SimulationsPlus

Putting Clients First Drives Growth And Fuels Innovation

INVESTOR DAY

NOVEMBER 14, 2023

NASDAQ: SLP

Agenda

- OPENING REMARKS | SHAWN O'CONNOR, CEO
- PBPK & CHEMINFORMATICS | JOHN DIBELLA, M.S.
- CLINICAL PHARMACOLOGY & PHARMACOMETRICS | JILL FIEDLER-KELLY, M.S., FISoP, JONATHAN CHAUVIN, PH.D.
- QSP | BRETT HOWELL, PH.D.
- REGULATORY STRATEGIES | JOHN DIBELLA, M.S.
- SALES STRATEGY AND CLIENT APPROACH | JOSH FOHEY
- M&A | SHAWN O'CONNOR, STEVE CHANG, M.S.
- FINANCIAL OVERVIEW & GUIDANCE | WILL FREDERICK, CFO
- ESG | WILL FREDERICK, CFO
- Q&A
- CLOSING REMARKS | SHAWN O'CONNOR, CEO

Safe Harbor Statement

With the exception of historical information, the matters discussed in this presentation are forward-looking statements that involve a number of risks and uncertainties. Words like “believe,” “expect” and “anticipate” mean that these are our best estimates as of this writing, but that there can be no assurances that expected or anticipated results or events will actually take place, so our actual future results could differ significantly from those statements. Factors that could cause or contribute to such differences include, but are not limited to: our ability to maintain our competitive advantages, acceptance of new software and improved versions of our existing software by our clients, the general economics of the pharmaceutical industry, our ability to finance growth, our ability to continue to attract and retain highly qualified technical staff, our ability to successfully integrate the recently acquired Immunetrics business with our own, as well as expenses we may incur in connection therewith, and a sustainable market. Further information on our risk factors is contained in our quarterly and annual reports and filed with the U.S. Securities and Exchange Commission.

Opening Remarks

SHAWN O’CONNOR, CEO

Key Messages

- WE HAVE A LONG HISTORY OF INNOVATION IN BIOSIMULATION THAT IS TRANSFORMING DRUG DEVELOPMENT AND R&D
- WE HAVE A RICH FUTURE FOR GROWTH OPPORTUNITIES
- WE HAVE A HIGHLY EXPERIENCED SCIENTIFIC LEADERSHIP TEAM
- WE ARE ALIGNED WITH OUR CLIENTS TO MEET DEMAND FOR FUTURE GROWTH
- WE HAVE A STRONG FINANCIAL POSITION TO FUND OUR GROWTH

SLP At A Glance

Leading Provider of Software and Consulting Services in the Biosimulation Market

AI-powered technology solutions optimize the outcomes of drug discovery, development, research, and regulatory submissions processes. Our software-based technology both models and simulates how drugs and diseases behave in humans and in other species.

25+
YEARS

OVER 25 YEARS IN BUSINESS AND CONTINUING THE COMMITMENT TO IMPROVE PUBLIC HEALTH THROUGH INNOVATIVE SOLUTIONS

300+
CLIENTS

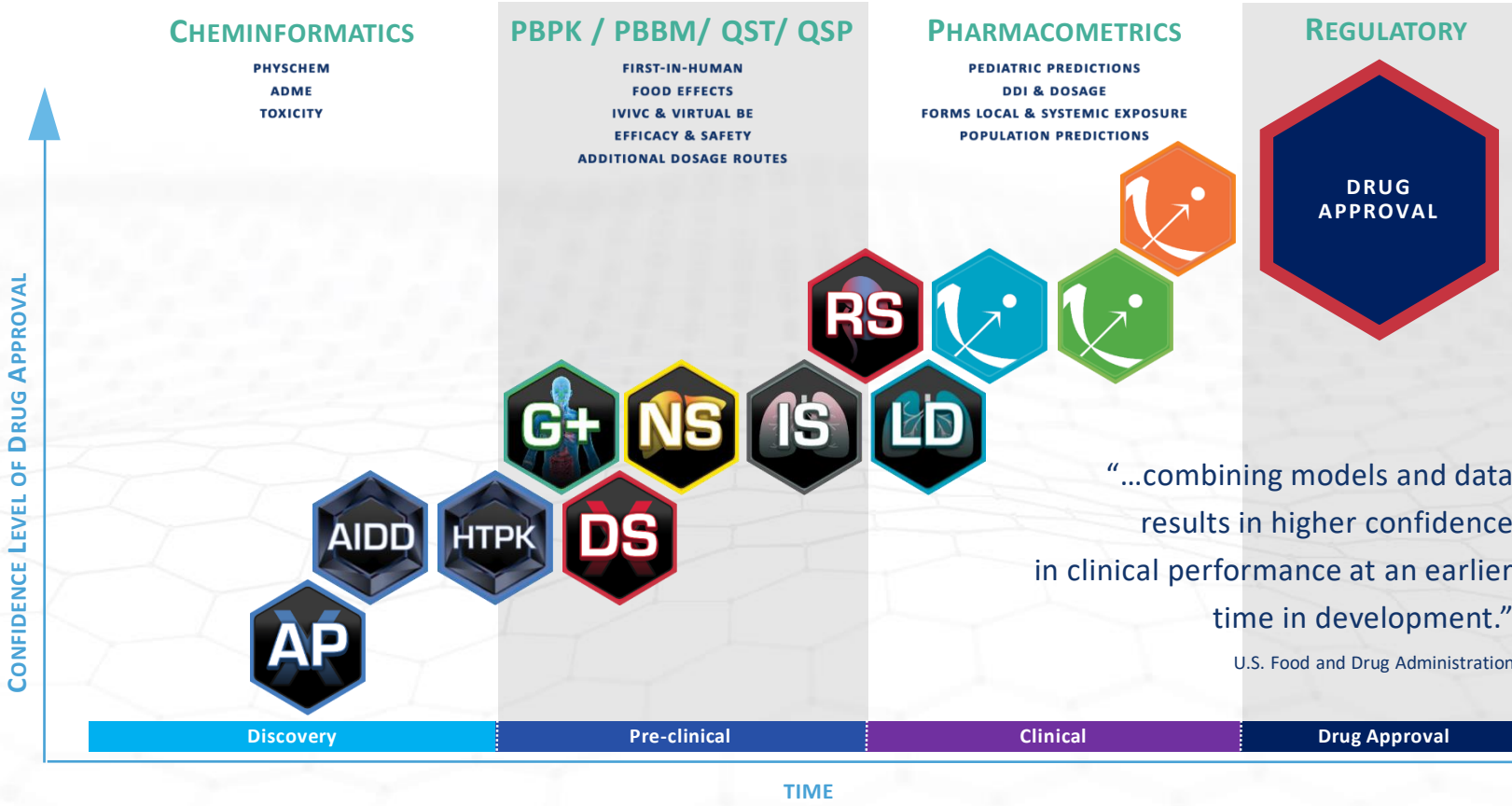
OUR CLIENTS TRUST OUR EXPERT CONSULTING THAT SUPPORTS DRUG RECOVERY, CLINICAL DEVELOPMENT RESEARCH AND REGULATORY SUBMISSIONS

18+
SOFTWARE SOLUTIONS

WE PROVIDE VALIDATED AI AND MACHINE LEARNING, MODELING AND SIMULATION SOFTWARE FOR NOVICE AND EXPERT USERS ALIKE

End-to-End Solutions Across the Development Life Cycle

Decrease development uncertainty, cost and time



"…combining models and data results in higher confidence in clinical performance at an earlier time in development."

U.S. Food and Drug Administration

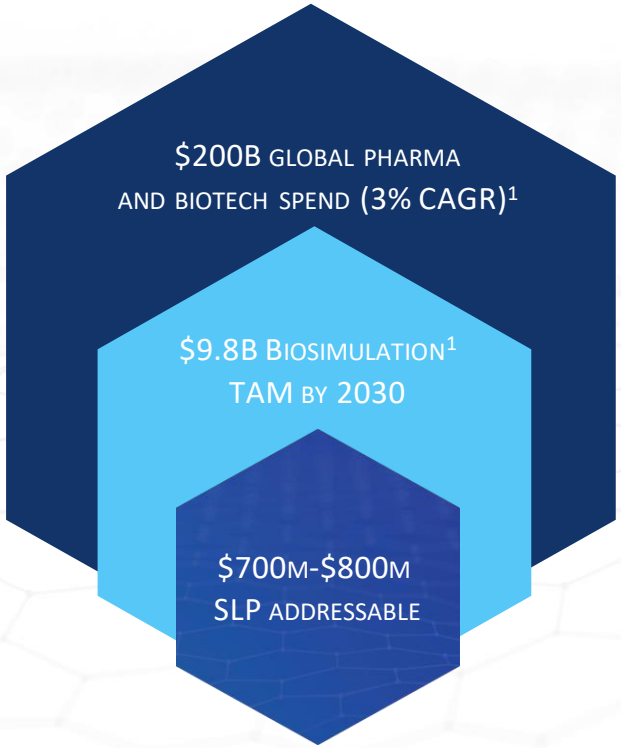
Our Goal Today

To give you a better understanding of our expertise and capabilities in each of these scientific domains, future developments and directions and how we deliver value to our clients

PUTTING CLIENTS FIRST DRIVES GROWTH AND INNOVATION

Leader in Large and Growing Market

Spending for biosimulation products continues to increase given need to bring drugs to market faster



- Biosimulation market valued at $2.8B in 2022 and is expected to expand at a 16.9% CAGR from 2022 - 2030[1]
- Strategy to grow addressable market within the Biosimulation TAM through both internal R&D investment and strategic acquisitions
  - SLP is growing faster than the Biosimulation TAM
  - Biosimulation growing at 4-5x total R&D spend
- Highly fragmented and underpenetrated market with only a few larger players
  - The global biosimulation market is segmented based on product, application, delivery model, and end users.

1 Company research, SkyQuest

Drug Development Challenges | Biosimulation Solution

Our core mission – accelerating the development and delivery of better, safer, and more effective drugs

CHALLENGES

- The median cost of developing a new drug averages $1.5 to $2 billion and the timeline can range from 10-15 years.
- On average only 11% of all drug candidates are approved

SIMULATIONS PLUS SOLUTIONS

- **Simulations Plus** offers AI-powered technology solutions to help optimize the outcomes of the drug discovery, development, research and regulatory approval processes to bring drugs to market faster
- **Simulations Plus** solutions can help increase the number of candidates approved by streamlining the drug development process, creating efficiencies that lead to drug efficacy and safety, higher regulatory approval, improved commercial success and much more

