To: Ian Gibbons[igibbons@theranos.com]; Stefan Hristu[shristu@theranos.com]
From: Gary Frenzel
Sent: Mon 11/10/2008 7:19:04 PM
Subject: FW: Follow up to our meeting

hey guys this is the response from Pfizer, we are not to respond yet. G

Gary Frenzel
Senior Manager Assay Systems
Theranos
3200 Hillview Ave,
Palo Alto, Ca 94304

==========

From: Weber, Shane [mailto:Shane.Weber@pfizer.com]
Sent: Monday, November 10, 2008 10:36 AM
To: Gary Frenzel
Cc: Weber, Shane
Subject: RE: Follow up to our meeting

Hi Gary,

Thanks for your prompt phone call to me on Friday. Yes, Thursday, 1 PM West Coast, 4 PM East coast works for a teleconf.

Yes, I am sorry that there have been multiple Pfizer points of contact over the years for Theranos.

I am interested more broadly as to what the instrument is and planned to be and not just in understanding the performance and utility of the Theranos System in the oncology study.

I am responsible for platforms for which Pfizer has a diagnostic interest and for which there is a clinical validation. If the platform is still in clinical validation than I may introduce you and the Theranos team to some who is more appropriate. But for now let's start with me for the Thursday teleconf.

As we agreed in our discussion, I was to provide copies of the documents that I am working off so we are on the same page and some questions of interest to start our conversation on Thursday.

For me, the goal is to understand the Theranos system.

Let's use my teleconf codes to save Theranos some costs.
Toll free USA
Participant pass code

Please feel free to forward to your team.

Have you confirmed if we are under CDA, if so, one way or two way and when it expires.

Best,
Shane

I have the Theranos summary to Aidan Power, the Introduction to Theranos Systems, the Informed Consent and the IRB Submission. I have read them. I attach these so we are all working off the same versions of the documents. If I do not

have the correct versions please send them, thank you. I have also read US patent 7,291,497 B2.

What I do not have are:

1. The original Theranos and Pfizer agreed work proposal that contains aims, goals, measurable milestone outputs and work plan. The IRB Submission document appears to reflect some original work plan, is that correct?
2. The Interim Report on Assay Development submitted to Pfizer Q2 2007.

In the summary document you refer:

3. To meeting with the Pfizer team. Who was the Pfizer team?
4. To Pfizer point of contacts changing several times. Who chronologically were the Pfizer point of contacts?
5. Pfizer portal at Theranos. Please provide me access to the Pfizer portal at Theranos

Would you please send, provide or answer. Thank You.

Please:
What are the assays that are currently run? Is the list on Slide 8, Introduction to the Theranos System the current list?

How many assays are currently run in multiplex mode? What are the multiplex assay panels?

The VEGF, sVEGFR2 and PlGF were done as a multiplex assay? What was the sample type? Blood, serum or plasma?

What were the calibrators? Were they done in the same sample type?

What was the reference method used? Was the reference assay a multiplex assay or three single assays? Where was it run? Who ran it?

How often does the instrument need to be calibrated?

How often do the on board chemistry controls need to be run?

What is the process from finger prick to blood sample to the assay cartridge? Is this integrated or does the patient prick the finger then squeeze blood into an orifice of the assay cartridge?

Does the instrument receive a finger into an orfice, prick and process into plasma? If not, are there plans for such an instrument?

Why is the Theranos VEGF and VEGFR2 assay not interfered with by Avastin but the reference method assay(s?) for VEGF and VEGFR2 are interfered?

Was there longitudinal time correlation of changes in VEGF, PlGF and VEEGFR2 with CT-MRI tumor reduction? Was any other tumor load reduction measured and correlated with these three analytes?

Slide 12, Introduction to the Theranos System shows a C peptide measurement and correlated to a reference assay. What was the reference assay, where was it run and by who? How many patients are there in this slide?

Slide 17, Introduction to the Theranos System shows a patient with a 30 day longitudinal time measurement. How many patients were so measured out of the number enrolled? Please provide this type of plot for all of the patients measured. Was there any correlation of responders versus non-responders? Or level of response?

Slide 21, Introduction to the Theranos System show three patients with 72 hour longitudinal time measurements. How many patients were so measured out of the number enrolled? Please provide this type of plot for all of the patients measured. Was there any correlation of responders versus non-responders? Or level of response?

Do you have data and reports that address these goals from the September 2006 Study Plan? If so please send. Is the Introduction to the Theranos Systems slide deck the report that addresses these goals below?

1.1. To profile trend results in panels of angiogenesis proteins over time and correlate those values to physical shrinkage in tumor size by leveraging Theranos systems to optimally sample in a way not possible using the central laboratory. These results can be used as baselines against which to index field data in future studies for dose ranging and compound optimization.
1.2. To evaluate the Theranos System in monitoring the progression of the cancers in the hands of clinical personnel and patients who are currently receiving anti-angiogenesis drugs including but not limited to (Specify drugs) for the treatment of their disease.
1.3. To quantify the result time, accuracy, and advantage of obtaining real-time environmental and blood data as well as stored clinically relevant data in patient records with the Theranos System with the current preferred laboratory measurement and data collection methods.
1.4. To quantify and compare the efficacy dynamics of three therapies and interventions
1.5. To demonstrate the impact of Theranos systems on compliance with a therapy / program to better slow the progression of these cancers
1.6. To pilot the TheranOS (Theranos Operating System) including the healthcare provider and patient portals as well as the data reports generated.

Is there an instrument version that measures single nucleotide polymorphisms?

Is there an instrument version that detects antibiotic resistant organisms?

Can the instrument take a swab sample?

Is there a site in the Mid-Atlantic or New England that I could visit to see the instrument?

From: Gary Frenzel [mailto:gfrenzel@theranos.com]
Sent: Thursday, November 06, 2008 8:19 PM
To: Lipset, Craig; Elizabeth Holmes; Weber, Shane
Cc: Marc Thibonnier; Carolyn Balkenhol; Stefan Hristu
Subject: RE: Follow up to our meeting

Hello Shane,
Do you think your team will be available Monday the 10th? We have a series of conference calls in the morning but think we can have the right group together after 11:00 am PST. Please let me know if this is ok or suggest a time that would work for you. Thanks Gary

Gary Frenzel
Senior Manager Assay Systems
Theranos
3200 Hillview Ave,
Palo Alto, Ca 94304

==========

From: Lipset, Craig [mailto:Craig.Lipset@pfizer.com]
Sent: Thursday, November 06, 2008 11:14 AM
To: Elizabeth Holmes; Weber, Shane; Gary Frenzel
Cc: Marc Thibonnier; Carolyn Balkenhol; Stefan Hristu
Subject: RE: Follow up to our meeting

Thank you, Elizabeth.

Gary – Please coordinate with Shane Weber, who leads our Diagnostics group here in NY. When a time is set, please let me know as I would like to join if my calendar permits.

All the best,
Craig

From: Elizabeth Holmes [mailto:eholmes@theranos.com]
Sent: Thursday, November 06, 2008 1:32 PM
To: Lipset, Craig
Cc: Marc Thibonnier; Carolyn Balkenhol; Stefan Hristu; Gary Frenzel
Subject: RE: Follow up to our meeting

Craig –

This is great.

I have copied Gary Frenzel to this email. You met Gary on your visit to Theranos; he runs our Assay Systems group. He will set up a call with the relevant people internally.

Marc, our CMO, and Stefan Hristu, the Client Solutions lead for that study, will likely be on that call.

Elizabeth.

Theranos Angiogenesis Study:

Report Prepared for Dr. Aidan Power
Pfizer, Inc.

Introduction:

Background:
Theranos Systems allow for comprehensive longitudinal profiling of multiplexed protein panels in fresh whole blood to extract earlier and more accurate reads on (individual patient) pharmacodynamic response. The ability to take more frequent measurements of complex assays through at-home, finger-stick tests allows for efficacy dynamics to be more accurately profiled.

Theranos Systems are used to fast-track the approval of key drugs and to rapidly expand the label of existing drugs by generating early reads and publications on efficacy dynamics in new indications (such as various solid tumors) and patient populations.

The primary objective of this program was to comprehensively demonstrate the functionality of Theranos Systems such that future studies could fully leverage the power of comprehensive longitudinal time-series profiling for rapid compound optimization.

For this angiogenesis program, Theranos was asked to develop multiplexed point-of-care assays for VEGF and PlGF for use in monitoring patient pharmacodynamic response to anti-angiogenesis therapies. The development of VEGFR2 in that multiplex was not funded, but desirable as a tool for use in future studies.

Within several months, Theranos successfully developed and validated a multiplex of VEGF, PlGF, and VEGFR2 for use in fresh whole blood point-of-care systems. The Interim Report on Assay Development was submitted to Pfizer in Q2 '07.

Theranos' point-of-contact at Pfizer changed several times during this period. Theranos was originally encouraged to work with Memorial Sloan-Kettering Cancer Center to introduce the Systems and run the patient study there. The progress on initiating that relationship was slow. Theranos was particularly interested in the MSKCC relationship as they were reported to have a good population of Sutent patients. Furthermore, Theranos had not been able to obtain archived samples and needed samples with drug present across the clinically relevant ranges for use in final calibration in order to start large-lot production.

After meeting with the Pfizer team and in parallel with completion of the interim validation report, Theranos proceeded with contracting another site, Tennessee Oncology Cancer Center (TNONC), with which it had pre-existing relationships. Theranos funded TNONC outside of the budget provided by Pfizer. As discussed at the interim update meeting with Pfizer, the first patient began participating in the study in July of 2007. Enrollment of Sutent patients at this site was very slow; upon further discussions with the Pfizer team the enrollment criteria were broadened to include patients on other anti-angiogenesis therapies with whom trends in the relevant markers could still be profiled. Multiple IRB submissions were filed. Final IRB and Informed Consent Forms are attached to this report.

In the interest of making progress quickly, Theranos went into production without having received any samples with clinically relevant concentrations of the therapies. Additional lots were produced with more clinically relevant specifications after receiving samples from TNONC.

Study design and status:
Patient screening began in early 2007, once the final site was selected, enrollment began. In July of 2007, Theranos' first patient was enrolled in the clinical trial. This trial consists of late-stage (4th

line) cancer patients across various tumor types receiving anti-angiogenesis therapy at the Sarah Cannon Research Center at Tennessee Oncology (TNONC) in Nashville, Tennessee. The patients enrolled in the study reside in very remote locations across the eastern US. Almost all patients are not computer literate, and most are from low income families - many patients cannot afford phone lines.

The Theranos angiogenesis system was being evaluated for clinical efficacy and as a means of more accurately and effectively monitoring cancer therapy and the progression of solid tumor cancers from a mechanism of action perspective. 27 patients have been enrolled. Various cycles of therapies are monitored as well as physical changes in tumor size. Five of the patients have retracted consent to the study, four of them due to family problems and one due to mental and physical instability. Thus, a total of 22 patients are in the process or have already completed the study. Eight more patients are needed in order to reach the intended study total of 30 patients. While comprehensive functionality and clinical benefit has been demonstrated, enrollment will continue to meet the original patient target. Enrollment is unpredictable and slow – systems for the remaining patients have been deployed to Theranos' east coast storage facility and are available for installation on-demand. All installations and shipments completed for this study were done on-demand with ~ 24 hours notice due to the difficulty of enrolling these patients at this site. Theranos' client solutions team has performed at-home installations and pick-ups for many weak patients.

For each patient, a total of up to 14 time points are collected during a projected month-long study, 3-4 time points taken at the clinic and the other 10-11 time points taken in-home. Both finger-stick and venous samples are taken during each clinic visit, while finger-stick samples are run in-home. The venous draw samples are run on the Theranos System in the clinic at the time of the draw; these samples are also processed such that the plasma and/or serum can be analyzed on the Theranos System and a reference method at Theranos. For the 22 patients currently enrolled, a total of 308 samples have been analyzed.

Some venous samples have been processed to provide an archive of (currently) 41 anti-coagulated plasma and serum samples which were frozen and have subsequently been analyzed at Theranos.

Theranos assay system description:

The Theranos system is comprised of consumer-oriented readers, single-use cartridges containing assay chemistry and controls, and a data collection system that communicates through cellular networks with the instrument to provide assay protocols and to compute and display results.

The steps required of a new patient are to take the machine out of the box and plug it into power source. The touch-screen then walks each patient through the process of poking his/her finger, depositing blood into the cartridge, and placing the cartridge in the reader drawer. The instrument then processes the assays and sends the data through the cellular network in real-time to a secure web-portal.

Theranos Systems allow for quantitative, multiplexed longitudinal time-series measurements to map correlation between the change in rate of blood-borne markers over time to surrogate and clinical end-points such as CTMRI scans.

System Specifications:

- Designed for at home use. Can also be used in physician's offices, ICU, and laboratories.
- Multiplexed measurement of biomarkers.
- Customizable for different/new assays on demand.
- Average 6 assays per cartridge
- Serial measurements to comprehensively profile pharmacodynamic response through trends
- Runs fresh whole blood, plasma or serum samples
- Finger-stick – small sample size (10-20 uL)
- Mix and match selection of analytes on demand.
- Wide measurement range

- pg/Ml – mg/Ml (1 billion fold)
- ❖ High sensitivity
  - 0.2 pg/Ml (2 parts per 10-billion)
- ❖ Recovery %: ~100
- ❖ System CV post-calibration (inter-intra reader, cartridge, and assay) %: <10
- ❖ On-board chemistry controls
- ❖ Factory calibration (no user calibration)
- ❖ Wireless communication of results to appropriate user through cellular network
- ❖ Proprietary algorithms to interpret time trend results

The existence of a technology infrastructure for home, real-time blood monitoring allows to collect information which cannot be seen using conventional blood tests:

- ❖ Small sample (finger-stick) + more frequent sampling of a small subset of analytes enables:
  - Identification of appropriate analytes (not possible if samples are not taken more frequently than for laboratory methods due to lack of trend profiles) << Small sample enables
  - Earlier detection of efficacy and safety dynamics or acute problems so intervention (dose) can be more effective
  - Convenience of monitoring through-out time-course before an event
- ❖ Higher sample integrity; real-time sample analysis on fresh whole blood on a standardized platform which can be deployed internationally removes assay noise associated with commercially available tests
  - Eliminate false reads on concentrations (caused by analyte decay rates in plasma) and inherent noise in data and patient correlations (caused by processing)

For this study, an instrument was deployed in the home of each patient; others are used at the Cancer Center.

Three assays are performed simultaneously in multiplex by the system on a finger-stick of fresh whole blood. The analytes are Vascular Endothelial Growth Factor (VEGF), soluble VEGF receptor R2 (sVEGFR2, usually referred to as VEGFR2) and Placental Growth Factor (PLGF). Each assay is controlled using within-cartridge control measurements.

The system is calibrated at Theranos. As detailed above, several cartridge lots have been used, each independently calibrated.

Traceability of calibration: Calibration is traced to authentic analytes dissolved at known concentrations in a plasma-like matrix. Calibration materials are prepared as mixed solutions of the three analytes. Assignment of calibrator concentrations is then made to values found for measurements of calibrators using reference assays.

System Performance Goals:

Assay	Reportable low pg/mL	Reportable high pg/mL	Precision CV, %
VEGF	20	10,000	10
VEGFR2	150	15,000	10
PLGF	20	1,000	10

Assay ranges achieved: The goals for assay ranges have been achieved. Due to the inability to receive samples for calibration at the beginning of the studies, the upper limit of calibration for VEGF was restricted to 3,000 pg/mL in the first cartridge lots, but then extended[1] to 10,000 pg/mL. For early cartridge lots the PLGF assay lower limit of sensitivity was 50 pg/mL so many early results for PLGF were out-of-range low. Lots produced after receiving samples for calibration have reportable ranges below 20 pg/mL.

Specificity: The specificity of the assays depends on the pairs of antibodies chosen for each assay. In the first instance, we rely on the antibody vendor information. Selected pairs are known to have good specificity in ELISA assays. Key issues for these analytes are (1) the structural relationship of VEGF and (2) the fact that VEGF binds to sVEGFR2. We have shown that the Theranos assay system is not affected by the presence of VEGF and VEGFR2 and PLGF in the same samples. In many patients in this study, the drug Avastin is used. This drug is an antibody that binds to VEGF. It is obvious that ELISA assays for VEGF (and perhaps VEGFR2) using antibody pairs are likely to be interfered with by Avastin. As documented below, Theranos assays for VEGF and VEGFR2 appear to function with minimal interference from Avastin. In contrast, the selected reference assay for VEGF is strongly interfered by Avastin.

Theranos System Performance:

Assay accuracy:
Accuracy has been evaluated by analysis of clinical samples. Two sets of samples have been used: (1) A set of 12 serum samples from cancer patients (obtained from a commercial vendor), (2) 41 archived serum and plasma samples from this study. Because Avastin was used to treat many of the patients in the TNONC study and this antibody strongly interferes with the reference method, we used the commercially available samples for VEGF.

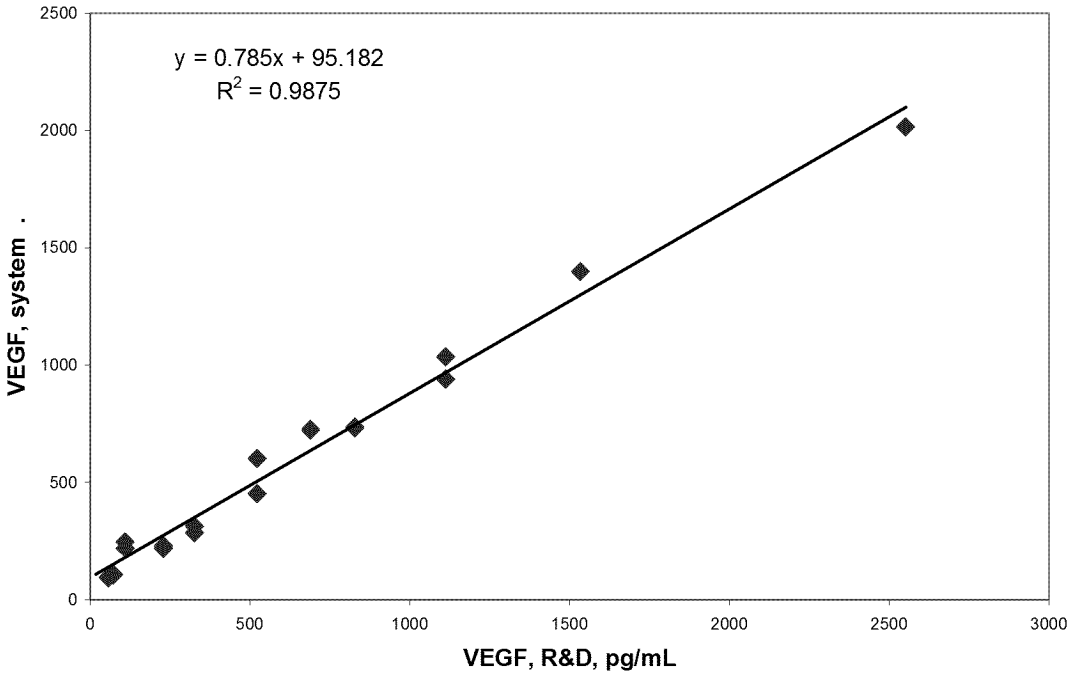
Twelve serum samples were assayed (singlicate) in the Theranos system and in duplicate for the reference method with the following results:

VEGF: y (Theranos) = 0.785 x (reference) + 95.2; R^2 =0.99. Range 96 – 1985 pg/mL. One sample was rejected from the analysis giving very high results in the Theranos system and low results in the reference assay. Based on the study data, it seems likely this patient was being treated with Avastin.

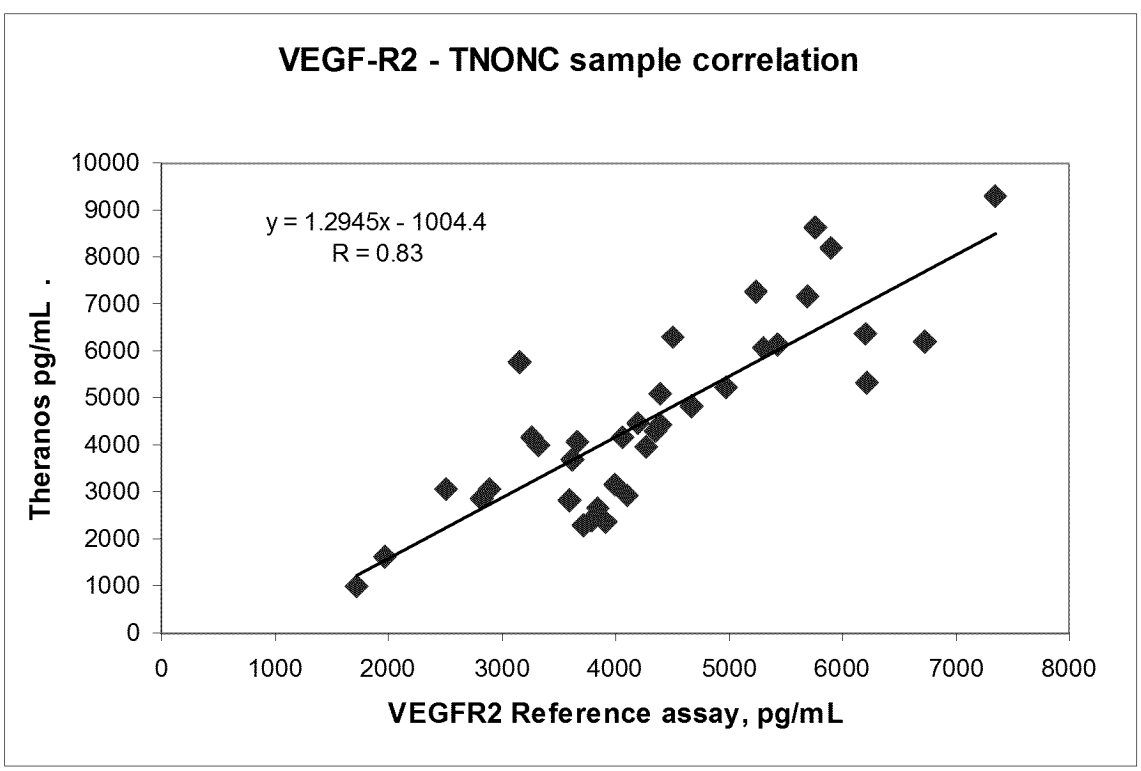
[1] All three assays have a linear dose-responses extending far above the highest calibrator used.

