

Message

From: Elizabeth Holmes [/O=THERANOS ORGANIZATION/OU=FIRST ADMINISTRATIVE GROUP/CN=RECIPIENTS/CN=EHOLMES]
Sent: 12/15/2009 7:32:42 PM
To: thomas.breuer@gskbio.com
CC: Sunny Balwani [sbalwani@theranos.com]
Subject: Follow up to our meeting

Dear Thomas,

It was great to meet you.

In follow up to our conversations, I have attached three documents to this email.

The first is a consolidated summary of the GSK infrastructure we've designed in follow up to our interactions with people on the corporate side in information systems and strategy. We took ten slides on the applications in Biologicals and added them to the end of that summary – slides 28-38. The first slide highlights the ability to use the existing surveillance infrastructure to rapidly test the efficacy of existing vaccines against drifted strains of influenza virus using Theranos' strain-specific real-time antibody tests and the formulas we've established for the relationship between dose, antibody levels, and clinical outcomes.

The second is a copy of the validation report from the GSK staff who tested Theranos technologies in RTP. As you can see in that attachment, GSK's lab Director concluded that "Theranos Systems eliminate the need for a lab." The report shows the ability to get better sensitivity and real-time data using Theranos.

The third is a copy of a case study on Theranos' analytics also reviewed by GSK staff in detail during their due diligence process. This review focused on the ability to improve probability of success of realizing a target product profile with Theranos analytics. The case study details another company's use of Theranos analytics in registrational studies where the system increased POS from 15-80% and saved 18-24 months in clinical development timelines.

The Theranos Solution is a fully integrated and automated system for data capture, analysis, and care delivery. The data capture capability in combination with the predictive analytics capability has been the key to our success in accelerating development timelines.

We are very much looking forward to following up with your clinicians in Philadelphia. Is there a convenient time this week we could meet or arrange a video-conference? Please let us know how best to follow up.

Kind regards,
Elizabeth.

Elizabeth Holmes
President and CEO
Theranos, Inc.

Tel: 650.470.6111
Fax: 650.838.9804

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Theranos, Inc., 3200 Hillview Avenue, Palo Alto, CA, 94304
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GTS

GSK's Strategic Enterprise Infrastructure

This presentation and its contents are Theranos proprietary and confidential.



Contents

• Background

- GTS ROI
- GTS Deliverables
- GTS in Biologicals



Introduction to Theranos, Inc.

Theranos is a Silicon Valley-based healthcare company founded in 2003.

- Theranos provides fully customized solutions that impact a diverse range of stakeholders in health care by providing actionable information far earlier than historically possible
- Our current and past clients include 9 of the top 15 major pharmaceutical companies, mid-sized bio-pharmas, prominent research institutions and U.S. and foreign government health organizations



About Theranos

Founder and CEO Elizabeth Holmes left Stanford University to start Theranos around her patents for next-generation healthcare systems. She has built the company from inception to rapid commercial growth today.

Vice Chairman Sunny Balwani joined Theranos after leaving Microsoft to successfully build and sell his own company for over \$400M

Other Management Team Members:

- Dr. Channing Robertson, Dr. Seth Michelson, Jodi Sutton, Dr. David Lester, Dr. Marc Thibonnier

Theranos' investors and board members include, amongst others:

- Donald L. Lucas, the first venture capitalist in Silicon Valley, and a legend behind many of today's Fortune 500 companies
- Larry Ellison, Founder and CEO of Oracle Corporation
- Bob Shapiro, former CEO and Chairman of Monsanto and Pharmacia Corporations (now Pfizer); former director of NYSE, Citibank, and other major corporations
- Draper Fisher Jurvetson; ATA Ventures (spin-out of Institutional Venture Partners)

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Theranos & GSK

- GSK completed a comprehensive validation of Theranos Systems in 2008
 - Validation was independently conducted run by GSK staff at RTP
 - Validation concluded “Theranos Systems eliminate the need for a lab”

- Over the past four years, leads from all three business units across all therapeutic areas have evaluated and expressed interest in the Theranos infrastructure

- Theranos and GSK have a fully executed MSA

- Integrated architecture of Theranos infrastructure requires adoption at top corporate levels

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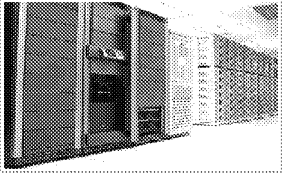
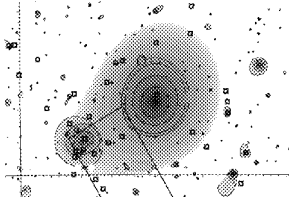
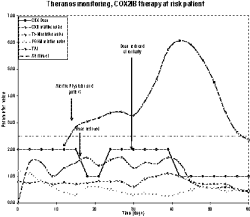


Theranos Infrastructure Technologies

Theranos Field Systems

| | | |
|---|--|---|
|  |  |  |
| Devices | Cartridges | Mobile Applications – Ex. the Health Assistant |

TheranOS – Theranos Operating System

| | | |
|---|---|--|
|  |  |  |
| Data Infrastructure | Models and Algorithms | Decision Support Applications – Ex. Virtual Studies |



GTS

- * GTS is a fully integrated, enterprise wide health data capture (including blood testing), analysis and care delivery solution
- * Accelerates clinical development timelines, improves probability of success (POS) of realizing each target product profile, and increases physician and patient adoption (increases sales)
- * Comprised of Theranos Field Systems and the TheranOS
 - Integration of technologies and more frequent sampling identifies predictive signatures that have not been possible to characterize using the conventional analytical infrastructure (movie v. snapshot) to better and more rapidly characterize efficacy and safety
 - Infrastructure is self-learning and is refined with every new data point collected across any business unit
 - Provides predictive decision support tools for clinicians
 - Provides actionable, “smart” content back to patients to facilitate behavior modification
 - Data Collection, Analysis & Surveillance Infrastructure in emerging countries becomes care delivery infrastructure



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▪ GTS ROI

- GTS Deliverables

- GTS in Biologicals



Economic Impact for GSK

- Accelerate Clinical Development/Trial Timelines
- Improve Probability of Success of Realizing Target Product Profiles
- Increase Physician and Patient Adoption – Increase sales



Economic Impact for GSK

- Accelerate Clinical Development/Trial Timelines
 - Elimination of Logistical constraints (shipping samples, analyzing data, bringing patients into clinics, recruiting patients without knowing their response profiles, etc.) and
 - Faster, more integrated studies (adaptive trials and decision making)

cumulatively reduce development timelines by (~3) years to facilitate earlier filings.

- Theranos' large pharmaceutical clients have valued the fully loaded cost of each day gained in time to market at \$1M/day



Economic Impact for GSK

- Improve Probability of Success of Realizing Target Product Profiles
 - 5x improvements in probability of success for each asset
 - Salvage assets and improve labels (more first line therapies)
 - Realizing the improvement in attrition rate across the entire portfolio versus just one compound continually reduces the fully loaded cost of R&D
- 5x improvement in probability of success correlates with greater than 10% ROI on the total investment into a compound, averaging greater than \$200M/asset



Economic Impact for GSK

- Increase Physician and Patient Adoption
 - Evidence based guidelines for starting/stopping/re-starting therapies to increase physician comfort with prescribing
 - Rapid publications for expanded use – new indications and amelioration of safety concerns
 - Improved care delivery through individualized feedback tools and better access to medicines through Theranos' decentralized testing infrastructures (in pharmacies, through health ministries, etc.)
- Increase sales by several multiples over current adoption/projections



Return on Investment

- The value of GTS lies in the fact that it is a fully integrated solution for data capture, integration, analysis, (and therapeutic delivery) across business units.
- The integrated solution provides compounding ROI over any particular business unit or drug-specific component.
- The key to significant ROI on GTS is programmatic deployment, which yields short term cost savings against the initial customization investment in addition to longer term ROI measured in terms of time saved and improved POS of realizing the target product profile for each asset.

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Immediate ROI: Executing on Healthcare Diversification Strategy

GTS is the vehicle for execution of GSK's strategic priorities and realization of the associated impact to earnings and growth

- Accelerated timelines ... simplifying GSK's operating model
- Improved POS ... delivering more products of value
- Increased adoption ... growing a diversified global business

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- GTS in Biologicals

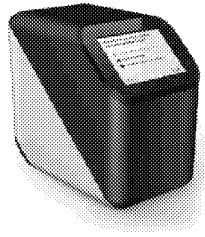


Theranos is the only company with full integration between sample analysis and analytical capabilities

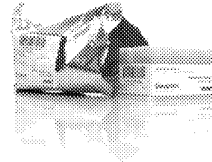
GTS integrates patient sample analysis with sophisticated analytical capabilities to increase R&D ROI.

| Capability | Clinical Trial Simulator | Physiological Modeler #1 | Physiological Modeler #2 | Central Lab | CRO |  |
|---|--------------------------|--------------------------|--------------------------|-------------|-----|---|
| Patient recruitment | | | | | ✓ | ✓ |
| Investigator/site mgmt | | | | | ✓ | ✓ |
| Sample handling | | | | ✓ | ✓ | ✓ |
| Sample analysis | | | | ✓ | ✓ | ✓ |
| Data management | ✓ | ✓ | ✓ | | ✓ | ✓ |
| Basic analytical package * PK/PD modeling * Clinical trial simulation | ✓ | ✓ | ✓ | | | ✓ |
| Physiological model | | ✓ | ✓ | | | ✓ |
| Dynamic learning models and real-time data acquisition | | | | | | ✓ |
| Clinical study report | | | | | ✓ | ✓ |

Theranos Field Systems



Devices



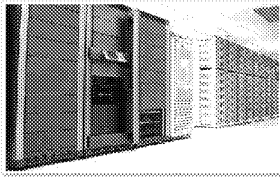
Cartridges



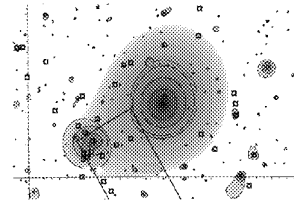
Mobile Applications –
Ex. the Health Assistant

- Measure whole blood analytes from a finger stick in real-time at any desired point of care (home, clinic, or mobile units)
- Simultaneously collect behavioral and lifestyle information through intuitive graphical touch screen interface
- Data from each device automatically and securely transmitted to TheranOS in real-time through cellular network
- Actionable information sent back to devices and applications (i.e., the Health Assistant, Virtual Studies Application)
- Point-of-care analysis of fresh whole blood eliminates conventional testing infrastructure issues, such as:
 - Analyte decay rates
 - Volumes of blood and frequency of blood draws
 - Decreases sample volume by 98%
 - Sampling schemes no longer restricted
 - Cost and logistics of sample shipments

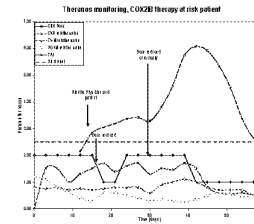
TheranOS



Data infrastructure



Models and Algorithms



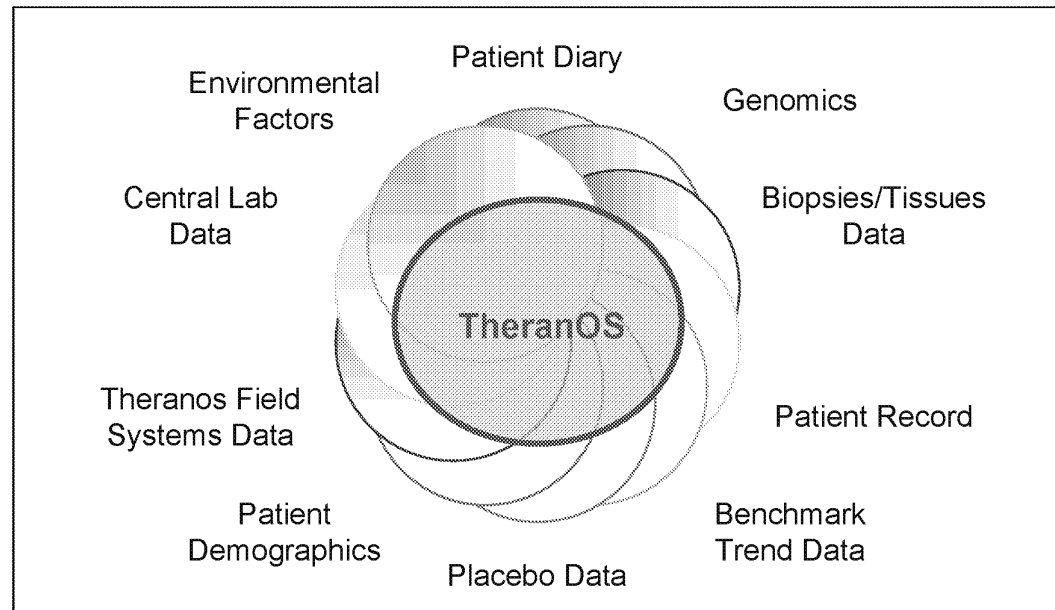
Applications –
Virtual Study

- * Data Infrastructure
 - Automatically imports data from any desired source.
 - Translates it into one standardized format.
 - Self-learning data engine
- * Models
 - Dynamically models the integrated data sets in real-time
 - Fully integrated and inter-connected physiological, statistical, and epidemiological system
 - Characterize each compound's mechanism-of-action.
 - Characterize all pathophysiologies associated with realizing each compound's target product profile
- * Customized Applications
 - Clinical trials simulation
 - Adaptive trials management, in compliance with existing regulatory guidelines
 - Accessed through secure online web portal



TheranOS: Proprietary Data Integration, Translation

- Proprietary import tool on web portal allows for automatic importation and standardization of data from all clinical databases.
- All data is automatically integrated with Theranos Field Systems data, centralized, and passed through predictive models.