Source: Company research

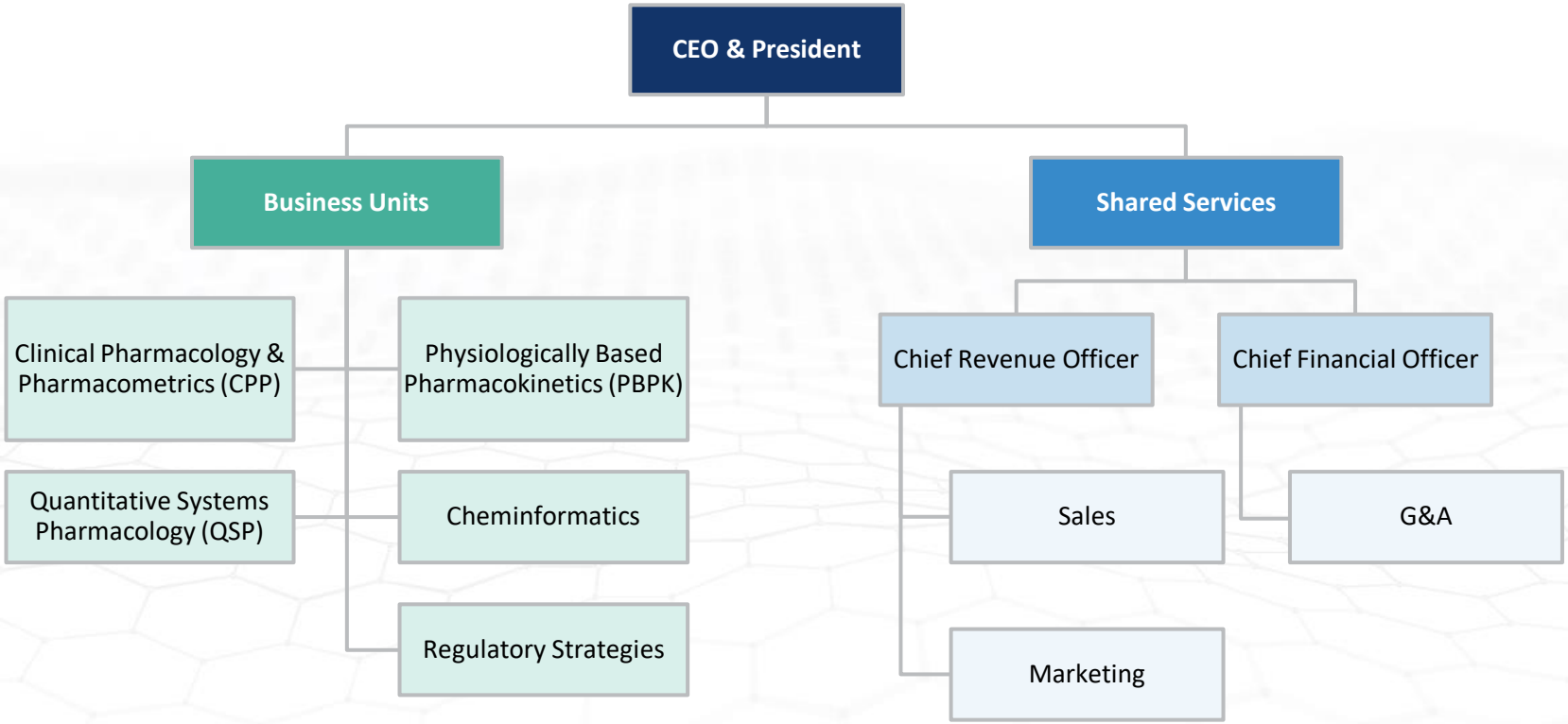
How We View Artificial Intelligence

- We have been utilizing AI technics and approaches in our solutions since our beginning
- Data is key: our tenure in serving the drug development industry has provided significant access to data necessary to perfect and refine predictive algorithms with key partnerships and collaborations with industry leaders and regulatory agencies
- ADMET Predictor is the best example of our AI predictive capabilities
- AI enhancements that improve data analytics are a component of each of our scientific domains with improvements currently planned into the future
- We embrace the excitement and potential improvements that AI can and will bring to drug development
- We have and will continue to utilize AI technologies to enhance our products and services

Strategic Objectives

- MAINTAIN LEADERSHIP IN MIDD
- EXPAND OUR PRODUCTS AND SERVICES
- PURSUE STRATEGIC ACQUISITIONS
- GROW AT OR ABOVE MARKET
- GROW PROFITABILITY AT OR ABOVE TOP LINE GROWTH

New Organizational Structure



Seasoned Management Team and Scientific Leadership

Highly experienced management team with deep life science industry expertise, track record of growth and strong returns

Shawn O'Connor
Chief Executive Officer

Will Frederick
Chief Financial Officer

Josh Fohey
Vice President, Business Development

Brett Howell, Ph.D.
President
Quantitative Systems Pharmacology Solutions (QSP)

Jill Fiedler-Kelly, M.S., FISoP
President
Clinical Pharmacology & Pharmacometrics Services Solutions (CPP)

John DiBella, M.S
President
Physiologically Based Pharmacokinetic (PBPK) Solutions, Cheminformatics Solutions, Regulatory Strategies Solutions

Jonathan Chauvin, Ph.D.
President
Clinical Pharmacology & Pharmacometrics Software Solutions (CPP)

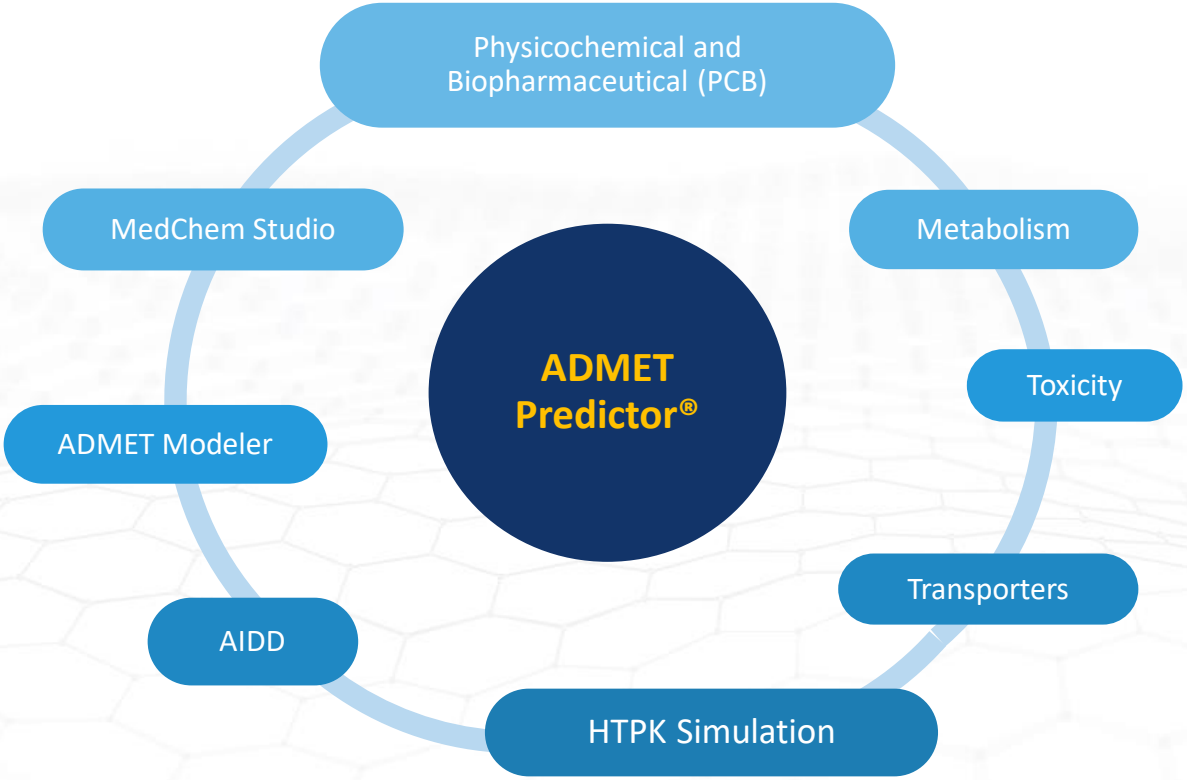
Steve Chang, M.S.
President
Immunetrics

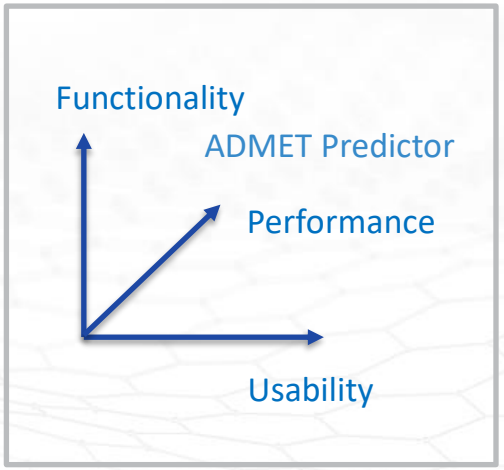

VIDEO
SimulationsPlus

Cheminformatics & PBPK

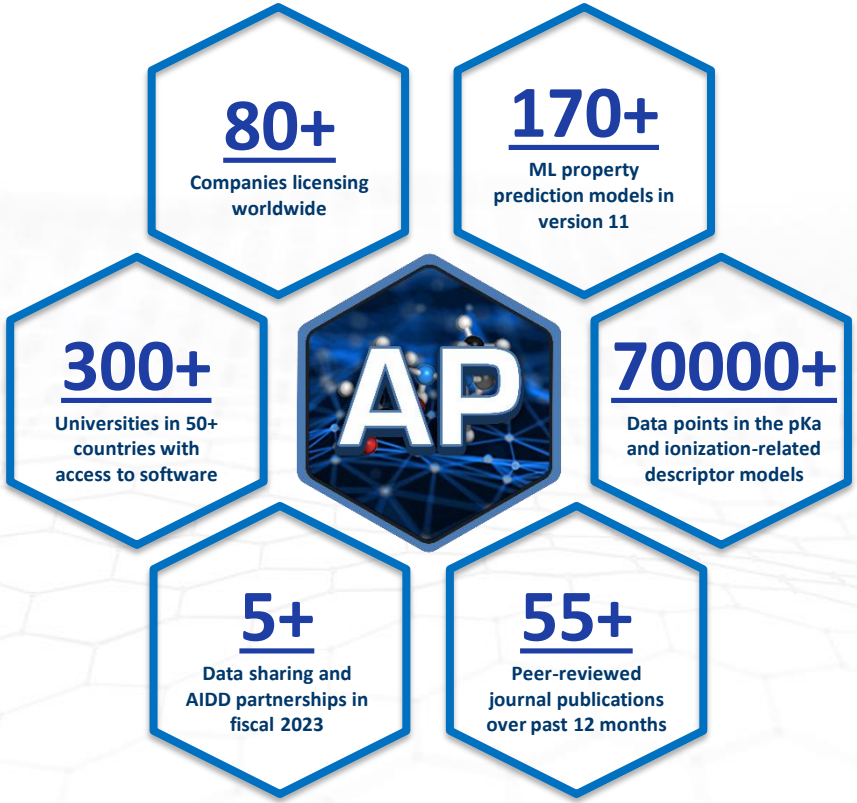
JOHN DIBELLA, M.S.

Cheminformatics | ADME-Tox Property Predictions and AIDD





ADMET Predictor By the Numbers



Cheminformatics Partnerships in Fiscal 2023

- pKa models have been rebuilt using proprietary data received from three new industrial partners
  - Partner 1: ~19,000 compounds
  - Partner 2: ~2,400 compounds
  - Partner 3: ~4,100 compounds
- Total number of ionization constants has increased from 33,640 to 70,810
- Continues successful record of industrial partnerships that originated with Bayer's 2011 contribution of 17,000 proprietary compounds

Simulations Plus Enters New Strategic Collaboration to Discover Anticancer Therapies Through Its AI-Driven Drug Design Technology

Drug discovery services partnership with Sino-American Cancer Foundation focuses on the development of actionable hits against the MTHFD2 target

March 28, 2023 08:30 AM Eastern Daylight Time

LANCASTER, Calif.--(BUSINESS WIRE)--Simulations Plus, Inc. (Nasdaq: SLP), a leading provider of modeling and simulation software and services for pharmaceutical safety and efficacy, today announced that it established a strategic research collaboration with the Sino-American Cancer Foundation (SACF). This collaboration will leverage Simulations Plus' staff and Artificial Intelligence-driven Drug Design (AIDD) technology in the ADMET Predictor® software platform to support the discovery and design of novel inhibitors of methylenetetrahydrofolate dehydrogenase 2 (MTHFD2), an emerging cancer target.