3200 Hillview Palo Alto, CA 94304
phone: 650.838.9292 fax: 650.838.9165 www.theranos.com

Single cartridge clinical results

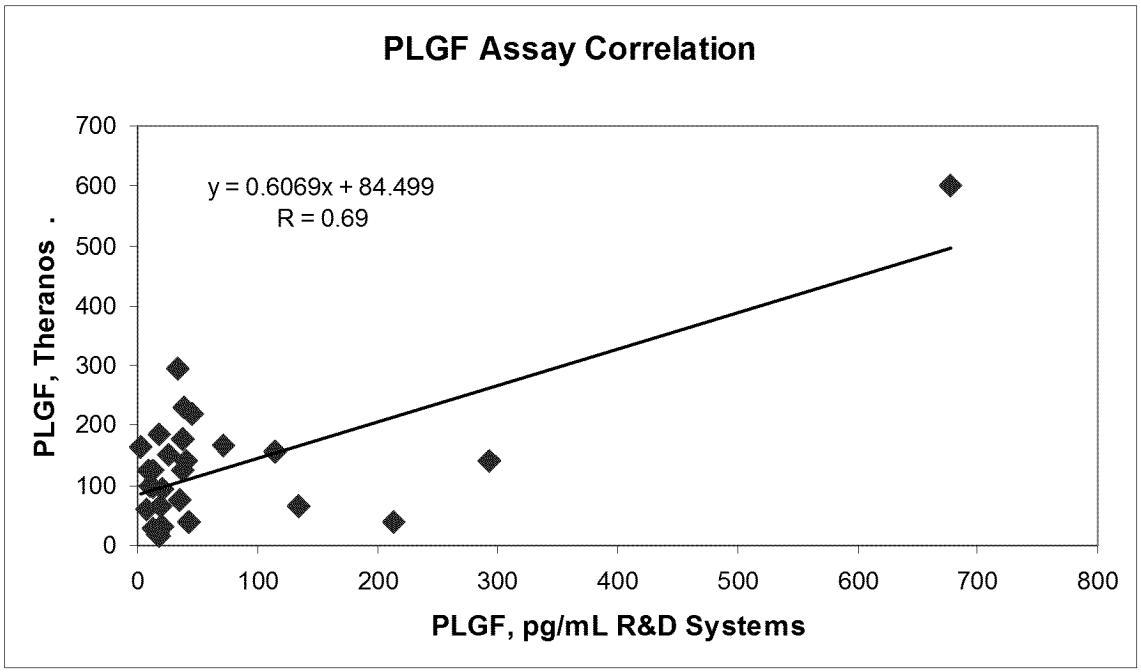


For VEGFR2, 39 TNONC samples were assayed in tripli cate in the Theranos system and duplicate for the reference method. The results were: y (Theranos) = 1.29 x (reference) + 1004; R =0.83. Range 1015 – 9285 pg/mL.



3200 Hillview Palo Alto, CA 94304
phone: 650.838.9292 fax: 650.838.9165 www.theranos.com

For PLGF 36 samples were measureable with the following results: y (Theranos) = 0.61*x (Reference); R = 0.69; Range 16 – 600 pg/mL



Effect of Avastin on the reference VEGF assay: Comparison of reference and Theranos VEGF assay results for venous samples were not correlated. Many Theranos results were in the thousands of pg/mL where reference assay gave a low value. Since it was noted that many of the patients had been treated with Avastin which binds to VEGF, Theranos did a study of spike recovery for the reference method. VEGF (400 pg/mL) was added to each sample and the assay repeated. Results are shown below:

Avastin Present	VEGF average, pg/mL Ref	VEGF average, pg/mL Theranos
N	149	588
Y	136	8359

	VEGF spike recovery, %
N	66.5
Y	-1.3

It is evident that Avastin completely blocks the reference assay response. Presumably, Avastin binds at a site on VEGF close to or identical with one of the antibodies used in the reference method. The reference assay thus responds only to free VEGF whereas the Theranos assay is not blocked and measures both Avastin-bound and free VEGF.

Assay precision:

Inter-Instrument Precision
Venous samples from patients were run across four instruments.

Assay	Reportable low pg/mL	Reportable high pg/mL	Precision CV, %
VEGF	20	10,000	8.0
VEGFR2	150	15,000	7.3
PLGF	20	1,000	9.2

Precision next to available reference methods was evaluated during calibration. Singlicate measurements from six instruments were used next to commercially available 'gold-standards.' The CVs reflect the calibration schemas before and after receiving clinical samples for calibration, the variances in the LOD between Theranos' assays and the commercially available kits as well as Theranos' ability to measure both free and bound VEGF.

Single lot calibration data

Analyte	Range (pg/mL)	Average CV, %
VEGF (lot 3)	30 – 10,000	12.0
VEGF (lot 1)	30 – 3,000	10.0
VEGFR2 (lot 3)	1,000 – 10,000	4.8
VEGFR2 (lot 1)	50 – 800	17.6
PLGF (lot 3)	5 – 780	26.9
PLGF (lot 1)	50 – 800	9.1

Precision was also measured by analysis of the 41 archived clinical samples in assays and for VEGF 12 commercial samples.

Analyte	Range (pg/mL)	Average CV, %
VEGF	30 – 10,000	16.7
VEGF[2]	96 – 1985	5.7
VEGFR2	1,000 – 10,000	20.4
PLGF	5 – 780	28.7

Dilution linearity:

Data gathered during lot calibration.

VEGF, pg/mL	Recovery, %
10000	(100)
2970	102
990	95
297	105
100	109
30	105
10	101

VEGFR2, pg/mL	Recovery, %
10560	(100)
7920	92.9
5280	100.9
3960	104.8
2640	97.7
1320	100.8

PLGF, pg/mL	Recovery, %
780	100.0
312	87.6
156	102.8
47	106.3
16	92.4
5	99.4

[2] Commercial samples

3200 Hillview Palo Alto, CA 94304
phone: 650.838.9292 fax: 650.838.9165 www.theranos.com

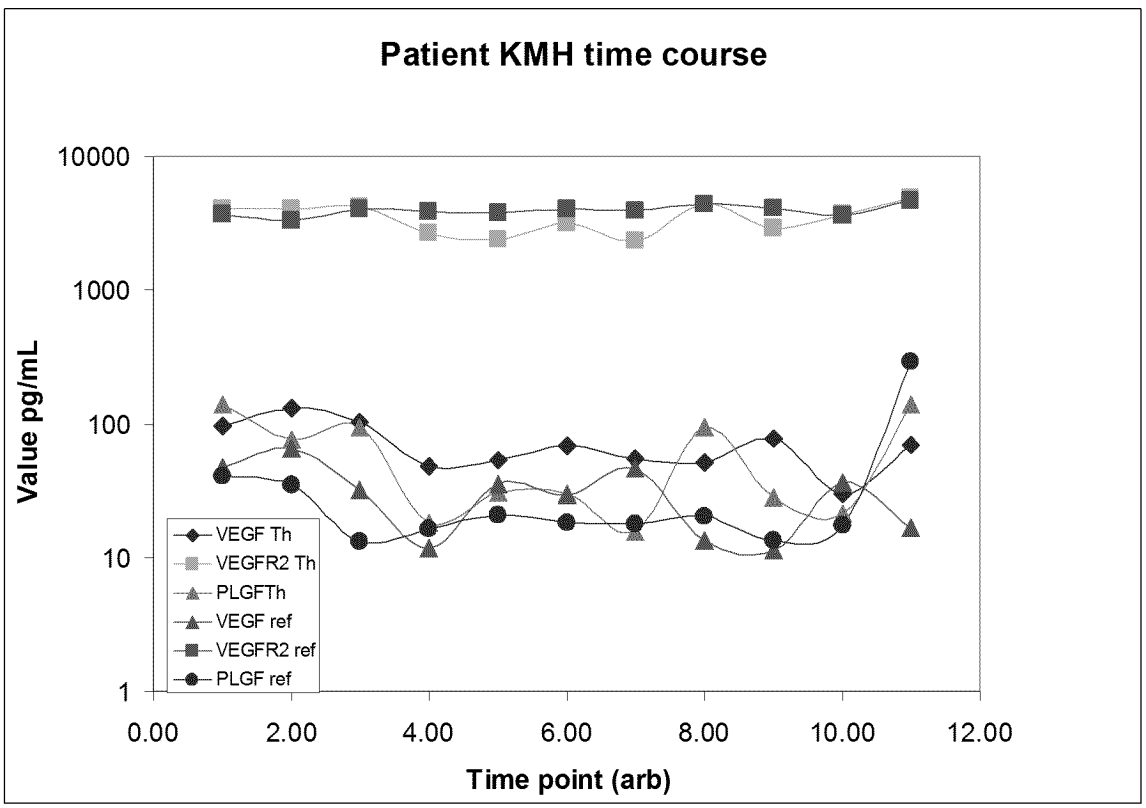
For all assays, recovery was close to 100 % in the reportable range.

Limit of detection (LOD):
Data gathered during calibration. The LOD is defined at a 95 % confidence level.

Analyte	LOD, pg/mL
VEGF	< 20
VEGFR2	< 200
PLGF[3]	< 20

Use of the system in field studies:

The system has been deployed to patient's homes and has downloaded protocols and uploaded data wirelessly. Some patients plugged phone lines (POTs modems) into the device if they were worried about cell reception. Data for every patient has been profiled on a secure, Pfizer-specific server.
Exemplary Sutent patient's[4] results are shown below. We show data for plasma samples drawn from the subjects at the clinic in comparison with reference method results.



Conclusions:

1. The Theranos System performed with equivalent or superior performance to reference assays while running in an extremely rugged ambulatory environment.
2. The ability to generate longitudinal profiles of angiogenesis proteins over time serves as a more effective mechanism for generating early, rapid reads on efficacy dynamics than

[3] Later stage cartridge lots
[4] Patient not on Avastin

'snap-shot' based measurements using the conventional testing infrastructure. See variance in patient time-course profiles on Pfizer web-portal through www.theranos.com.

3. The lack of samples with which to calibrate resulted in delays in production of lots that were calibrated for the appropriate range. Once calibrated, the performance of the system next to the reference methods improved.
4. Inter-system accuracy is excellent.
5. VEGF assay accuracy is good for some cancer patient subjects, but since the system responds to total VEGF but not free VEGF we were not able to verify accuracy for the TNONC samples.
6. VEGFR2 assay accuracy is quite good for TNONC venous samples.
7. PLGF assay accuracy next to the reference method was not good, but most of the samples are at very low concentration and the reference kit's LOD is higher than Theranos'.
8. Avastin does not block the Theranos assay.
9. The Theranos System can measure both bound and free VEGF.

3200 Hillview Palo Alto, CA 94304
phone: 650.838.9292 fax: 650.838.9165 www.theranos.com

INFORMED CONSENT AND AUTHORIZATION FORM TO PARTICIPATE IN A RESEARCH STUDY

REFMAL____: A Study to use the Theranos System in Monitoring the Progression of _____ in Ambulatory Patients Being Treated with _____ Therapies

INVITATION TO PARTICIPATE

You have been asked to participate in a research study entitled A Study to use the Theranos System in Monitoring the _____ in Ambulatory Patients Being Treated with _____ Therapies ("the Research Study") because you are currently receiving either oral DRUG NAMES as treatment for your type of cancer. The Research Study is being conducted at the SITE NAME in collaboration with Theranos™, a healthcare systems company that is developing an ambulatory monitoring system to monitor the effects of prescription medications in patients.

The purpose of this Informed-Consent-Authorization Form (this "Form") is to tell you about what will happen during this Research Study and the risks of participating, so that you can make an informed decision as to whether or not you would like to participate. The Form also includes other important information about the Research Study, including an explanation of the Protected Health Information that the Investigators may collect and use during this study and with whom they may share that information during the research Study and after the research Study is completed (more information about this is discussed in the authorization to use and disclose protected health information section). If there is anything in this Form that you do not understand, please ask questions before making any decisions.

Your decision to participate in this research Study is entirely voluntary and you do not have to participate. If you decide to participate, you can stop participating at any time. If you decide not to participate, or if you join the Research Study and later decide to stop, you will not experience any penalty or loss of benefits.

PURPOSE

You and your physician have decided that treatment with either DRUG NAMES is currently the best option for the management of your disease. The purpose of this Research Study is to evaluate the use of a new ambulatory drug monitoring system known as the Theranos System by patients who are being treated with either DRUG NAMES.

The Theranos System is a small handheld monitor that can detect changes in the levels of biochemical markers in a patient's blood that occur after taking a drug. The information is then wirelessly communicated to the medical personnel who are monitoring the patient.

PROCEDURES

If you decide to participate in this research study, you will be asked to visit the outpatient clinic on two separate occasions one week apart. At the first visit, you will have a single 10 millilter (2 teaspoons) blood sample drawn from a vein in your arm. This blood sample will be processed, frozen, and shipped to the study sponsor for analysis by conventional methods. The clinic staff will then teach you how to use the Theranos System (the new ambulatory drug monitoring system). You will be taught how to use a lancet (a small needle) to prick your finger and obtain blood that can be drawn up into a cartridge that you will be provided. You will then insert the cartridge into a separate device known as a reader, which will quickly analyze the sample and wirelessly transmit the data to a remote computer database located at the study sponsor. This procedure will be repeated a second time (the finger stick, loading the cartridge, and using the reader) while you are in the clinic to make certain that you are comfortable with the procedure and will be able to repeat the procedure alone at home. You will be asked to obtain two additional blood samples by fingerstick at home. These samples may be done at any time on Day 3 and Day 5 of the following week. On day 8, you will be asked to return to the clinic. At this time, you will have a second 10 milliliter (2 teaspoons) blood sample drawn from a vein in your arm. This blood sample will also be processed, frozen, and shipped to the study sponsor for analysis by conventional methods. You will also be asked to perform one final finger stick and blood analysis with the Theranos System.

During the week that you are participating in this trial, you will be asked to complete a patient diary on the internet on your computer at home. You will be asked to record the dose of either DRUG NAMES that you are taking and the specific time of day that you took your dose. You will also be asked to record any side effects that you may be experiencing with your treatment.

RISKS

Blood draws can cause mild pain and bruising at the injection site, potential painful and swollen veins, or blood clots (thrombosis). In addition, you might experience dizziness when the blood is drawn. On rare occasions, an infection may develop at the site of needle insertion. In the unlikely event of infection, you will receive standard medical treatment.

BENEFITS

You will not receive any direct benefit from taking part in this Research Study. It is hoped that in the future, knowledge gained from this study may help other people.

ALTERNATIVES

You may choose not to participate.

COMPENSATION

You will not receive any sort of compensation for participating in the Research Study. Information obtained from the Research Study may be used to develop drugs, products, or other inventions that have commercial rewards. You will not obtain any financial benefit from such commercial developments. You will not be paid or receive any compensation for permitting your blood samples and data to be included in the Research Study.

STUDY SPONSOR/FUNDING

The sponsors of the research study are the SPONSOR NAMES. SPONSOR NAMES is dedicated to conducting oncology research at various locations throughout the country. SPONSOR NAMES has entered in a contract with SITE NAME under which physicians at SITE NAME conduct research for SPONSOR NAMES. SITE NAME and its physicians are compensated by SPONSOR NAMES for conducting research on SPONSOR NAMES' behalf.

COSTS

SITE NAME will be responsible for all costs associated with obtaining and testing your blood samples in this study.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

1. What information will be used or disclosed?

As part of the Research Study procedures, the Research Team will collect Protected Health Information. Your Protected Health Information could directly identify you; for example, it might include your name, social security number, or your medical record number. In addition, SITE NAME has previously provided you with its Notice of Privacy Practices (the "Notice") that explains, among other things, the definitions of Treatment, Payment and Health Care Operations and the types of uses and disclosures of your Protected Health Information that SITE NAME can make for Treatment, Payment, and Healthcare Operations purposes.

2. Who is Authorized to Use and Disclose Your Protected Health Information?

You hereby authorize SITE NAME and the Research Team to use and disclose your Protected Health Information solely for the purposes of the Research Study. Remember, that certain members of the research Team, for example the Research Study Manager, are SPONSOR NAME employees, not SITE NAME employees. These SPONSOR NAME employees will have access to your entire SITE NAME medical record and to the Protected Health Information collected during the Research Study.

3. With Whom Will We Share Your Protected Health Information?

By signing this Informed Consent-Authorization Form, you authorize SITE NAME to use and disclose your Protected Health Information that is created or collected in the course of this Research Study to regulatory agencies, SPONSOR NAME, and other individuals and organizations that analyze your Protected Health Information in connection with this Study (the "Recipients").

Once SITE NAME discloses your Protected Health Information to the recipients, SITE NAME cannot guarantee that Recipients will not re-disclose your Protected Health Information to other persons who may not be bound by this Informed Consent-Authorization Form, or otherwise be permitted to use or disclose your Protected Health Information in ways that you do not intend.

4. When Does This Authorization Expire?

This Informed Consent-Authorization does not expire. If, however, you wish to revoke your authorization for SITE NAME to use and disclose your Protected Health Information for the purposes described in this Form and to the Recipients described, please see Section XII.5.

5. What Happens If You Withdraw From the Research Study or Revoke Your Authorization to Use and Disclose Protected health Information?

Your authorization for SITE NAME to use and disclose your Protected Health Information will remain in effect unless you give written notice of your decision to revoke your authorization to the Privacy officer listed below (who will then provide this revocation to the appropriate parties, including the Principal Investigator). Your written revocation will be effective immediately upon SITE NAME's receipt of your written notice. However, your revocation will not have any effect on any action taken by SITE NAME in reliance on this authorization before it received your written notice of revocation. For example, if the Research Team has already collected and reviewed your Samples and your Protected Health Information, it may not be possible to withdraw your Protected Health Information from the aggregated Research Study results. However, the Research Team will not collect any further Protected Health Information about you.

6. How Will Your Protected Health Information be Protected?

We will take reasonable and appropriate measures to maintain the confidentiality of your Protected Health Information, subject to the anticipated disclosures discussed previously in the risks and procedures sections. In order to protect your Protected Health Information, the Research Team will code your Samples so that only the Research Team, SITE NAME, and SPONSOR NAME will know which sample corresponds with you. Your Protected Health Information and sample data will be kept in locked databases.

7. Who Do I Contact About Protected health Information?

If at any time during this Research Study, you feel that you have not been adequately informed of your rights with respect to the privacy of your Protected Health Information, or feel that the privacy of your Protected Health Information has not been adequately protected, you can contact the SITE NAME Privacy Officer during normal working hours (8:30 a.m. to 5:00 p.m.) and ask to speak with:

Name: NAME
Telephone: NUMBER
Address: SITE NAME , PLLC
ADDRESS

OTHER CONSIDERATIONS

If you do not understand anything related to this study or have a problem related to your taking part in this study, please contact the principal investigator at once:

NAME, the 24-hour telephone number is NUMBER.

You should contact Dr. NAME, Chairman, Institutional Review Board at NUMBER if at any time you have questions regarding this research, your participation in it, or your rights as a research subject.

It may be necessary to contact you at a future date regarding new information about this study. For this reason, we ask that you notify the institution where you received treatment on this study with any changes in address.

SIGNATURES

I have read and understand the terms of this Informed Consent-Authorization Form and I have had an opportunity to ask questions about the Study and to discuss the Study with my doctor and other health care providers and my family and friends.

A Study to use the Theranos System in Monitoring the Progression of Solid Tumor Cancers in Ambulatory Patients Being Treated with Anti-Angiogenesis Therapies

Protocol Number: NUMBER

Principal Investigator: NAME

Sponsors: Theranos
1430 O'Brien Drive, Suite C
Menlo Park, California 94025

Date Final _____

1. OBJECTIVES

1.1. To profile trend results in panels of angiogenesis proteins over time and correlate those values to physical shrinkage in tumor size by leveraging Theranos systems to optimally sample in a way not possible using the central laboratory. These results can be used as baselines against which to index field data in future studies for dose ranging and compound optimization.

1.2. To evaluate the Theranos System in monitoring the progression of the cancers in the hands of clinical personnel and patients who are currently receiving anti-angiogenesis drugs including but not limited to (Specify drugs) for the treatment of their disease.

1.3. To quantify the result time, accuracy, and advantage of obtaining real-time environmental and blood data as well as stored clinically relevant data in patient records with the Theranos System with the current preferred laboratory measurement and data collection methods.