TheranOS Data Infrastructure

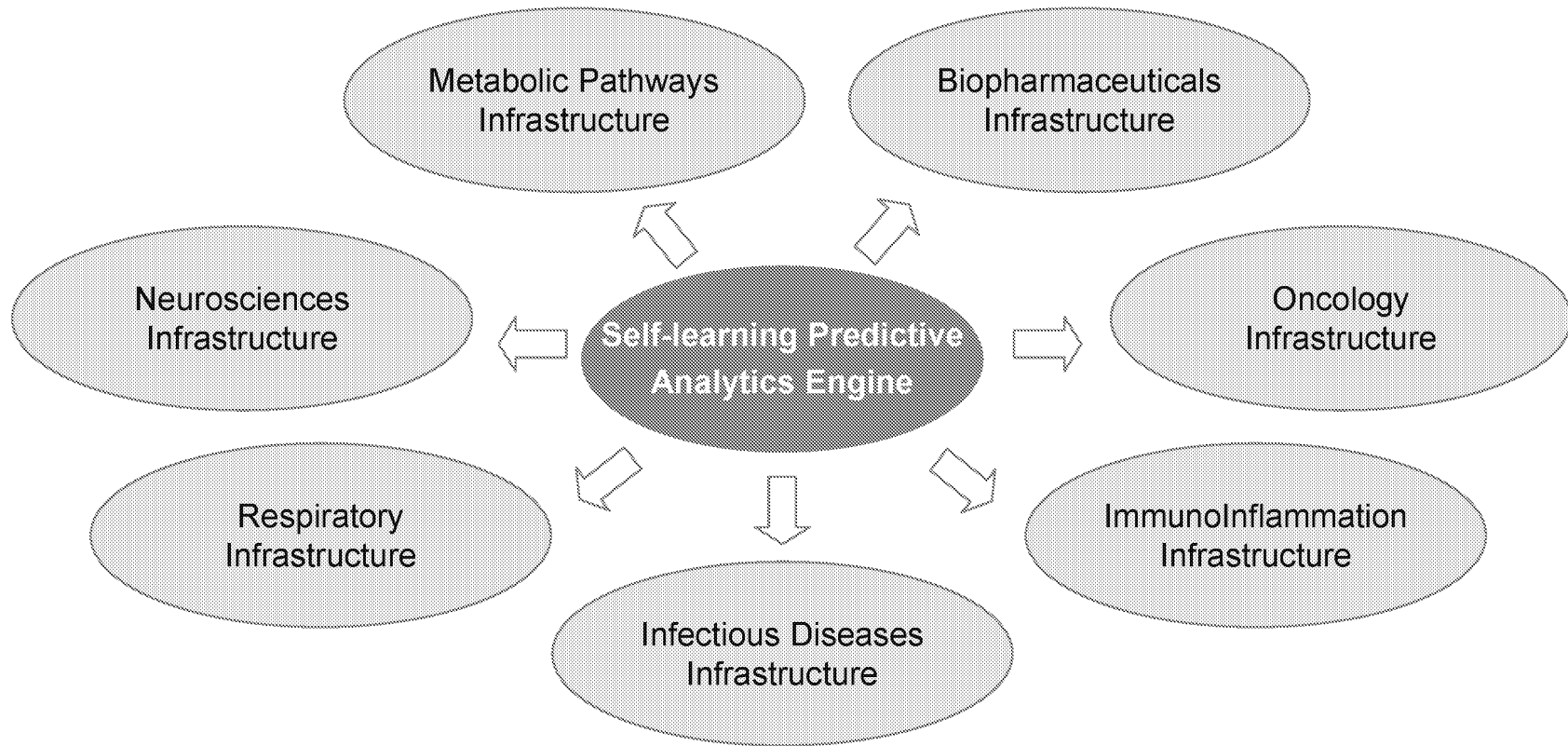


GTS Architecture Drives Deployment Plan

- A cornerstone of GTS' architecture is the inflammation engine.
- The central role of inflammation in the disease process and tissue damage/repair, allows one to apply the GTS infrastructure across various therapeutic areas and business units.
- Deployment of a customized inflammation platform provides the ability to rapidly integrate data from different pathophysiological states for predicting and establishing novel therapeutic indications.
 - GTS engine learns from every new data point and models become increasingly predictive -compounding predictive power
- Drug-specific models and cartridges are built on GTS' pathway architecture to conform to existing business unit structure.
 - TheranOS allows for data integration & exploitation across a broad range of existing data capture tools.



Rapid Customization of GTS: Therapeutic Area Infrastructures





Decision support applications:

TheranOS Software for each Therapeutic Area:

- Probability Mapping Application
- Health Assistant
- GTS Assistant
- Adaptive Studies
- Ontologies
- Predictive Signatures
- Biomarker Identification Application (BIA)
- Virtual Study Application
- Others

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Data Collection Library & Care Delivery Tools:

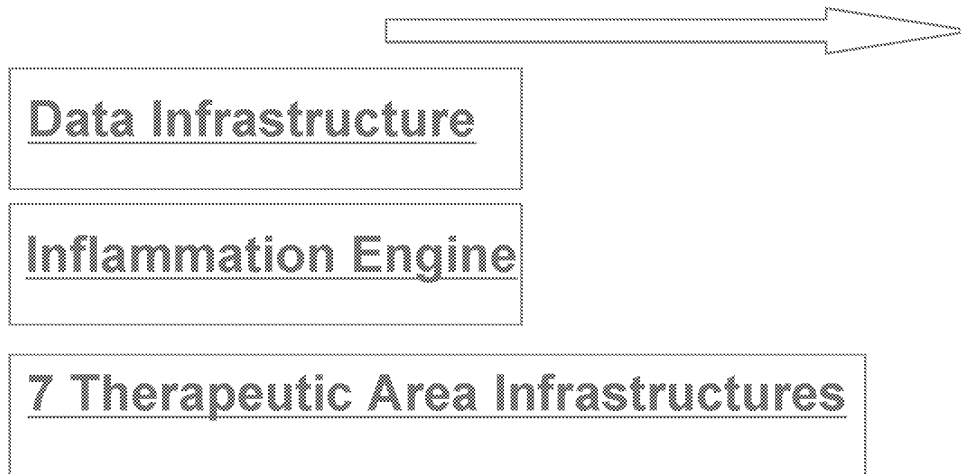
For each therapeutic area:

- Cartridge tests – libraries of ~250 tests per disease area
- Device touch-screen software applications and embedded sensors – blood pressure, weight, others
- Mobile phone applications

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Rolling infrastructure set-up

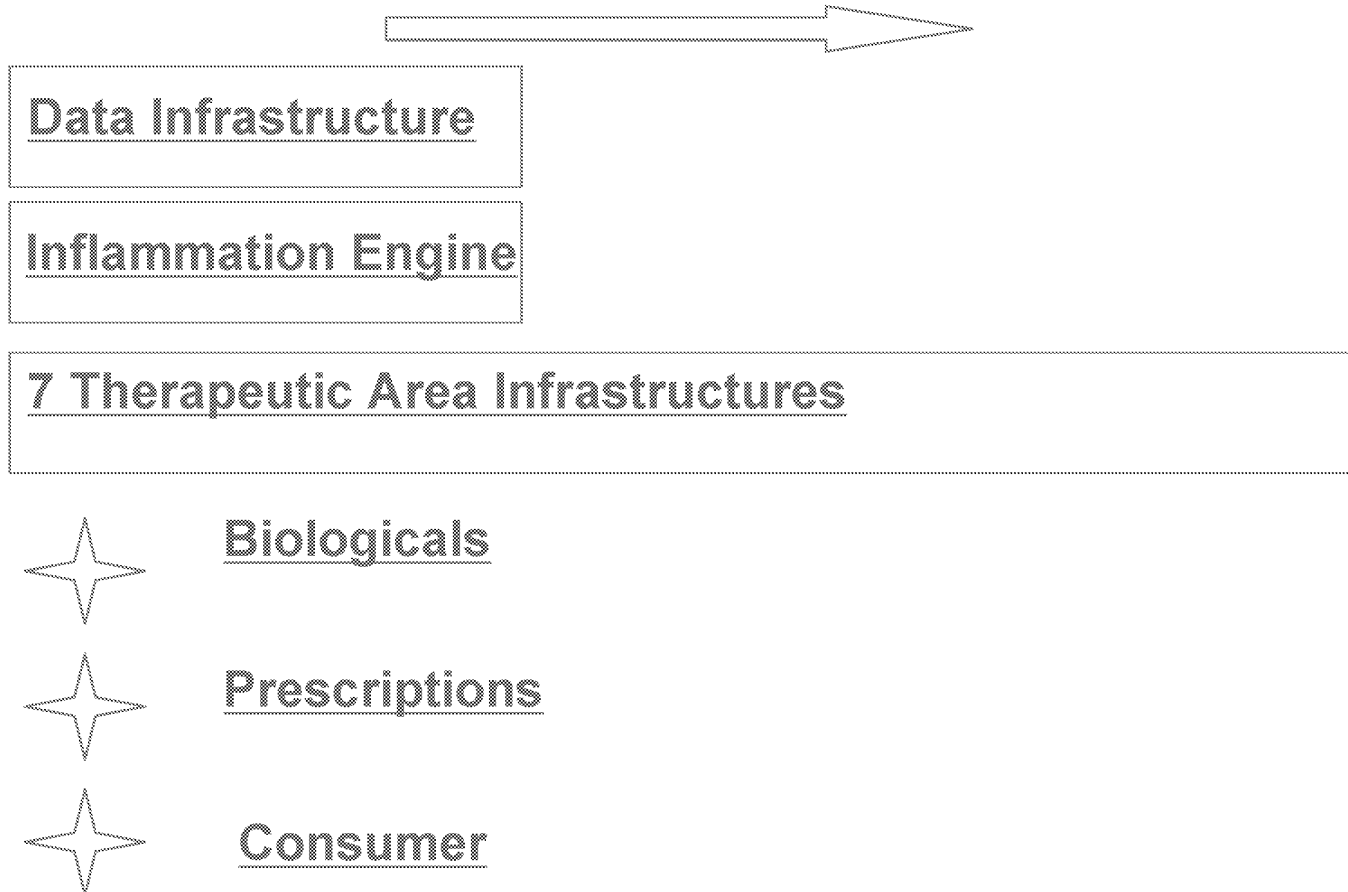


Customization and activation of base GSK data infrastructure and learning engines followed by rolling set up of 7 therapeutic area infrastructures

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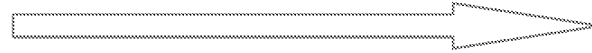
Rolling infrastructure set-up



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Rolling infrastructure set-up



Biologicals: Influenza (vaccine) → Oncology
→ Others



Prescriptions: Unprecedented Early
Development Compounds, REMS, LpPLA-2
→ Early Development, Phase III, Phase IV &
Post marketing studies



Consumer: Weight loss (alli) → Smoking
Cessation → Others

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Deployment of GTS

- Customization, Installation, and License of enterprise infrastructure
- Deployment of consumables for studies
- License expansion – Deployment of additional drug-specific models/consumables



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GTS in Biologicals



Rapid Validating Efficacy of Existing Vaccines Against Drifted Strains of Influenza Virus

- Theranos characterized relationship between dose, clinical efficacy, and antibody titers to influenza strains on its validated point-of-care systems.
- Assays identify functional, strain-specific antibodies from a finger-stick of fresh whole blood.
- Once deployed in a clinical study, patients could be immediately challenged with the actual virus and followed for 2+ weeks to assess whether the existing vaccine is efficacious.
- If not, the same infrastructure could be used to rapidly assess optimal dose and efficacy of a new vaccine.

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Influenza Surveillance Infrastructure

Real-time development and deployment of antibody, cytokine, and efficacy/safety marker measurements from finger-stick of blood /nasal swab run on point-of-care device

- Characterize velocity of antibody decay
- Accelerate development of new vaccines to mutations
- Quantitatively characterize efficacy and safety profiles to ameliorate concerns and differentiate GSK vaccines
- Guide optimal administration of vaccines
- Provide real-time measurement of efficacy and immunity

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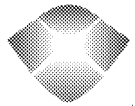


Influenza Surveillance Infrastructure

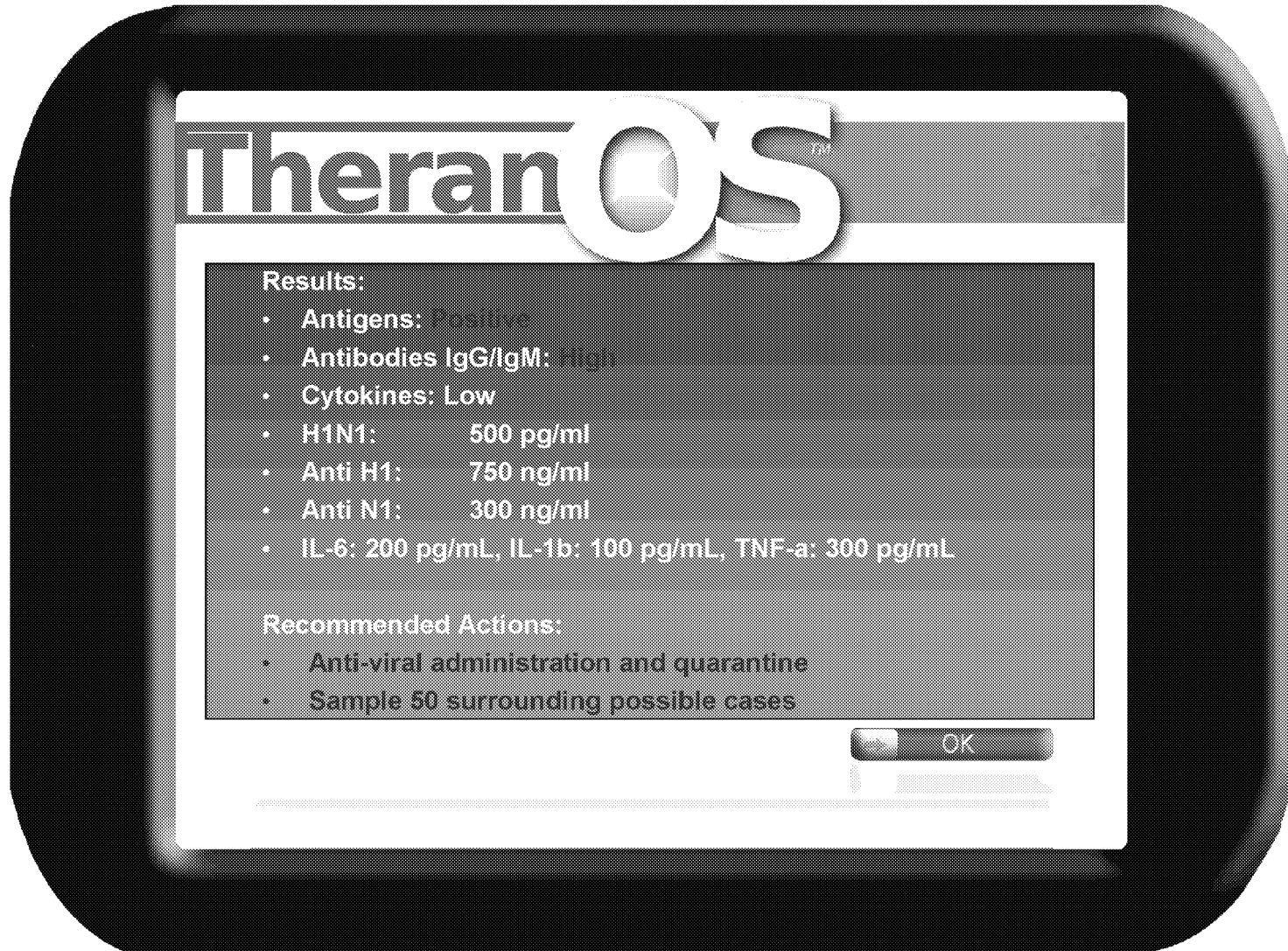
Modeling and simulation of efficacy and safety dynamics and projected spread and mutation of the virus