Simulations Plus Enters Partnership to Apply AI/ML Technologies to Design Novel Compounds

Promising intellectual property resulting from the collaboration with Polish Academy of Sciences will be jointly owned for further development opportunities

March 15, 2023 08:30 AM Eastern Daylight Time

LANCASTER, Calif.--(BUSINESS WIRE)--Simulations Plus, Inc. (Nasdaq: SLP), a leading provider of modeling and simulation software and services for pharmaceutical safety and efficacy, today announced that it entered into a collaborative research agreement with the Institute of Medical Biology of the Polish Academy of Sciences (IMB PAS) to jointly design new compounds for the RORγ/RORγT nuclear receptors using its cutting-edge artificial intelligence (AI) / machine learning (ML) technology in the ADMET Predictor® software platform.

Cheminformatics | The Future

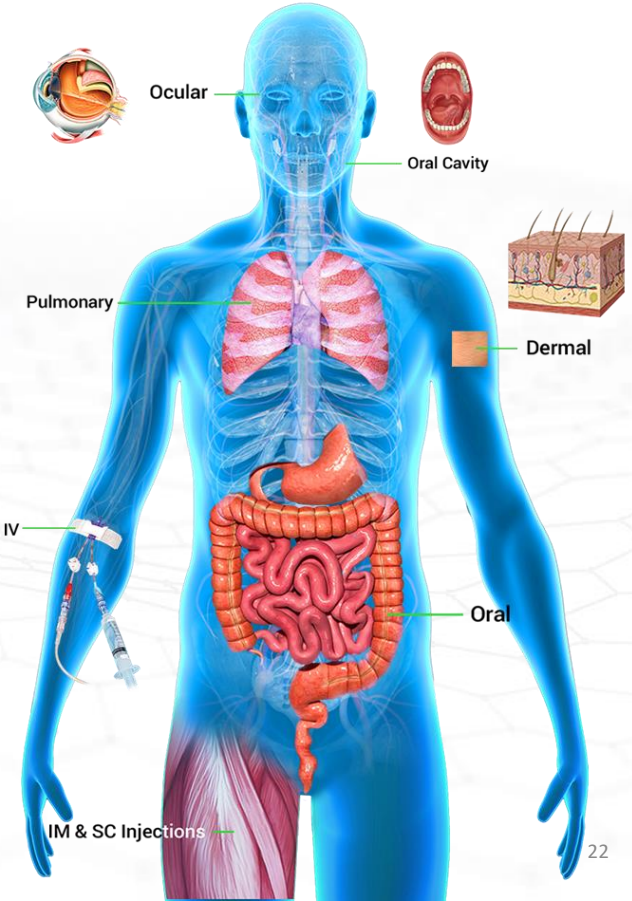
- Expansion of machine learning models to inform inputs into other software offerings at the company
- Explore new AI/ML technologies to improve model performance and assist with data compilation/curation
- Develop additional descriptors (2D and 3D) to extend chemical coverage space into new territories
- Enhance AIDD approaches with new functionalities – retrosynthesis predictions, novelty searches
- …and more

Cheminformatics | Why We Win

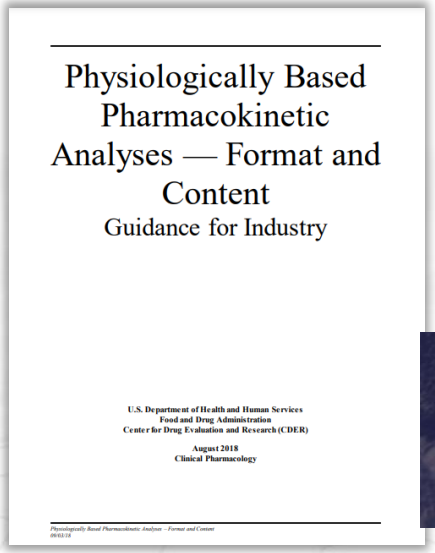
- We're ranked #1 for accuracy in published independent comparisons for different ADME endpoints
- Simulations Plus has the top-rated machine learning + top-rated PBPK models tightly integrated in ways no other company can accomplish
- We have generative AI with embedded GastroPlus PBPK simulations to uniquely design/optimize molecules
- Access to premium, carefully curated data, which others do not have, to feed our machine learning models
- Hundreds of peer-reviewed journal articles published citing ADMET Predictor
- Flexible licensing & deployment models provides options to a wide range of clients across industries
- Expert team of data scientists, developers, and support staff provides the coaching, maintenance, and training companies need to successfully incorporate AI/ML modeling into their discovery programs

What Do We Mean When Describing PBPK Modeling?

- Physiologically based pharmacokinetic (PBPK) models represent animals and humans virtually as a collection of organs and tissues, each defined by a system of mathematical equations
- PBPK models are developed using quantitative values (“parameters”) and equations that describe characteristics (e.g., body weight, blood flow rate, physicochemical properties, formulation) and mechanisms (e.g., dissolution, precipitation, absorption, metabolism)
- PBPK models built for animals can often be extrapolated to humans – and, in a similar vein, models built for healthy adults can often be extrapolated to other populations (e.g., pediatrics, disease states)



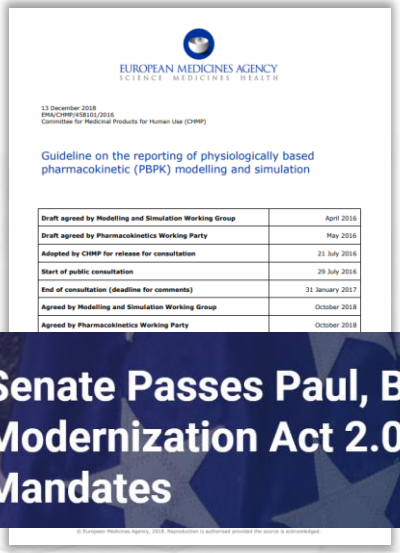
PBPK Modeling to Support Regulatory Interaction | The Push


Physiologically Based Pharmacokinetic Analyses — Format and Content
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

August 2018
Clinical Pharmacology

2018

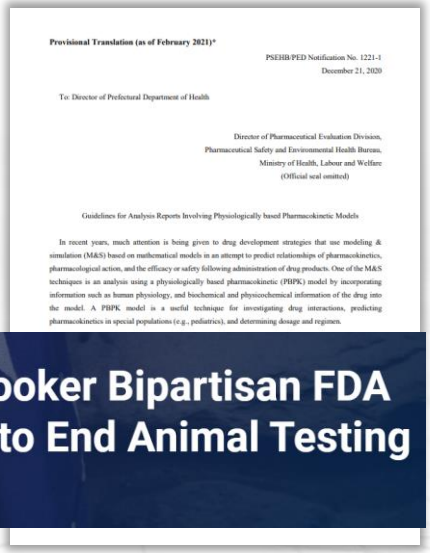

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 December 2018
EMA/CHMP/458101/2016
Committee for Medicinal Products for Human Use (CHMP)

Guideline on the reporting of physiologically based pharmacokinetic (PBPK) modelling and simulation

Draft agreed by Modelling and Simulation Working Group	April 2016
Draft agreed by Pharmacokinetics Working Party	May 2016
Adopted by CHMP for release for consultation	21 July 2016
Start of public consultation	29 July 2016
End of consultation (deadline for comments)	31 January 2017
Agreed by Modelling and Simulation Working Group	October 2018
Agreed by Pharmacokinetics Working Party	October 2018

2018


Provisional Translation (as of February 2021)*

PSEHB/PED Notification No. 1221-1
December 21, 2020

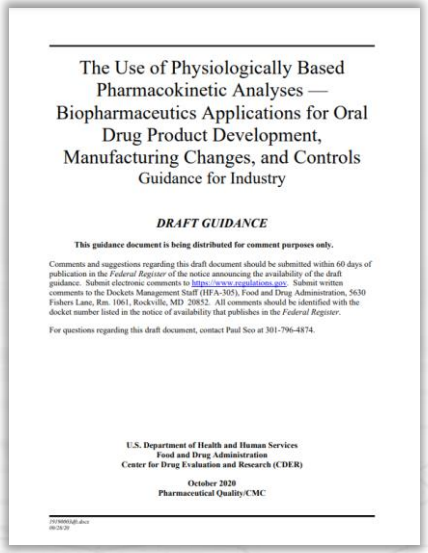
To: Director of Prefectural Department of Health

Director of Pharmaceutical Evaluation Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Guidelines for Analysis Reports Involving Physiologically based Pharmacokinetic Models

In recent years, much attention is being given to drug development strategies that use modeling & simulation (M&S) based on mathematical models in an attempt to predict relationships of pharmacokinetics, pharmacological action, and the efficacy or safety following administration of drug products. One of the M&S techniques is an analysis using a physiologically based pharmacokinetic (PBPK) model by incorporating information such as human physiology, and biochemical and physicochemical information of the drug into the model. A PBPK model is a useful technique for investigating drug interactions, predicting pharmacokinetics in special populations (e.g., pediatrics), and determining dosage and regimen.

2020


The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Paul Seo at 301-796-4874.

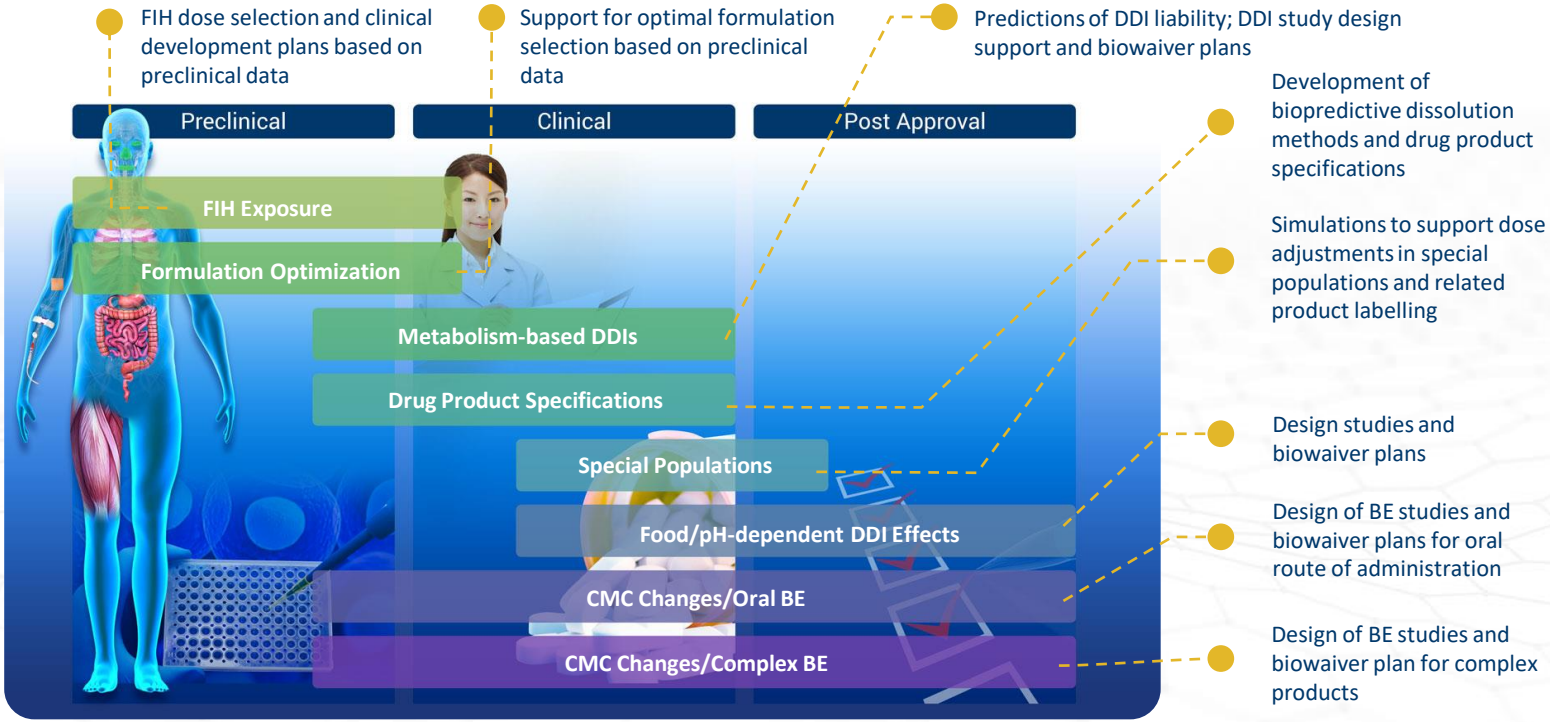
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2020
Pharmaceutical Quality/CMC