1.4. To quantify and compare the efficacy dynamics of three therapies and interventions

1.5. To demonstrate the impact of Theranos systems on compliance with a therapy / program to better slow the progression of these cancers

1.6. To pilot the TheranOS (Theranos Operating System) including the healthcare provider and patient portals as well as the data reports generated.

2. BACKGROUND

Theranos is a healthcare systems company that provides *real-time* clinical information to enable pharmaceutical companies to develop safer and/or more efficacious drugs, and to improve and expand the profile of marketed drugs.

Theranos' monitoring system allows healthcare providers and patients to monitor drugs, their metabolites and relevant biomarkers from whole blood in *real-time* at any testing frequency in a clinic, hospital setting or with ambulatory patients. When profiled through trends over time, biomarkers can be used to trace diseases, the efficacy and safety of therapy and the impact on patients from environmental factors. The Theranos System allows pharmaceutical companies and healthcare providers to rapidly gather and analyze serial data and obtain early signals of the benefits of a therapeutic treatment regime, of any adverse drug reactions (ADRs), and the recurrence of a disease after a period of remission.

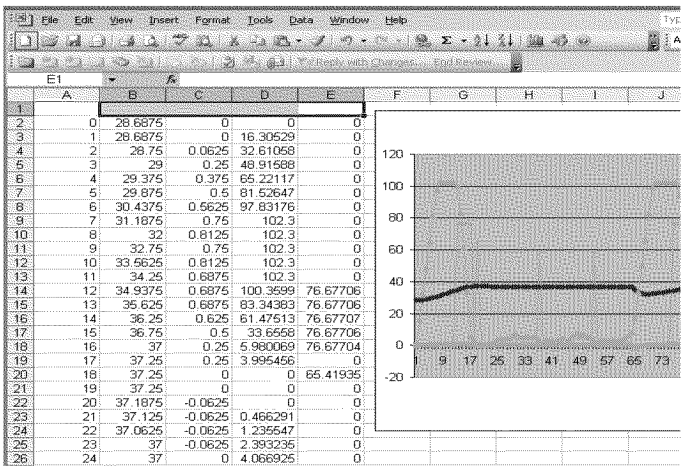
The Theranos System integrates customized clinical informatics with proprietary technology, and microfluidics into a portable/handheld monitor. The system has three components:

- The "Reader" – a device, capable of extracting *in vitro* assay data from assay Cartridges and transmitting data via a wireless link to a remote database that is accessible by hospitals, clinicians, and study coordinators.

- The "Cartridge" – a disposable cartridge containing Chemiluminescent based immunoassays to measure the concentration of products and/or defined biomarkers for efficacy and safety. This cartridge is capable of running both high-sensitivity and low-sensitivity multiple assays in 10 μL of whole blood that is obtained from a finger stick blood sample. Each cartridge can carry from one to a multiplex of biomarkers customized for each pharmaceutical partner. The Theranos System utilizes combinations of drug and biomarkers together with other critical patient information to map trends which serve as indicators of efficacy and safety.

The Cartridge and Reader are very easy for the patient to use. The patient utilizes a lancet that draws a droplet of blood. They hold their finger up to the collection spot on the cartridge which sips in the blood. The cartridge is put into the slot on the reader which automatically draws in the cartridge. The only thing left to do is for the patient to come back later and throw the cartridge away.

- TheranOS (Theranos Operating System) - a database and proprietary analytic communications software for retrieval, transmission, analysis and integration of data from the Theranos Cartridges and from patients' records. TheranOS offers query capability into the data from an individual level as well as at an aggregate level with flexible and customizable reporting options. Patient involvement is enhanced through the use of patient diaries, patient feedback and patient alerts that remind the patient to monitor themselves and/or to take their medication. Importantly, TheranOS is HIPAA and HL-7 compliant.



	A	B	C	D	E
1					
2	0	28.6875	0	0	0
3	1	28.6875	0	16.30529	0
4	2	28.75	0.0625	32.61058	0
5	3	29	0.25	48.91588	0
6	4	29.375	0.375	65.22117	0
7	5	29.875	0.5	81.52647	0
8	6	30.4375	0.5625	97.83176	0
9	7	31.1875	0.75	102.3	0
10	8	32	0.8125	102.3	0
11	9	32.75	0.75	102.3	0
12	10	33.5625	0.8125	102.3	0
13	11	34.25	0.6875	102.3	0
14	12	34.9375	0.6875	100.3599	76.67706
15	13	35.625	0.6875	83.34383	76.67706
16	14	36.25	0.625	61.47513	76.67707
17	15	36.75	0.5	33.6558	76.67706
18	16	37	0.25	5.980069	76.67704
19	17	37.25	0.25	3.995456	0
20	18	37.25	0	0	65.41935
21	19	37.25	0	0	0
22	20	37.1875	-0.0625	0	0
23	21	37.125	-0.0625	0.466291	0
24	22	37.0625	-0.0625	1.235547	0
25	23	37	-0.0625	2.393235	0
26	24	37	0	4.066925	0

Insert drug information here

Bevacizumab (Avastin®) is a monoclonal antibody against VEGF which binds and neutralizes all biologically active isoforms of VEGF. Avastin is approved, in combination with intravenous 5-fluorouracil-based chemotherapy, for first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum and in combination with carboplatin and paclitaxel for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC).

Sunitinib (Sutent®) is an oral multi-kinase inhibitor that targets several receptor tyrosine kinases including platelet-derived growth factor receptors (PDGFRα and PDGFRβ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2, and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET). (1) Inhibition of the phosphorylation of multiple receptor tyrosine kinases potentially results in inhibition of tumor growth and/or metastases, tumor regression, and inhibition of angiogenesis. In January 2006, the Food and Drug Administration (FDA) approved sunitinib for the treatment of gastrointestinal stromal tumor (GIST) and advanced renal cell carcinoma.

Sorafenib (Nexavar®) is also an oral tyrosine kinase inhibitor that targets multiple receptor kinases including CRAF, BRAF, mutant BRAF, KIT, FLT-3, VEGFR-2, VEGFR-3, and PDGFR-β resulting in decreased tumor cell proliferation and angiogenesis. (2) In December 2005, the FDA approved sorafenib for the treatment of patients with advanced renal cell carcinoma.

This pilot study will profile the correlation of longitudal time-series measurements of VEGF, PIGF and VEGFR2 to physical shrinkages in tumor size measured by CT-MRI scans with the Theranos System in ambulatory patients who are receiving your drug add in info as needed here for the treatment of their disease.

3.0 ELIGIBILITY CRITERIA (add therapy-specific criteria here)

3.1 Patients with any tumor type who are currently receiving commercially available anti-angiogenesis therapy including bevacizumab, sunitinib or sorafenib for the treatment of their disease. The specific dose and schedule of their anti-angiogenesis therapy including bevacizumab, sunitinib or sorafenib is at the discretion of the treating physician, but will be recorded in the patients record and the data collection forms.

3.2 Patients must be willing to perform lancet finger sticks at different time points over the study period.

3.3 Patients must be 18 years of age or older.

3.4 Patients must be able to understand the nature of the study and give written informed consent.

4.0 STUDY DESIGN

Sample Size: A total of 250 patients (male or female) will be enrolled.

Prior to the first patient beginning the trial, the clinic personnel at the Site/sponsor will be trained on the use of the Theranos System.

Each patient will be sent home with a reader and the appropriate number of individual cartridges required for the study. The clinic personnel will use the supplied bar code scanner to scan the individual bar codes for each cartridge and link it with a patient ID which will be entered via a screen within the TheranOS System.. The patient will also be supplied with the appropriate number of lancets and alcohol wipes. A lunch type cooler bag will be supplied for each patient to carry their cartridges and accessories home.

On the first clinic visit (DAY 1), clinic personnel will draw a single 10 ml venous blood sample from the patient as well as perform a finger stick utilizing the Theranos System. . The number of tubes to be collected will be as follows; one EDTA (plasma) and one plain red top. As a measure of drug response Circulating Endothelial Cells (CECs) in the venous blood draw will be calculated

The designated clinical personnel will demonstrate to the patient how to use the Theranos System while the patient is in the clinic. The designated clinical personnel will then oversee the patient as they use a lancet to obtain blood through a finger stick and then use the cartridge to draw in the blood sample. Once the sample is in the cartridge, the patient will insert the cartridge into the reader. While the reader runs the analysis on that cartridge, the patient will be instructed on the other aspects of the trial. Once the assay is processed the patient will return to the reader, dispose of the cartridge, and then use a second cartridge to repeat the blood procurement and analysis process one additional time.

Each patient will then be sent home from the clinic with a Theranos reader, 6 additional cartridges, supplies, and instructions to repeat the procedure at two additional time points (Day 3, and Day 5) while at home. On Day 8, the patient will return to the clinic. While in the clinic, an additional 10ml venous blood sample will be obtained from the patient. The patient will also perform a finger stick to obtain a blood sample for analysis on the Theranos System. The venous blood sample will be processed, frozen, and shipped by clinic personnel to Theranos for conventional evaluation (ELISA), and the results will be compared to the results obtained with the Theranos System.

This process will be repeated with patients taking home cartridges and supplies to support 2 at home finger sticks on Days 10, and Day 12. On Day 15, the patient will return to the clinic.. The patient will also perform a finger stick to obtain a blood sample for analysis on the Theranos System. The venous blood sample will be processed, frozen, and shipped by clinic personnel to Theranos for conventional evaluation (ELISA), and the results will be compared to the results obtained with the Theranos System.
The process will once again be repeated with patients taking home cartridges and supplies to support 2 at home finger sticks on Days 17, and 19 with the patient returning to the clinic on the 22nd. The patient will continue the cycle until the last clinic visit on Day 28. See table below for the remaining cycles of which the patient takes home the cartridges to support 2 at home finger sticks per week.

The patient will be administered your drug as directed or will take additional medications (need to input here) orally as directed by their physician and will record the following information in the patient diary on a daily basis (see Appendix A): (Certain information will also be completed by the clinical staff and time of medication being taken can be captured)

a. Medicines taken including the time of day and dose
b. Overall health assessment: including any side effects they may be experiencing

The following table summarizes the Data Points for Monitoring using the Theranos System and using traditional laboratory methods during the trial:

TABLE I: Data Points for Clinical Monitoring using the Theranos System (TS) and Laboratory Assay (ELISA)
- Calibration time-points – venous versus finger-stick

Data Point	Location	Assay
Day 1	Clinic	2 TS cartridges ELISA
Day 3	Home	TS
Day 5	Home	TS
Day 8	Clinic	1 TS cartridge ELISA
Day 10	Home	TS
Day 12	Home	TS

Day 15	Clinic	1 TS cartridge ELISA
Day 17	Home	TS
Day 19	Home	TS
Day 22	Clinic	1 TS Cartridge ELISA
Day 24	Home	TS
Day 26	Home	TS
Day 28	Home	TS
Day 29	Clinic	1 TS Cartridge ELISA
Day 31	Home	TS
Day 33	Home	TS
Day 36	Clinic	1 TS Cartridge ELISA
Day 38	Home	TS
Day 40	Home	TS
Day 43	Clinic	1 TS Cartridge ELISA
Day 45	Home	TS
Day 47	Home	TS
Day 50	Clinic	1 TS Cartridge ELISA
Day 52	Home	TS
Day 54	Home	TS
Day 57	Clinic	1 TS Cartridge ELISA

If needed, option to continue monitoring 2X's per week up to 57 days in total. This provides an opportunity to extend up to 12 more time points in total.

5.0 REPORTING RESULTS

Theranos will provide online tools to plot/correlate levels of soluble selected biomarkers using the Theranos System and the conventional laboratory (ELISA) method along with other relevant measurements, including data entered into the TheranOS System by the clinic or the patient. Additionally, Theranos will provide separately a descriptive analysis of the potential added-value to patient treatment, based on time differences between Theranos real-time data and data from conventional laboratory analysis.

For each test sample analyzed by the Theranos System, a data summary report will be generated and be available from the server. Assay results will be accessible and available to authorized personnel only. Information from patient diaries and additional data inputs to the database will be summarized for the investigator and the patient. The investigator must complete a questionnaire that will secure feedback on the Theranos System and provide comparative results with the clinical lab test. A CT scan will be provided to Theranos for each patient as a measure of

tumor response/volume at baseline to insure compatibility. Additionally the clinical staff will record any adverse events the patient may be experiencing with the treatment.

Appendix A – Patient Diary

Initial Questionnaire – Completed vby Clinic Staff

1. Please fill in the following information:
    a. Patient Age _____
    b. Patient Height_____
    c. Patient Weight_____
    d. Demographics
        1. Caucasian
        2. Black
        3. Hispanic
        4. Asian
        5. Other

2. Which of the following best describes your smoking status?
    a. I smoke daily
    b. I smoke occasionally
    c. I don't smoke now, but I used to
    d. I have tried it a few times, but never smoke regularly
    e. I have never smoked

3. How often do you usually have an alcoholic drink of any kind? This includes wine, beer and spirits.
    a. Every day
    b. 4-6 times per week
    c. 1-3 times per week
    d. Monthly or less
    e. I don't drink alcohol at all

4. How often do you exercise:
    a. Every day
    b. 4-6 times a week
    c. 2-3 times a week
    d. Once a week
    e. Less than once a month
    f. Never

5. What is the primary diagnosis the patient is being treated for:
    a. Colorectal Cancer
        i. Adjuvant

ii.Metastatic
1. Stage? II, III. IV

b. GIST
i. Adjuvant
ii.Metastatic
1. Stage? II, III. IV

c. Renal Cancer
i. Adjuvant
ii.Metastatic
1. Stage? II, III. IV

d. Breast Cancer
i. Adjuvant
ii.Metastatic
1. Stage? II, III. IV

e. NSCLC
i. Adjuvant
ii.Metastatic
1. Stage? II, III. IV

f. Other
i. Adjuvant
ii.Metastatic
Metastatic
1. Stage? II, III. IV

2. Please check all the medications the patient is currently being given:

Chemotherapies		
5-FU	fluorouracil	
Camptosar	irinotecan/CPT-11	
Eloxatin	oxaliplatin	
Gemzar	gemcitabine	
Hycamtin	Topotecan	
Paraplatin	carboplatin	
Xeloda	Capecitabine	
	leucovorin	
Other Chemotherapy		

General Therapies		
Anastrozole	arimidex	
Avastin	bevacizumab	
Bexxar		
Erbitux	cetuximab	
Gleevec		
Herceptin	Gemcitabine	
Iressa	Gefitinib	
Nexavar	sorafenib	

Revlimid	LENALIDOMIDE	
Sutent	sutinib malate	
Tarceva	Erlotinib	
Taxotere	Docetaxel	
Velcade	Bortezomib	
Other General Therapies		

Supportive Care		
Advil/other	ibuprofen	
Ambien/Lunesta/other sleep aids		
Anzament	dolasetron	
Aranesp	Erythropoietin	
Aspirin		
Epogen	Erythropoietin	
Kytril	granisetron	
Neulasta	pegfligrastim	
Neupogen	Filgrastim	
Paxil/other antidepressants		
Procrit	Erythropoietin	
Tylenol/other	acetaminophen	
Zofran	ondansetron	
Other Supportive Care		

Patient Daily Questions (Customize to study objectives)

1. On a scale of 1 to 10, how do you feel today?

   Very Good 10 9 8 7 6 5 4 3 2 1 Poor

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

2. Thinking about your health today, which of the following statements best describe your usual activities such as work, family or leisure activities.
   a. I have no problems with performing my usual activities
   b. I have some problems performing my usual activities
   c. I am unable to perform my usual activities.

3. Moderate activities, such as moving a table, moderate exercise, pushing a vacuum cleaner,.
   a. Yes, limited a lot
   b. Yes, limited a little
   c. No, not limited at all

4. Please check if you have any of these complaints today:
    a. Headache
    b. Nausea
    c. Body Pain
    d. Dizziness
    e. Reaction at infusion site
    f. Fatigue
    g. Depressed
    h. Shortness of breath
    i. Decreased appetite

5. Appendix B – Patient Post-Study Evaluation

Thank you for participating in a study to evaluate the Theranos System. By utilizing the Theranos System you've been able to provide information to your physician that could support their decisions around your ongoing therapy.

We would like to ask you a few questions about your use of the Theranos System.

1. Overall, how easy was it to use the Theranos System?
    a. Very easy
    b. Somewhat easy
    c. Somewhat hard at first, but it got easier
    d. Very hard

2. How would you rate the Patient User Manual?
    a. Very informative, with clear directions
    b. Informative but some of the directions need to be clarified
    c. Not helpful at all
    d. Didn't read it
    e. Didn't get a patient user manual

3. How would you rate the training you received at the clinic prior to taking the System home?

    Very Good 10 9 8 7 6 5 4 3 2 1 Poor

4. How would you rate the Theranos System on the following attributes
    - Ease of use

    Very Easy 10 9 8 7 6 5 4 3 2 1 Hard

    - Time Required

Very little time of time 10 9 8 7 6 5 4 3 2 1 Lots

- Patient Diary

Very easy to use 10 9 8 7 6 5 4 3 2 1 Hard to Use

- Drawing Blood

Painless 10 9 8 7 6 5 4 3 2 1
Painful

5. How well did the Theranos System work for you during the trial?
    a. Very Well
    b. Okay
    c. Had problems
        i. What problem(s) did you experience? Mark all that apply
            1. Drawing blood
            2. Filling the cartridge
            3. Loading the cartridge
            4. Getting a cellular signal
            5. Getting onto the website
            6. Filling out the patient diary
            7. Other (please explain)
        ii.(For each problem) How were you able to resolve your problem on _____?
            1. Figured out solution on my own
            2. Called clinic and they helped me
            3. Called Theranos Customer Care Center
                a. How would you rate the support you received?
                    i. Excellent
                    ii. Very Good
                    iii. Good
                    iv. Fair
                    v. Poor
                b. How was your problem resolved?
                    i. Customer Care Center talked me through the problem
                    ii. A replacement reader/cartridge was sent to me
                    iii. Other (please explain)

6. Overall, on a scale of 1 to 10 which process would you prefer to provide monitoring information to your physician?

Prefer monitoring at home Prefer going to clinic

10 9 8 7 6 5 4 3 2 1

6.0 REFERENCES

Add therapy-specific information

1. SUTENT® (sunitinib malate) capsules Product Package Insert. Pfizer Labs. February 2006.
2. NEXAVAR® (sorafenib) Product Package Insert. Bayer Pharmaceuticals Corporation. August2006.
3. AVASTIN (bevacizumab) Product Package Insert. Genentech

I have the Theranos summary to Aidan Power, the Introduction to Theranos Systems, the Informed Consent and the IRB Submission. I have read them. I attach these so we are all working off the same versions of the documents. If I do not have the correct versions please send them, thank you. I have also read US patent 7,291,497 B2.

What I do not have are:

1. The original Theranos and Pfizer agreed work proposal that contains aims, goals, measurable milestone outputs and work plan. The IRB Submission document appears to reflect some original work plan, is that correct?
2. The Interim Report on Assay Development submitted to Pfizer Q2 2007.

In the summary document you refer:

3. To meeting with the Pfizer team. Who was the Pfizer team?
4. To Pfizer point of contacts changing several times. Who chronologically were the Pfizer point of contacts?
5. Pfizer portal at Theranos. Please provide me access to the Pfizer portal at Theranos

Would you please send, provide or answer. Thank You.

Please:
What are the assays that are currently run? Is the list on Slide 8, Introduction to the Theranos System the current list?

How many assays are currently run in multiplex mode? What are the multiplex assay panels?

The VEGF, sVEGFR2 and PlGF were done as a multiplex assay? What was the sample type? Blood, serum or urine?

What were the calibrators? Were they done in the same sample type?

What was the reference method used? Was the reference assay a multiplex assay or three single assays? Where was it run? Who ran it?

How often does the instrument need to be calibrated?

How often do the on board chemistry controls need to be run?

What is the process from finger prick to blood sample to the assay cartridge? Is this integrated or does the patient prick the finger then squeeze blood into an orifice of the assay cartridge?

Does the instrument receive a finger into an orfice, prick and process into plasma?

Why is the Theranos VEGF and VEGFR2 assay not interfered with by Avastin but the reference method assay(s?) for VEGF and VEGFR2 are interfered?

Was there longitudinal time correlation of changes in VEGF, PlGF and VEEGFR2 with CT-MRI tumor reduction? Was any other tumor load reduction measured and correlated with these three analytes?

Slide 12, Introduction to the Theranos System shows a C peptide measurement and correlated to a reference assay. What was the reference assay, where was it run and by who? How many patients are there in this slide?

Slide 17, Introduction to the Theranos System shows a patient with a 30 day longitudinal time measurement. How many patients were so measured out of the number enrolled? Please provide this type of plot for all of the patients measured. Was there any correlation of responders versus non-responders? Or level of response?

Slide 21, Introduction to the Theranos System show three patients with 72 hour longitudinal time measurements. How many patients were so measured out of the number enrolled? Please provide this type of plot for all of the patients measured. Was there any correlation of responders versus non-responders? Or level of response?

Do you have data and reports that address these goals from the September 2006 Study Plan? If so please send. Is the Introduction to the Theranos Systems slide deck the report that addresses these goals below?

