criteria? Is the exposure dose proportional? Did the drug cause an increase in a biomarker? Use statistical tools in WinNonlin to integrate and report inferential analysis of study results. New descriptive statistics have been added, including 2.5% and 97.5% percentiles, user-specified percentiles, sample and population statistics for skewness and kurtosis, and range, min and max when weighting is used.

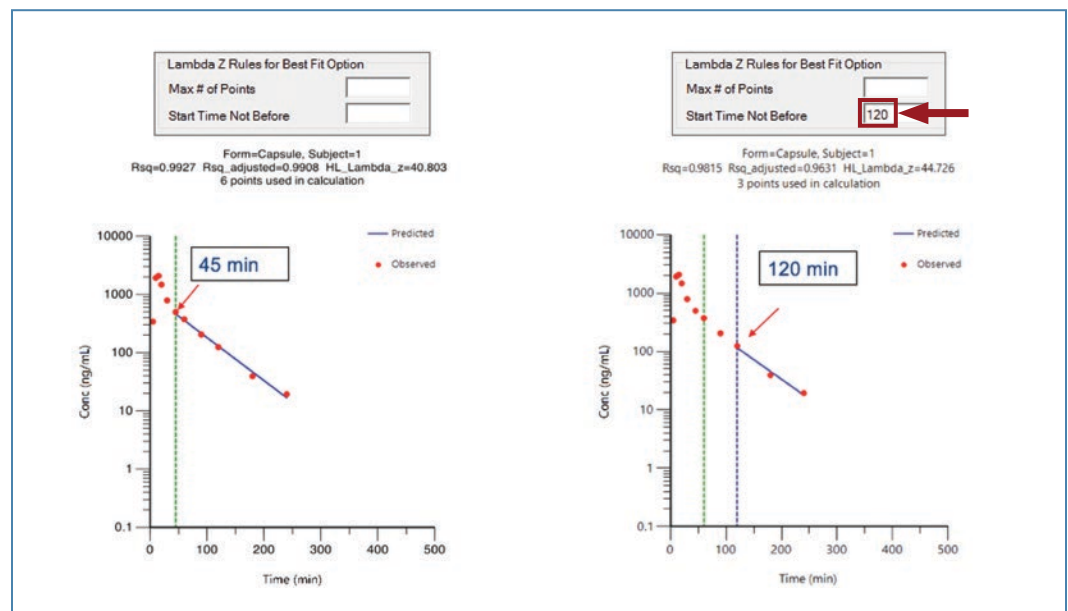|			
	Bioequivalence		Superposition
	Analysis of variance/General linear models		Semi-compartment modeling
	Deconvolution		Descriptive statistics

Phoenix WinNonlin takes non-compartmental analysis (NCA) to a new level by adding many commonly calculated NCA parameters to the standard output, providing the ability to define custom NCA parameters, business rules for calculating the terminal slope, and acceptance flags based on terminal slope quality assessments. These new features minimize post-processing work and increase transparency with analysis.

Business Rules for Terminal Slope Calculation

Organizations can set strict criteria for the calculation of the terminal slope in NCA. Those rules can be implemented directly in Phoenix's updated NCA tool. Users can specify the maximum number of points to be included in the regression or the earliest time to be used (see figure below). The settings are retained and can be reviewed for compliance with organization policies and procedures.

In addition, users can define acceptance criteria for adjusted r^2, % extrapolated AUC, or Span (lambda z sampling interval/$t_{1/2}$). All calculated values will be marked as meeting the criteria, not meeting the criteria, or missing. This permits easy post-processing of results based on quality standards for lambda z.

www.certara.com

# New Parameters for Non-compartmental Analysis

The automated calculation of over a dozen of parameters for plasma and urine will save time by reducing manual work and reduce errors with non-compartmental analysis in Phoenix WinNonlin.

- Plasma parameters
  - Swing (single dose and steady-state)
  - %Fluctuation (single dose and steady)
  - C_{last} (predicted)
  - C_{tau} (observed and predicted)
  - Span
  - AUC_{last}/Dose
  - AUC_{Tau}/Dose
  - AUC_{Tau} %Extrap
  - Lambda_z_intercept
  - $N_{samples}$
  - Dose

- Urine parameters
  - $Rate_{last}$ (predicted)
  - $AURC_{last}$/Dose
  - $N_{samples}$
  - Dose

- User-defined parameters
  - Computed concentrations at any time point (uses AUC calculation interpolation)
  - Arithmetic combinations of any NCA parameter (eg, partial AUC/Dose)

An Intuitive Graphical User Interface

Phoenix WinNonlin was designed to help users efficiently move from data to reporting results using a graphical workflow designed to visualize data flow and analysis pathways. Each workflow contains separate objects for each action—eg, data processing, NCA, PK/PD models, table creation, figures and plot creation, and reporting—which are linked together within an intuitive graphical user interface. Locking the workflow provides consistent results and eliminates QC checks for approved workflows. Traceable workflows increase productivity by nearly 2-fold.