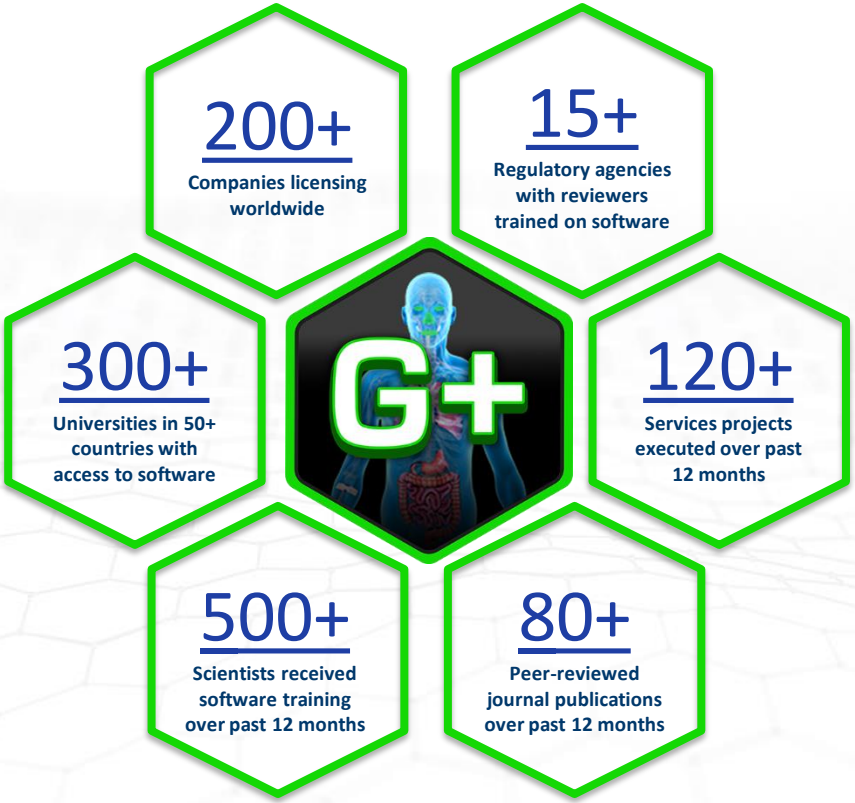
2020

Senate Passes Paul, Booker Bipartisan FDA Modernization Act 2.0 to End Animal Testing Mandates

Common PBPK M&S Industry Applications



GastroPlus By the Numbers



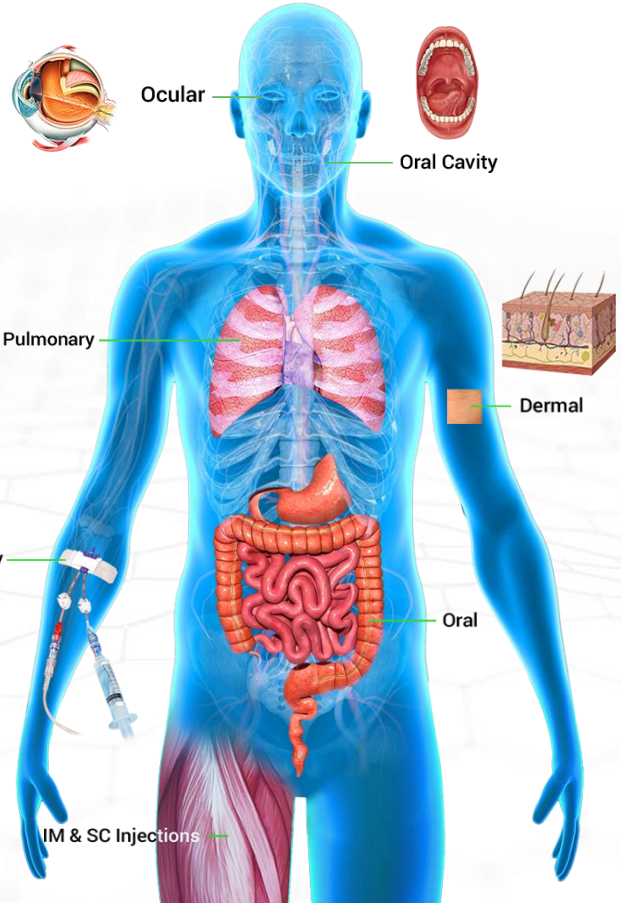
Partners Driving PBPK | Funded Scientific Collaborations

FDA: Ocular model extensions

FDA: Oral cavity model extensions

FDA: Pulmonary model extensions

FDA: Dermal model extensions



Large Pharma: Local GI disease extensions

FDA: Oral absorption model extensions

FDA: Virtual BE trial workflows

FDA: Long-acting injection model extensions

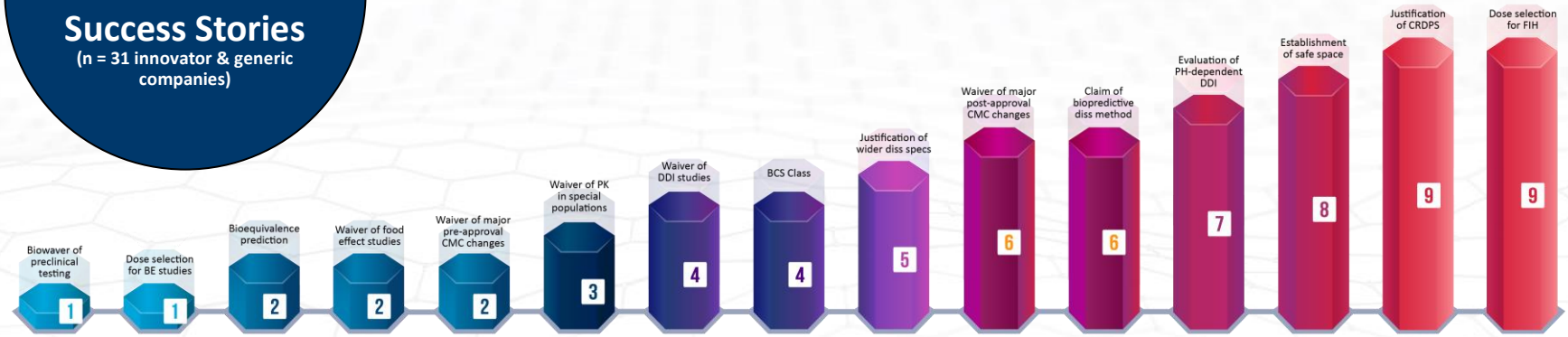
Regulatory Applications of GastroPlus (2020-22)

Client Survey Results

69

Success Stories

(n = 31 innovator & generic companies)



Examples of Approved Drugs Supported By GastroPlus

- ***Alecensa®***, pH-dependent DDI
- ***Braftovi® & Mektovi®***, Metabolic DDI
- ***Calquence®***, Drug product specifications / pH-dependent DDIs
- ***Farydak®***, pH-dependent DDIs
- ***Inlyta®***, Transporter DDI
- ***Kisqali®***, pH-dependent DDI
- ***Opsumit®***, Drug product specifications
- ***Mekinist®***, Transporter DDI
- ***Tamiflu®***, Pediatric dose support
- ***Invokana®***, Drug product specifications
- ***Piqray®***, Food effect
- ***Zurampic®***, Drug product specifications

A Recent Regulatory Win

Problem Statement:

- Commercial tablets for 2 dose strengths were being submitted by a mid-size pharma company
- Both FDA and EMA pushed back on the proposed Q80% time point of 45 minutes
- Dissolution testing of production batches showed dissolution rates close or failing proposed agency limits which would have led to OOS batches during routine manufacturing

The Solution: GastroPlus® PBBM

- Model was validated across clinical datasets and applied to run VBE and justify, together with a risk analysis based on ER data, wider proposed dissolution specifications for both dose strengths
- Cost = $0.25M USD (one-time charge)

What Were the Alternatives?

1. Do nothing and accept standard dissolution specs
   - Estimated 5-10% OOS batches = loss of $1M USD/year
2. OR Run a clinical trial to justify dissolution specifications
   - Manufacture clinical batches across 2 dose strengths at the proposed dissolution specifications
   - Conduct 2 human BE studies on 42 subjects in fed and fasted state for both drug products

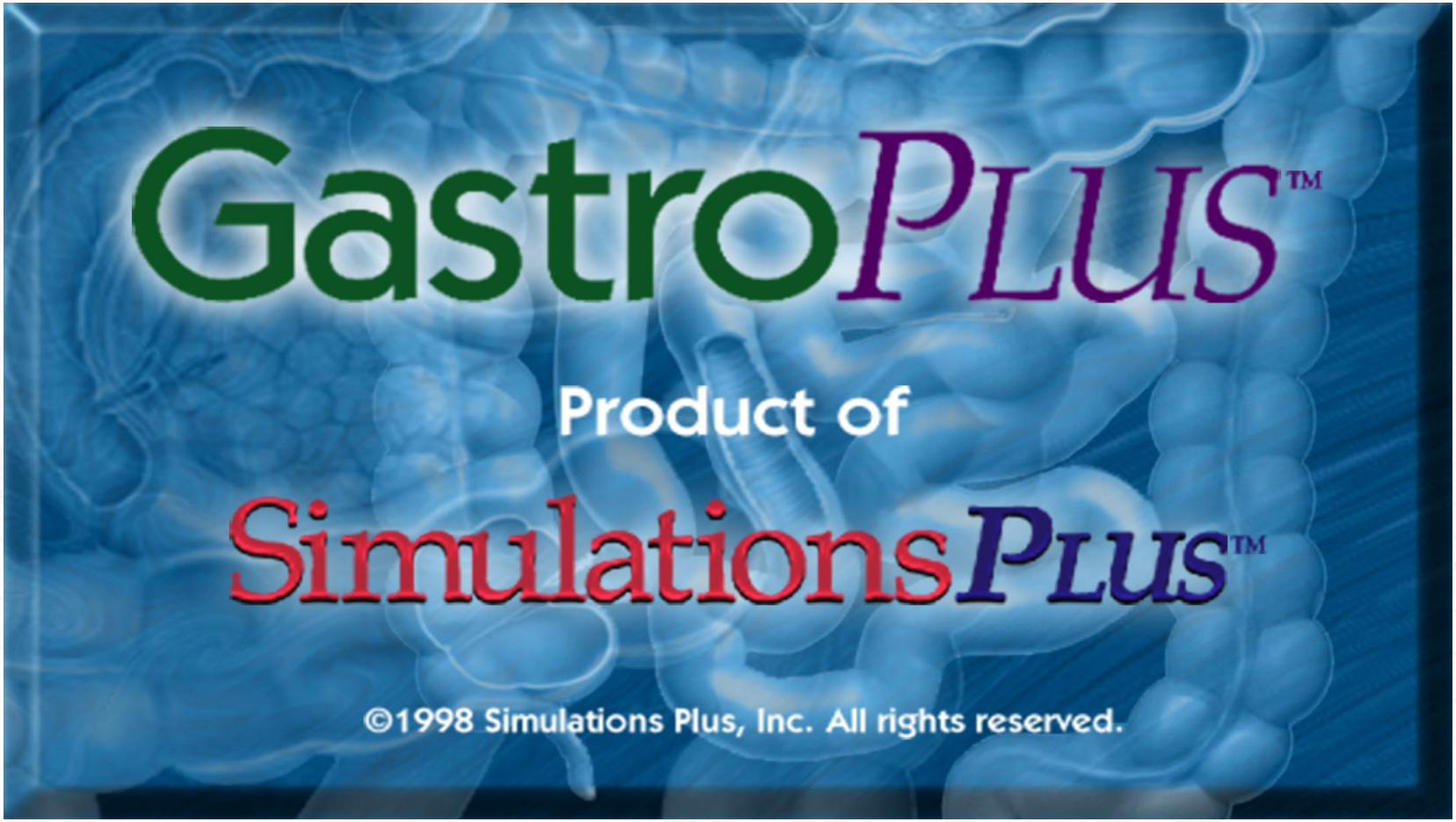
Scenario Costs:

Scenario 1. Do Nothing Estimated Cost =
5-10% OOS batches
Loss of $1M USD/Year

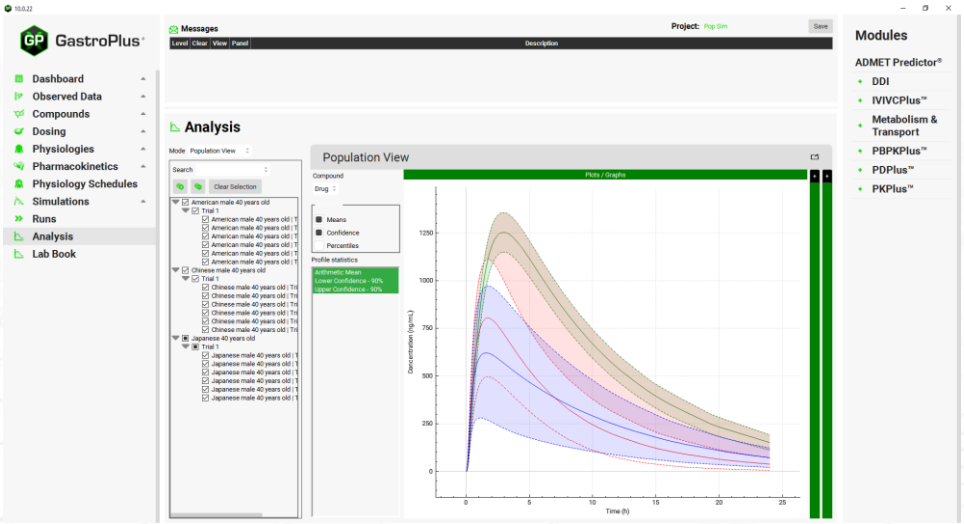
Scenario 2. Run a Clinical Trial Estimated cost =

$0.5M USD (manufacturing)
+ $7M USD (clinical studies)
+ 6-12 months to complete study & analysis

Celebrating the 25th Anniversary of GastroPlus



The Future of GastroPlus



The trusted science of GastroPlus is the same –
the workflows & logic will be around for years to come!

PBPK | The Future

- Integration of QSP and CPP technologies within the GastroPlus environment to expand product and service offerings
- Application of AI to provide expert PBPK coaching and support to users on a real-time basis to expand our client base
- Mechanistic delivery models around the body for different molecule types
- True polypharmacy simulation capabilities to mimic a patient's real-world medication schedule and better assess drug-drug interactions, fixed dose combination products, and more

PBPK | Why We Win

- Ranked #1 for accuracy in all published independent comparisons of PBPK software – laser focus on science and innovation for 25+ years
- 1000+ peer-reviewed journal articles published citing GastroPlus
- Over 20 funded grant partnerships with the FDA since 2015 – reflects significant trust and confidence from regulators expert team of modelers, developers, and support staff provides the coaching, maintenance, and training companies need to successfully incorporate PBPK modeling into their R&D programs
- Our expert team of modelers, developers, and support staff
- Flexible licensing models provides access to a wide range of clients across industries

Clinical Pharmacology & Pharmacometrics (CPP)

JILL FIEDLER-KELLY, M.S., FISoP,
JONATHAN CHAUVIN, PH.D.

The Clinical Pharmacology & Pharmacometrics Leadership Team

Jill Fiedler-Kelly – CPP Services

- Co-founded Cognigen in 1992
- Joined Simulations Plus when it acquired Cognigen in 2014
- +30 years of modeling and simulation experience
- Co-author of a textbook on population PK/PD modeling
- Adjunct Professor of Pharmaceutical Sciences at the University at Buffalo (SUNY Buffalo)

Jonathan Chauvin – CPP Software

- Lixoft in 2015
- Joined Simulations Plus when it acquired Lixoft in 2020
- Filed +30 patents and directed 20 publications in refereed committees, newspaper articles, and 50 conference papers

Clinical Pharmacology & Pharmacometrics | Introduction

Software and consulting synergy – benefits of MonolixSuite capabilities and efficiencies

- Combining the most user-friendly modeling and simulation software with the extensive experience of the highly respected consulting team offers an unmatched level of support for model-informed drug development programs
- ~$19M in revenue; 62% services, 38% software in fiscal 2023
- Over 95% client renewal rate based on fees for MonolixSuite
- Growth in fiscal 2023: >100 companies using MonolixSuite, 12 new consulting clients and 5 consultants in fiscal 2023
- Highly experienced leadership team with advanced technical degrees, >30 years experience in consulting and >20 years experience in the pharmaceutical industry

Clinical Pharmacology & Pharmacometrics | Services

Pharmacometrics Services…

- Quantitative support of model-informed drug development
  - Pharmacometric modeling to understand and explore variability in PK, PK/PD and exposure-response
  - Support for development and regulatory decision making: providing confidence in the rationale for next phase planning and providing support for regulatory challenges through quantitative analyses, technical reports, written responses, briefing books, and attendance at meetings
  - Embedded clinical pharmacology and pharmacometrics team member support
  - Comprehensive quality management system with validated and secure systems for data handling and analysis
  - Committed and supportive team partnering with our clients and working with integrity to turn clinical data into actionable insights

Clinical Pharmacology & Pharmacometrics | Software

Pharmacometrics Software…

- MonolixSuite is the gold standard for user-friendly pharmacometric modeling and simulation software
  - Non-compartmental analysis with PKAnalix
  - Nonlinear mixed effects population PK/PD modeling with Monolix
  - Model-based, high performance clinical trial simulations with Simulx
- Intentional design offers seamless and efficient workflow across analysis steps
- Intuitive graphical user interface, extensive documentation and dedicated support team facilitates a shorter learning curve for modelers and quicker time to gain confidence in capabilities

Collaborative team support on many fronts

Our pharmacometric consultants performed PK/PD modeling in support of a highly-anticipated novel therapy being investigated to treat a rare disease affecting children. Our team of experts subsequently assisted the Sponsor with preparation for an Advisory Committee meeting resulting in the successful attainment of accelerated approval granted by FDA.

Leveraging the strength of the software

A team of modeling experts from the CPP business unit are using Monolix to develop a PK/PD platform model framework that will enable our client to quantitatively support go-no go decision making for oncology compounds based on linking early biomarker data to predict late clinical endpoints.

Support for decision making across all development stages

Modeling support provided to a client applying AI to precision engineer medicines was used to make critical decisions to enable development-related decision making for pipeline candidates.

The services team provided pharmacokinetic and exposure-response modeling support for a compound offering novel treatment for a rare genetic disease affecting children and adults; following approval by FDA, the modeling work was used to support labelling statements that describe dosing recommendations for the compound.

Clinical Pharmacology & Pharmacometrics | The Future

- Investing in expanding MonolixSuite functionality with input from in-house consultant users as well as the entire client base to:
  - Support further integration into the global environment and ecosystem of tools supporting model-informed drug development
  - Provide continual improvement of workflow and interoperability across application domains
- Opportunities for collaboration between QSP and CPP scientific areas of focus to support client needs:
  - Leveraging mechanistic QSP models developed to support early decision making to expedite the analysis of clinical data from first-in-human studies
  - Leveraging empirical PK/PD models by adding complexity with the characterization of additional endpoints and pathways
- Incorporation of AI and ML methods in pharmacometric analyses and associated data processing activities may allow for further increases in efficiency and streamlining of workflows to expedite the generation of results

Clinical Pharmacology & Pharmacometrics | Why We Win

Unparalleled Offering

- Synergistic combination of extensive experience and expertise in providing quantitative support for model-informed drug development programs across therapeutic areas and the best-in-class, most user-friendly software tool for efficient modeling & simulation workflow

- Consulting teams believe that the relationships we build with our clients are essential to our success: communicating with transparency and integrity and commitment to support for confident decision-making supported by high-quality modeling and simulation from beginning to end

- Software and services supported by solid infrastructure and quality management system

Quantitative Systems Pharmacology Solutions (QSP)

BRETT HOWELL, PH.D.

QSP | Introduction

Software and consulting synergy…

- QSP is an exciting and rapidly growing field of biomedical research
- Our QSP team combines a knowledge of mathematics, disease pathophysiology and pharmacology to help our clients make better decisions
- Our QSP team now has the broadest range of therapeutic area coverage of any QSP team in the industry

QSP | Library of Existing QSP and QST Models

QSP: Inflammatory and Fibrotic Diseases

- Non-alcoholic fatty liver disease / steatohepatitis (NAFLD/NASH)
- Idiopathic pulmonary fibrosis (IPF)
- Interstitial lung disease (ILD) associated with systemic sclerosis
- Wound healing after myocardial infarction (MI)
- Uric acid disposition in gout
- Dysregulation of alternative and terminal pathways (AP, TP) of complement

QST: Liver and Kidney Safety

- Drug induced liver injury (DILI)
- Drug induced acute kidney injury

QSP: Immuno-Oncology

- Acute myeloid leukemia (AML)
- Multiple myeloma (MM)
- Solid tumor (NSCLC, melanoma)
- Diffuse large B-cell lymphoma (DLBCL)

QSP: Autoimmune Diseases

- Rheumatoid arthritis (RA)
- Psoriatic arthritis (PSA)
- Psoriasis (PSO)
- Atopic dermatitis (AD)
- Systemic lupus erythematosus (SLE)
- Ulcerative colitis (UC)
- Crohn's disease (CD)

QSP | Services

- Platforms across therapeutic development landscape including diseases
- Our coverage positions us to increase engagements
- Unique combined understanding of:
  - Drug effectiveness at treating disease
  - Safety
  - Negative drug side effects
- Optimize the balance between a therapies positive and negative impacts on the patient
- Offer milestone-based consulting project structures

QSP | Software

- Includes proprietary infrastructure built within these environments:
  - Thales: drives oncology and autoimmune models
  - MATLAB: drives pharmacology focused models
  - Julia: drives our NASH / NAFLD model
  - C++: drives our liver and kidney safety platforms
- All of our platforms are available for licensing by our clients, enabling our clients with QSP teams inhouse to partner with us in a collaborative way

QSP | Success Stories

U.S. FOOD & DRUG ADMINISTRATION

Home / News & Events / FDA Newsroom / Press Announcements / FDA Approves Novel Drug to Treat Moderate to Severe Hot Flashes Caused by Menopause

FDA NEWS RELEASE

FDA Approves Novel Drug to Treat Moderate to Severe Hot Flashes Caused by Menopause

Share Tweet LinkedIn Email Print

More Press Announcements

For Immediate Release: May 12, 2023

Español

Today, the U.S. Food and Drug Administration approved Veozah (fezolinetant), an oral medication for the treatment of moderate to severe vasomotor symptoms, or hot flashes, caused by menopause. Veozah is the first neurokinin 3 (NK3) receptor antagonist approved by the FDA to treat moderate to severe hot flashes from menopause. It works by binding to and blocking the activities of the NK3 receptor, which plays a role in the brain's regulation of body temperature.