1.1. To profile trend results in panels of angiogenesis proteins over time and correlate those values to physical shrinkage in tumor size by leveraging Theranos systems to optimally sample in a way not possible using the central laboratory. These results can be used as baselines against which to index field data in future studies for dose ranging and compound optimization.
1.2. To evaluate the Theranos System in monitoring the progression of the cancers in the hands of clinical personnel and patients who are currently receiving anti-angiogenesis drugs including but not limited to (Specify drugs) for the treatment of their disease.
1.3. To quantify the result time, accuracy, and advantage of obtaining real-time environmental and blood data as well as stored clinically relevant data in patient records with the Theranos System with the current preferred laboratory measurement and data collection methods.
1.4. To quantify and compare the efficacy dynamics of three therapies and interventions
1.5. To demonstrate the impact of Theranos systems on compliance with a therapy / program to better slow the progression of these cancers
1.6. To pilot the TheranOS (Theranos Operating System) including the healthcare provider and patient portals as well as the data reports generated.

Is there an instrument version that measures single nucleotide polymorphisms?

Is there an instrument version that detects antibiotic resistant organisms?

Can the instrument take a swab sample?

Is there a site in the Mid-Atlantic or New England that I could visit to see the instrument?

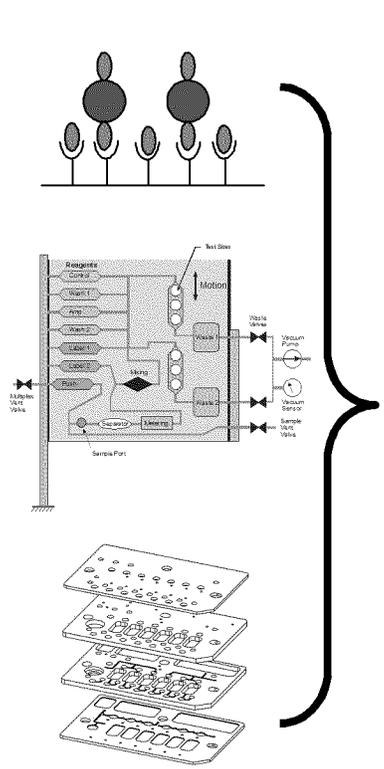
theranos
redefining healthcare

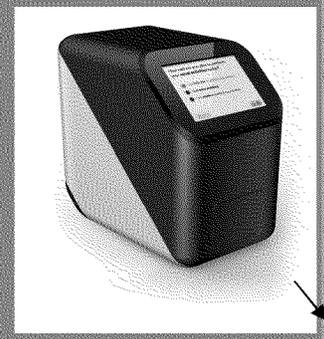
An Introduction to Theranos Systems

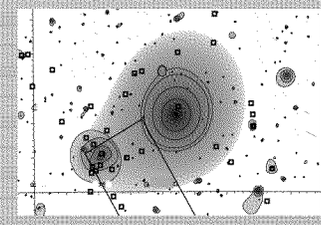
theranos
redefining healthcare

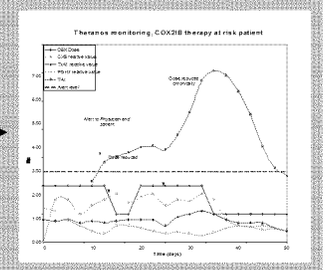
Theranos Infrastructure

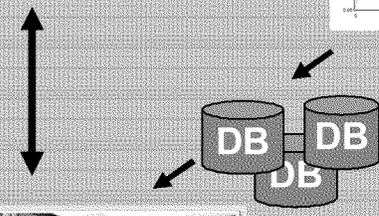
The Healthcare Operating System for Mechanism Based Medicine

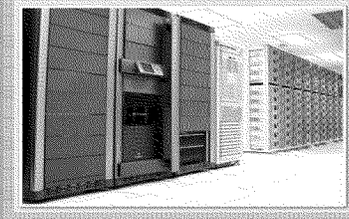


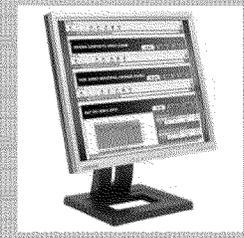












TheranOS

Cartridges Reader

Consumer Systems

Informatics Applications

Data infrastructure

theranos
redefining healthcare

The existence of a technology infrastructure for home, real-time blood monitoring allows to collect information which cannot be seen using conventional blood tests:

- Small sample (finger-stick) + more frequent sampling of a small subset of analytes enables
  - Identification of appropriate analytes (not possible if samples are not taken more frequently than for laboratory methods due to lack of trend profiles) << Small sample enables
  - Earlier detection of efficacy dynamics or acute problems so intervention (dose) can be more effective << Frequent sampling enable
  - Ease of use; Convenience of monitoring through-out time-course before an event

- Higher sample integrity; real-time sample analysis on fresh whole blood on a standardized platform internationally
  - Eliminate false reads on concentrations due to analyte decay rates and inherent noise due to processing

- Increased sensitivity over commercially available standards (<1pg/ml and high mg/ml simultaneously at <5% CV assay spec) to allow for detection of protein multiplexes in at clinically relevant concentrations

theranos
redefining healthcare

Actionable Information Systems

- Fewer patients in future studies; Eliminate shipping and lab costs
- Real-time simultaneous PK/PD –faster, better, dose-response characterization
- Comprehensive longitudinal time series profiling –account for velocity of progression toward outcome; characterize direction changes in-process
- "Mechanism maps": trends in panels of proteins over time and change in rate of multiplexed panels correlated to clinical endpoints, stored on server, and mapped in the context of the full pathophysiology of the disease for use in indexing future patient data to better quantify a patient state
  - **Analogous to thyroid tests, need multiple variables to effectively make decisions**
- Integrated link to (adaptive) trial and health management system

theranos
redefining healthcare

Summary: Actionable Information Systems for Compound Optimization and Enhancement of the Value of Therapies

1. **Phase I-III: Fast-track compound to market with broadest label possible**

2. **Phase IV and Post-Marketing: Rapidly expand label to more indications and sub-patient populations; ameliorate safety concerns; cross comparison studies for rapid publications with hard data**

- Exposure models (real-time, more comprehensive PK)
  - Adaptive dosing
    - (Exposure versus biology)
  - In-patient dose titration to ID optimal dose and schedule for sub-patient populations
- Dynamics (real-time, more accurate efficacy and safety dynamics),
  - Generate profiles that could not previously be mapped
- Consumer oriented interactive information collection & delivery systems
  - Data collection, patient compliance, and engagemen

- Therapy: Health Program
- Predictive pathophysiology: Data rich patient poor studies

theranos
redefining healthcare

Customized Studies

(Phases run in parallel)

1. Existing Cartridges: Ship Systems Immediately for Studies
   - Customized Cartridges: 2-5 Months
2. Antibody Development:
   - Theranos to Develop: 6-12 Months
3. Gathering of project specifications:
   - 1-2 Weeks
4. Customization of TheranOS to include but not limited to:
   - Patient Diary
   - Data Collection System
   - Data Integration System
   - Data Transfers (export into CSV)
   - Data Analysis System and Reporting (automatic graphical multivariate analyses, mapping of real-time data into pathophysiology maps)
   - Ongoing

TOTAL TIME TO STUDY INITIATION BASED ON PROJECT NEEDS (other than Antibody Development) –1-5 Months

theranos
redefining healthcare

System Design

Designed for at home use and can also be used in clinics (will be CLIA waived)
Multiplexed measurement of biomarkers
- Max 6-8 per cartridge

Serial measurements to detect trends
Fresh whole blood, plasma or serum samples
Finger-stick: Small sample size (10-20 uL)
Mix and match selection of analytes
Wide measurement range
- pg/mL – mg/mL (1 billion fold)

High sensitivity
- 0.2 pg/mL (2 parts per 10-billion)

Analyte Recovery: ~100 %
System CV (inter-intra assay, inter-intra cartridge, inter-intra reader): <10%
On-board chemistry controls
Factory calibration (no user calibration)
Wireless communication of results to appropriate user
Proprietary algorithms to interpret time trend results

theranos
redefining healthcare

Theranos Assay Library* Q1-08

Cytokine Markers	Cardiovascular Markers	Metabolic Markers
GCSF	BNP	Adiponectin
iCAM-1	CKMB	GIP
IL-1 through IL-8	LTB4	GLP-1
IL-10, IL-12	Fibrin D-Dimer	GLP-2
CRP	LPS-binding protein	Glucagon
IL-15	Myoglobin	Insulin and pro-insulin
TGFβ	Procalcitonin	Leptin and grelin
TNFα	Protein C	Peptide YY and NPY
TNFβ	Troponin-I	Glucose
Oncology Markers	**Apoptosis Markers**	**Other Markers**
EGFR	M30	Cystatin-C
PIGF	M65	IgE - free and total
PSA	Nucleosomal DNA	Progesteron
sVEGF R2	**Bone Markers**	Prothombrin
VEGF	Osteoclast panel	sCD14
FLT-3	Osteoblast panel	Troponin-T
kit	Osteocalcin	α-Glutathione S-Transfera

* (Includes existing assays and those currently under development)

theranos
redefining healthcare

Sensitivity matches or exceeds best available methods in real samples

GLP-1: 0.17 pM (drug company study)
IL-6: 0.4 pg/mL (in house study)

theranos
redefining healthcare

Antibodies to small molecules

Theranos team led by world-class expert and comprised of key Syntex principals

- Small molecules
  - Covalently attached ("haptens")
  - To "carrier" proteins
    - Albumin, IgG, KLH
    - High Hapten/Protein ratio
  - Repeated immunization (hyperimmunization)
  - Freunds' adjuvant
- Evoke strong immune responses
- Monoclonal/Polyclonal antibodies can be made
- Theranos system requires MAbs specific to compound and/or its metabolites
  - If available from prior Analytical Chem/DMPK assays, assay development & validation on Theranos readers is relatively quic
  - If MAbs not available, Theranos will raise those antibodies by haptenating compound, developing & validating assay –lead time 6 to 9 months

theranos
redefining healthcare

Antibody Development Process

Hapten Design

- ❑ Inspect Structures
- ❑ Define which molecules are to be recognized by Ab
- ❑ Define structural elements likely to evoke Ab
- ❑ Select linking sites
- ❑ Design hapten or hapten precursor

Preparation of Haptens

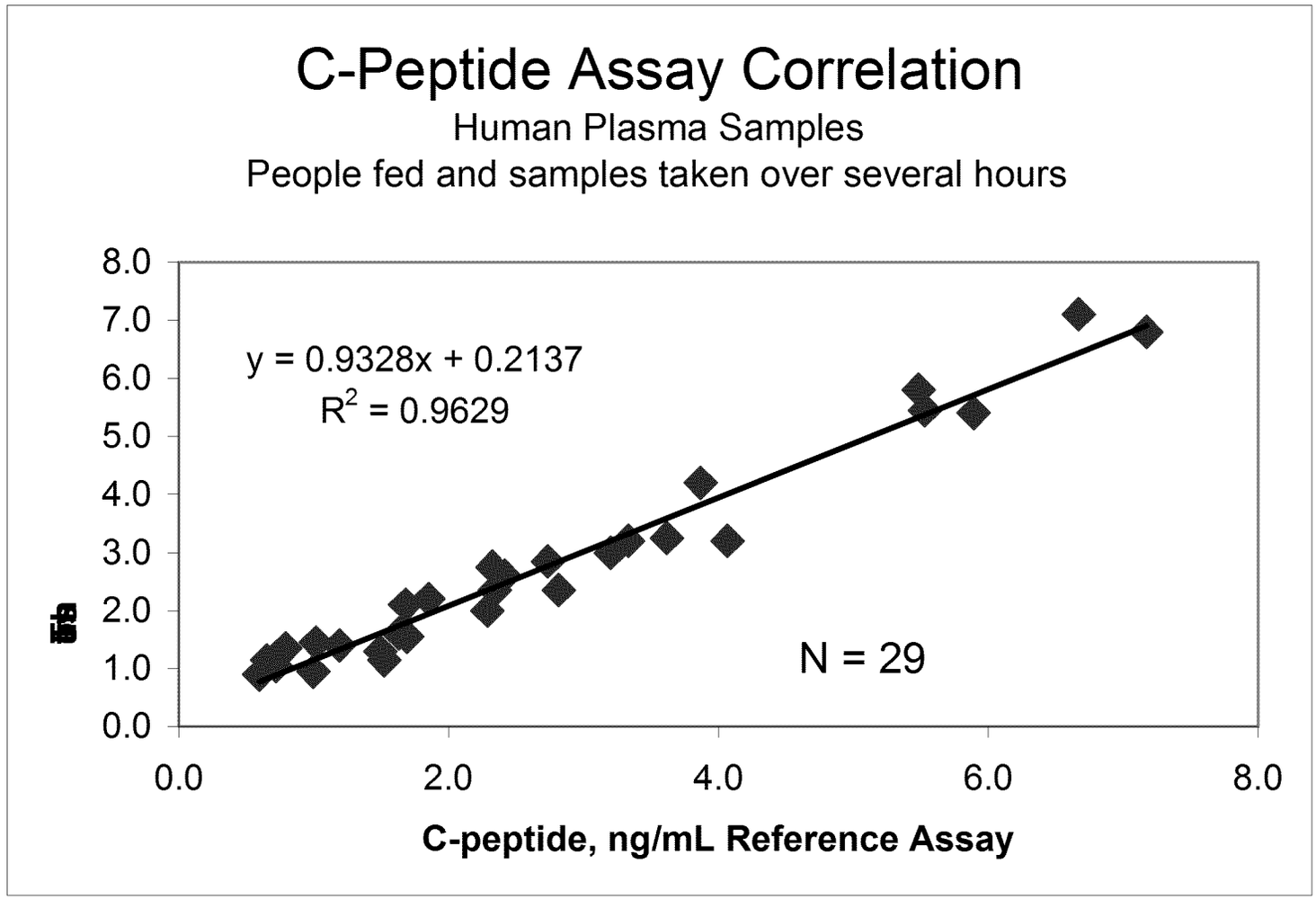
- ❑ Starting materials can be the drug or drug intermediates available from drug company
- ❑ Drug company may do some straightforward synthetic work
- ❑ Synthesis requiring only a few straightforward steps can be outsourced to local synthesis shops
- ❑ Activation (if needed) is done at Theranos

Steps in Antibody Production

- ❑ Outsourced from Theranos
- ❑ Polyclonal and monoclonal programs
- ❑ Early screening at vendor
- ❑ Selection of candidate animals
- ❑ Fusions and cloning
- ❑ Clonal Selection
- ❑ Strong candidates screened at Theranos in specific assay format
- ❑ Bulk production (MC's 100mg, PC's 10s of mls)
- ❑ Clones stabilized and archived (two locations)