Workflows enable users to spend less time preparing and manipulating data and results. Scientific and QA reviewers can use tools for rapid error identification to reduce review time.
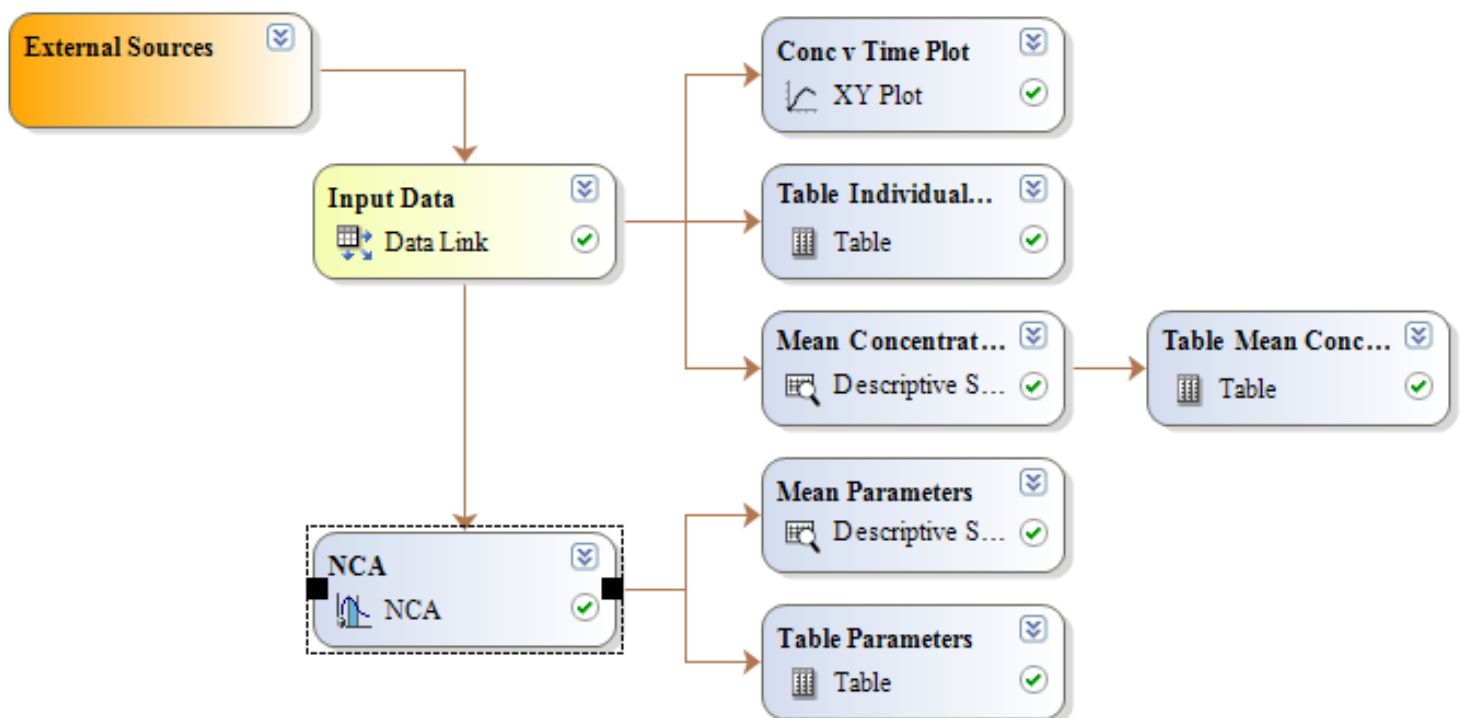
Powerful Integrated Graphics Engine and Table Generator

