

Dear GastroPlus User,

Over the past several years, the Simulations Plus team has been revolutionizing oral small molecule PBPK/PBBM modeling with one of the most significant changes in the <u>GastroPlus</u> platform to date. This release aims to transport you to a new paradigm focused on ease-of-use and deep understanding, all using the same trusted and established science. We are committed to ensuring our platform continues to exceed your expectations, and in that spirit, we're thrilled to announce the release of the entirely reimagined GastroPlus X (GPX <sup>TM</sup>). Our development team continues to work hard to make GastroPlus the most advanced and reliable simulation program for drug absorption, pharmacokinetics, pharmacodynamics, and drug-drug interactions in the world.

# 1. Our new GPX<sup>™</sup> platform is packed with exciting new features and functionalities that are bound to ignite your modeling activities. Below are some highlights that will transport you to the new paradigm!

- NEW! Logical, User-friendly Interface
  - o Smooth and Efficient Workflow through Views, Panels and Subpanels
  - o Vertical and context scrolling throughout the application
  - Data groupings for optimal organization of information
  - Pop-out Views & Panels to utilize multiple monitors
  - One Modeling Project = One GPX Project. No more need for support files
  - Message Center
    - Guide the user through model building
    - Ability to check your set up before simulations
  - Legacy Import
    - Ability to import historical GP databases from previous versions for use in the new paradigm
- NEW! Refined Model-Building Paradigm
  - Reusable assets for flexible and efficient modeling
  - Parallel running of simulations improves speed by orders of magnitude
  - Project templates & asset export/import allow supercharged modeling and collaboration
  - Saved simulation and run settings reduce redundant work
  - Model multiple forms for powerful PBBM modeling
- NEW! Analysis View interactive, report-ready plotting and data analysis for reviewing, understanding and comparing simulation results
  - Easily examine detailed results for population simulations, optimization and parameter sensitivity analyses (PSA) directly in the GPX interface
  - Summary View
    - Interactive statistical analysis embedded within the software
    - Ability to view across all runs and simulations
    - Copy statistics for reports or presentations
    - Reorder columns for better analysis and decision making
- NEW! Compounds View



- New features for multiple solubilities in different solvents and with different solubilizers
- NEW! Dosing View
  - Create dosing schedules that range from simple to complex, administering everything from a single formulation to a combined loading dose and maintenance schedule
- NEW! Physiology View
  - Combine physiologies in a time-dependent manner in the Physiology Schedules View
- NEW! Pharmacokinetics View
  - Create multiple compartmental PK models per compound for individuals or species
- NEW! Simulations View
  - Mix-and-match compounds, dosing schedules, physiology schedules, and pharmacokinetic settings to mimic real-world scenario simulations
  - Ability to dose multiple compounds in a single simulation
  - New simplified absorption model for simplified PBPK modeling of preclinical/clinical datasets
- NEW! Runs View
  - Perform multiple simulations simultaneously
  - Run PSA, population simulations, or optimization using existing simulations
  - New Virtual Bioequivalence (VBE) mode for quickly conducting virtual BE trials
  - Ability to save all settings for PSA, Population Simulations, VBE, and Optimization
- Lab book
  - Enhanced notes saved in the project with improved organization and readability to support communication across teams
- DDI Module
  - Polypharmacy perform DDI simulations with unlimited compounds
  - Significantly increased speed and performance for average or population-based DDIs
- IVIVCPlus<sup>TM</sup> Module
  - Ability to deconvolute in vivo dissolution from individual subjects and build robust IVIVCs
  - More flexibility on mixing and matching observed data to dissolution
- Metabolism and Transport Module
  - Individual scale factor for enzymes and transporters for easy exploratory modeling
  - New enzyme and transporter expression levels in different species
- <u>PBPKPlus<sup>TM</sup> Module</u>
  - Interactive PBPK model interface allows for real-time parameter customization
- <u>PKPlus<sup>TM</sup> Module</u>
  - Leverage powerful PKanalix® algorithms
- <u>ADMET Predictor<sup>®</sup> Module:</u>
  - o Synchronized with ADMET Predictor® v11 models
  - Improved processing speed for compound import
- NEW! Verification Suite
  - An automated method for users of GPX to verify that the product is installed properly and all licensed modules are working as expected in the user's environment
  - Test multiple simulations in various run modes, comparing the outputs to a set of reference "gold-standard" results (as determined by Simulations Plus)
  - Convenient reporting in an un-editable summary report and detailed .csv file

### 2. Installation of GastroPlus on your computer/network



Our software is designed to run on Windows 11 (64-bit), Windows 10 (64-bit) or Windows Server 2022 (64-bit). A minimum of 8 GB of RAM is recommended for optimal performance. GastroPlusX requires at least 1GB of available hard-drive space for installation. The software can be installed from the \*.zip package retrieved from our ShareFile <u>online portal</u>, either as a "standalone" installation on your computer or as a "network installation" on your local area network. Refer to the installation manual or our <u>website</u> for instructions.

Before GastroPlus can be run from your installation, it must be activated. The activation process is handled via email with our licensing department at <u>licensing@simulations-plus.com</u>.

## 3. GastroPlus X tutorial

GPX includes an updated tutorial guide.

This guide contains step-by-step instructions for running different GastroPlus simulations. Data for running these simulations are also provided wherever necessary, along with the nature and source. The tutorial data files are present in the Tutorials folder *after* installing GastroPlus on your computer.

## 4. Customer support

As part of our Personal Consultation Program, Simulations Plus has assigned scientists to serve you in your use of GastroPlus. Feel free to contact them for guidance on techniques for using the program better, suggestions, and bug reports.

We stand ready to help. If you would like advice on techniques for using the program most effectively in your research, please contact us.

Telephone:	+1-661-723-7723
E-mail:	support@simulations-plus.com
Website:	www.simulations-plus.com

Thank you for the trust and confidence you place in GastroPlus. We look forward to assisting in any way we can.

Best regards,

John DiBella President, PBPK/CHEM Solutions Simulations Plus, Inc. (NASDAQ: SLP)

#### The Development Team:

Manas Shah Mark Pflieger Suriya Arulselvan Ann Gbruoski Asanka Wickramasinghe Jason Pearson Kai Shen Noam Morningstar-Kywi



Michael Chinander Dechuan Zhuang Harsha Patil Bryan Holland

#### Scientists:

Haiying Zhou Becky Graves Jim Mullin Maxime Le Merdy Priyata Kalra Daniela Silva Nathalie Toublanc Robert Fraczkiewicz Michael Lawless Michael B. Bolger Neil Miller Viera Lukacova

#### Security, Installation, Testing, and Documentation Support:

Mark Pflieger Aleksandra (Ola) Mikosz Jeff Dahlen Kevin Cooper Victor Aguilar Lisa Behr Jennifer Dilts Oguz Kaan Fiona Plait Farah AlQaraghuli Celeste Vallejo

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