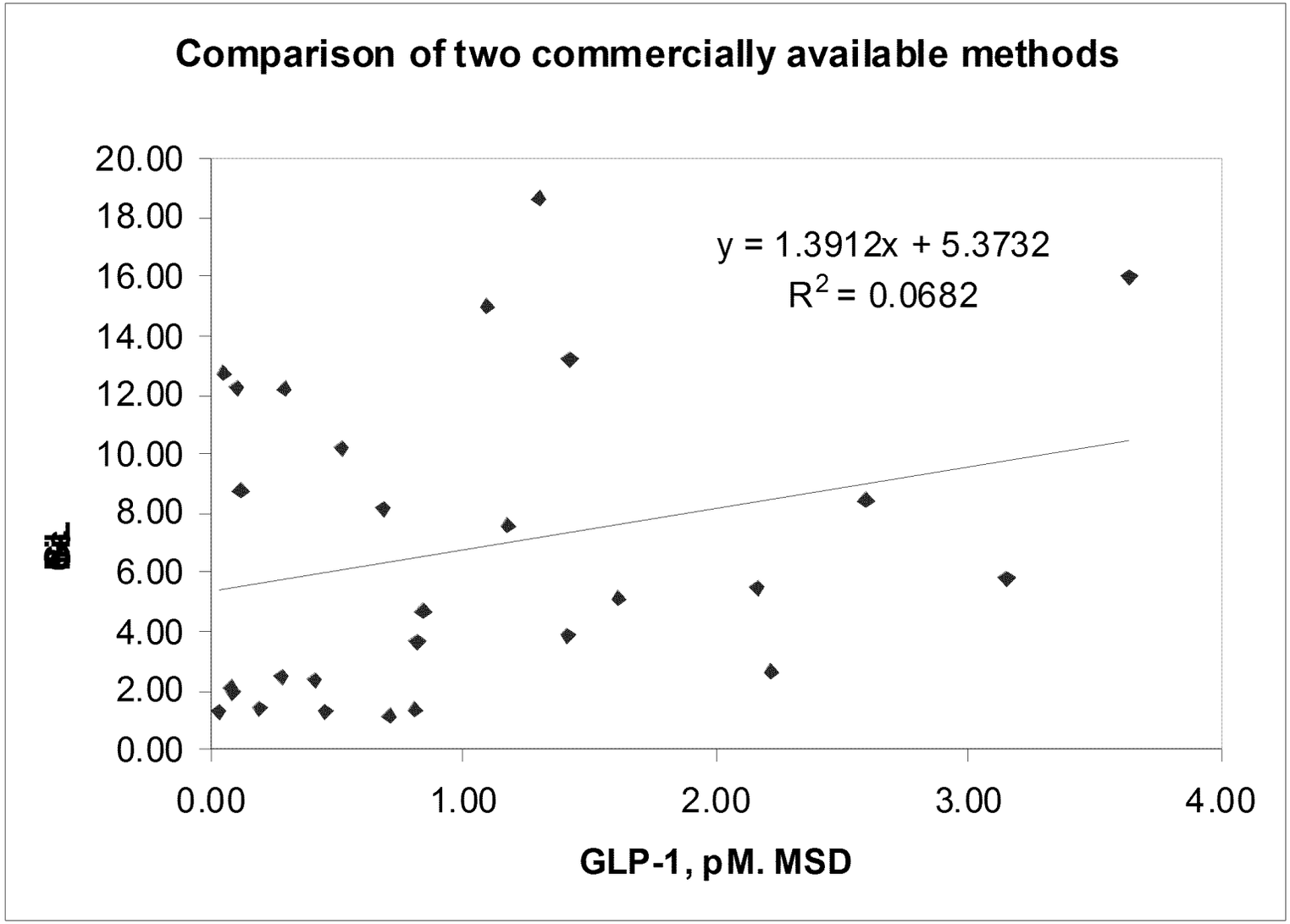
C-Peptide Assay

theranos
redefining healthcare



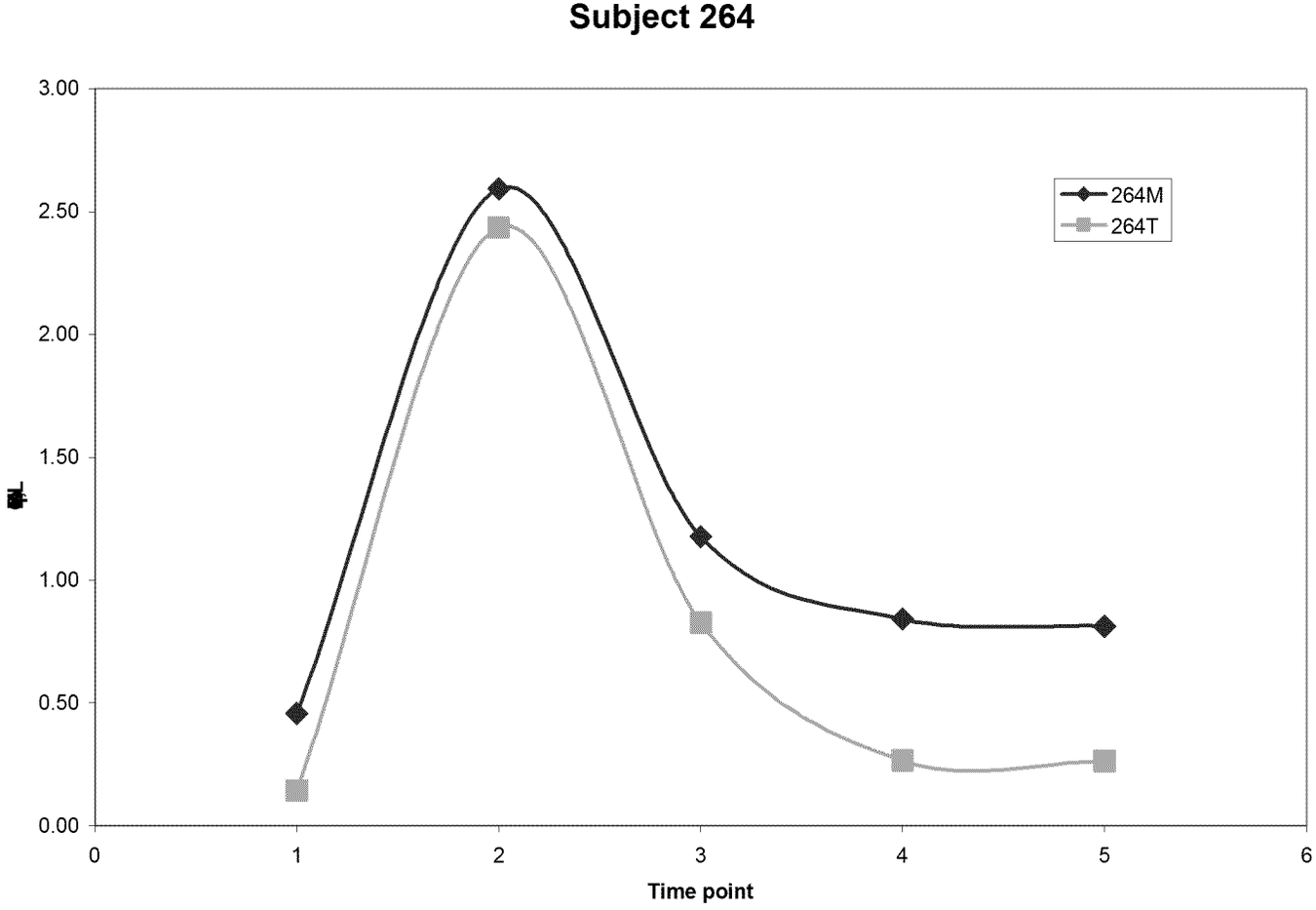
theranos
redefining healthcare

Current Gold-Standards



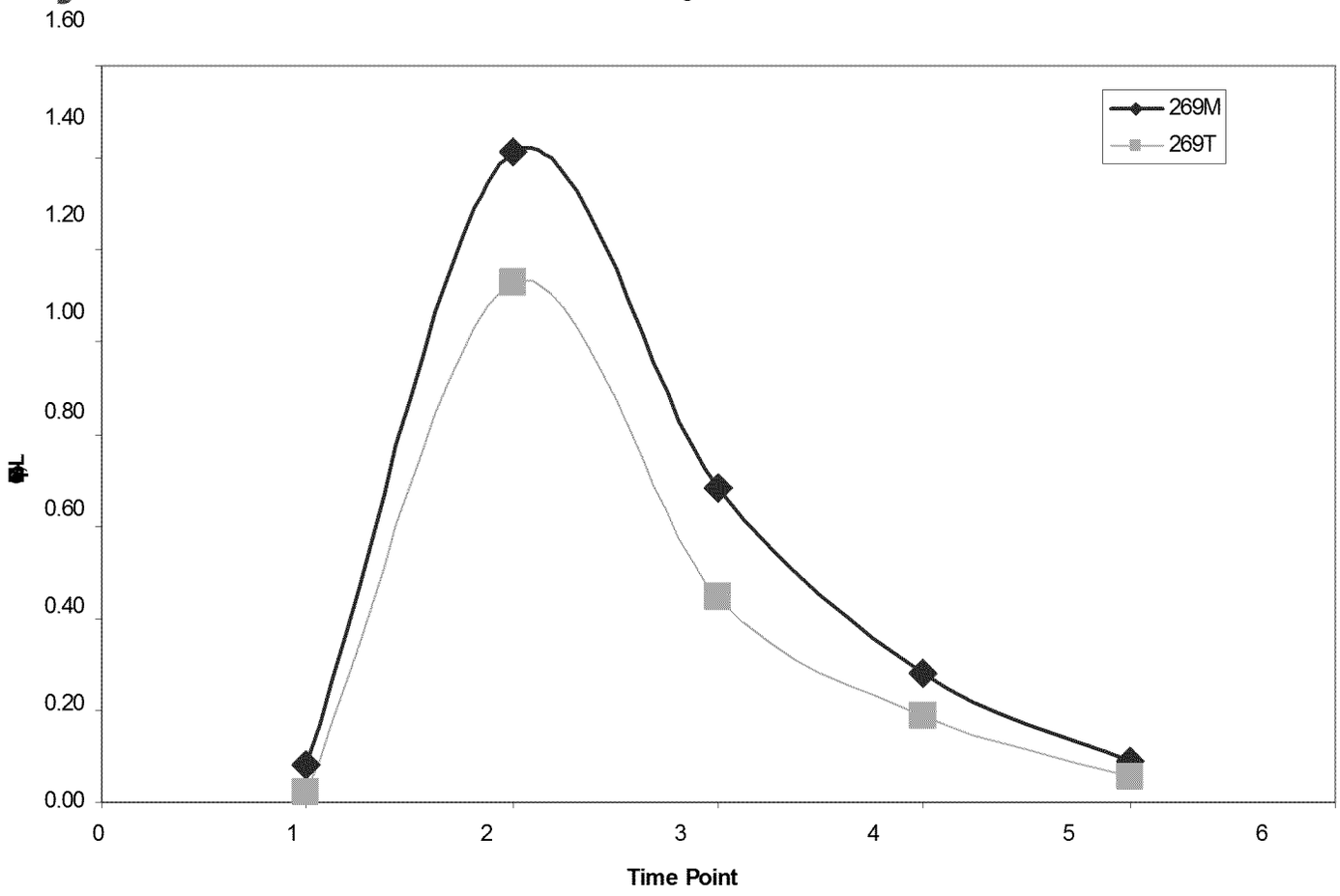
theranos
redefining healthcare

Subject 264: GLP-1

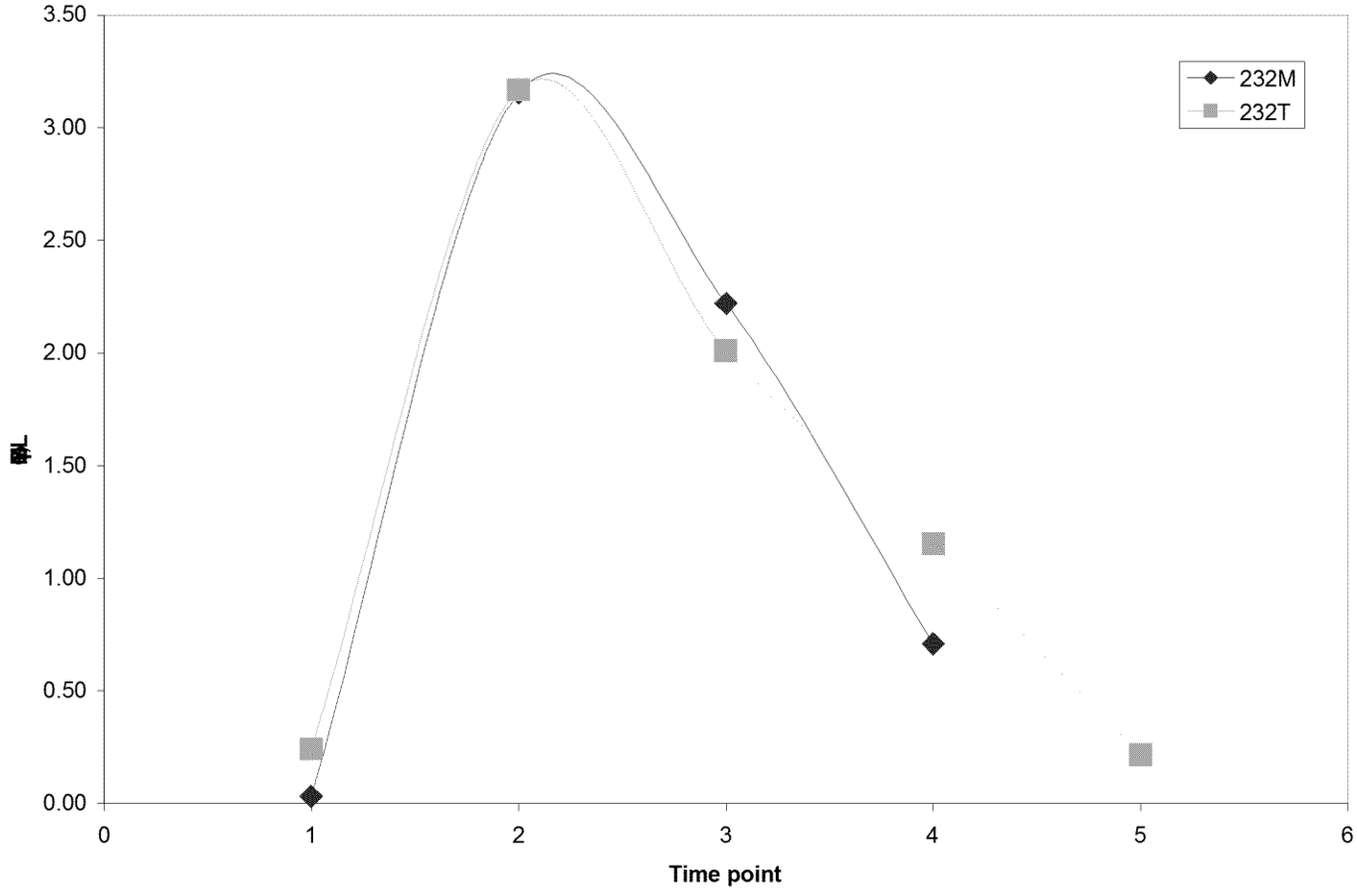


theranos
redefining healthcare

Subject 269: GLP-1



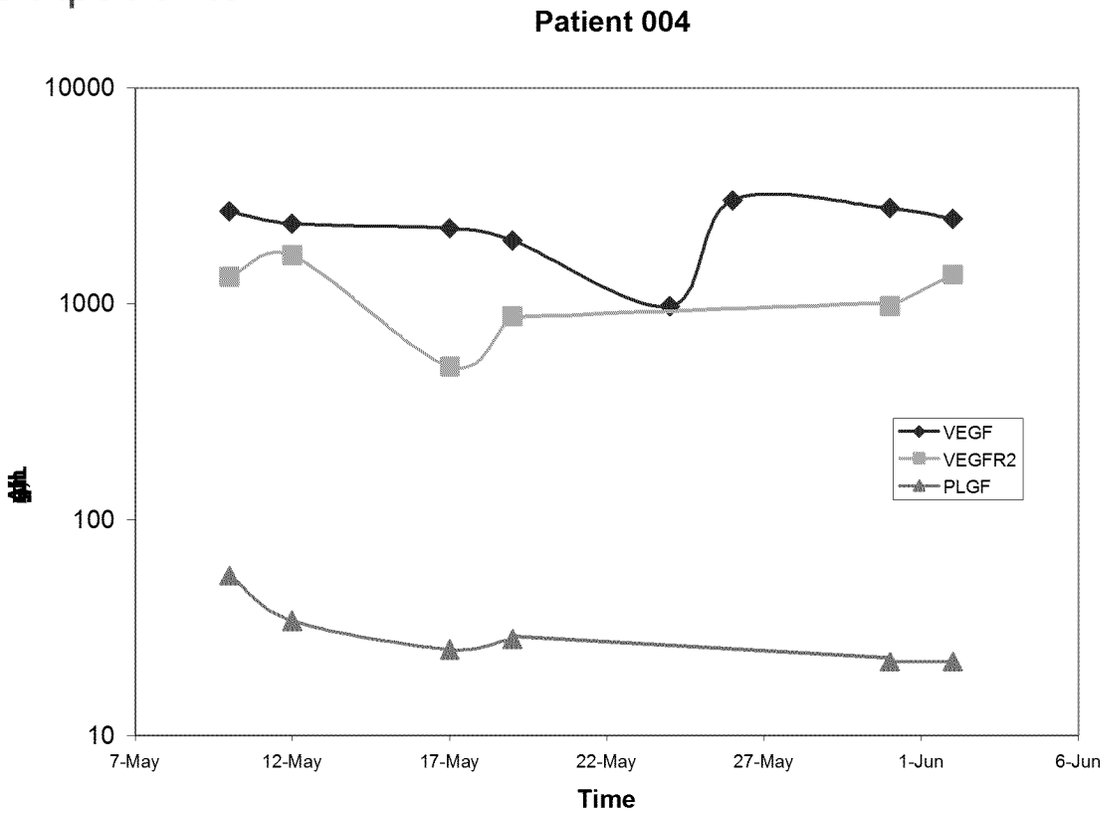
Subject 232 –GLP-1



theranos
redefining healthcare

Monitoring Three Biomarkers of Angiogenesis

Cancer Outpatients

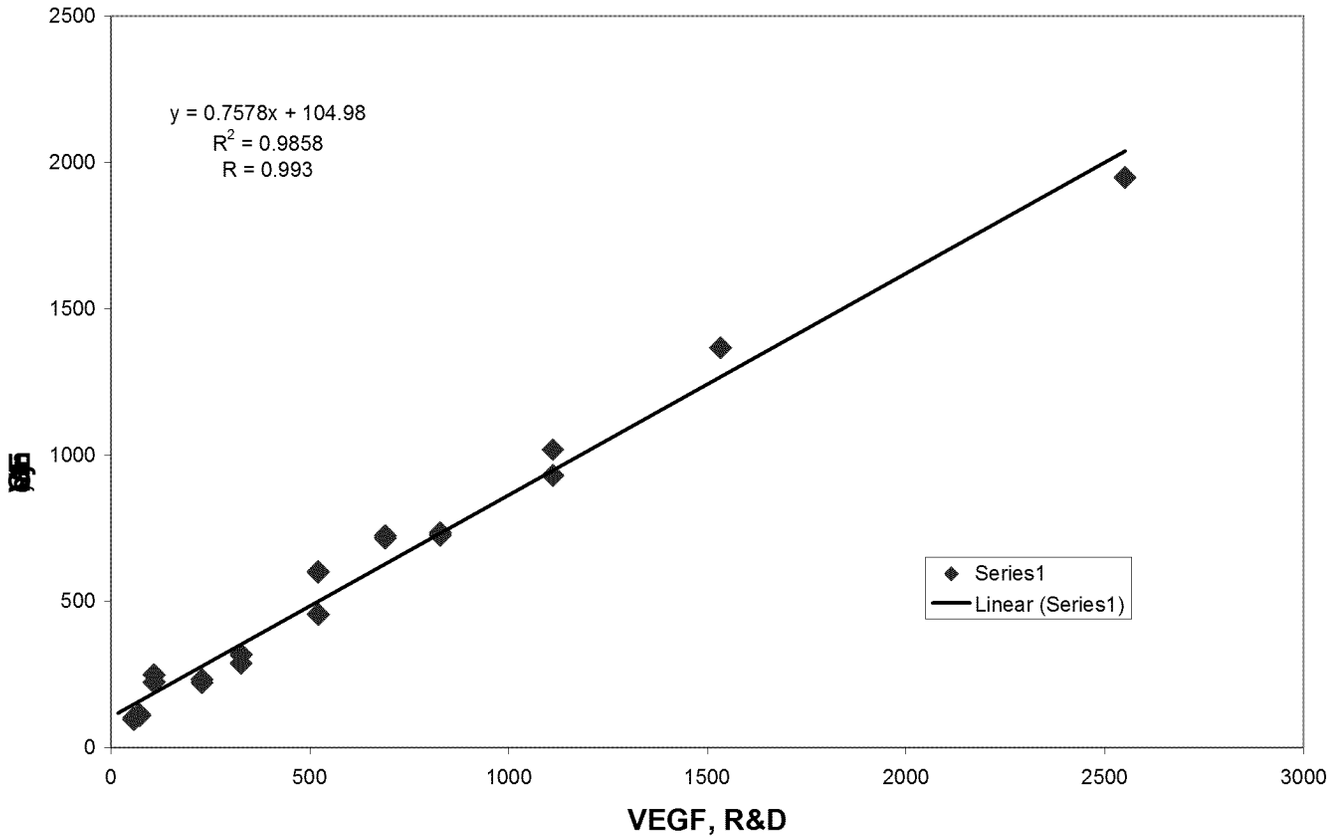


theranos
redefining healthcare

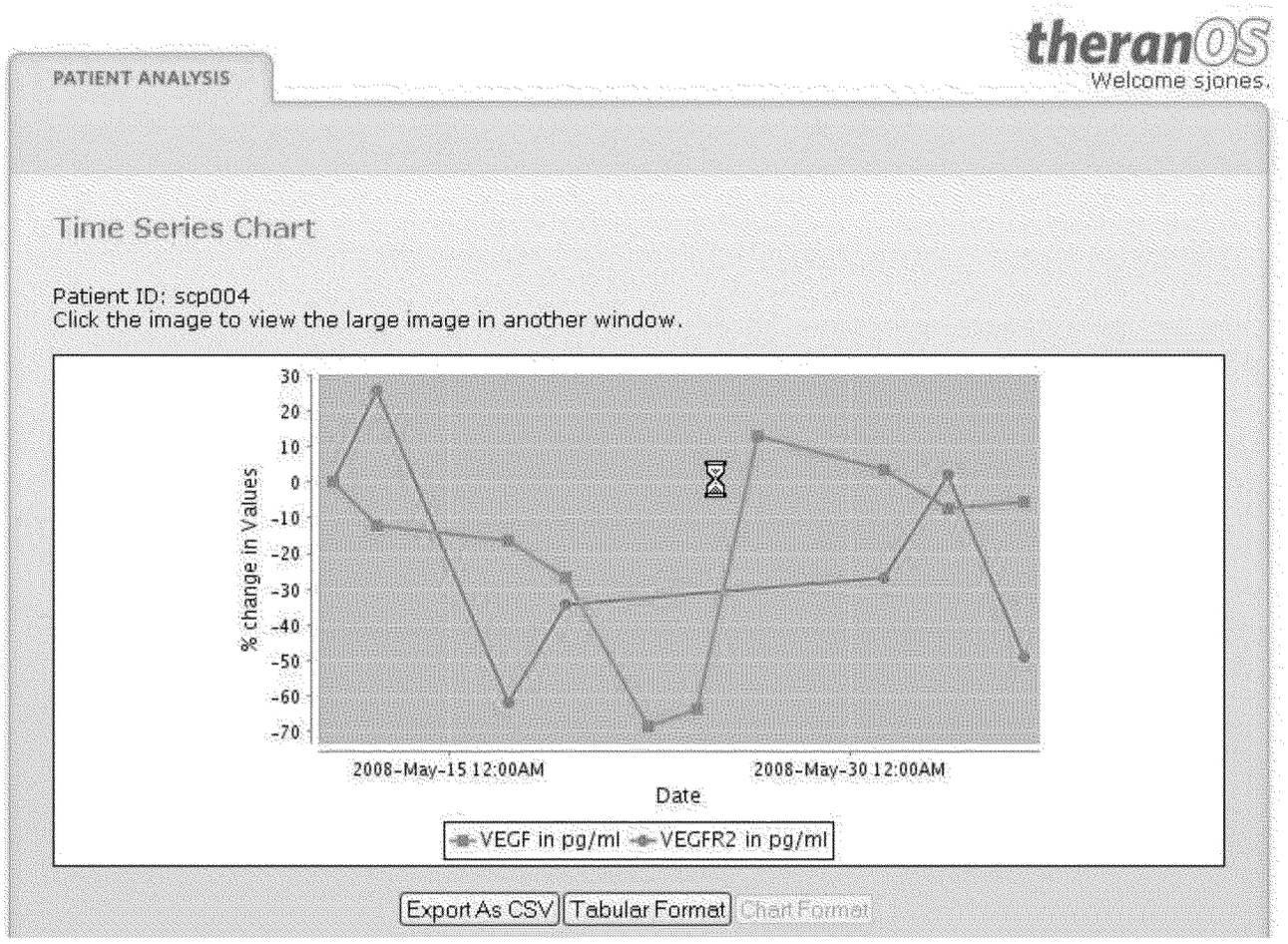
Analytical Validation

(plasma samples)