- In-silico comparative effectiveness studies to optimally power head-head studies with antibody/efficacy cartridges
- Virtual studies to rapidly optimize dose and minimize safety issues
- Rapidly power (adaptive) studies
- Detect any mutation of the H1N1 virus as it emerges.
- Project spread of disease and mutations

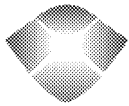
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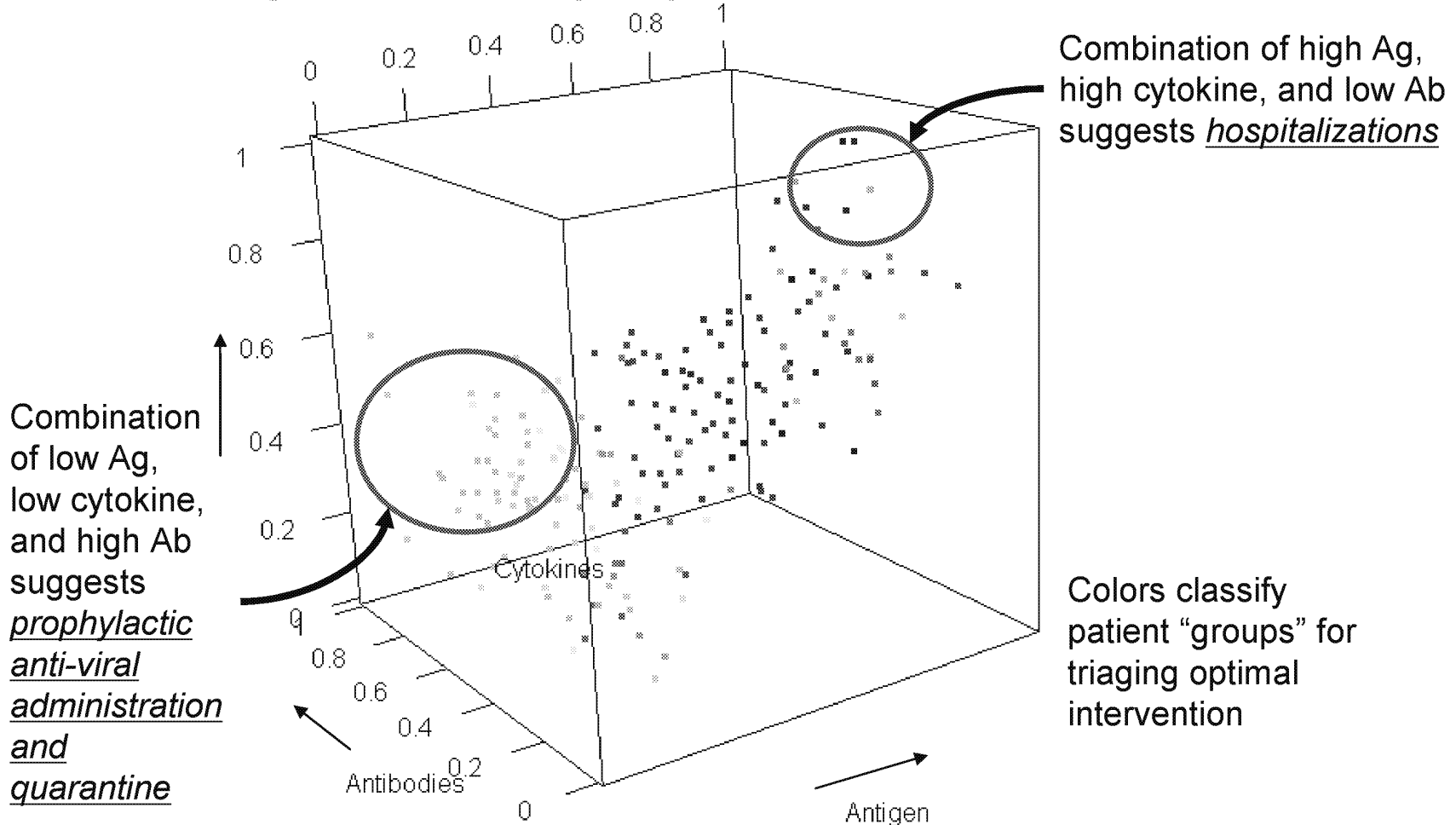
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theranos

redefining healthcare

Recommended Actions Depend on Levels of Antigen, Antibody, Cytokine and Other Markers



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THS Modeling Platform Capabilities

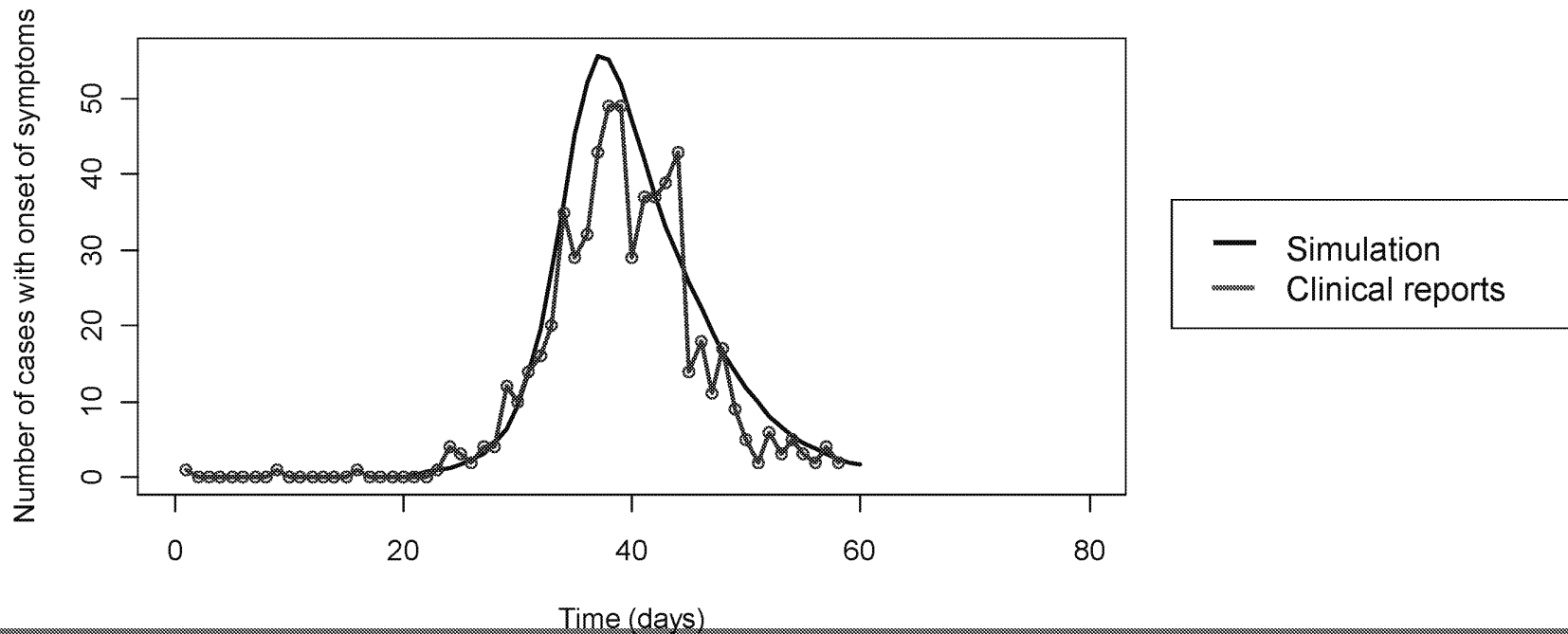
1. Predicts spread of an infectious pathogen in a heterogeneous human population.
2. Reflects the impact of regional demographics and patient risk factors.
3. Enables evaluation of healthcare mitigation policies, for example:
 - Surveillance/testing strategies
 - Hospitalization, home isolation, and quarantine policies
 - Prophylactic vaccination and anti-viral treatment policies
 - School and workplace closures; other social distancing measuresEnables cost assessment and evaluation of quality adjusted life years (QALY) saved by comparing alternative mitigation approaches.
4. Is fully integrated with real-time data acquisition, enabling model updates based on the latest data acquired from multiple sources
5. Includes automated, frequent model updates.
 - Leads to more accurate projections for spread.
 - Allows health agencies to rapidly adapt to changing conditions.

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THS Model Accurately Reproduces Spread of La Gloria Outbreak

- All models are validated by reproducing historical data

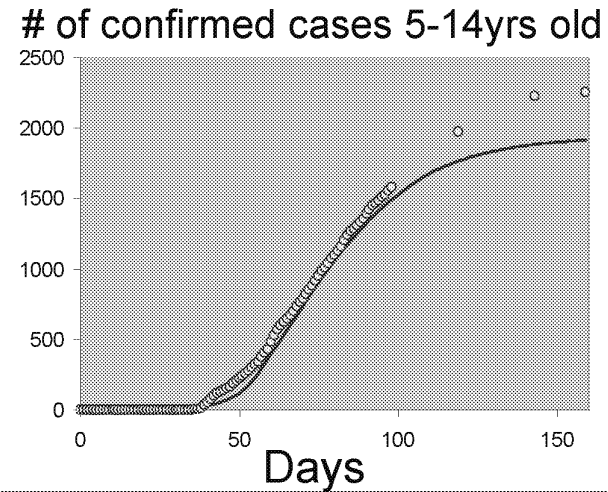
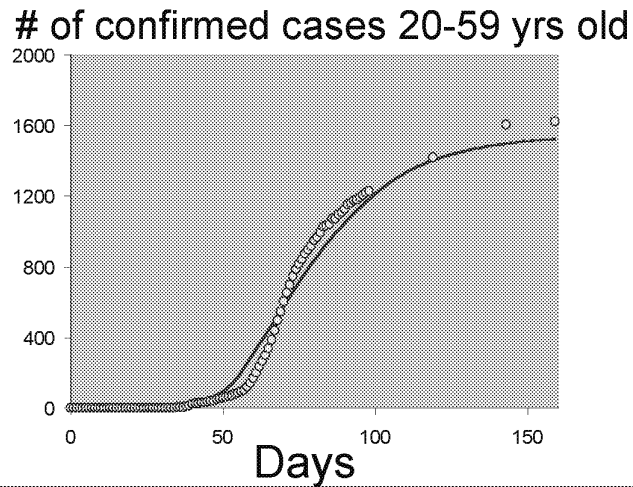
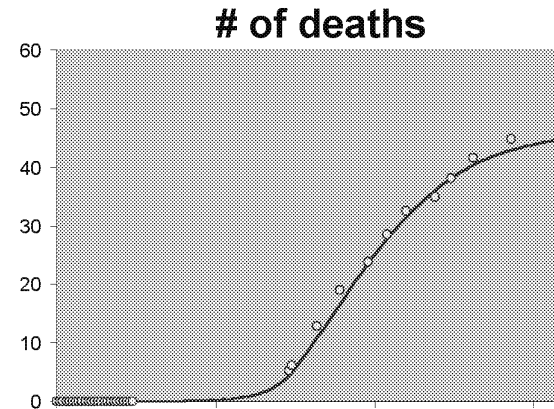
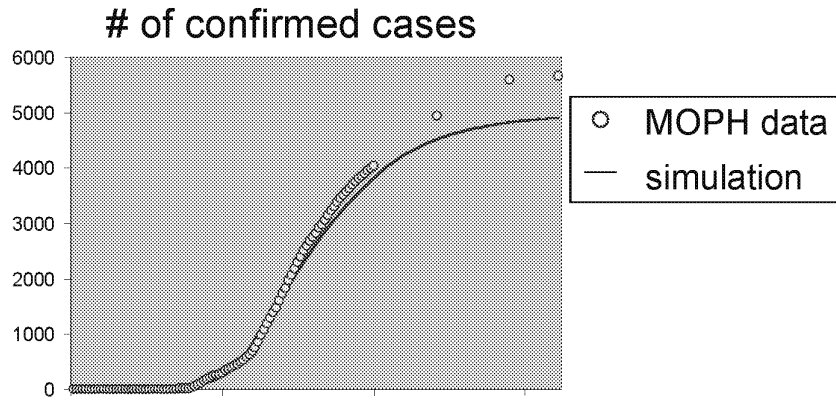


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Model Reproduces Bangkok Publicly Reported H1N1 Data Including Deaths and Age-Dependence

Total cases ~20,000; reported cases significantly less.