FIERCE Pharma

Pharma Manufacturing Marketing Special Reports Fierce 50

PHARMA

Pfizer buys migraine partner Biohaven for $11.6B, betting on CGRP drugs in grand return to neuroscience

By **Angus Liu** · May 10, 2022 10:15am

Quantitative Systems Pharmacology (QSP) Model Predicts Lack of Efficacy for Cenicriviroc, a CCR2/5 Antagonist, in NAFLD/NASH Patients

Christina Battista, Lisl KM Shoda, Grant T Generaux, Scott Q Siler

DILIsym Services Division, Simulations Plus Inc., Research Triangle Park, NC

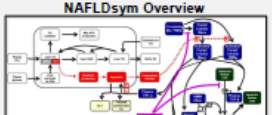
AASLD The Liver Meeting® Nov. 12-15, 2021 DIGITAL EXPERIENCE

INTRODUCTION

A phase 3 clinical trial (AURORA) for cenicriviroc (CVC), a CC chemokine receptor 2 and 5 (CCR2/5) antagonist, was recently terminated due to lack of efficacy[1].CVC was thought to suppress the inflammatory response and decrease collagen deposition by reducing recruitment of macrophages and activation of hepatic stellate cells,respectively[2,3] CVC exposure and its effects were implemented within a quantitative systems pharmacology (QSP) model, NAFLDsym (Figure 1), to see if simulations captured the lack of efficacy observed in the AURORA study and to explore if

RESULTS

NAFLDsym Overview



Simulation results using *in vitro* estimates for CVC potency

Simulated CVC 150 mg QD for 2-years	Mean Percent Change from Pre-treatment
Liver fat (%)	0 ± 0
Plasma ALT (U/L)	0 ± 0
NAS (score)	0 ± 0
Fibrosis Score (stage)	-1 ± 0

Simulations with increased CVC potency

Simulated CVC 150 mg QD for 2-years	Mean Percent Change from Pre-treatment			
	1x potency	2x potency	10x potency	100x potency
Liver fat (%)	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Plasma ALT (U/L)	0 ± 0	0 ± 0	1 ± 0	1 ± 1
NAS (score)	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Fibrosis Score (stage)	-1 ± 0	-1 ± 0	-5 ± 12	-15 ± 17

QSP | The Future

Several Exciting QSP Initiatives

- Big emphasis on expansion into more indications within oncology
- Therapeutic area expansion in other arenas
- New client sponsored development is ongoing in neurology
- Combination of AI with QSP modeling

QSP | Why We Win

Four key reasons why our clients choose to work with our QSP team:

1. Focused on diseases of relevance to our clients and the flow of capital
2. The QSP group is composed of a large team of knowledgeable experts, making the offering scalable and adaptable
3. Software + services: these two offerings allow us to tailor our solutions for large, medium, and small companies within Pharma and biotech
4. Ecosystem: the exposure modeling tools (e.g., PBPK and PMx) to feed drug concentrations into them is unparalleled in the industry

Regulatory Strategies

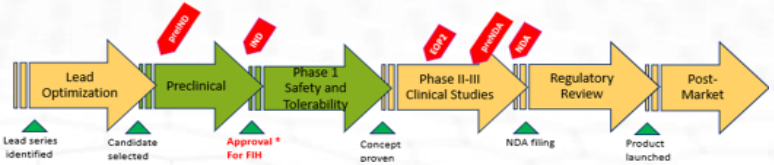
JOHN DIBELLA, M.S.

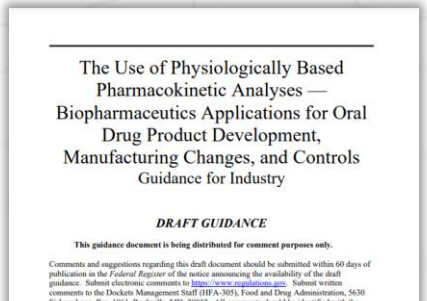
Regulatory Strategies | What We Offer

Comprehensive knowledge of drug product development

Expertise in regulatory milestones and requirements

Holistic understanding of M&S regulatory requirements and applications





The Use of Physiologically Based Pharmacokinetic Analyses — Biopharmaceutics Applications for Oral Drug Product Development, Manufacturing Changes, and Controls
Guidance for Industry

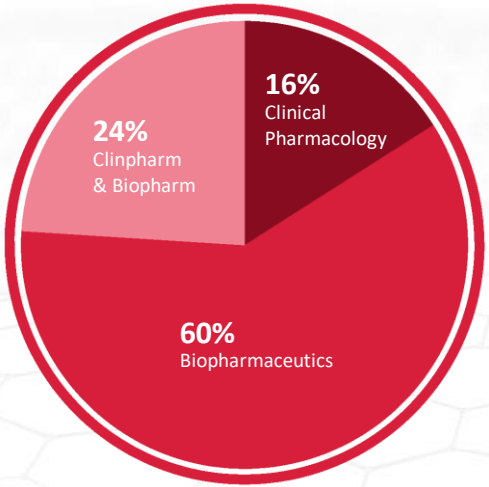
DRAFT GUIDANCE

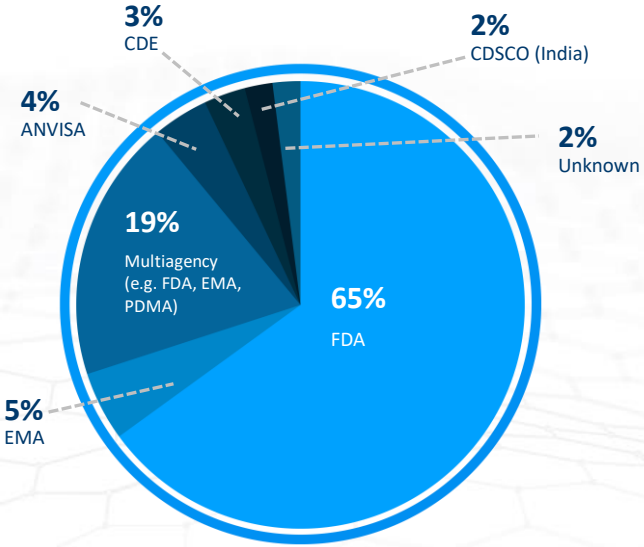
This guidance document is being distributed for comment purposes only.

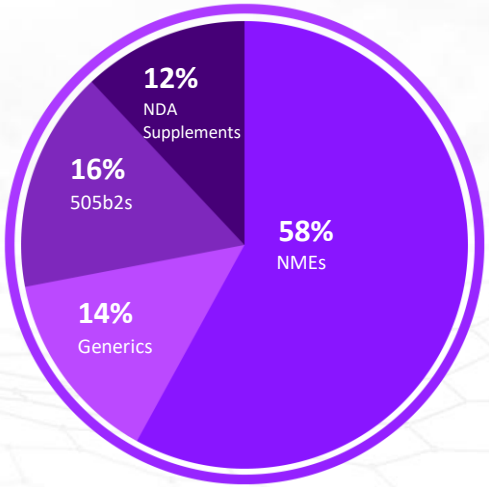
Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630

Regulatory Strategies | How We Help

A proven partner for regulatory strategies and M&S consulting support





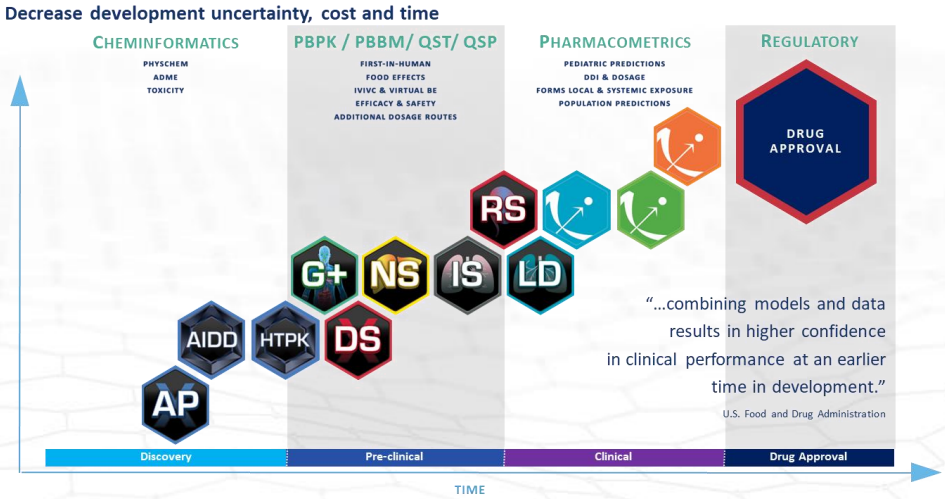


Sales Strategy and Client Approach

JOSH FOHEY
VICE PRESIDENT, BUSINESS DEVELOPMENT

Sales Strategy and Client Approach

Simulations Plus is a cutting-edge modeling and simulation company specializing in serving pharmaceutical companies at every stage, from early discovery to post-approval.

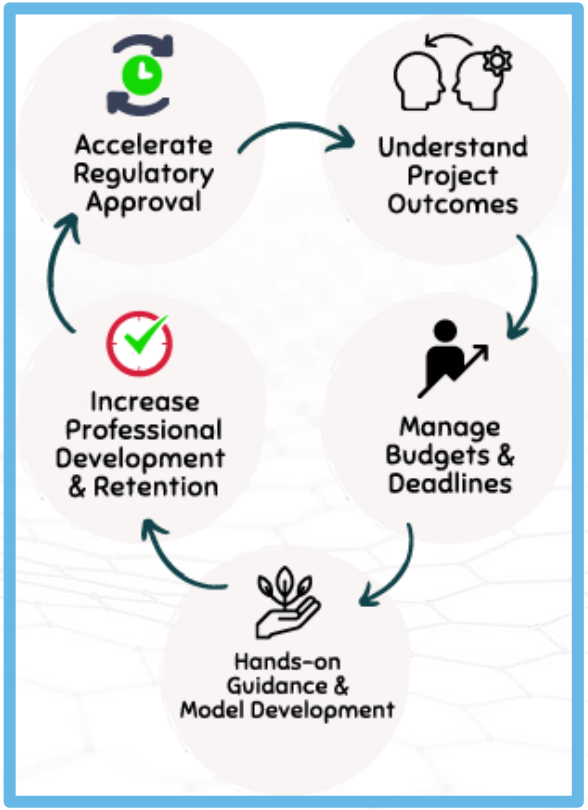


Sales Strategy and Client Approach | Expertise

- Our expertise lies in harnessing the power of machine learning in chemistry, as well as employing advanced methodologies such as PBPK , QSP, QST, pharmacometrics, and regulatory support.
- Our mission is to accelerate the delivery of safe and efficacious medicines to patients worldwide, revolutionizing the pharmaceutical landscape through the integration of industry leading technologies and scientific expertise.