VEGF clinical results

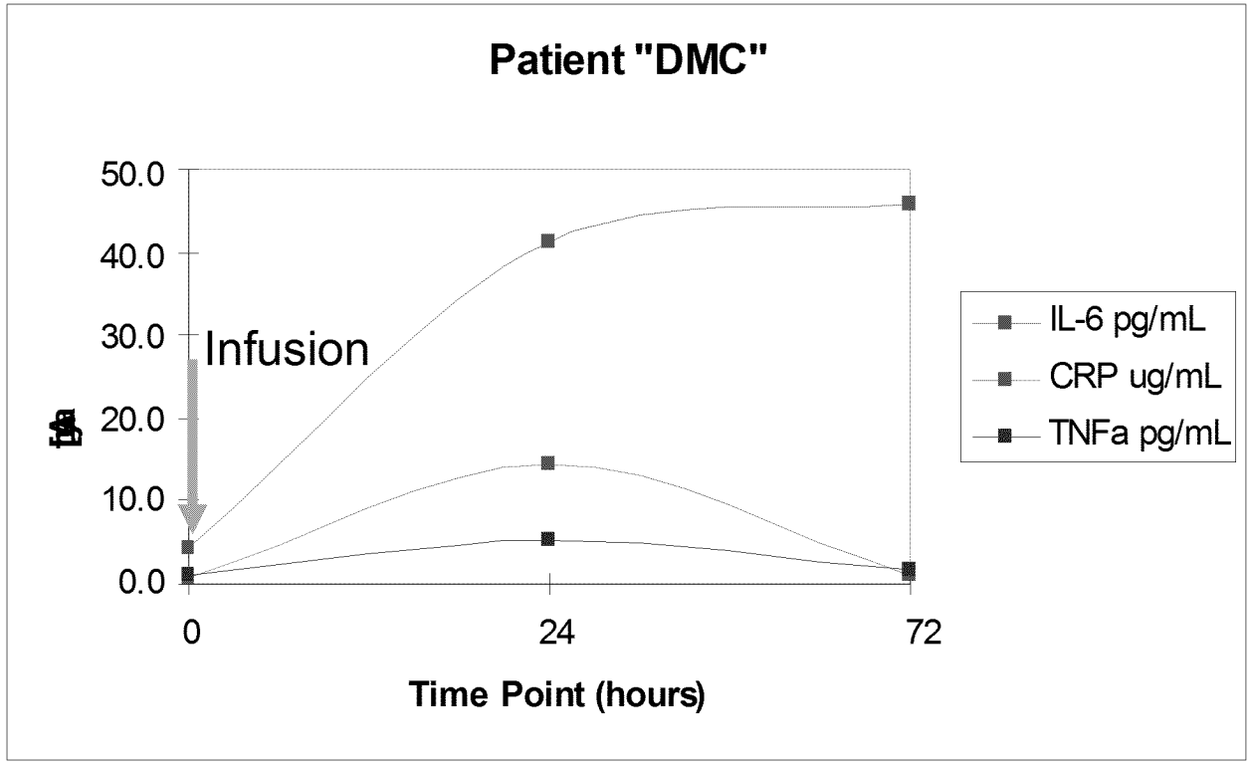


Response to Avastin Therapy (anti-VEGF)



theranos
redefining healthcare

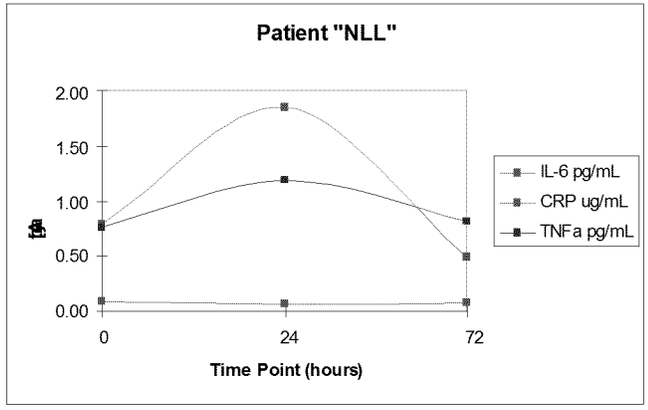
Typical results for one subject

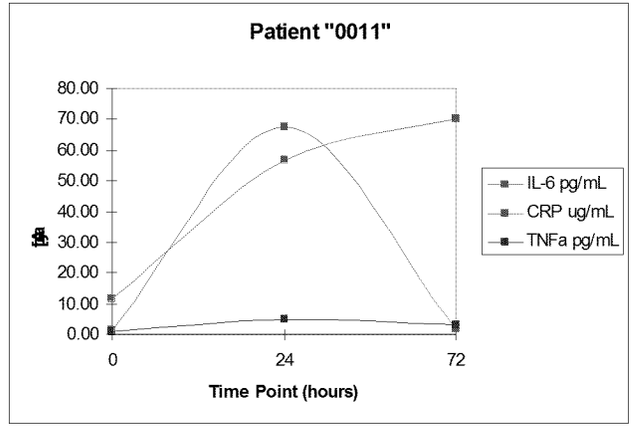


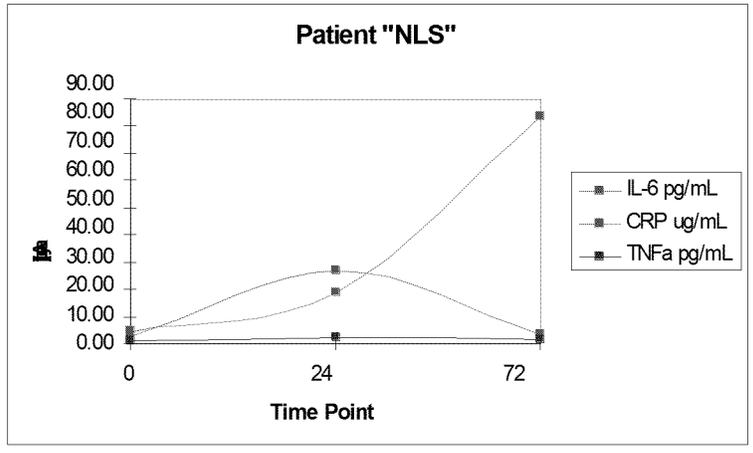
theranos
redefining healthcare

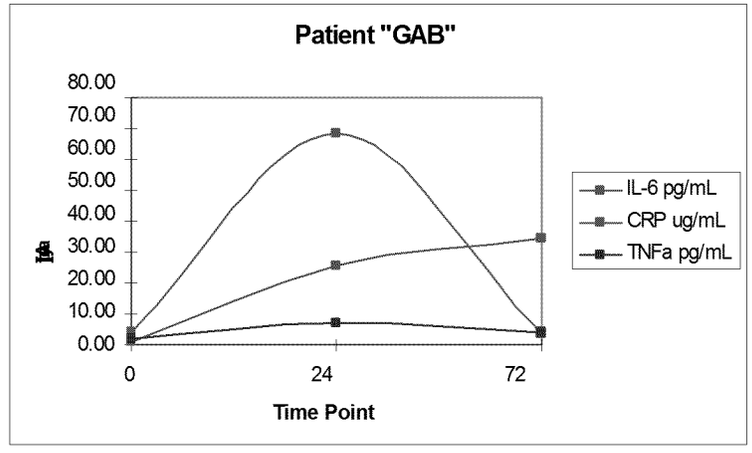
Huge variation between subjects

Both absolute levels and changes over time vary greatly









theranos
redefining healthcare

Cartridges

- Disposable cartridge loaded with Chemiluminescence immunoassays able to test up to 8 different assays on a single cartridge.
- The System utilizes combinations of drug and biomarkers together with other critical patient information including imaging to map trends which serve as indicators of efficacy and safety.
- The System's Chemiluminescence platform provides the capability to measure both high-sensitivity and low-sensitivity analytes on the same cartridge with a total system CV of <10%.
- Automated micro-fluidic disposable allows for rapid sample interference removal and reagent addition for increased sensitivity

theranos
redefining healthcare

Reader

- The Reader is the center for Remote Patient Care.
  - Wirelessly controls blood tests
  - Graphical user interfaces serves as next generation patient diary & compliance tool
    - Captures diary data and energy consumption and expenditure information
  - Communication portal for patient to healthcare provider/clinical coordinators
- Capable of extracting *in vitro* assay data from any combination of therapeutic analyte specific Cartridges
- Processing time averages 30 min.
- Training of new users is fast & easy
- Touch Screen enables real-time link to TheranOS web portal
- Hardware is customized for pre-clinical, ICU, and physician's office applications.

theranos
redefining healthcare

Portal to Enhance Remote Interactions with Patients

Engage patients in managing their disease

- Integration of individualized programs based on patient input to touch-screens, blood data, and indexing these factors against stored profiles which are linked to content from leading clinical centers of excellence designed to affect positive behavioral modifications in a personalized way

Captures data in an ambulatory setting reducing requirements of patients to return to the clinic & enabling early, adaptive and rapid decision making

- Fully integrated data infrastructure
- Increased patient compliance and higher integrity in patient diary data
- Direct interaction between physician and patient (two ways)

theranos
redefining healthcare

The Theranos System: Remote Interaction

Friendly User Interface

- Readers have web-standards based touch screens
- These screens are dynamically fed with content in real-time
- Collects data through graphical touch-screen input
- Modes for different visual needs, e.g., “High Contrast,” “Large Buttons”

Dynamic, updateable content

- Surveys fed and retrieved from server
- Additional content can be generated or modified at any time

theranos
redefining healthcare

The Theranos System: Behavior Modification

Theranos strives to change patients' behavior to enable long-term, healthy living through targeted content

Class-based content is delivered based on patients' goals, protein levels, and their diaries

- Patient classes are identified at program initiatio
- Content is individualized with streamlined information that touches individuals' predispositions and mindsets
- Content is based on informatics performed on integrated data sets & tied to patient class and progress as shown through the monitoring data
- It represents leading psychological approaches to weight loss motivation and therapy, delivered in small, memorable chunks.
- The content is derived from Theranos Human Centered Design team with a link to leading centers of excellence

theranos
redefining healthcare

Next generation GUI-based programs

Increased Compliance with a Program

- Visual input and feedback
- Cognitive demand is reduced giving patients a higher level of satisfaction
- Center for home healthcare, where patients are most comfortable
- Programs are individualized
  - Not search-based
- Account for sleep, stress, environmental pressures and practical mechanisms of eating healthily and exercising
  - Coupons –local restaurants near user location
  - Mobile Platform

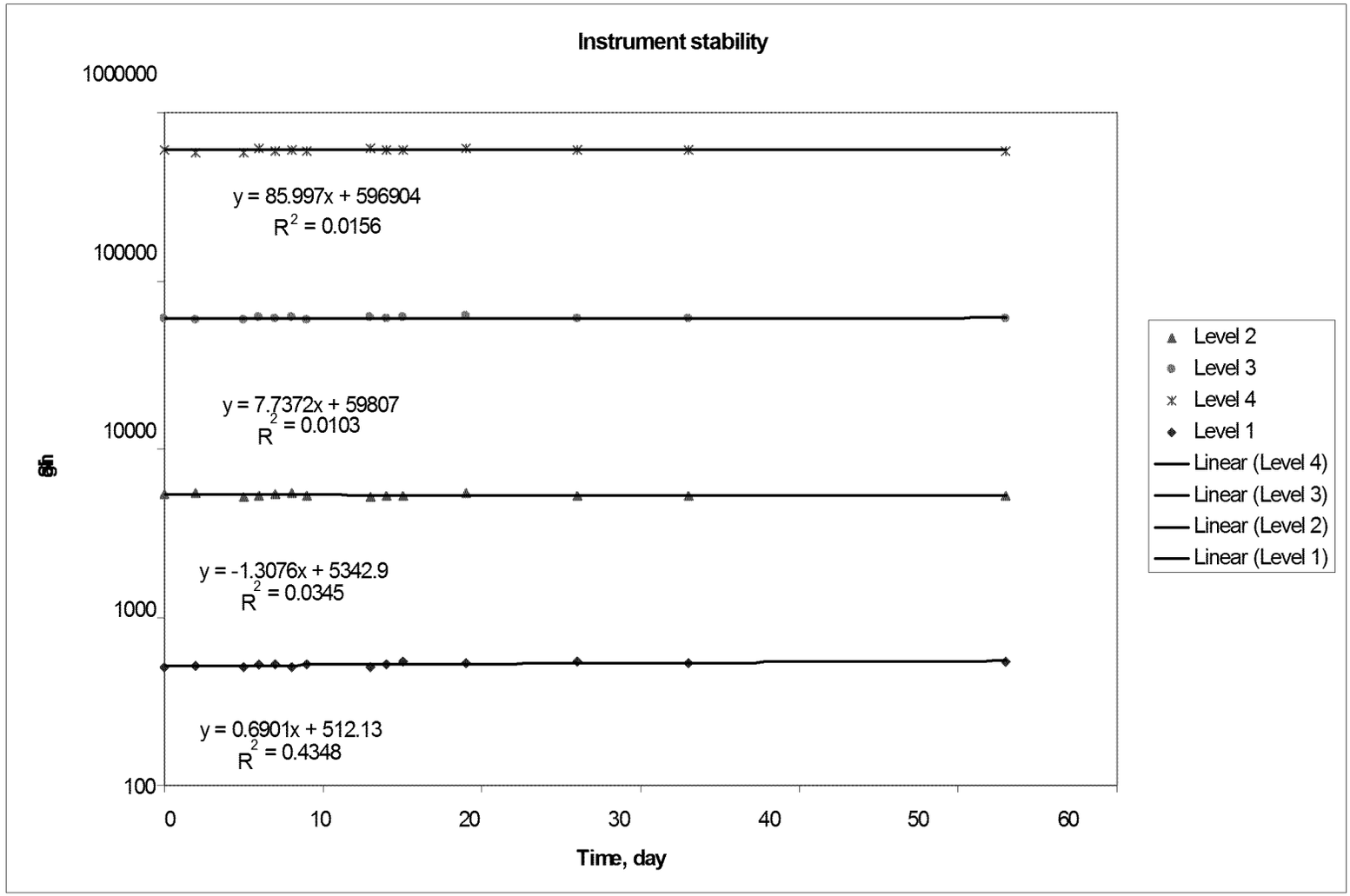
theranos
redefining healthcare

The Theranos System: Benefits

- The Theranos approach allows patients to manage their own disease and gives targeted feedback about their progress
  - Animated, targeted, and psyche-based content engages patients in managing their own dependence and allows them to build a relationship with the System
- Direct interaction between physician and patient (two ways) during drug development and post-marketing
- Theranos enables early detection, with rapid and adaptive treatment strategies
- Survey API supports adaptive, seamless design studies and content
  - Clinic can adjust survey or content through XML
- Open data infrastructure provides full integration with other systems
  - Can link data with other monitoring data, such as other assays or research metrics from other aspects of study
- Patients are more likely to provide **honest data** because Theranos Readers analyze biological markers as well as survey data

Instrument optics stability

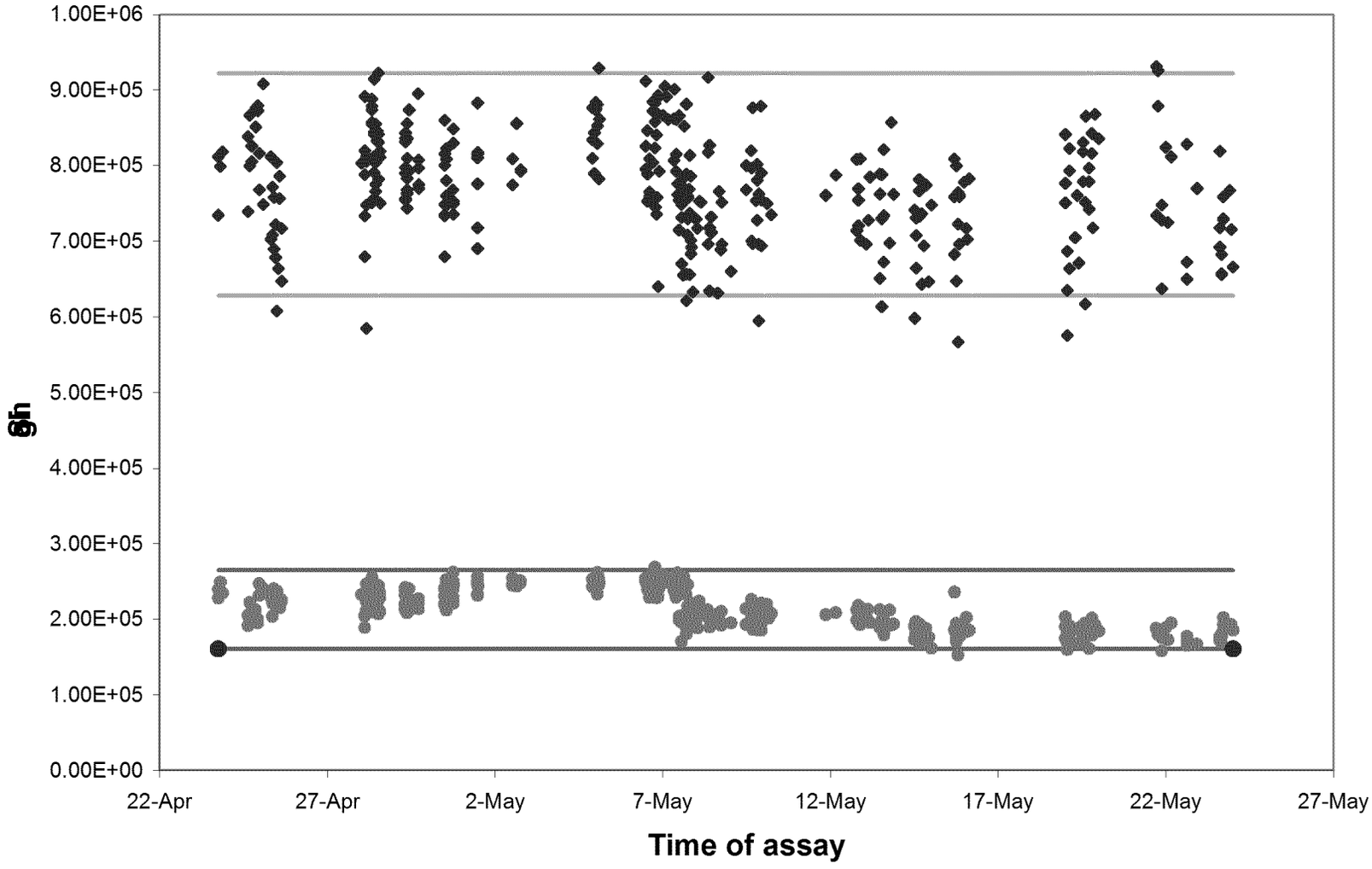
Perfectly stable over two months



theranos
redefining healthcare

Controls verify system performance

Clinical study over one month System calibration was stable
Two assays, 20 instruments, 360 cartridges



theranos
redefining healthcare

Comprehensive meta-analysis System: Adaptive Systems Biology in Practice

- Users at Pharma will be able to Graphically view all the known patient information in a central software program irrespective of where it is stored and add information to that repository dynamically so that the changes of proteins can be seen in the context of the full picture of disease progression. (i.e. proteins linked to imaging data linked to demographics linked to health records)
- The data repository is controlled by TheranOS (Theranos Operating System), a central mathematical software program which allows Pharma to visually see, interpret, and analyze all of their data in one place, and is linked to a disease management system .
- Better and dynamic analysis -- Once an initial data is analyzed using Theranos proprietary algorithms, the Database is updated automatically as more data is collected serving as a trial decision making tool or system for establishing baselines against which to map future dosing schedules or get early reads on efficacy and safety across key populations
- Data is extracted from any existing database and linked into a central mathematical database which allows users to visually see, interpret, and analyze data in one place which is linked to an (adaptive) clinical trial management system.
- Temporal algorithms applied to map data predictively
- Web portal customized for researchers, patients and clinicians

theranos
redefining healthcare

The Dynamics of Biology:
Sampling and Context

Statistical sampling is a means to an end

- It allows one to quantify underlying processes in a rigorous way
- Based on any family of underlying hypotheses process, it allows one to interpret the results in the context of the purported biology at hand
- Biology is a time based dynamic, thus requiring longitudinal sampling to tell its complete story

Variation in the underlying target populations requires that the sampling characterize individual behavior as a "class" effect

theranos
redefining healthcare

The Theranos Methodology:

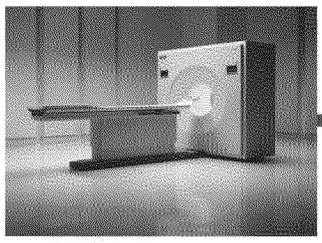
Turning Patterns into Probabilities

- Complex biology requires one sample the dynamics of each contributing underlying dynamic in the process, i.e. multivariate
- Patterns of proteins can be compared with statistical rigor as to their similarity
- Similarity can be quantified as a statistical distance, forming a mathematical metric space.
- Given a family of reference populations (e.g., CR, PR, SD, NR), the distance metric can be associated with a Bayesian probability of class assignment
- Together, this methodology defines a landscape or geometry and allows one to locate any patient at any time point in that space
- Therefore, individual trajectories can be characterized in that space as to position, speed, and heading

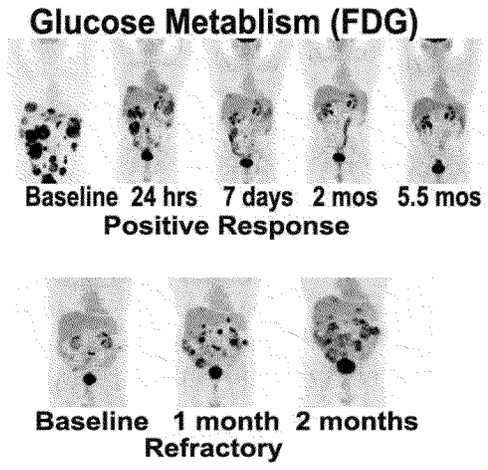
theranos
redefining healthcare

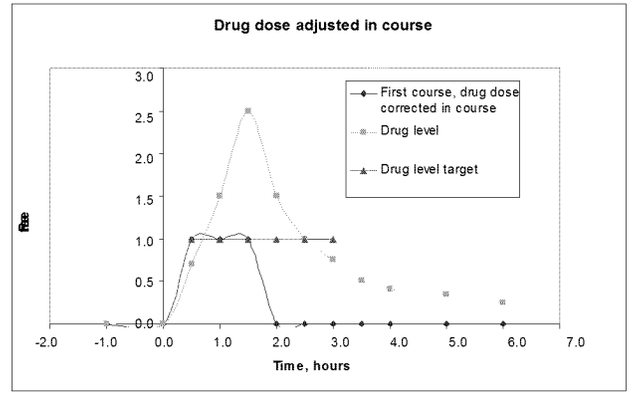
Establishment of Baseline

- The CAB system enables the development of correlations between blood test trends, efficacy and safety.
- The first step is to establish baseline data within the system. Animal and/or human data generated correlating trends in panels of proteins with endpoints such as molecular imaging serves as the foundation. This data can be drawn from the body of evidence on a particular therapy.