The integrated graphics engine in Phoenix WinNonlin automatically creates publication-quality plots and figures and well-organized tables to help create standardized PK/PD reports more efficiently. More flexible charting and plotting tools have been added, including ordering the presentation of categorical axes, allowing for offsets, changing font style and size, customizable legend placement, and more. High native resolution plots and figures can be easily customized to meet user specifications without the need for third party software packages. Do you have standard plots and figures in your organization? Custom plot templates can be shared by everyone and loaded with one command.
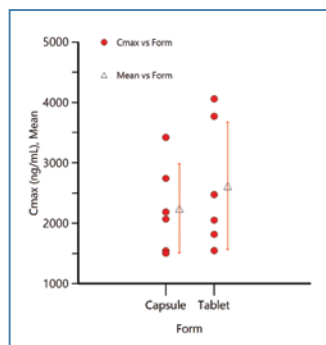
X-Categorical Plot with Error Bars and Offsets
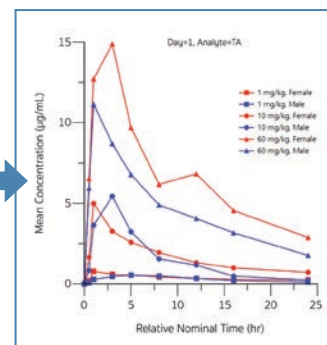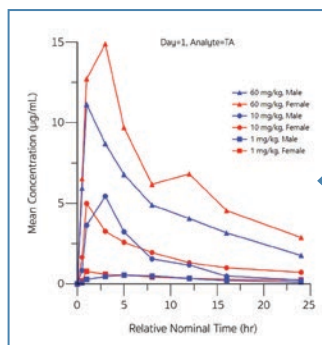
Group Label Order Change

Tools for Data Processing and Preparation

Analysis dataset preparation is a breeze with Phoenix WinNonlin's data processing tools. The Phoenix workflow traces data from the moment it is imported through the final analysis, preventing data loss and costly re-analysis.

Integrated data processing functions—sorting, splitting, filtering, transforming, merging , appending, stacking, pivoting, joining, and more—provide full visibility into the incoming data and the results of each data set.

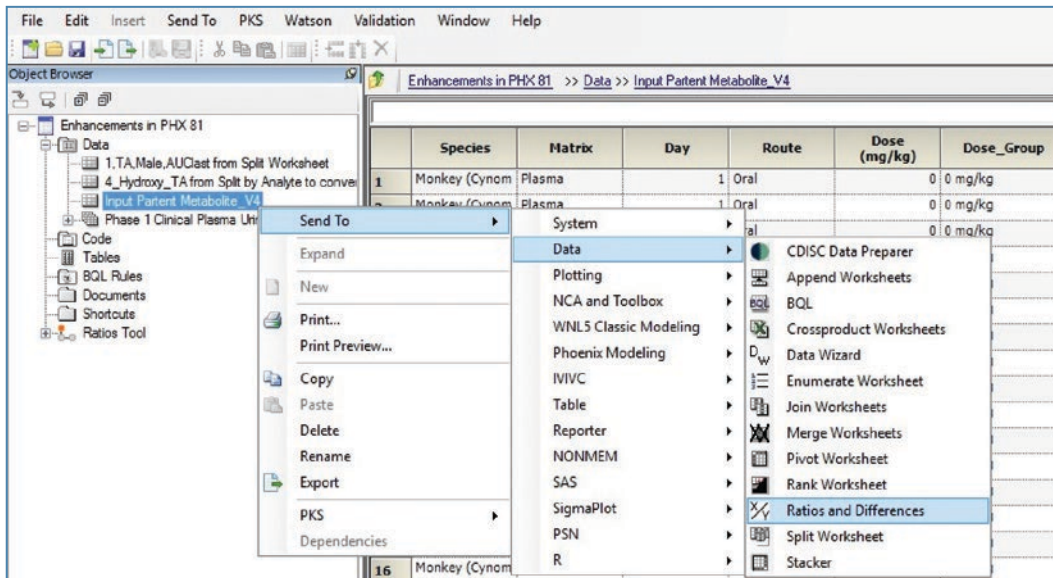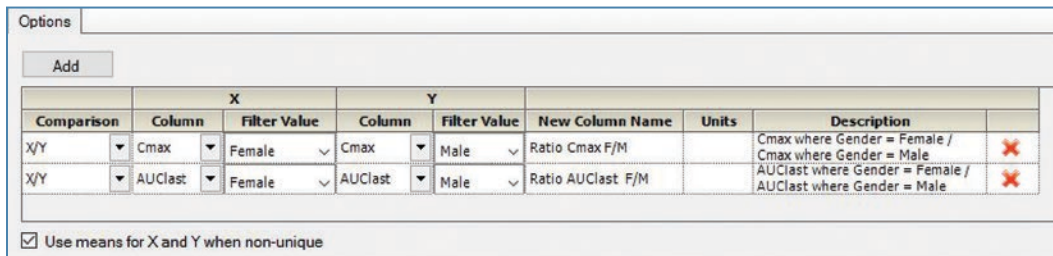|			
	CDISC Data Preparer		Merge Worksheets
	Append Worksheets		Pivot Worksheet
	BQL		Rank Worksheet
	Crossproduct Worksheets		Ratios and Differences
	Data Wizard		Split Worksheet
	Enumerate Worksheets		Stacker
	Join Worksheets		

Ratios and Differences Tool

The new Ratios and Differences tool automatically calculates NCA ratios, including renal clearance, accumulation ratio, linearity index, parent to metabolite exposure ratios, and more.