Sales Strategy and Client Approach | Growth

- Bringing together strategic partnerships
- Bundling our solutions to maximize the value proposition of our partnership
- More therapeutic alignment with our partners to cater offerings



Sales Strategy and Client Approach

CHEMINFORMATICS

- Accuracy of property predictions
- Lead candidate selection and redesign with HTPK/AIDD
- Discovery services to accelerate development and scale ecosystem

PBPK

- More versatility and enhanced functionality vs competitors
- Machine learning inputs
- Regulatory standard

CPP

- Consult and Coach
- Monolix Differential
- Experts to guide your program and learning

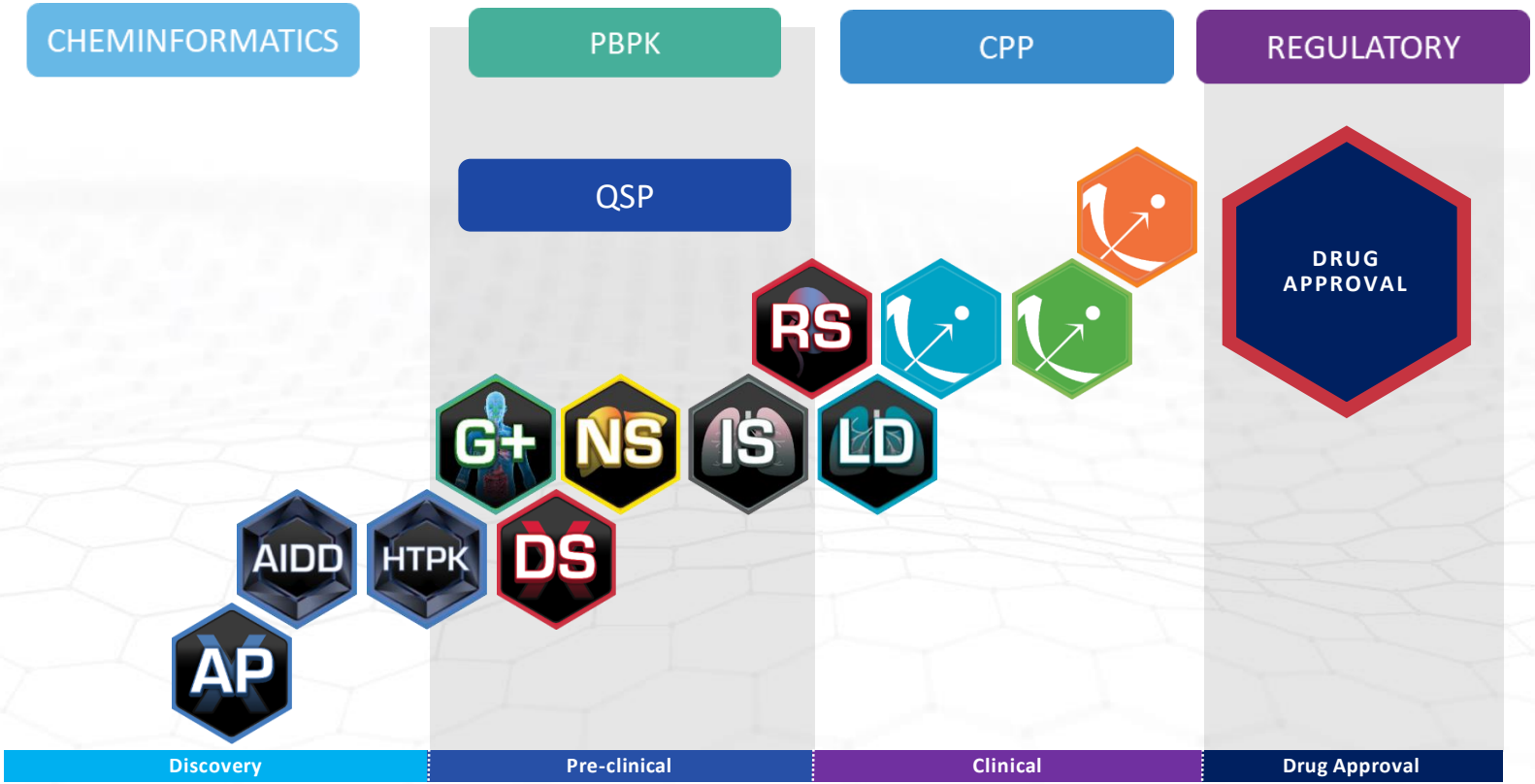
QSP

- Maximize therapeutic and disease understanding
- Optimize dose selection and clinical execution
- Prioritize your investments and mitigate program risk

REGULATORY

- Save experimental work when coupled with modeling
- Better design and optimize clinical trials
- Expertise to hold your hand through regulatory scrutiny

New Structure Aligns with Client Needs



Sales Strategy and Client Approach | Fiscal 2023

- **Increased bookings** for large pharma partners
- Sold to over **400 accounts**
- **Increased client engagement** in Alliance Management (Concierge Program)
- **Over 90% of the bookings** from Pharmaceutical companies
- **Over 80% of software bookings** were renewals with upsells or price increases
- **Increased number of optional tasks** on services projects

M&A and Integration

SHAWN O'CONNOR, CEO
STEVE CHANG, M.S.

M&A Strategy Supplements Organic Growth

- Target business expands our TAM or accelerates capture of market share in existing TAM
- Target technology/services are compatible with our existing capabilities
- Target culture is compatible with our culture
- Target valuation is reasonable
- Target is accretive

M&A | Integration & Immunetrics Case Study

Integration and consolidation efficiencies

- QSP is a critical and growing field
- Immunetrics has increased the range of therapeutic areas addressed by our QSP software and services offerings by more than 50%
- Ideal fit as the business leverages our existing infrastructure by expanding its therapeutic resources into largely underserved areas, including immunology and oncology
- Immunetrics chose Simulations Plus for its well-respected reputation
- Integration is going very well

FINANCIAL OVERVIEW & GUIDANCE

WILL FREDERICK, CFO

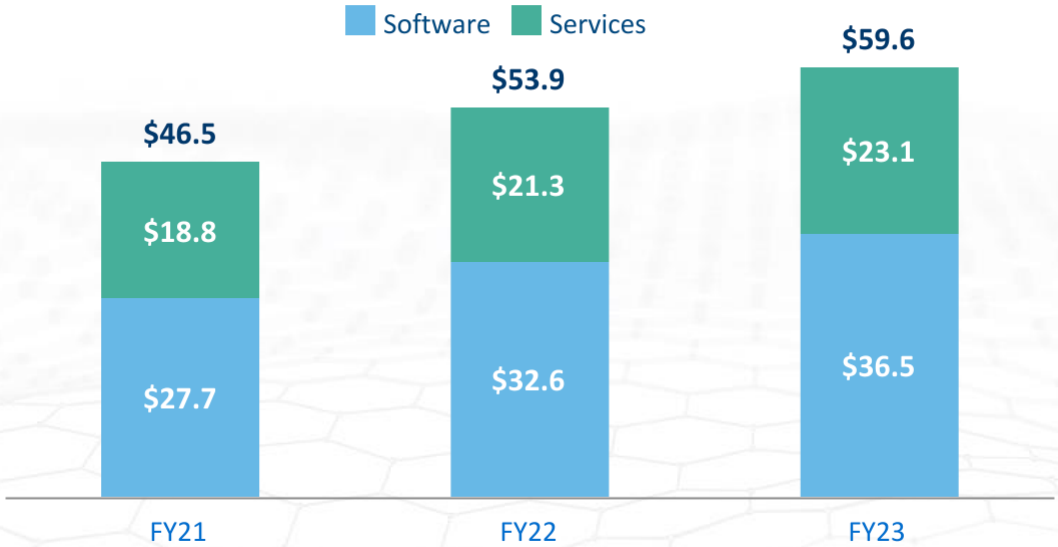
Fiscal 2023 Highlights

- Strong revenue and earnings results for fiscal 2023
- Conditions in our market remain similar to what we have seen past several quarters
  - Small biotech slowdown
  - Large Pharma spending cautiousness
- Integration of Immunetrics going well
- Achieved revenue and adjusted diluted earnings per share guidance

1 Refer to Non-GAAP Disclosures in the appendix

Revenue Trends

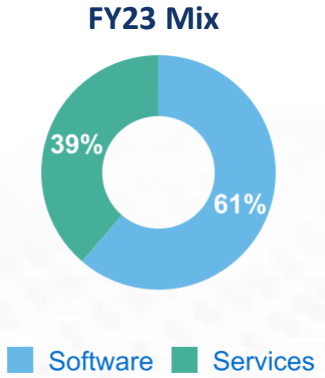
(in millions)

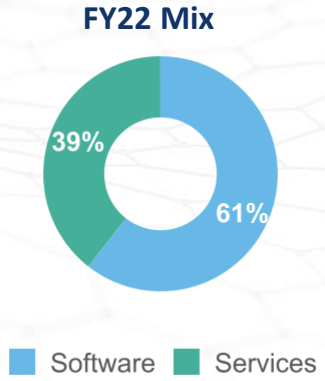


+11%
Total Revenue

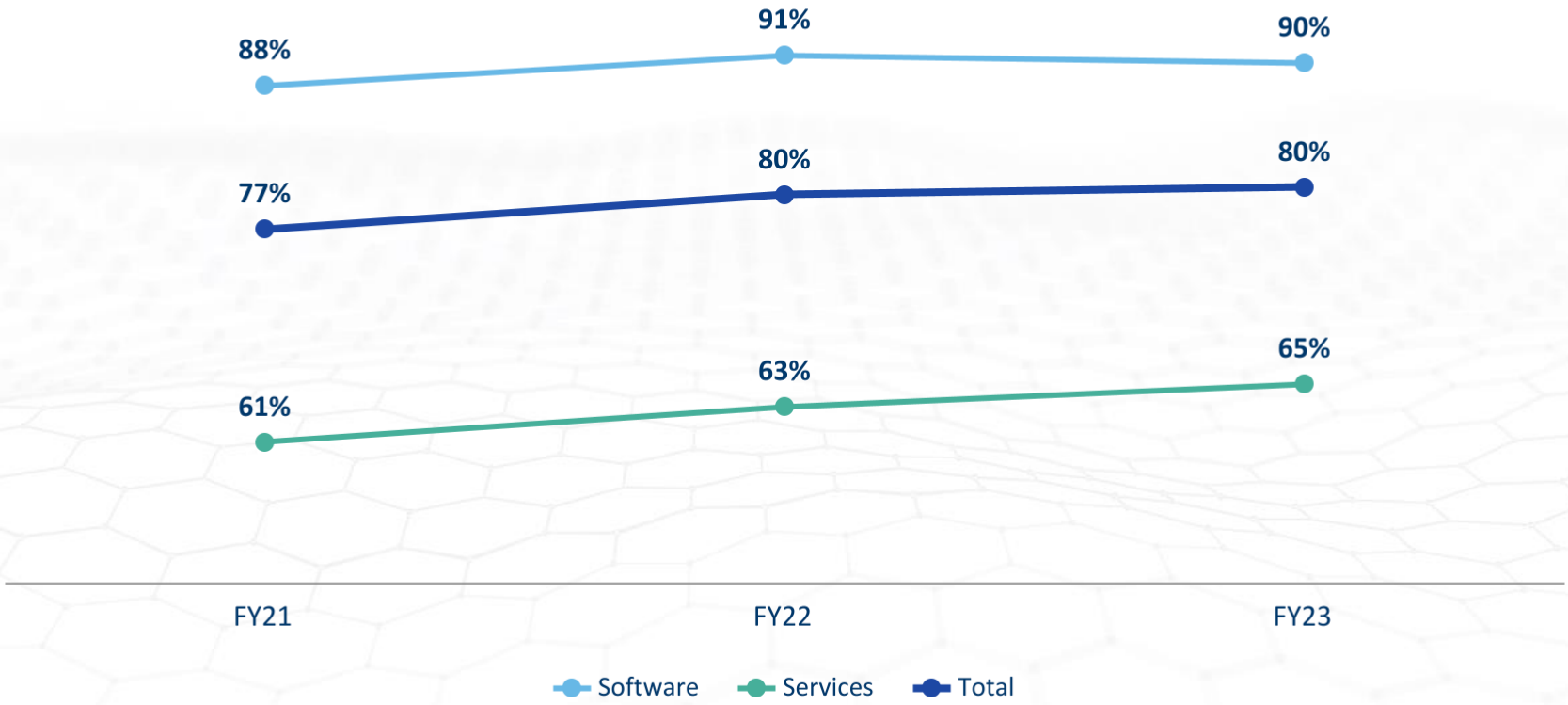
+12%
Software Revenue

+8%
Services Revenue



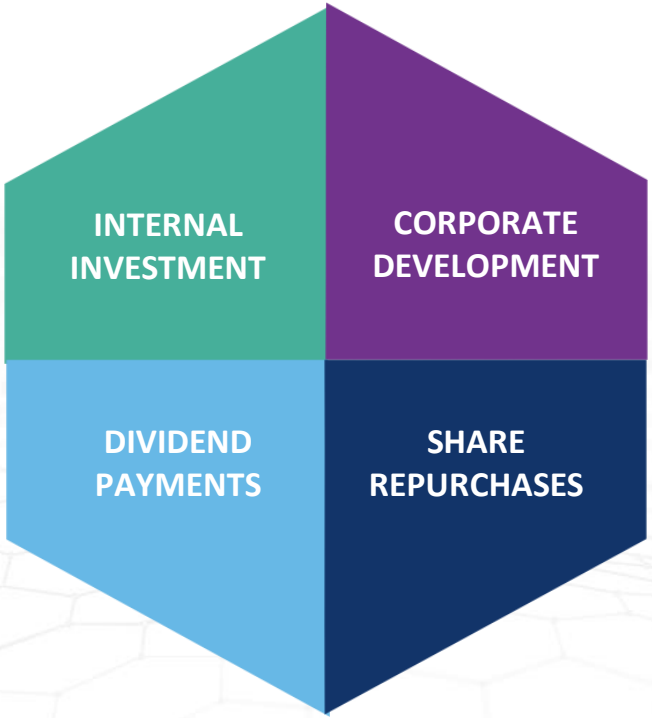


Gross Margin Trends



Capital Allocation Strategy

- Employee Engagement and Development
- Product Development
- ERP Processes and Technology