PET Scanner

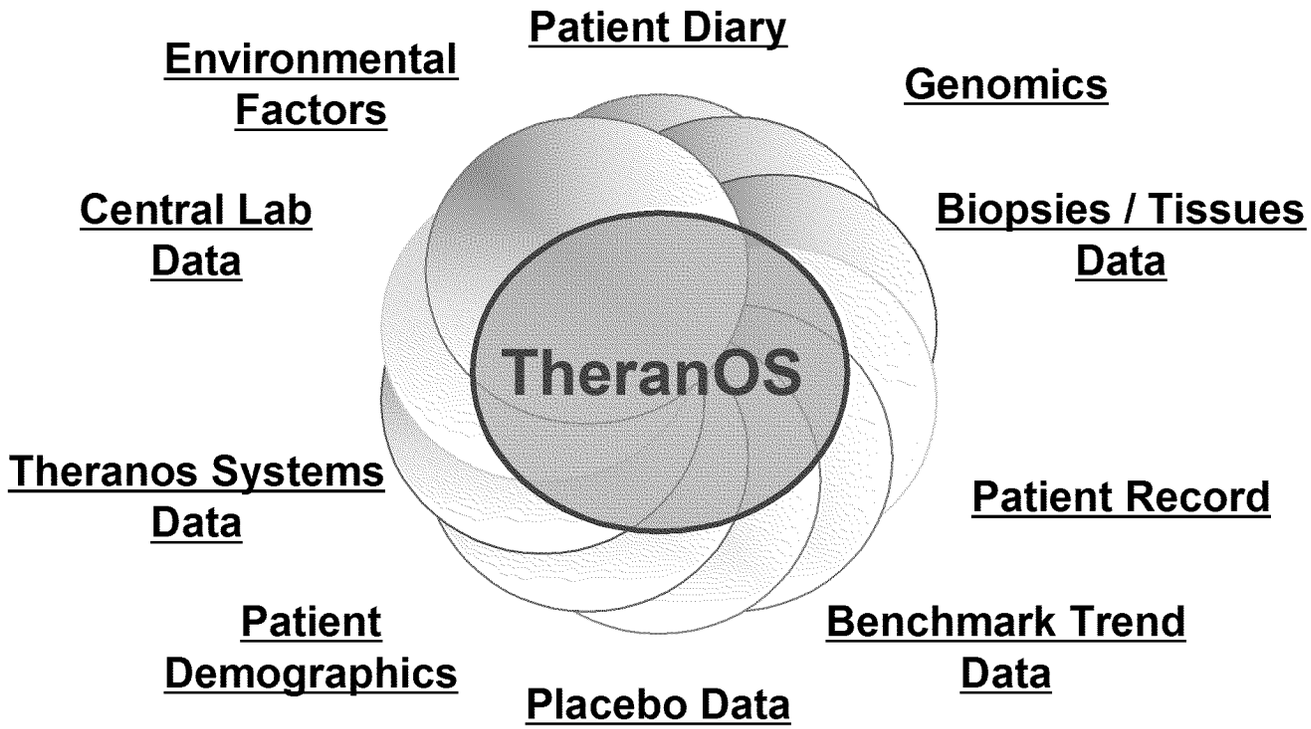




theranos
redefining healthcare

Centralized Data Repository

Integration of blood and patient diary data with all other physiologically relevant information.

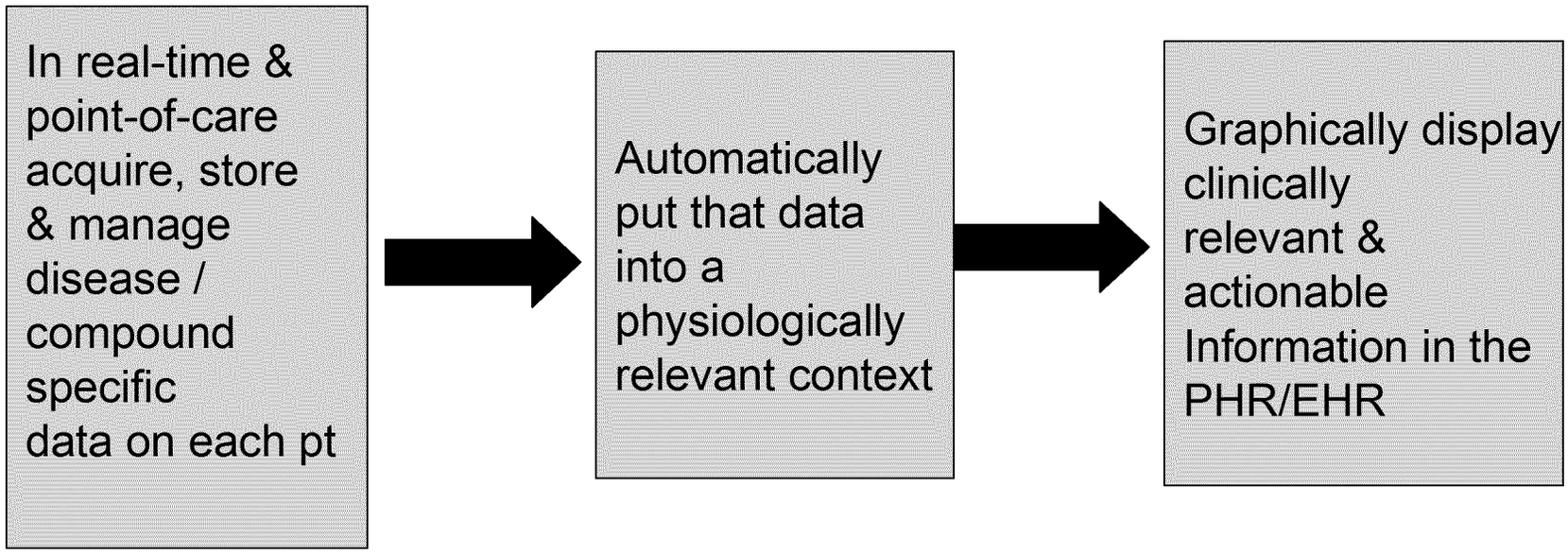


Simulation, Linear Regression, Bayesian Analyses

Efficacy of Drug(A) in Indication(B) = $\sum$ (Factor 1)(Weight (1) + Factor (2)Weight(2) + Factor(3)Weight(3) ….

theranos
redefining healthcare

TheranOS: Healthcare Operating System Turning Disease Specific Data into Clinically Relevant Information



Theranos
POC Systems

Theranos
Multivariate
Analysis
System

Theranos
Clinical
Visualization
System & Applications

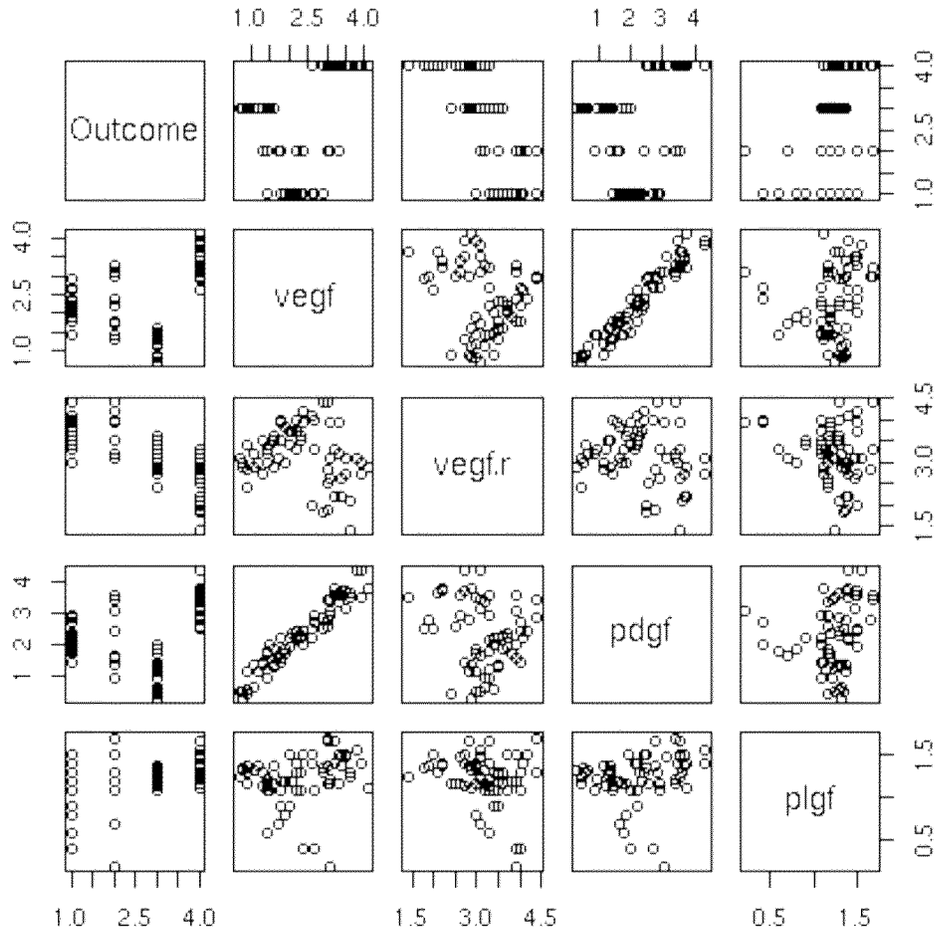
theranos
redefining healthcare

Approach to Pilot Programs

- Apply TheranOS "mapping" algorithms to historical data to create baseline profiles
- Leverage multiplexed longitudinal time-series profiling to map efficacy dynamics more comprehensively (predictive)
- Enhance baseline with pharmacodynamic data from pilot programs
- Index future patient data against stored baselines through TheranOS to obtain rapid, early reads on progression

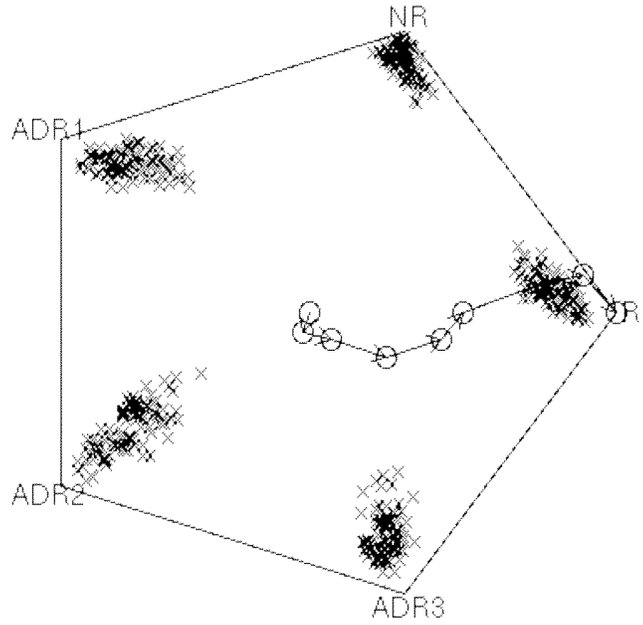
theranos
redefining healthcare

The Analyte Space



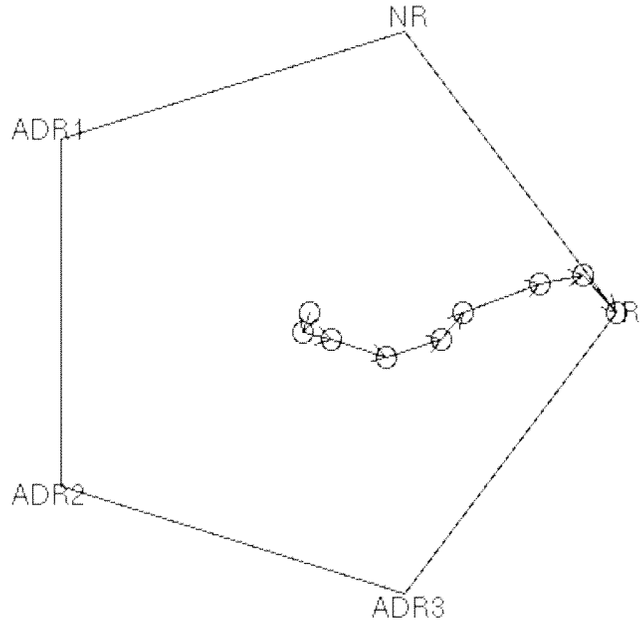
theranos
redefining healthcare

Analytes mapped into a probability space of clinical outcomes



theranos
redefining healthcare

Assess probability of a patient approaching an outcome



theranos
redefining healthcare

Summary: System Features

- Integrated data systems (all information linked into one database in an actionable format)
- Dynamic maps depicting the onset adverse events at a physiological level across a broad range of indications
- Real-time reporting, analytics, and risk management tools which model methods for patient treatment optimizations or ameliorating risk based on integrated data analyses (dose adjustments, drug combinations, patient selection criteria)
- Next-generation consumer systems for better mapping disease progression and efficacy at a patient level; pharmacovigilance and surveillance
  - Monitor patients continuously and in real-time; rapidly identify progress toward events in the field by mapping patient data against stored profiles; better identify the cause of those events
  - Action can be taken in real-time based on premeditated models for response to various events
  - Integrated therapy-"patient program" combinations
    - Optimized therapy regimens
    - Enhanced clinical outcome
    - Robust clinical efficacy assessments
    - Less dependence on physician background

theranos
redefining healthcare

System Applications

- Optimize dosing and efficacy across patient types
  - Adaptive dose ranging studies to customize compound for maximum efficacy and safety in key patient populations (dose to efficacy and not just safety; account for compliance)
- Better conduct risk management and safety surveillance
  - Electronic pharmacovigilance; better data generation
- More rapidly identify efficacy and safety of combination therapies
- Better characterize efficacy dynamics in cross comparison studies; publications to ensure reimbursement
- Post marketing studies to rapidly optimize compounds for new indications and sub-patient populations; label expansion.
  - Enhance value of therapy through interactive consumer monitoring, targeted information for patients, and controlled feedback
  - Early Insight on efficacy dynamics across multiple indications and sub-patient populations in parallel

theranos
redefining healthcare

Case Study: Analysis to better quantify biomarker patterns indicating a patient's status

Stanford AML study

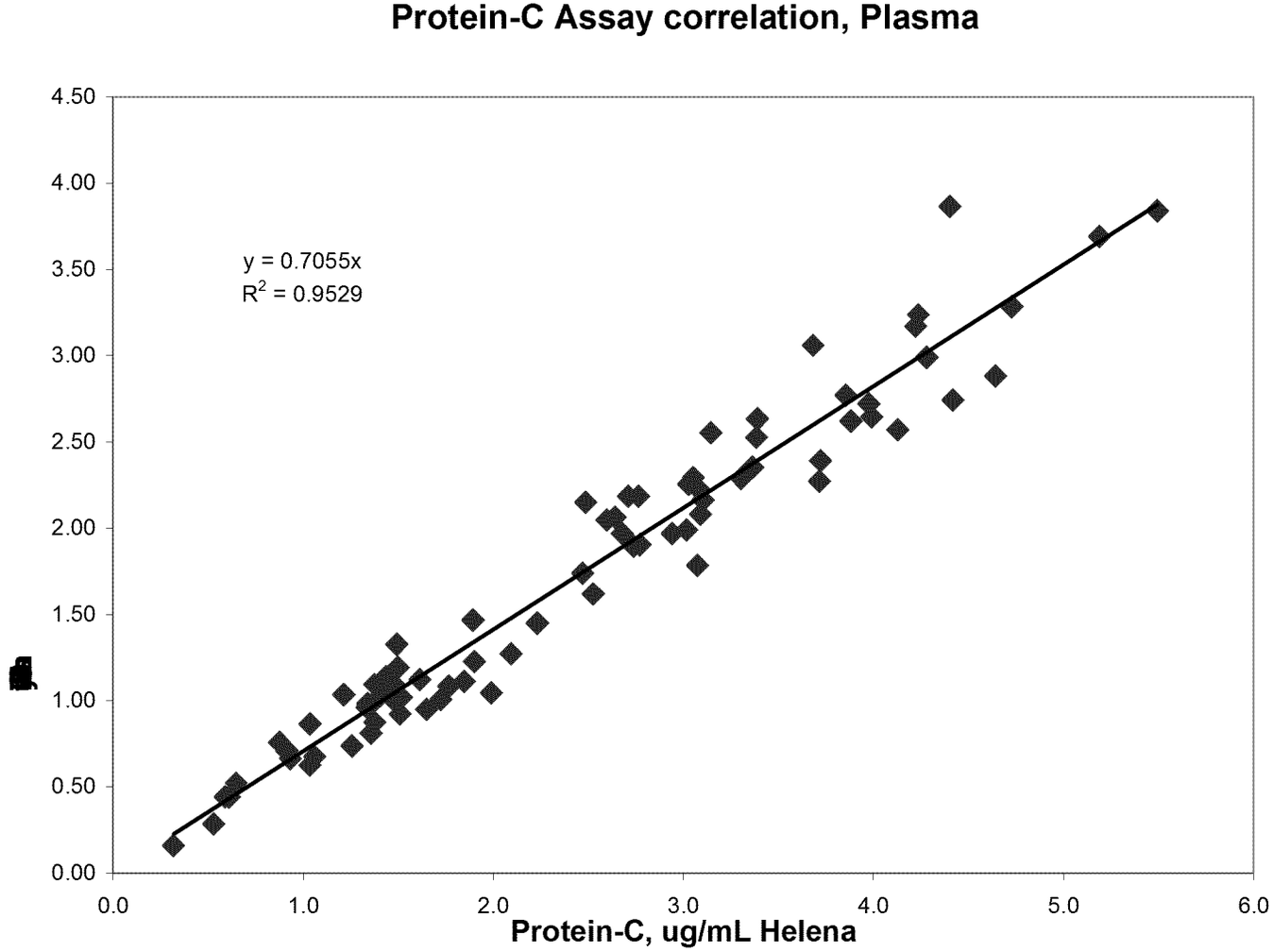
10 markers profiled

- 8 shown here

Values for patients who in the course of the study became septic and who did not are shown.