Step 1. Select Data

Step 2. Map Data and Add Options

Step 3. Obtain Results

Phoenix WinNonlin Makes Compliance Work Much Easier

The analysis of PK, PD, and TK data requires users to follow regulations to ensure compliance with regulatory agencies around the world. Each object includes a validation tab to confirm proper operation, a history tab that keeps an audit trail of changes, and a settings output that records the settings used for analysis.

Validation Suite, now fully integrated into Phoenix WinNonlin, eliminates the need to install a separate application. Automatic execution of detailed test scripts completes the validation of WinNonlin in minutes, not days. Validation is completed in less than 30 minutes with locked PDF reports containing links to saved reference files, user output files, and difference files. Updated validation template documents are aligned with the latest regulatory guidance computer system validation such as ICH E6 Good Clinical Practice (GCP) R2.

Full integration of Phoenix WinNonlin with the Phoenix Knowledgebase Server (PKS) enables the management of clinical and non-clinical PK and PD data and analyses in compliance with the US FDA electronic records and signatures regulation (21 CFR Part 11).

The Phoenix workbench provides an integrated solution to efficiently share pre-clinical and clinical knowledge throughout an organization and track a drug through the development lifecycle via a secure and consistent workflow.

Flexible and Powerful Compartmental Modeling Tools