- Acquisitions (Immunetrics Q4)
- Investment Opportunities
- Strategic Partnerships and Alliances

- $0.06 per share paid Feb. 6th
- $0.06 per share paid May 1st
- $0.06 per share paid Aug. 7th
- $0.06 per share paid Nov. 6th

- $50M share repurchase program
- $20M accelerated share repurchase (ASR) in Q3

We are committed to investing in our employees, products, and providing value to our shareholders

Fiscal 2024 Guidance

	Guidance
Total Revenue	**$66M to $69M**
Total Revenue Growth	**10% to 15%**
Software Revenue Mix	**55% to 60%**
Services Revenue Mix	**40% to 45%**
Diluted EPS	**$0.66 to $0.68**

Financial Profile

Delivering Double-Digit Revenue Growth / Industry Leading Margins

	FY18	FY19	FY20	FY21	FY22	FY23	5 Yr CAGR
REVENUE $ in millions	$29.7	$34.0	$41.6	$46.4	$53.9	$59.6	**12.3%**
	FY18	**FY19**	**FY20**	**FY21**	**FY22**	**FY23**	**6 Yr Avg**
GROSS MARGIN %	73.1%	73.4%	74.4%	77.2%	79.9%	80.0%	**76.4%**
EBITDA MARGIN %	43.3%	39.1%	34.4%	31.2%	33.3%	19.2%	**33.4%**

- Double digit revenue growth
- Strong recurring revenue supported by a 90%+ Software Fee Renewal Rate
- High gross/EBITDA margins to drive strong operating leverage
- High-margin, recurring revenue over the life of the client relationship
- Product mix skews toward higher margin software sales
- $115.5 million in cash and short-term investments to fund growth

ESG

WILL FREDERICK, CFO

Sustainability Framework

Social

Advance science and innovation through partnerships and collaboration to benefit global health, while minimizing the negative social impacts of traditional research.

Environment

Minimize the environmental impacts of our operations, directly and indirectly, by waste reduction, recycling practices, and by using renewable energy providers where possible

Business Governance

Ensure thorough oversight of enterprise and ESG risks associated with our business, leveraging policies and procedures, training and awareness, and controls.

Human Capital

We embrace a culture of engagement, empowerment, and equity to attract, support, and retain a talented and diverse workforce dedicated to promoting scientific innovations.

STRATEGIC PRIORITIES FORM THE FOUNDATION OF OUR SUSTAINABILITY FRAMEWORK

Fiscal 2023 ESG Achievements

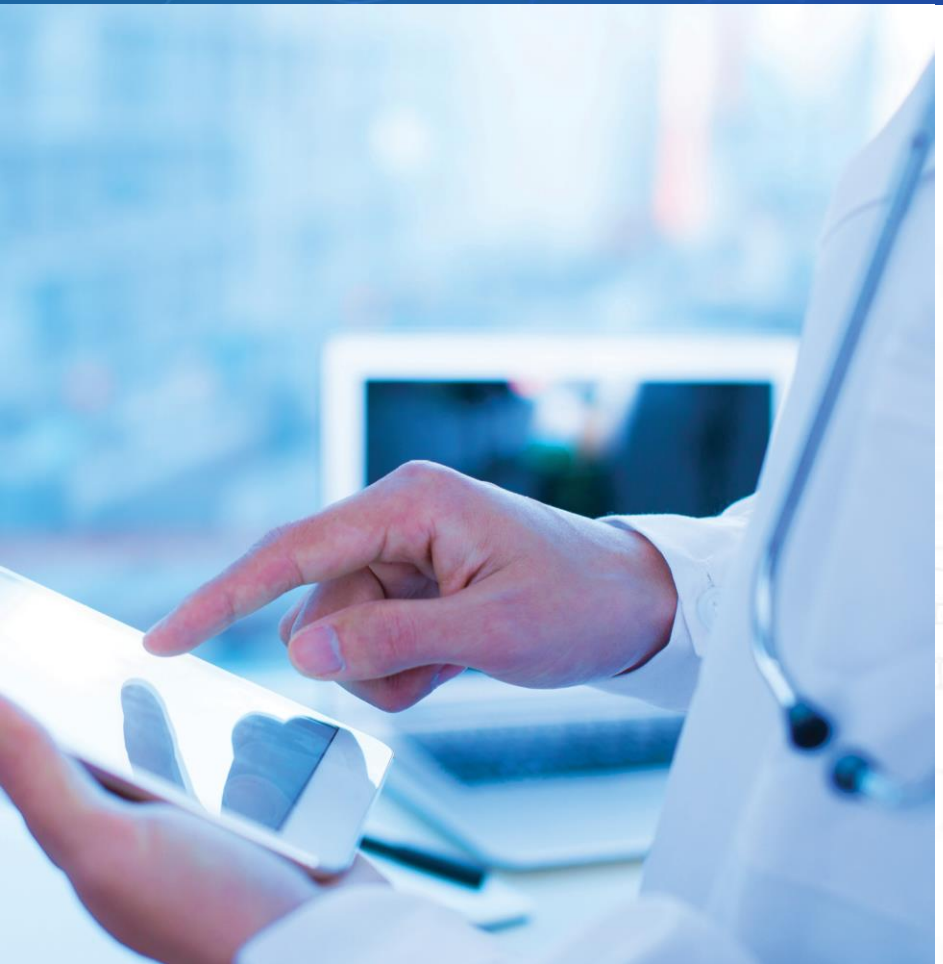
ENVIRONMENT	SOCIAL	HUMAN CAPITAL	GOVERNANCE
Reduced footprint of US-based facilities by 35% from 19,300 sf to 12,400 sf.	Updated company privacy policy and processes in the PDP Program to reflect changes to global personal data protection laws.	Established a paid parental leave program to support working parents.	Engaged a third-party consulting firm to carry out a board evaluation process and joined NACD to support ongoing director education.
Established a process to gather GHG emissions data points and set targets for expected SEC disclosure requirements.	Developed and published Human Rights Policy to support our commitment to human rights.	Implemented employee engagement & recognition software to further promote and foster a culture of appreciation and inclusion.	Implemented pay vs. performance analysis for SEC disclosure of company financial performance measure used to determine executive compensation.
Implemented LearnUpon LMS and Adobe e-signature to reduce in-person training travel and printed materials with virtual on-demand programs using digital materials.	Expanded University+ program to 307 free software licenses across 51 countries to further education in our industry and support the next generation of scientists.	Conducted employee engagement survey to ensure culture alignment and success of internal programs and benefits.	Updated Code of Conduct policy to reflect that we and our business partners meet the standards of business governance, environmental sustainability, and human rights.

Questions

CLOSING REMARKS

SHAWN O’CONNOR, CEO

Our Path to Win



- **Unparalleled offerings and client-centric business model**
- Leaders in model informed drug development because we are **focused on areas that our clients find most important**
- Continue to lead the industry in **ease of use** for our software offerings
- Continue to build upon our **strong relationship-based model** to expand existing clients and win new clients

Conclusion | Key Messages

- WE HAVE A LONG HISTORY OF INNOVATION IN BIOSIMULATION THAT IS TRANSFORMING DRUG DEVELOPMENT AND R&D
- WE HAVE A RICH FUTURE FOR GROWTH OPPORTUNITIES
- WE HAVE A HIGHLY EXPERIENCED SCIENTIFIC LEADERSHIP TEAM
- WE ARE ALIGNED WITH OUR CLIENTS TO MEET DEMAND FOR FUTURE GROWTH
- WE HAVE A STRONG FINANCIAL POSITION TO FUND OUR GROWTH

SimulationsPlus

Putting Clients First Drives Growth And Fuels Innovation

NASDAQ: SLP

https://www.simulations-plus.com/

Appendix

Workplace Recognition Awards

Diversity at Simulations Plus

Top 5%

A+

Diverse employees at Simulations Plus have rated Perks And Benefits, Meetings, and Team as the highest categories they have scored

CEO Rating at Simulations Plus

A+

CEO Rating at Simulations Plus is rated A+
Last updated months ago

TOP 5%

Simulations Plus ranks in the Top 5% of other companies on Comparably with 51-200 Employees for CEO Rating Score

Simulations Plus' CEO, Shawn O'Connor, has 60 employee ratings and a score of 89/100, placing them in the Top 5% of similar size companies on Comparably with 51-200 Employees and Top 5% of other companies in Los Angeles. When breaking the CEO score down by factors such as department, gender, and ethnicity, we see that females at Simulations Plus rate Shawn O'Connor higher than males, giving the CEO a score of 94/100.

Non-GAAP Definitions

Adjusted EBITDA

Adjusted EBITDA is defined as earnings (loss) before interest, taxes, depreciation and amortization, stock-based compensation, (gain) loss on currency exchange, any acquisition- or financial-transaction-related expenses, and any asset impairment charges. Currency exchange excluded represents the exchange rate fluctuations on the foreign currency denominated transactions. The impact of transactions in foreign currency represents the effect of converting revenue and expenses occurring in a currency other than the functional currency. The Company believes that the non-GAAP financial measures presented facilitate an understanding of operating performance and provide a meaningful comparison of its results between periods. The Company's management uses non-GAAP financial measures to, among other things, evaluate its ongoing operations in relation to historical results, for internal planning and forecasting purposes and in the calculation of performance-based compensation. Adjusted EBITDA represents a measure that we believe is customarily used by investors and analysts to evaluate the financial performance of companies in addition to the GAAP measures that we present. Our management also believes that Adjusted EBITDA is useful in evaluating our core operating results. However, Adjusted EBITDA is not a measure of financial performance under accounting principles generally accepted in the United States of America and should not be considered an alternative to net income or operating income as an indicator of our operating performance or to net cash provided by operating activities as a measure of our liquidity. The Company's Adjusted EBITDA measure may not provide information that is directly comparable to that provided by other companies in its industry, as other companies in its industry may calculate non-GAAP financial results differently, particularly related to nonrecurring, unusual items.

Adjusted Diluted EPS

Adjusted diluted EPS is calculated based on net income excluding the impact of any acquisition- or financial-transaction-related expenses, any asset impairment charges, and tax provisions / benefits related to the previous items. The Company excludes the above items because they are outside of the Company's normal operations and/or, in certain cases, are difficult to forecast accurately for future periods.

The Company believes that the use of non-GAAP measures helps investors to gain a better understanding of the Company's core operating results and future prospects, consistent with how management measures and forecasts the Company's performance, especially when comparing such results to previous periods or forecasts.