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Selected Oncology Applications

- Rapid expansion of use through predictive visibility (models) and early reads (cartridges) on efficacy and safety in new indications
 - MAGE-3 expansion
- Virtual and rapid head-head studies for comparative differentiation
 - Cervarix differentiation – characterization of velocity of antibody decay and need for re-boost
- Combination tests for low cost, real-time identification of antigen levels/presence of genetic signature from finger-stick of fresh whole blood run on point-of-care device in pharmacies, physician's offices, and other remote locations
 - MAGE-3 “responder” identification

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Deployment of GTS

- Decision support applications provide compounding predictive power
 - Inflammation/immunology/humeral response models form foundation of data analytics engine
 - Data analytics engine facilitates data integration and connectivity between disease-specific infrastructures:
 - Viral & Allergy Vaccines
 - Bacterial Vaccines
 - Emerging Diseases & HIV
 - Cancer Vaccines
- Data collection, analytics and surveillance infrastructure facilitates Care Delivery in emerging countries through placement of devices in remote locations



Excerpts from GSK Metabolic Study Report

Nelson Rhodes, Director GSK Metabolic Biomarker Laboratory
Surekha Gangakhedkar, Theranos Assay Systems Lead

Background information:

The Theranos system was evaluated at GSK to profile active GLP-1 and C-peptide values and these data were compared to “gold standard” ELISAs using frozen human plasma from study XXXXXXXX. The key project objectives (found in the attached statement of work) were:

- To assess the performance of the Theranos System in measuring a multiplex for GLP-1 and c-peptide values (the “Cartridge Analytes”) as compared to the current gold standard ELISAs (which are not multiplexed).
 - Specifically, the study will assess Theranos’ capabilities to detect points that the reference assays failed to accurately detect by running samples with C-peptide values in a standard range (ng/mL) and GLP-1 values between 0-3.2 pM
- To assess the functionality, specificity, reproducibility, accuracy, and precision of the Theranos System.
- Assess the Theranos data reporting and transfer functions

Thirty plasma samples (assayed in duplicate) were chosen based on historical GSK data for total GLP-1 levels from subjects given a mixed meal and two finger prick blood draws were performed. Five Theranos machines were used with active GLP-1 and C-peptide cartridges that required 20µL of plasma. MesoScale Discovery’s (MSD) active and total GLP-1, Linco (Millipore) active GLP-1, and Linco (Millipore) C-peptide ELISAs were run as comparator assays.

GSK Metabolic Biomarker Lab comments:

- Data show good correlation
 - $r^2 = 0.90$ for GLP-1 (MSD vs. Theranos)
 - $r^2 = 0.96$ for C-peptide (Linco vs. Theranos)
- Inter-instrument precision (RLU average %CV = 11)
- Machines worked well
- Touch-screen interface was easy to use
- Cartridges were pretty straight forward (easy to handle and load)
- Assays took approximately 1 hour and 15 minutes per cartridge

Overall conclusions:

- The Theranos system eliminates the need for a lab and provided quality data
- The Metabolic Biomarker Lab has a favorable impression of the technology/system and recommends GSK clinical groups to work with Theranos

Data:

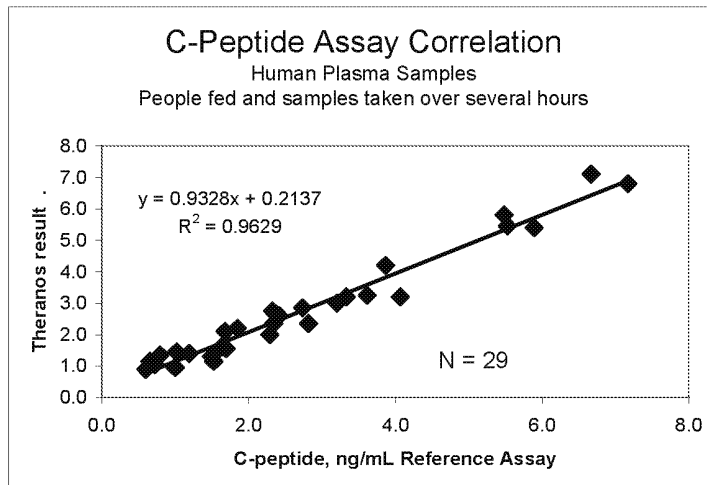
Study design

- Human subjects
- Food “challenge”
- Measure GLP-1 and C-Peptide multiplex over 5 time points
 - Linco Assay
 - MSD Assay
 - Theranos Assay

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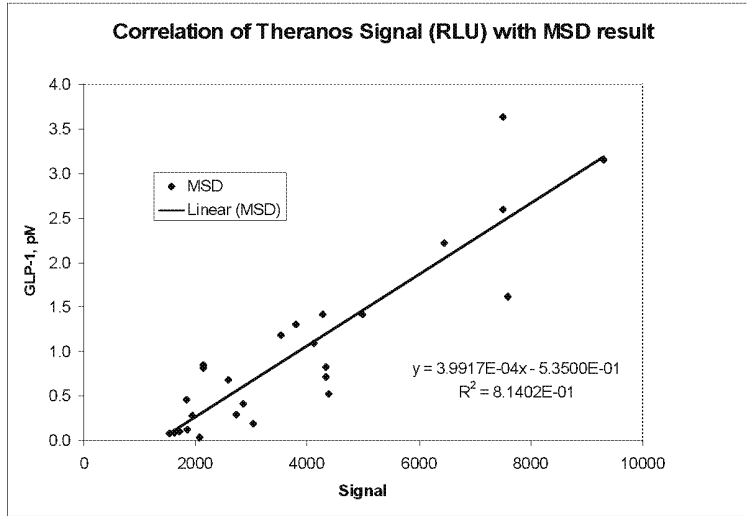
C-Peptide Assay

Averaged results



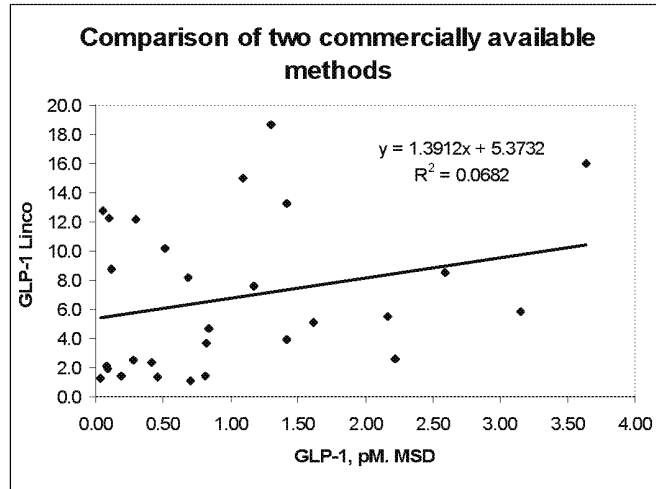
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Calibration to GSK matrix



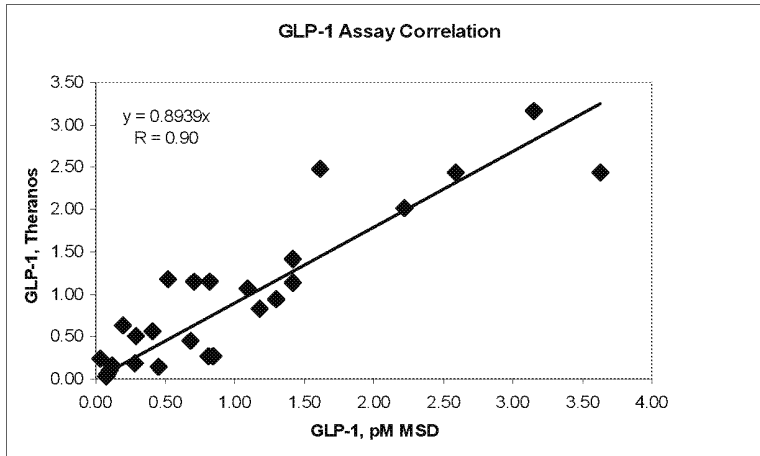
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Lack of correlation of predicate methods



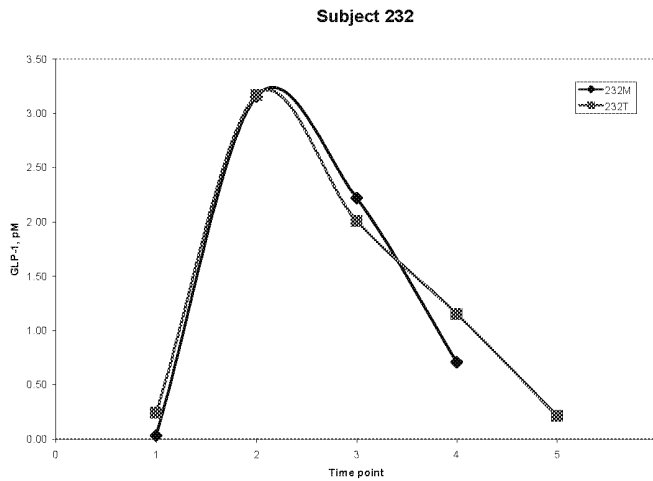
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Assay correlation



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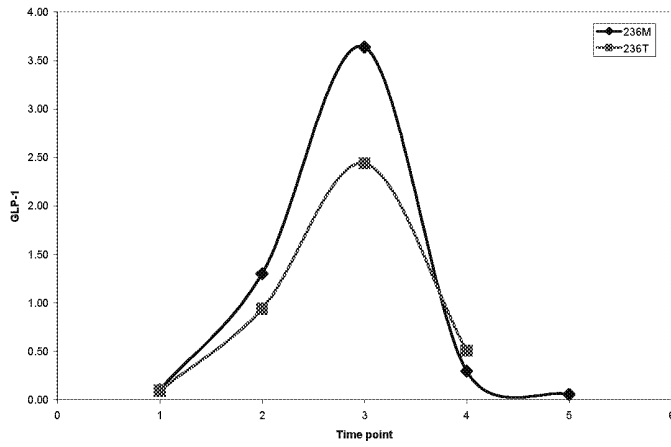
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Subject 236

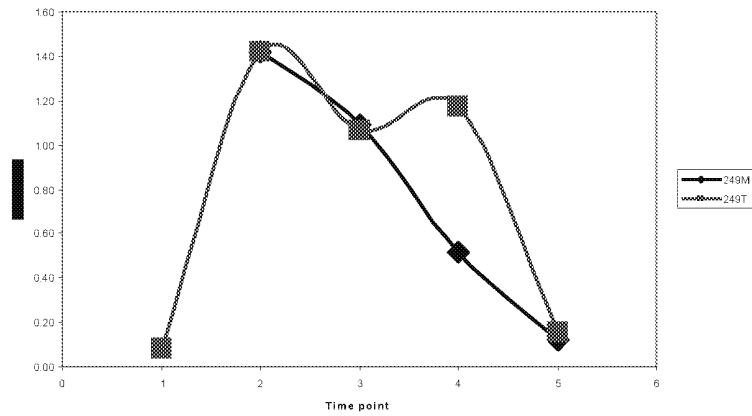
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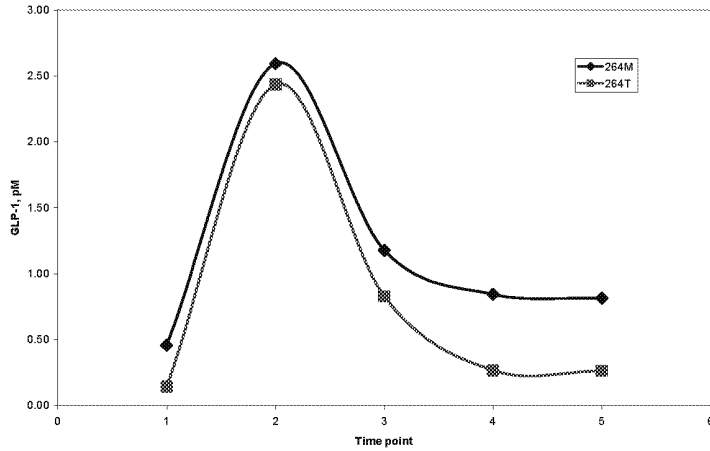
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Subject 264

Subject 264



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Summary Statistics GLP-1 Comparison

- Theranos LOD = 0.17 pM
- Dynamic range measured: 0-3.2 pM
- Mean = 0.9 pM (Th), 1.0 (MSD)

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TPS Case Study: Client ROI

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Virtual Study Application

TheranOS Virtual Study Application enables more efficient clinical study design, conduct, and analysis through in-silico:

1. Comparison of alternative clinical study designs
2. Exploration of drug effects on multiple physiologic outputs
3. Examination of patient response variance in order to power the clinical study
4. Optimization of dose regimens
5. Examination of the magnitude and variance of side effects



Virtual Study Application

TheranOS Virtual Study Application enables more efficient clinical study design, conduct, and analysis through in-silico:

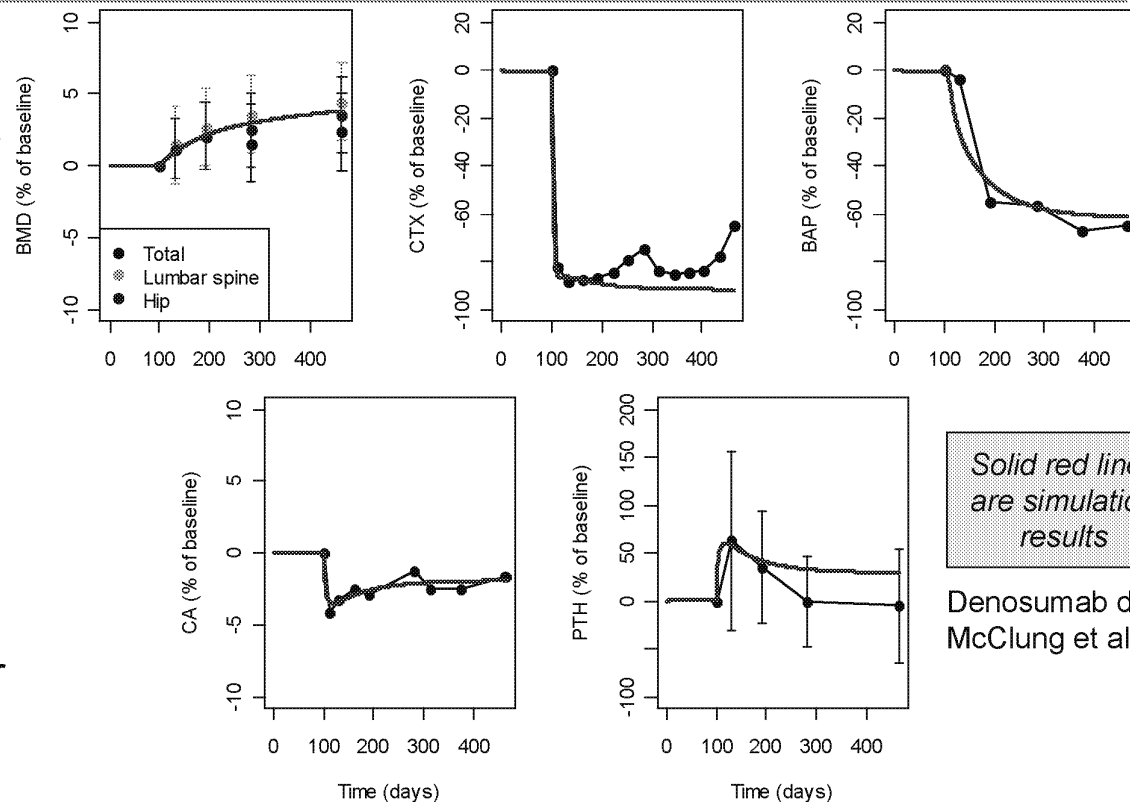
6. Identification and selection of sub-populations having different physiologic responses
7. Identification of predictive patterns for early reads on efficacy and safety
8. Refinement of enrollment criteria.
9. Probability analysis of likely clinical outcomes for a given design.
10. Head-head studies for comparative effectiveness
11. ...