WNL 5 Classic Modeling and Phoenix Modeling tools provide beginner to advanced users with suitable options. WNL 5 Classic Modeling has several built-in models including Dissolution, Indirect Response, Linear, Michaelis Menten, PD, PK, and PKPD models, and an option for user-defined models in ASCII format. Built-in, Graphical Editor and Textual editor options are available for Phoenix Modeling.
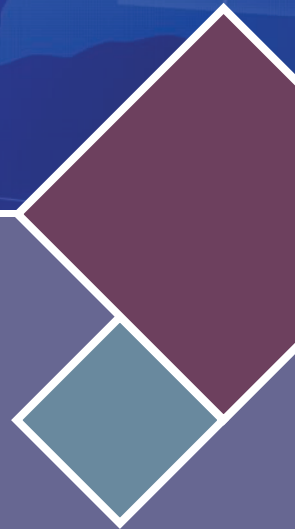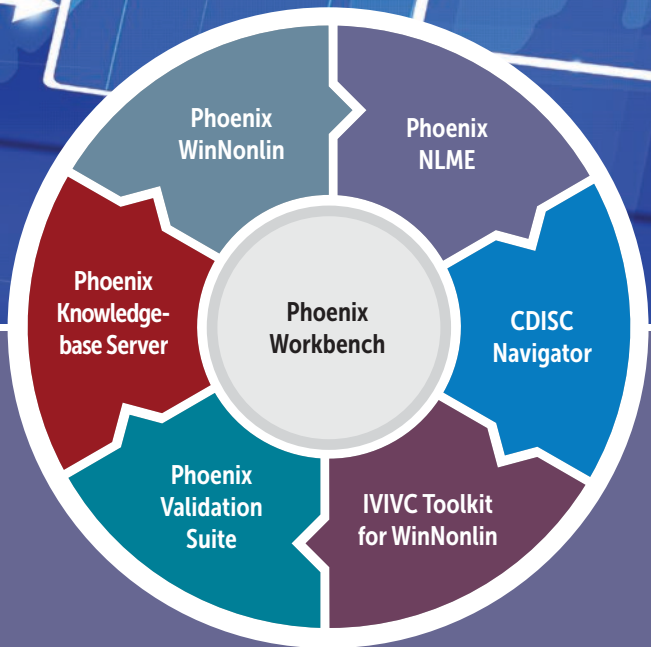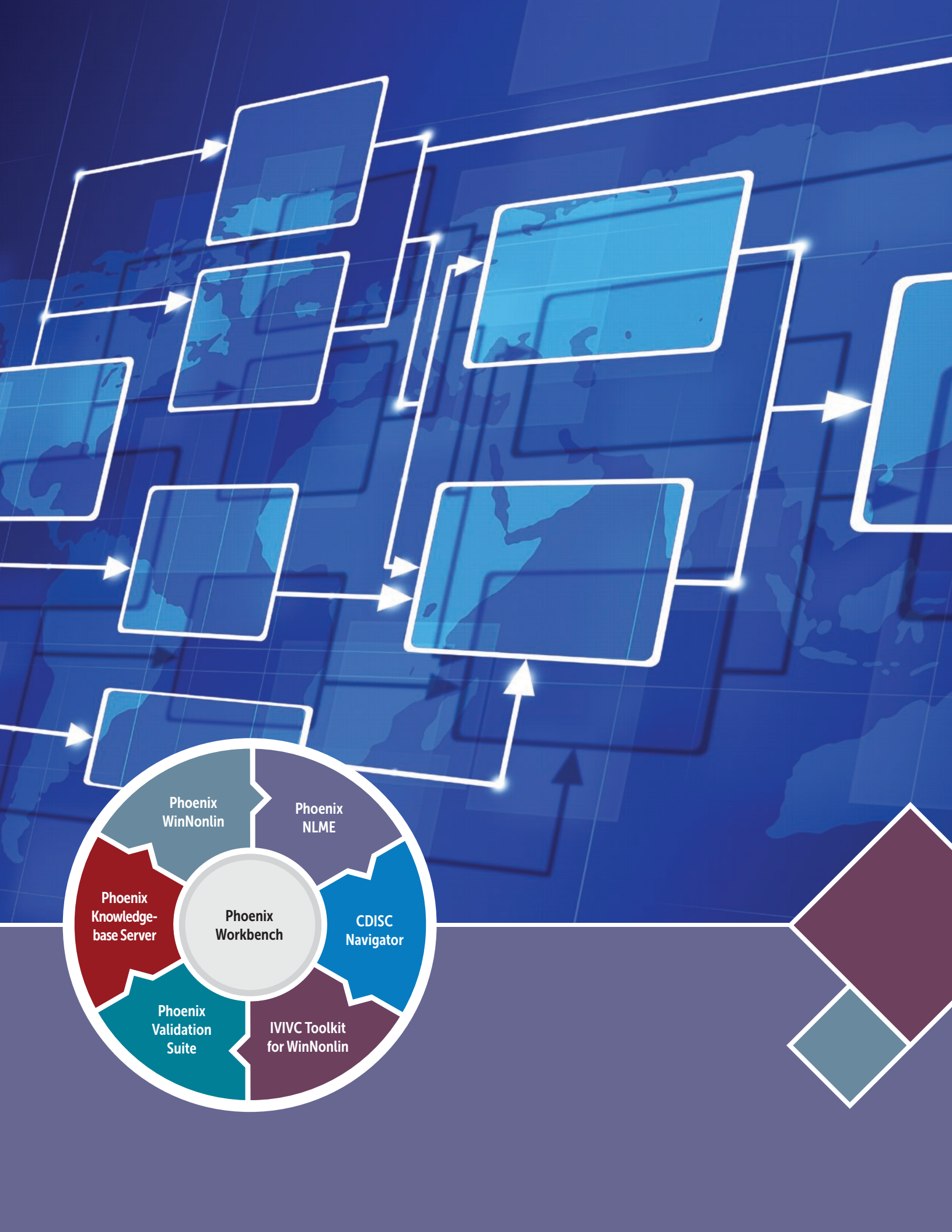
Access to Continuing Education and Support

Coming up to speed on WinNonlin is simple and easy with the graphical user interface. We provide a wide range of education and support tools to get users started and up to date with the most important advancements in modeling:

- Step-by-step user guide and examples

- Classroom and on-demand e-learning training courses available through Certara University (www.certarauniversity.com)

- The new Certara Professional Certification program offers online accreditation of user competency and proficiency analysis of PK/PD data using Phoenix WinNonlin 8.0 and 8.1 (www.certara.com/cpc)

- Webinars from world-renowned investigators and modelers

- White papers, educational blog posts, and access to an active user forum community (support.certara.com/forums)

Discover Why WinNonlin is the Industry Gold Standard for NCA, TK, and PK/PD Modeling and Simulation

Contact us at sales@certara.com to start using WinNonlin today.

Phoenix
WinNonlin

Phoenix
NLME

Phoenix
Knowledge-
base Server

Phoenix
Workbench

CDISC
Navigator

Phoenix
Validation
Suite

IVIVC Toolkit
for WinNonlin

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

For more information visit www.certara.com or email sales@certara.com.