Simulations can be run before a study is designed and dynamically throughout each study.

TheranOS Comprehensive Physiological Models

Using the interconnected physiological modeling engine, simulated optimal therapy regimens for maximum efficacy and minimal adverse events for asset that acts on multiple pathways.

- 95% target inhibition reproduced key behaviors reported in the clinical study of compound
- The model predicts the efficacy profiles of the drug, even without accounting for its *mechanism of action* (MOA models built for other drugs)
- Model identified a predictive signature of BMD that is measurable ~6 months prior to physical changes in BMD



Solid red lines are simulation results

Denosumab data: McClung et al 2006

▪ www.theranos.com

Example of TPS in Compound Development for Anemia and Bone-related Disease

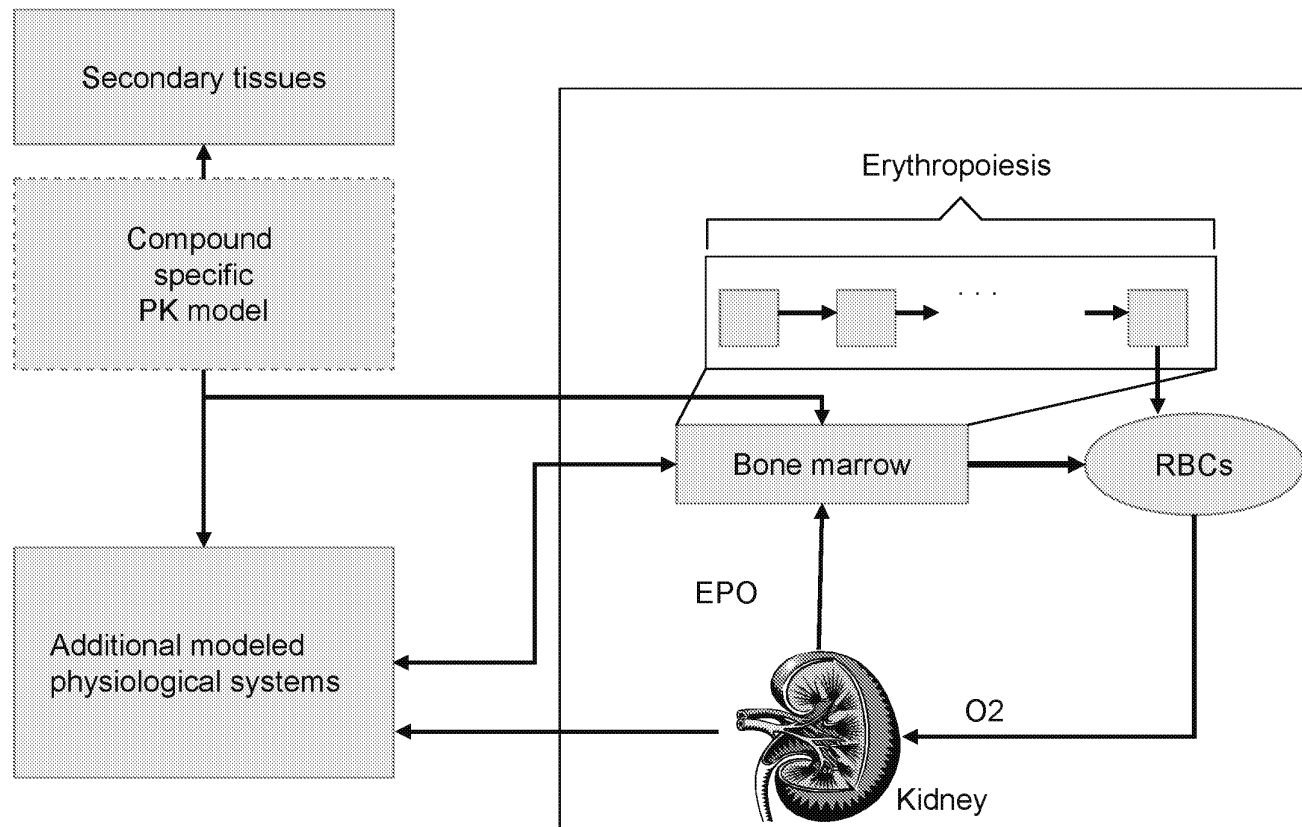
1. Customized TheranOS for automated data integration, analysis and real-time self-learning
 - Compounding predictive power from all Client-generated data
2. Developed and validated physiologic-based mechanistic modeling and simulation system
 - Captured effects of target inhibition by Compound treatment
 - Included target patient phenotypes based on literature and healthy patient responses to Compound
 - Optimized design, evaluation, execution of (adaptive) clinical trials for Compound
 - Led to novel biomarkers for efficacy and/or safety, enhancing patient treatment with Compound

Example (cont'd)

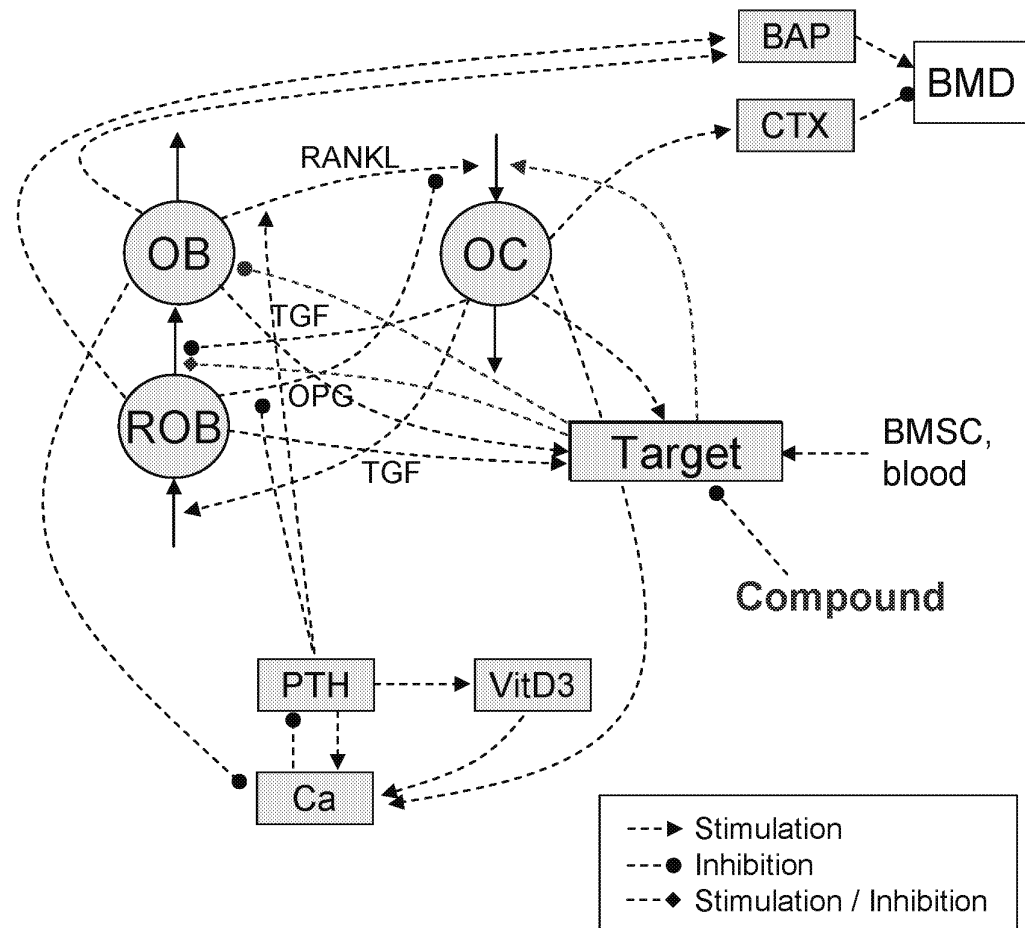
3. Virtual Study Application used to optimize Phase IIa trial design for target patient population
 - Recommended designs enhance power of trial
 - Increased probability of success
 - Provided support for regulatory reviews
 - Integrated data sets and models used by Client to run in-house simulations
 - Easy-to-use interface for in-house ownership/use of highly complex, proprietary modeling system

4. TheranOS applications integrated with Theranos Field Systems yielding compounding predictive power
 - Automated data integration, analysis, self learning and model refinement for trial design, analysis, and patient monitoring
 - Extended to include additional indications for Compound and for other compounds and their indications/target profiles

Schematic Overview of Physiological Model

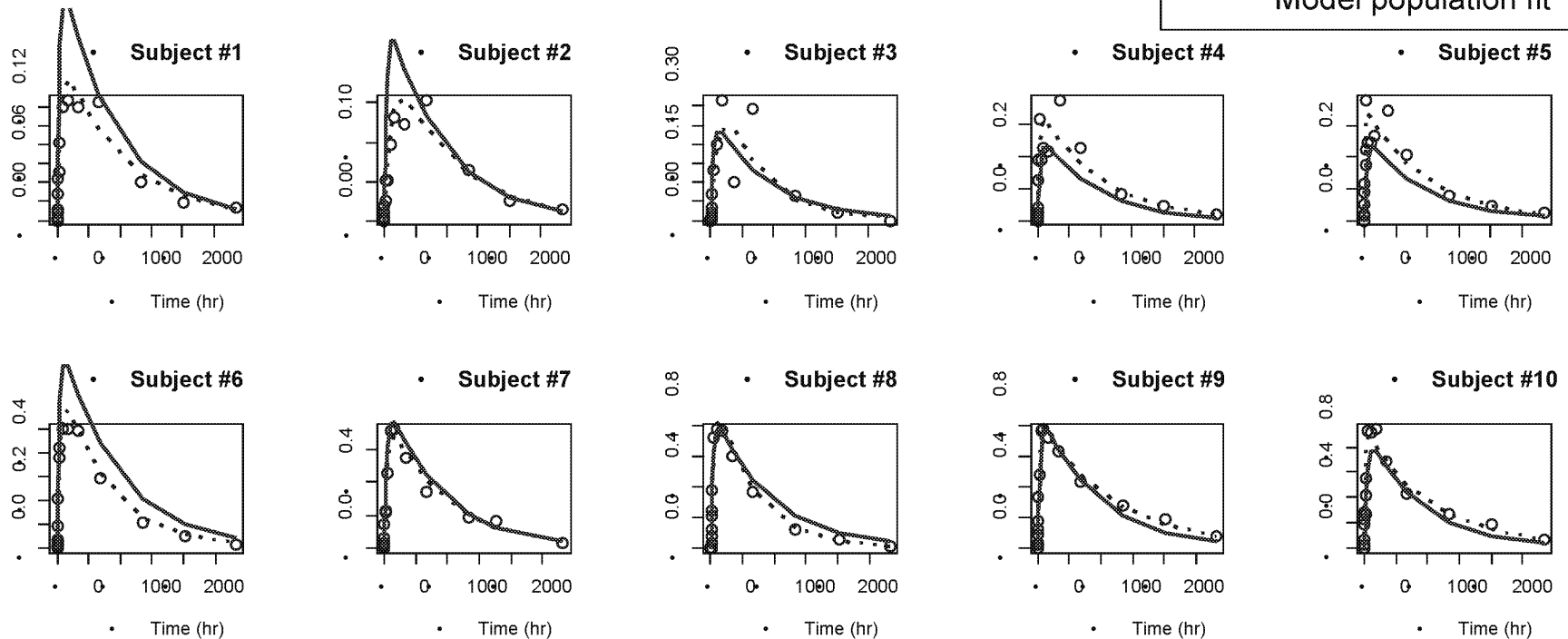
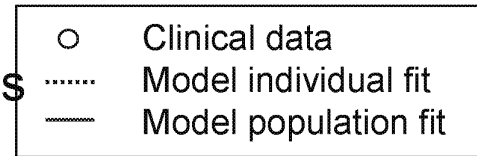


Summary Illustration of Quantitative Model Representing the Dynamics of Bone Metabolism

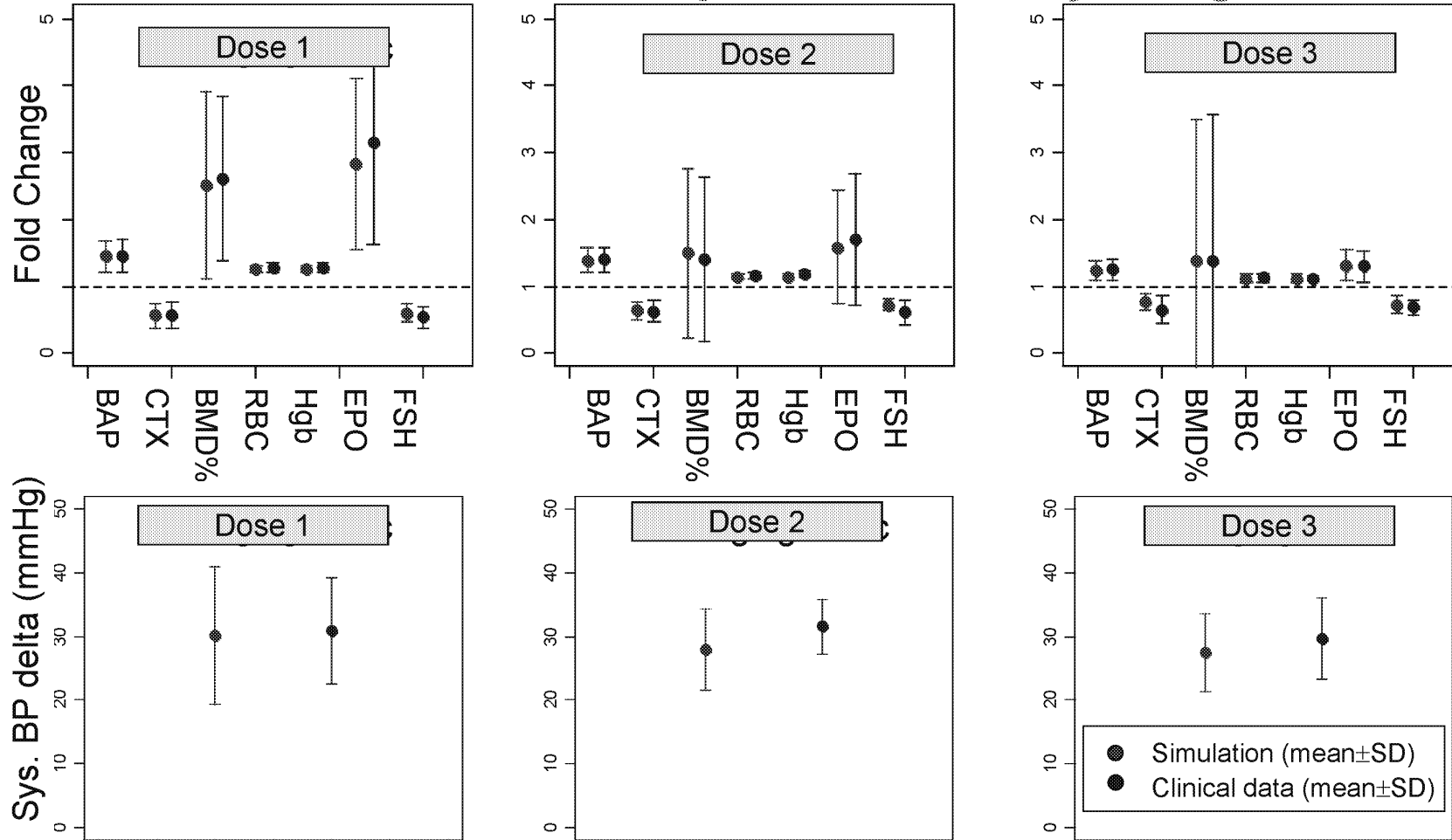


Pop-PK Mixed-Effects Modeling for Compound SC Administration

- First-order one-compartment model was used to fit the Compound SC PK data.
- Model data accurately predicts clinical PK profiles



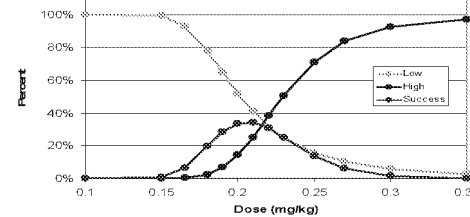
Simulated Peak Responses Predicted High, Mid, and Low Dose Response for All Physiologies



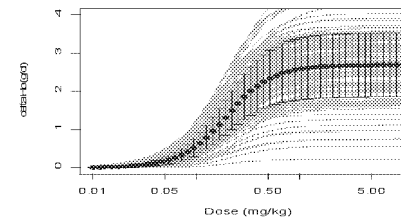
Virtual Study Application Increased Study POS

Simulations increased probability of study success by allowing users to optimize protocol and dosing titration schemes in-house prior to study initiation.

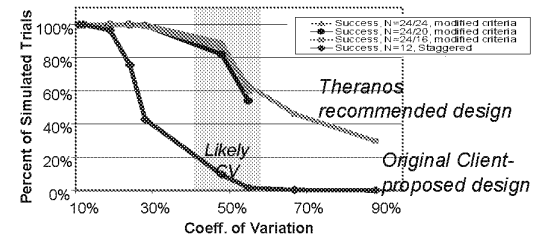
Simulation of probability of 'successful outcome' indicated high probability of study failure ...



... due to underlying variability of responses

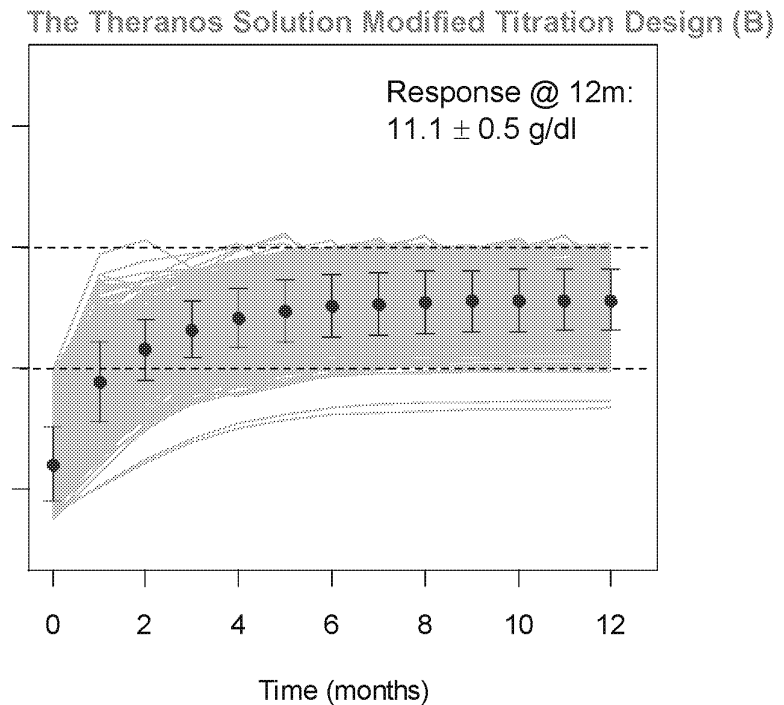
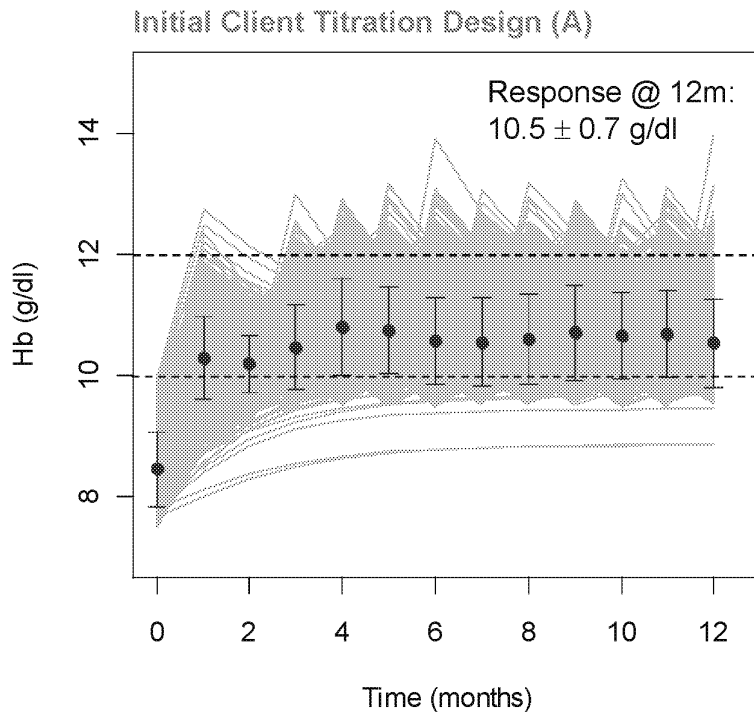


TPS optimized study design, dosing regimen, and titration parameters, increasing the probability of success 5x



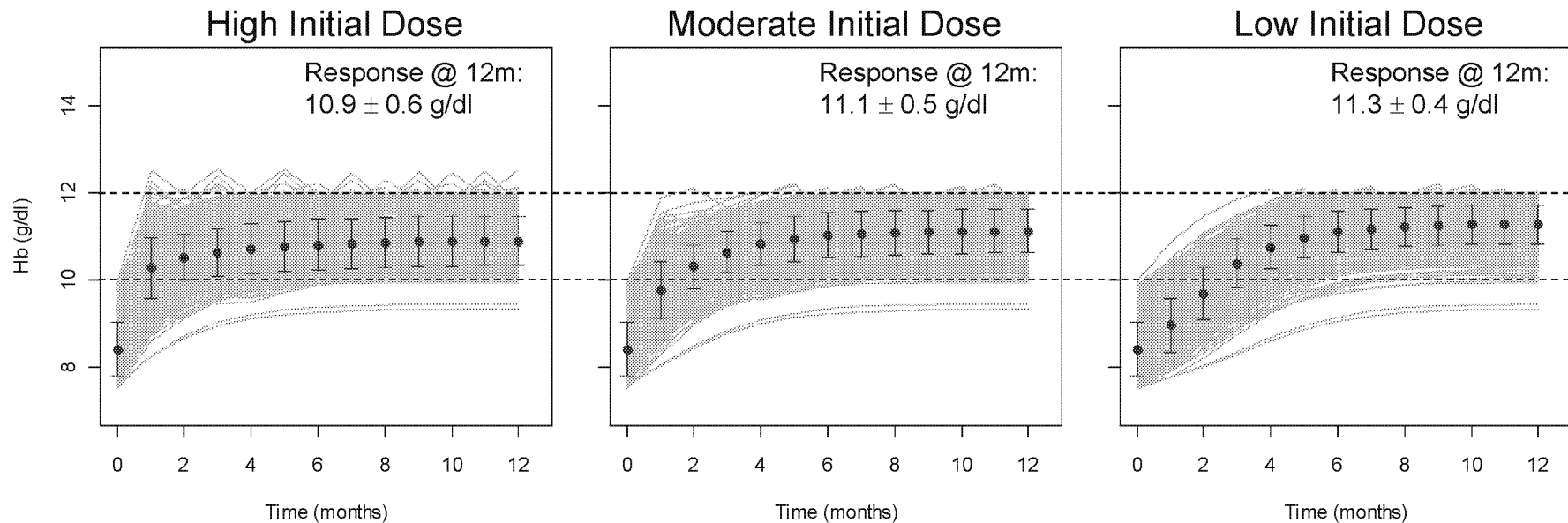
Virtual Study Application used to improve POS

New titration design resulted in lower variance, leading to fewer excursions above maximum desired response and significantly decreasing frequency of safety issues.



Further Dose Titration Optimization

Further optimization of dose titration yielded even better efficacy and safety across three initial dose scenarios.



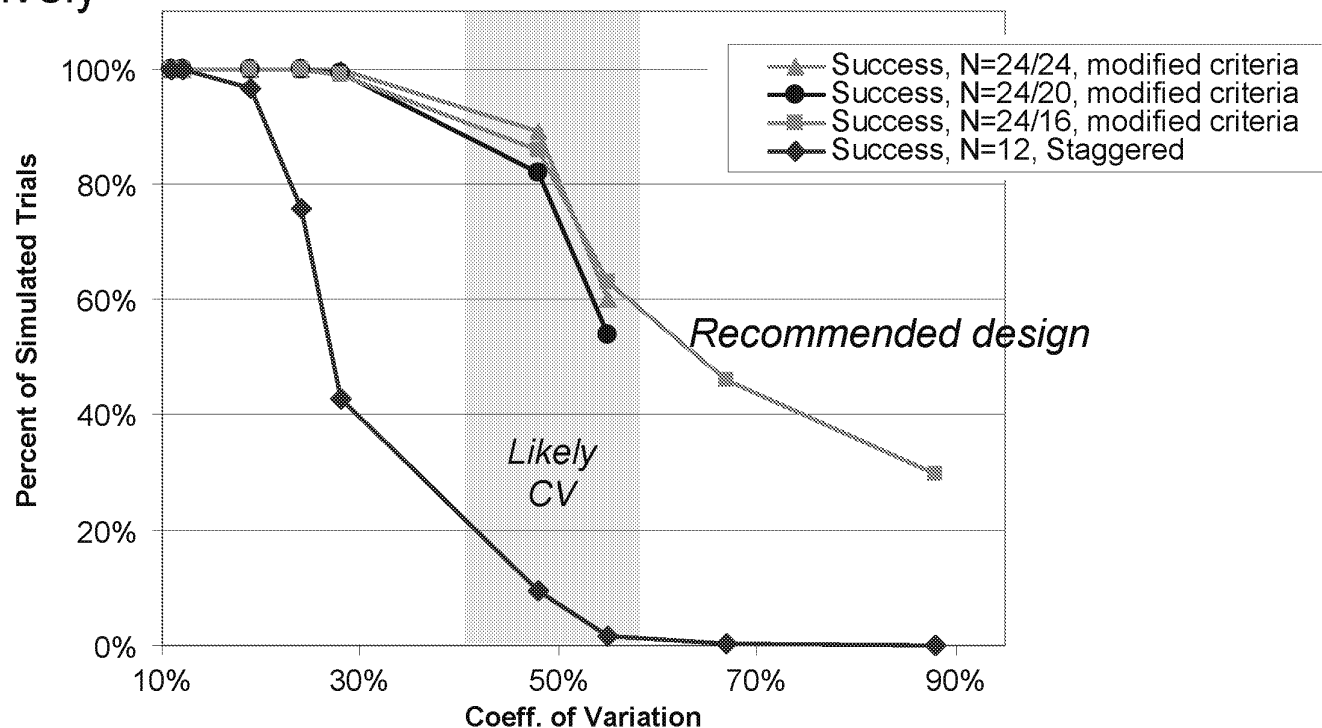
Safety and Efficacy Profile

Based on this safety and efficacy profile, the final design was recommended, as it:

- Significantly enhances both safety and efficacy under all conditions for heterogeneous patient populations
- Improves long-term Hgb maintenance by reducing “on-off” dosing and wide Hgb swings
- Reduces variance of Hgb response and treatment dose
- Is robust to initial dose given to the cohort

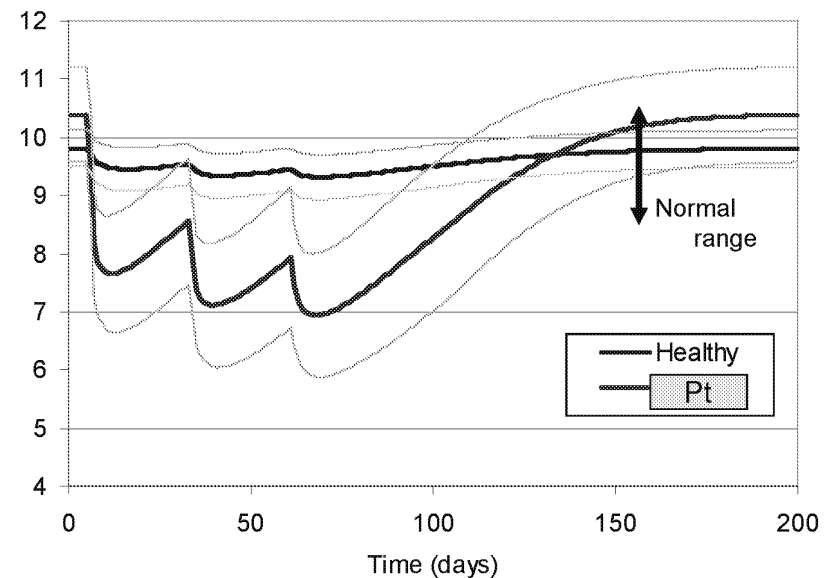
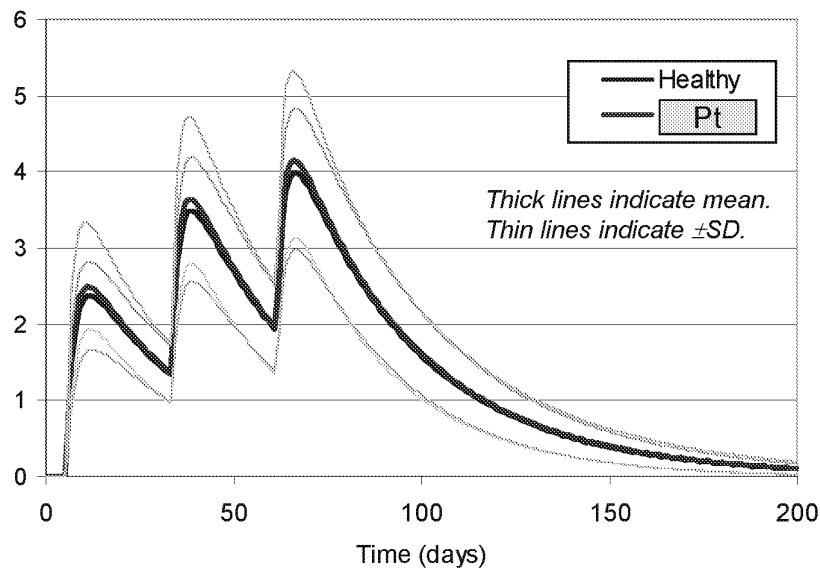
Proposed Semi-Parallel Trial Design is Estimated to Increase the Probability of Success from ~15% to ~80%

Recommendation: semi-parallel design has good chance of success for n=24 and n=16 in initial cohort and parallel cohorts, respectively



Model Illuminates Secondary Safety Concerns

Model indicates that Compound treatment may lead to secondary safety concerns in target patients undergoing treatment, if not taken into account.



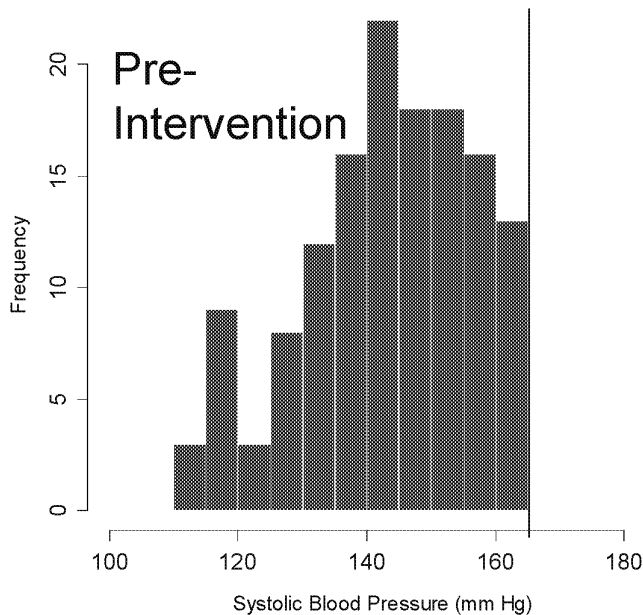
Secondary Safety Concerns

Model indicated that Compound treatment may lead to secondary safety concerns in target patients undergoing treatment

1. Severe hypocalcemia after intravenous administration of bisphosphonates has been observed in patients with poor mineral regulation.
2. Target patients present a particular risk due to limited endogenous mineral regulation.
3. Phase I studies with Compound in healthy patients show limited Ca effects due to normal mineral regulation in these patients.

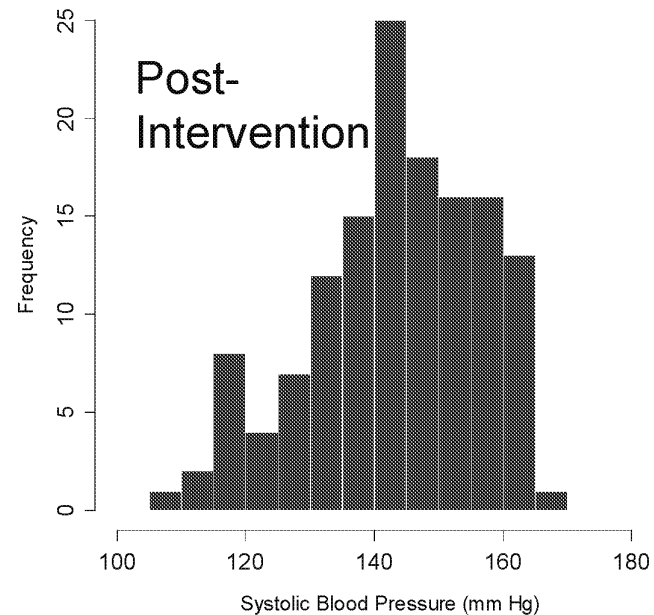
Enhanced TheranOS Patient Cohort

After safety review, shows excellent agreement with Client data on variability in pre- and post- BP of patients.



Population mean: 150.6 mmHg
Population SD: 18.0 mmHg

Population mean: 149.3 mmHg



143.2 mmHg } [Rohrscheib et al,
13.3 mmHg } CJASN , 2008]

141.0 mmHg } Data from Client,
Oct 27 2009

Summary of Dose Titration Optimization for Hgb Maintenance and BP-Related Safety Profile

Dose titration designs

| Endpoints | | B3 | B3a | B4 | B5 |
|--|--|--|-----|--|---|
| All Patients | Safety profile (% population with high BP events) | 8 | 17 | 8 | 10 |
| | Hgb response at 1 month after last dose, (% responder patients within target Hgb range, 10-12 g/dL) | 62 | 91 | 78 | 86 |
| Excluding patients with baseline BP>160 mmHg | Safety profile in absence of high baseline BP patients >160 mmHg, (% population with high BP events) | 0.8 | 6 | 0.8 | 1.6 |
| | Hgb response at 1 month after last dose, (% responder patients within target Hgb range, 10-12 g/dL) | 67 | 91 | 82 | 90 |
| Implementation logistics | Information required for calculating each dose | <ul style="list-style-type: none"> • ΔHb since last dose • ΔHb since 1st dose • Current Hb | | Additional Info <ul style="list-style-type: none"> • Baseline BP | Additional Info <ul style="list-style-type: none"> • Current BP • Max ΔBP since last dose • Max sys BP since start of trial |

Summary of Trial Design Results and Insights Based on Modeling and Simulation

Using TheranOS model, optimized dose titration and Phase II clinical designs for target patients to meet clinical objectives, improve success probability, and accelerate development timelines

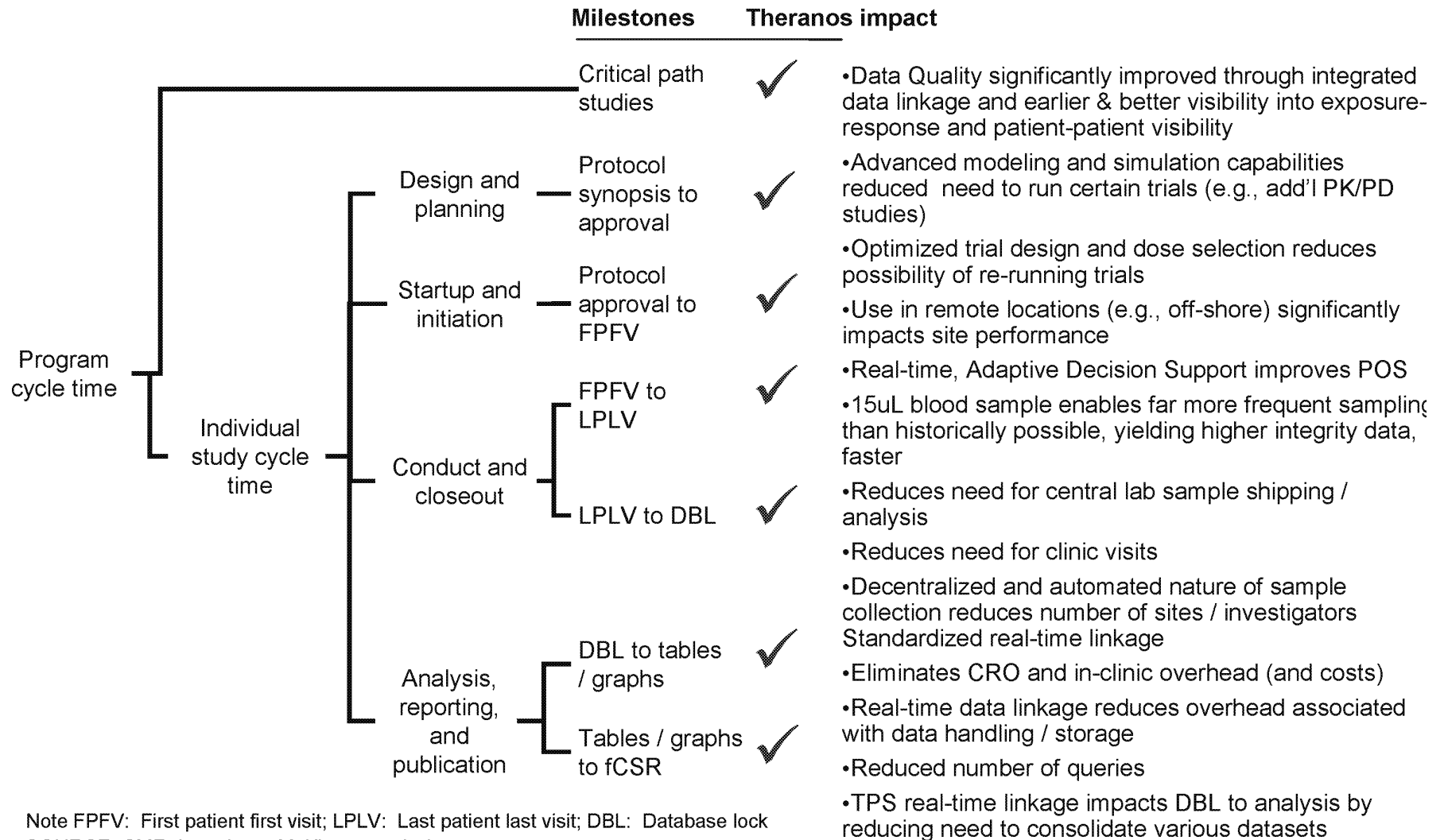
- Dose titration design predicted to improve efficacy across cohort of heterogeneous patients with improved safety profile (limits large/rapid Hgb excursion)
- Evaluated and proposed initial starting Compound dose for target patients to enhance response magnitude and rate with suitable safety profile
- Proposed semi-parallel trial design and modified success criteria predicted to increase statistical power from 15% to 80%

Selected insights based on model development included:

- Rapid hypertensive response may be due to three contributing factors: direct pharmacological effect, rise in viscosity (RBC), delayed rise in EPO (vasoconstriction).
- Identification of candidate biomarker (CTX/BAP ratio) for the prediction of BMD % change
- Delayed transient increase in EPO may be indicative of abnormal RBC/Hgb function.
- Compound treatment predicted to lead to secondary safety marker in target patients.



ROI: Accelerating Timelines and Improving POS



Note FPFV: First patient first visit; LPLV: Last patient last visit; DBL: Database lock
SOURCE: CMR; interviews; McKinsey analysis

Client ROI from POS Analyses & Recommendations

- Overview
 - Client with PoC study design question
 - Compound being used in anemia
- The Theranos Solution utilization
 - Theranos builds systems model to simulate PoC studies
 - Theranos recommends new PoC study design
- The Theranos Solution impact
 - Theranos increased probability of success from ~15% to ~80%
 - Theranos study design eNPV impact of ~\$202 million

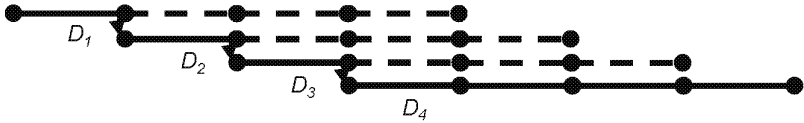
The Theranos Solution – Overview

Build predictive model and use it to design proof-of-concept study.

Overview

- Theranos asked to build a predictive model for a drug with highly complex interacting physiologies and tightly limiting safety concern
- Theranos used the model to help design a proof-of-concept study that improved odds of success

Client design

- Client had originally designed a proof of concept study that included
 - Staggered dosing regimen
- 
- Titration regimen that had high degree of variability in patient responses (bouncing between too strong or too weak a response)
- Client had indicated that if the compound failed in the PoC study, there were 3 likely outcomes
 - Terminating compound development
 - Re-doing PoC study
 - Taking forward multiple doses forward for Phase 2b

The Theranos Solution – Utilization

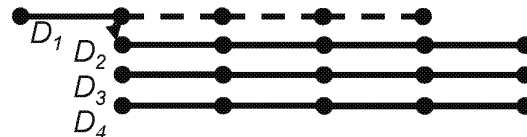
Built complex model and proposed optimized study design within 6 months.

Timeline of events

- Feb, Theranos receives request
- Mar, Theranos receives data to begin modeling
- Jun, Complex systems model built from scratch, with initial physiologically meaningful results
- July, Systems model and simulations completed with solution delivered to Client

Theranos Solution

- The Theranos Solution improved odds of success in a number of ways, including:
 - Building a complex systems model
 - Proposing a new proof of concept study design based on extensive simulation of underlying physiology including
 - Proposing a semi-parallel dosing regimen



- Proposing a new titration regimen that reduced the likelihood of excursions above the maximum desired response and reduced the number of low-responders

The Theranos Solution – Impact on Success

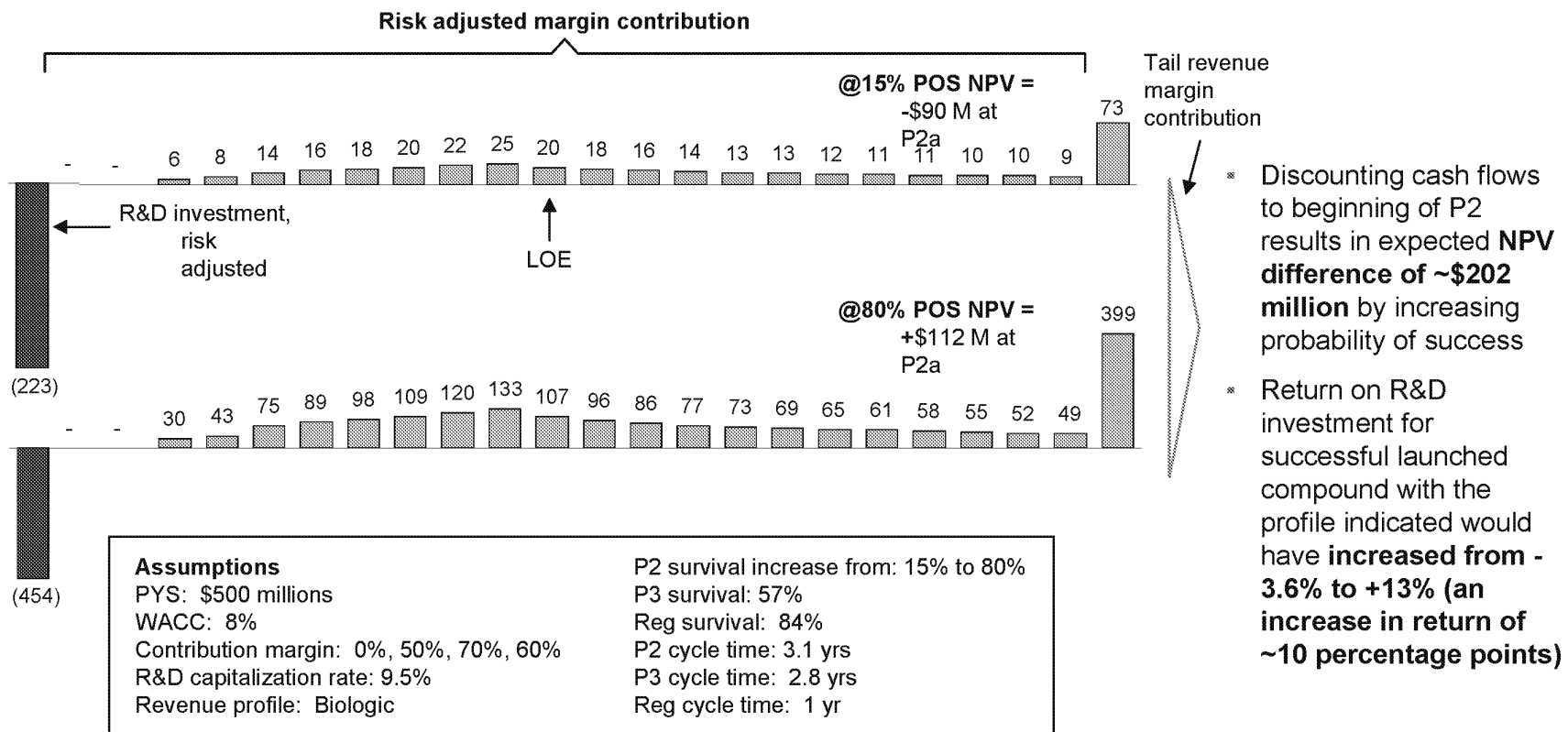
Optimized study design increased probability of success from ~15% to ~80%.

Theranos Impact

- Probability of success through study design
 - New study design optimized dosing and titration regimens to patient responses, resulting in improved odds of success from ~15% to ~80% by causing:
 - Fewer excursions above highest dose range
 - Faster average onset of action
- Guidance to regulatory agency
 - Theranos accompanied client at meetings with regulatory agency to present new study design and rationale (and then designs for all following studies)
- Client reaction
 - Client believes The Theranos Solution study design significantly reduced likelihood of (re-)running additional studies; Estimates an impact of 18+ months saved in clinical development timeline

- *Theranos improved Quality by improving probability of success through optimized study design with eNPV impact of \$202 million (see next slide)*
- *Theranos also improved Speed/Cost by reducing the need to re-do PoC study (typical PoC 18-24 months, \$10-\$20 million)*

Improving probability of survival in PoC from 15% to 80% resulted in eNPV of ~\$202 million for late market drug entrant



SOURCE: PharmaProjects; DiMasi et al. 2002 Journal of Health Economics

The Theranos Solution – Impact on ROI

Assumptions:

- Late-to-market drug
- Potential safety issues
- Competing against established drugs
- Minimal peak year sales and success probabilities

Initial Probability of Success of 15%

- At Phase 2, value of the drug is -\$90 million
- Economically unfeasible at proposed success rate
- Development is likely to be stopped
- Considering development investment to date, IRR = 3.6%

Theranos Improvement to Probability of Success of 80%

- At Phase 2, value of the drug became +\$112 million
- Theranos added ~\$202 million value
- Theranos effectively increases ROI to 13%.

Eliminating the need to repeat a single study accelerated development (estimated 18-24 months)

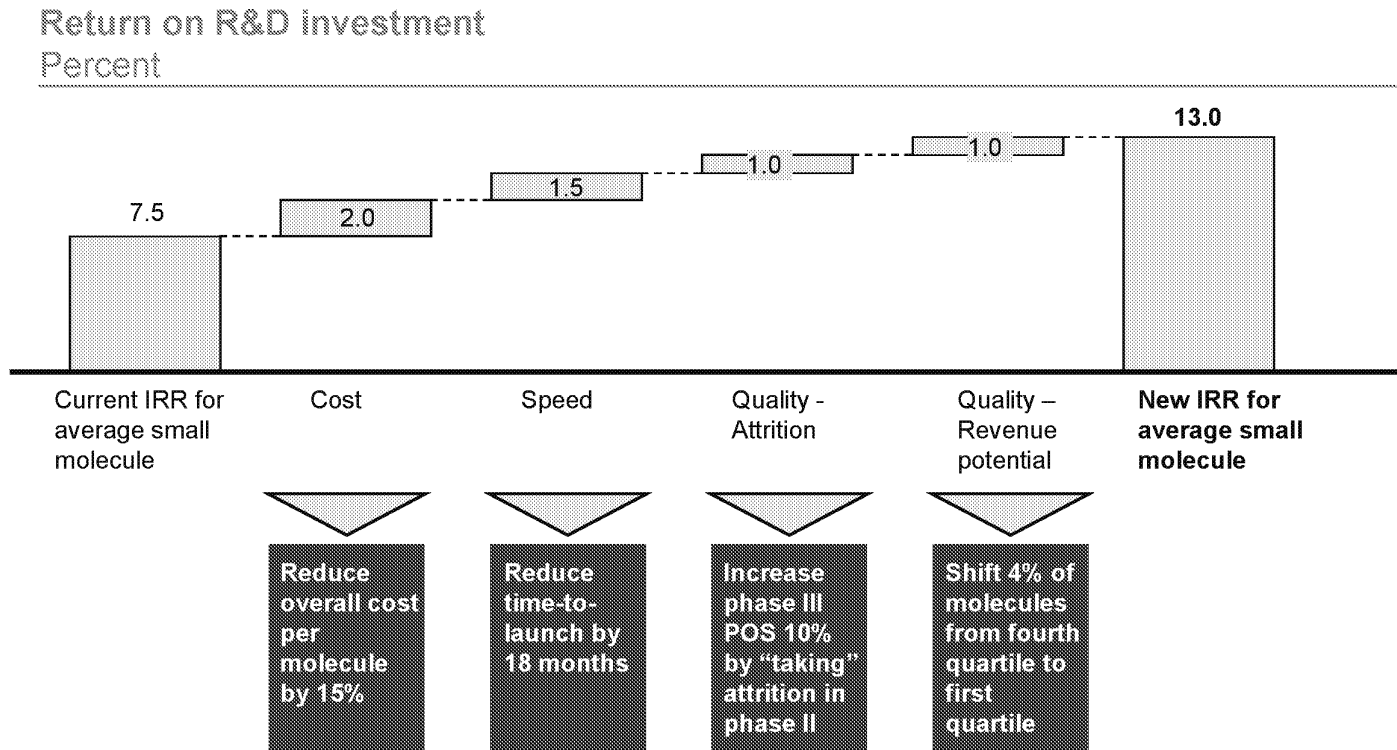
TPS impact

- Return on R&D investment for successful launched compound **increased ~10 percentage points**
 - Further reduction of fully loaded cost of R&D and increase of revenues from time savings
- By realizing the improvement in attrition rate across the entire portfolio versus just one compound, biopharmaceutical companies are realizing a further reduction in the fully loaded cost of R&D, because in an aggregate portfolio fewer wasted trials yield lower spend for the overall portfolio irrespective of development timelines.



Increasing Return on R&D Investment

External research shows that pulling several operational levers can increase return on R&D investment.

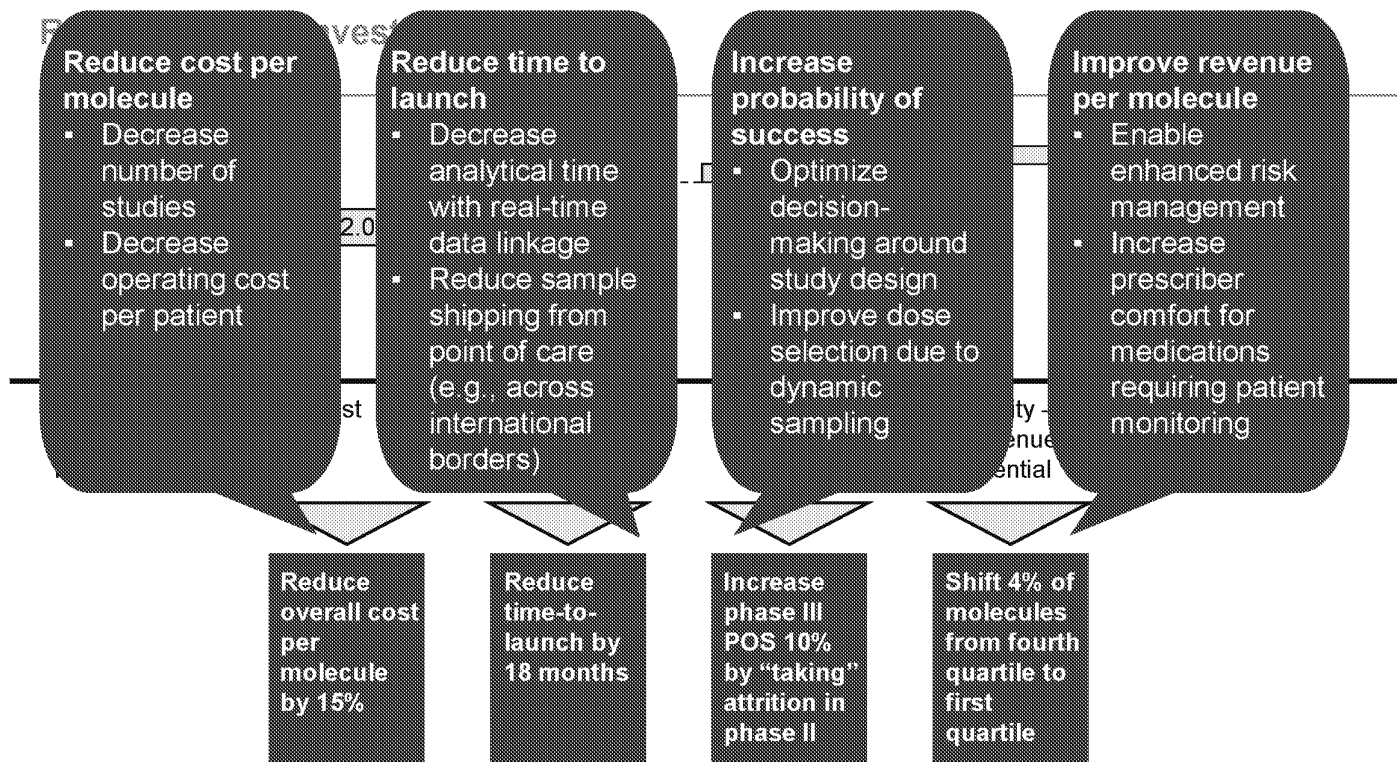


SOURCE: E. David, et al. "Pharmaceutical R&D: The Road to positive R&D returns", *Nature Reviews Drug Discovery*

Theranos Confidential



Theranos can help achieve these improvements.



SOURCE: E. David, et al. "Pharmaceutical R&D: The Road to positive R&D returns", *Nature Reviews Drug Discovery*

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