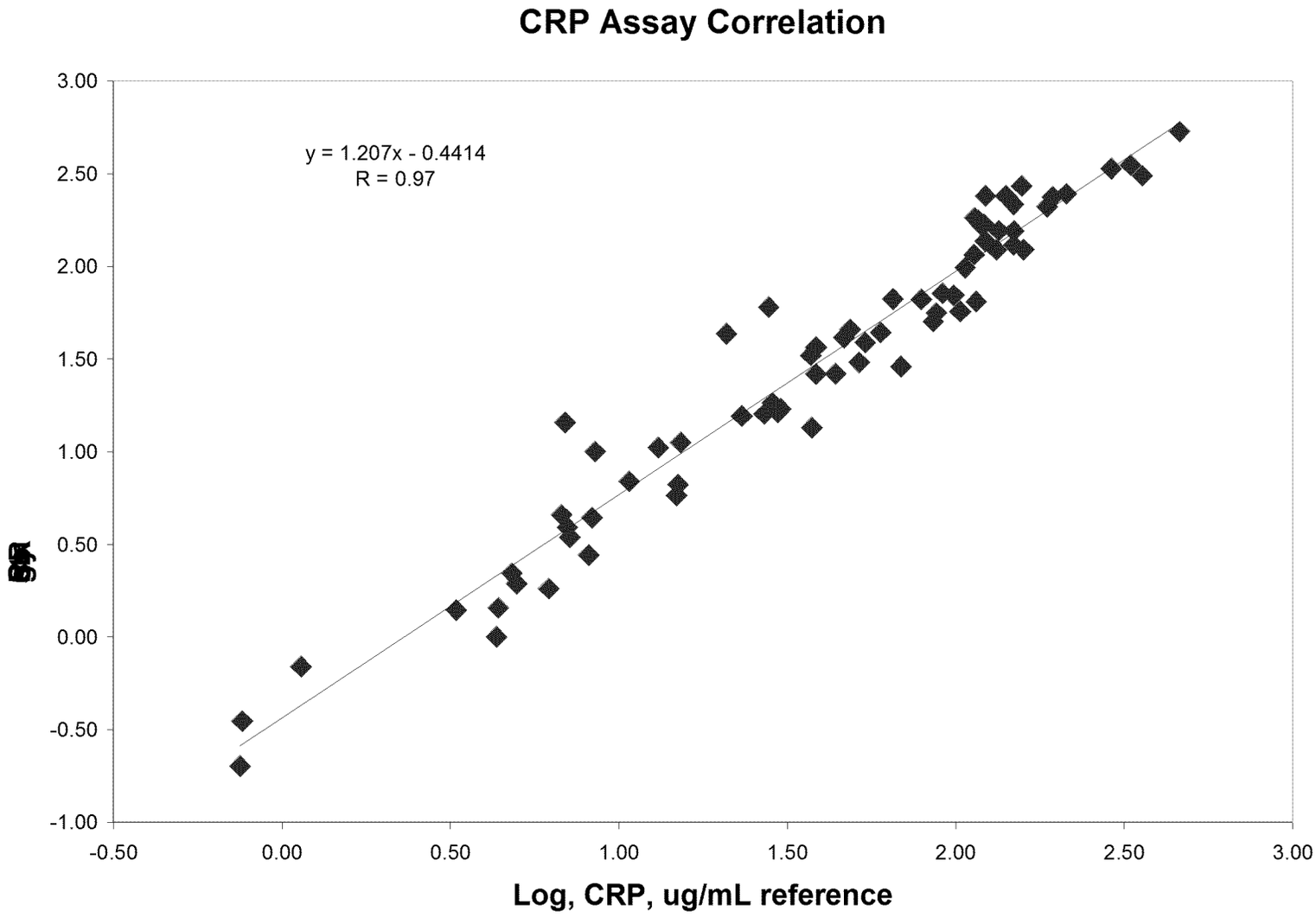
theranos
redefining healthcare

AML/Sepsis: Assay accuracy



theranos
redefining healthcare

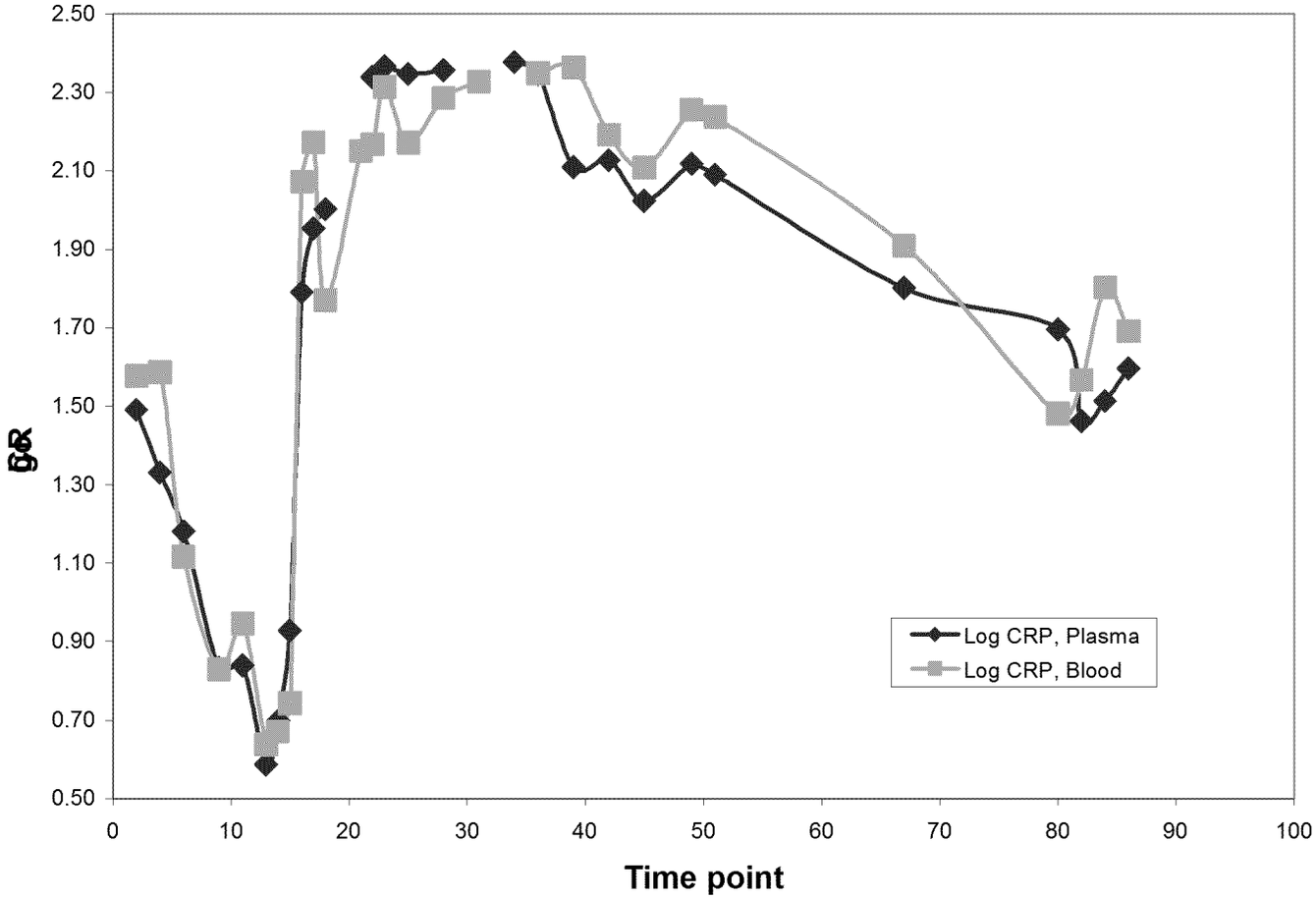
Method Correlation, CRP



theranos
redefining healthcare

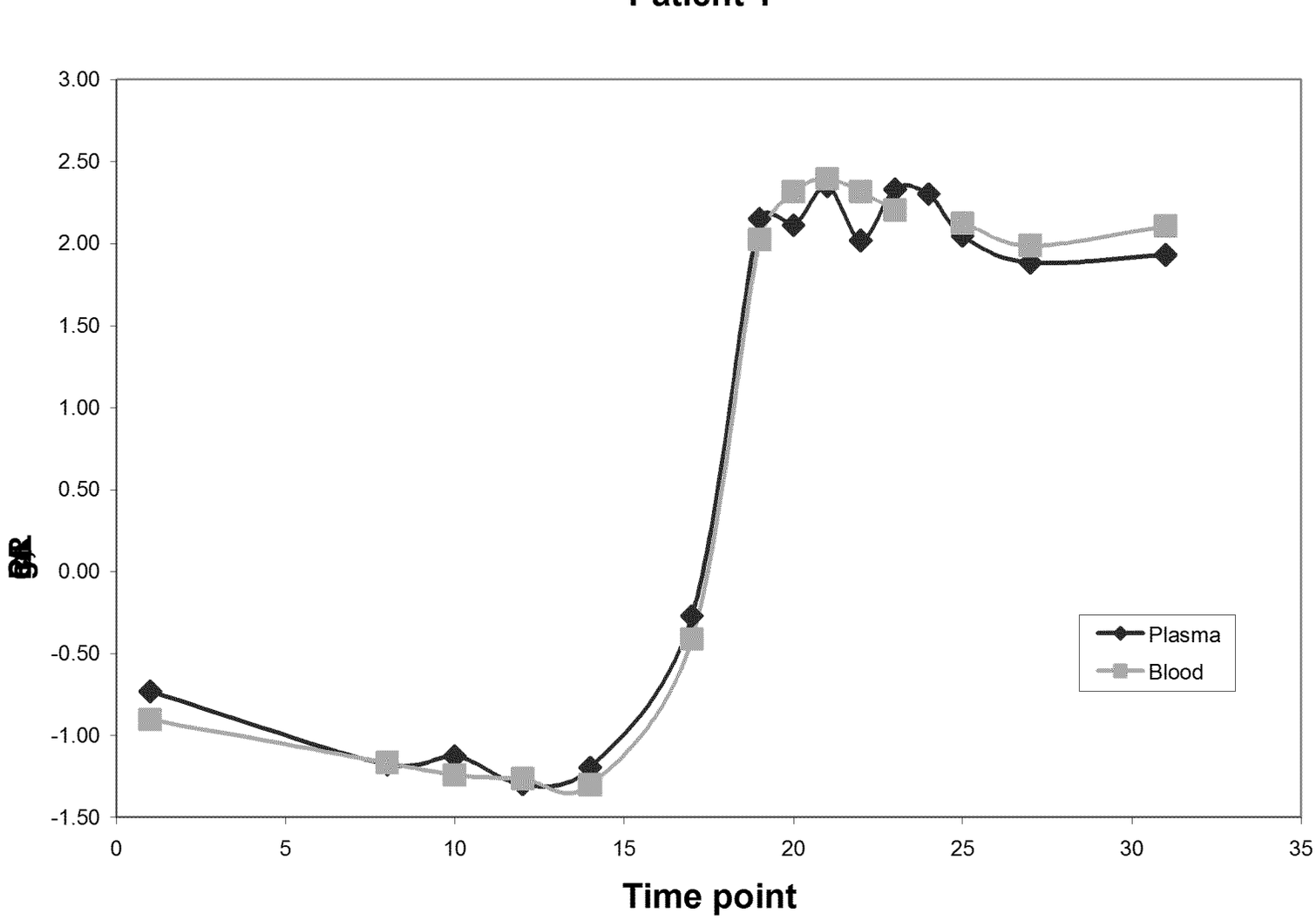
Results from blood and plasma track

Log value time course: CRP Patient 4



theranos
redefining healthcare

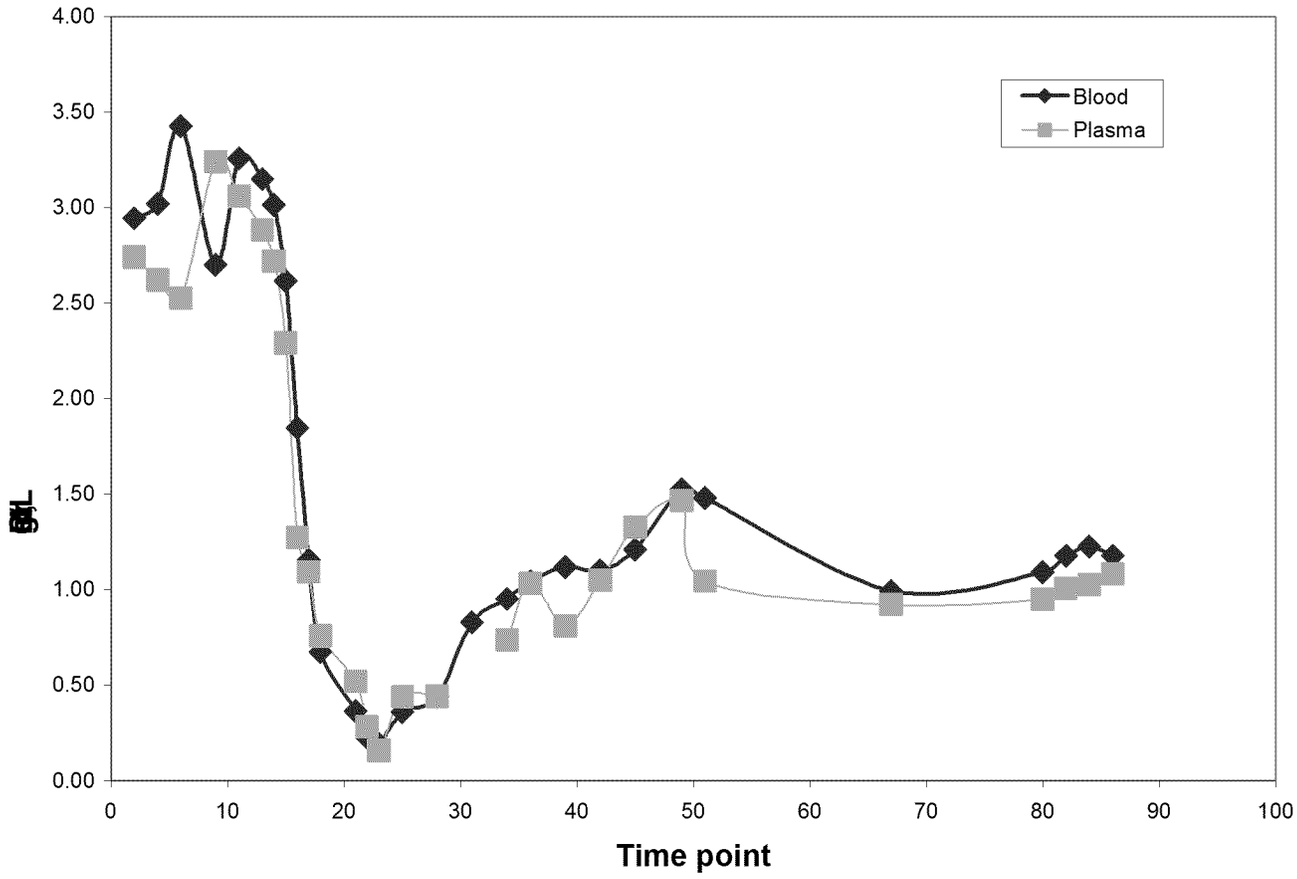
Patient 1: Plasma and blood



theranos
redefining healthcare

Blood versus plasma: Protein-C assay

Protein-C results: Patient 4 time course

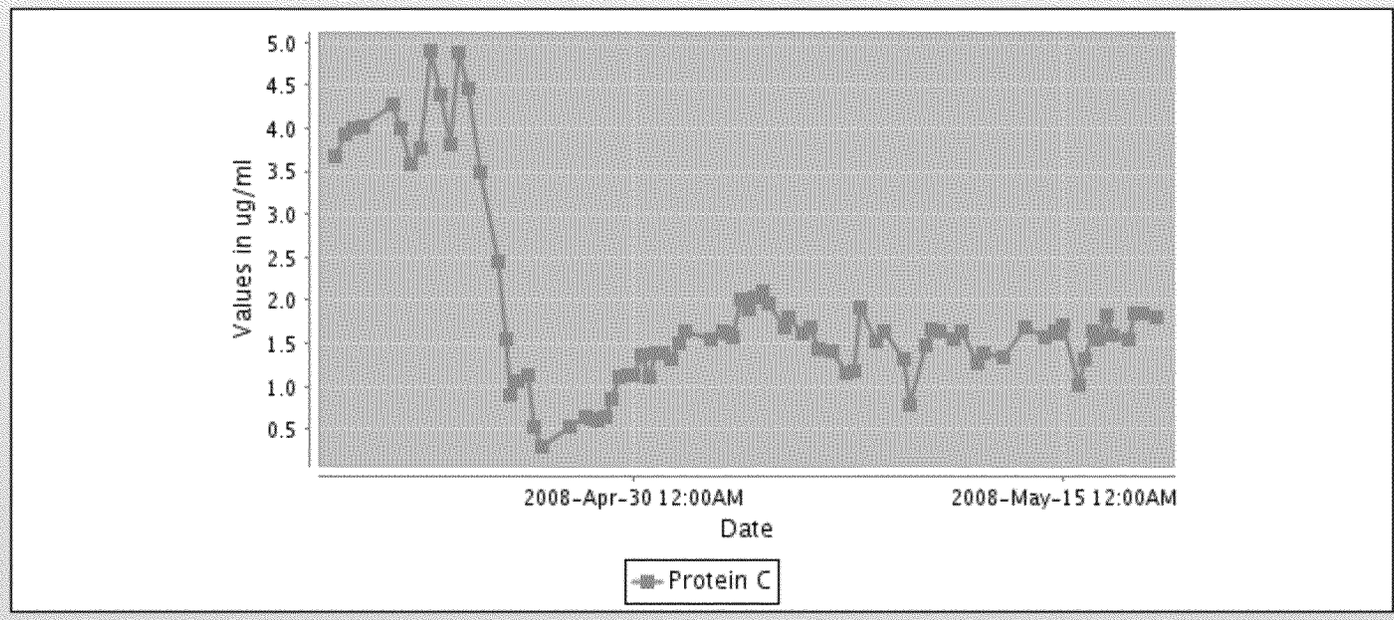


theranos
redefining healthcare

Theranos Server Output

Time Series Chart

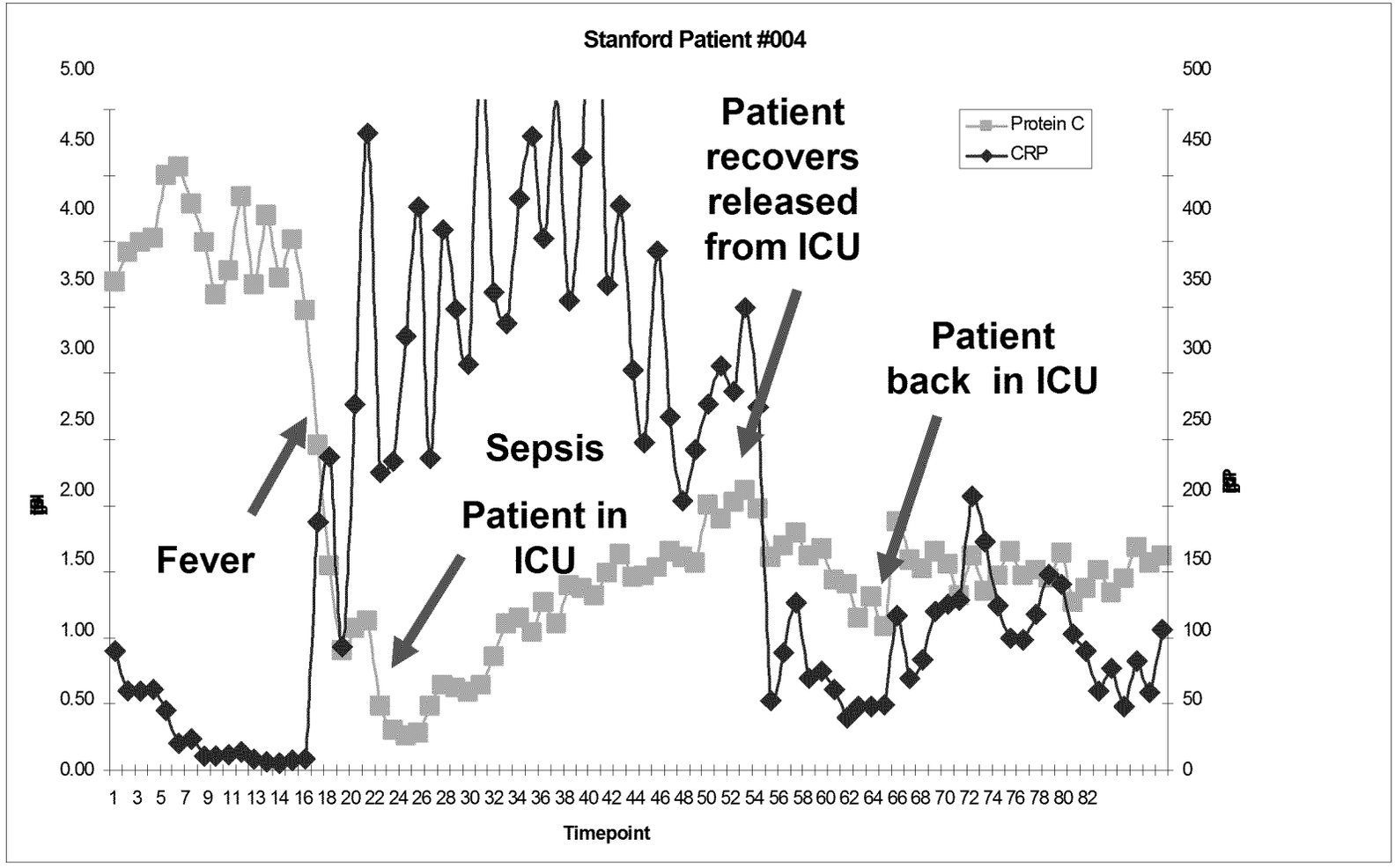
Patient ID: 004
Click the image to view the large image in another window.



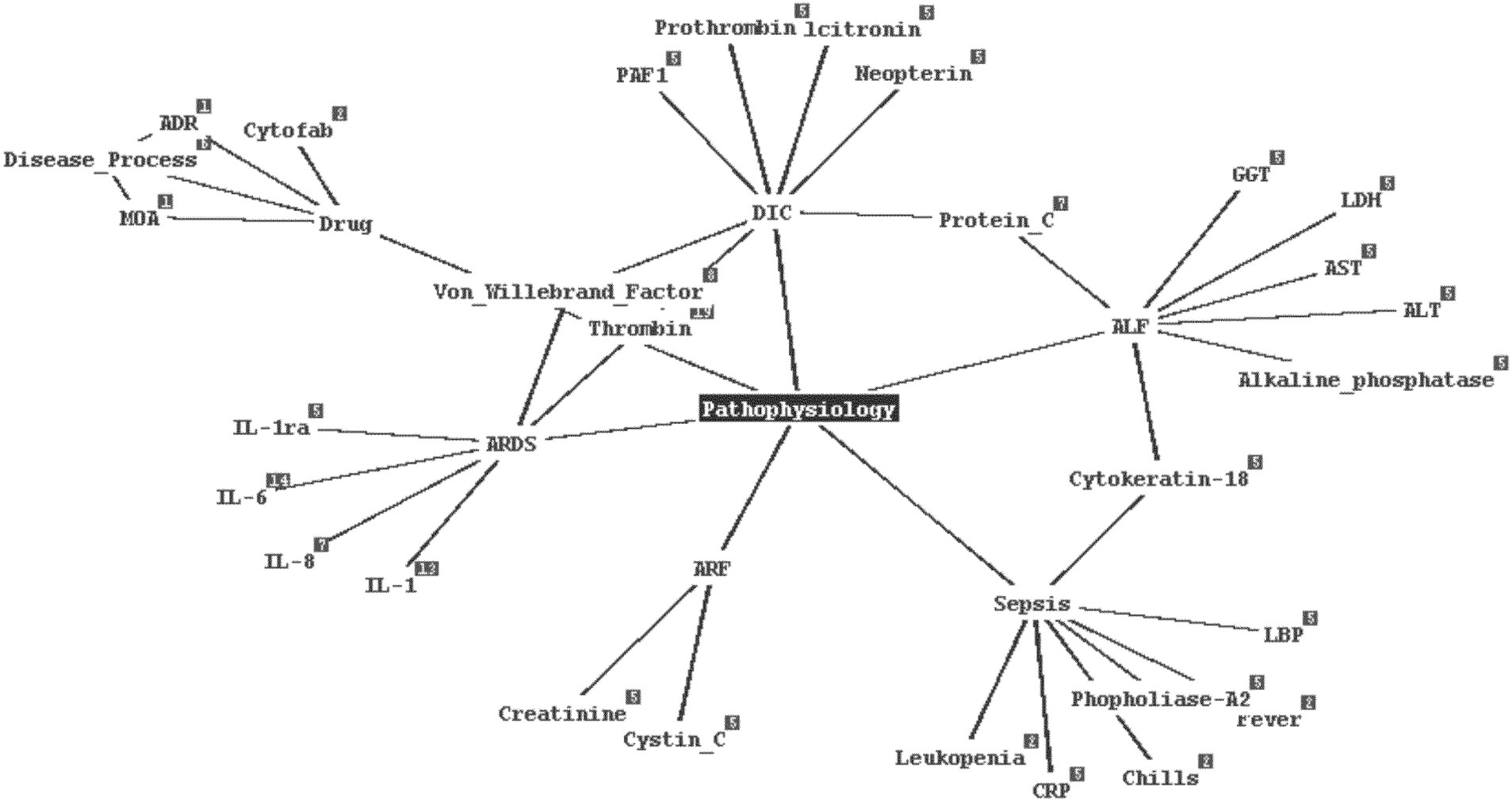
Export As CSV | Tabular Format | Chart Format

theranos
redefining healthcare

Patient 4: Relapse



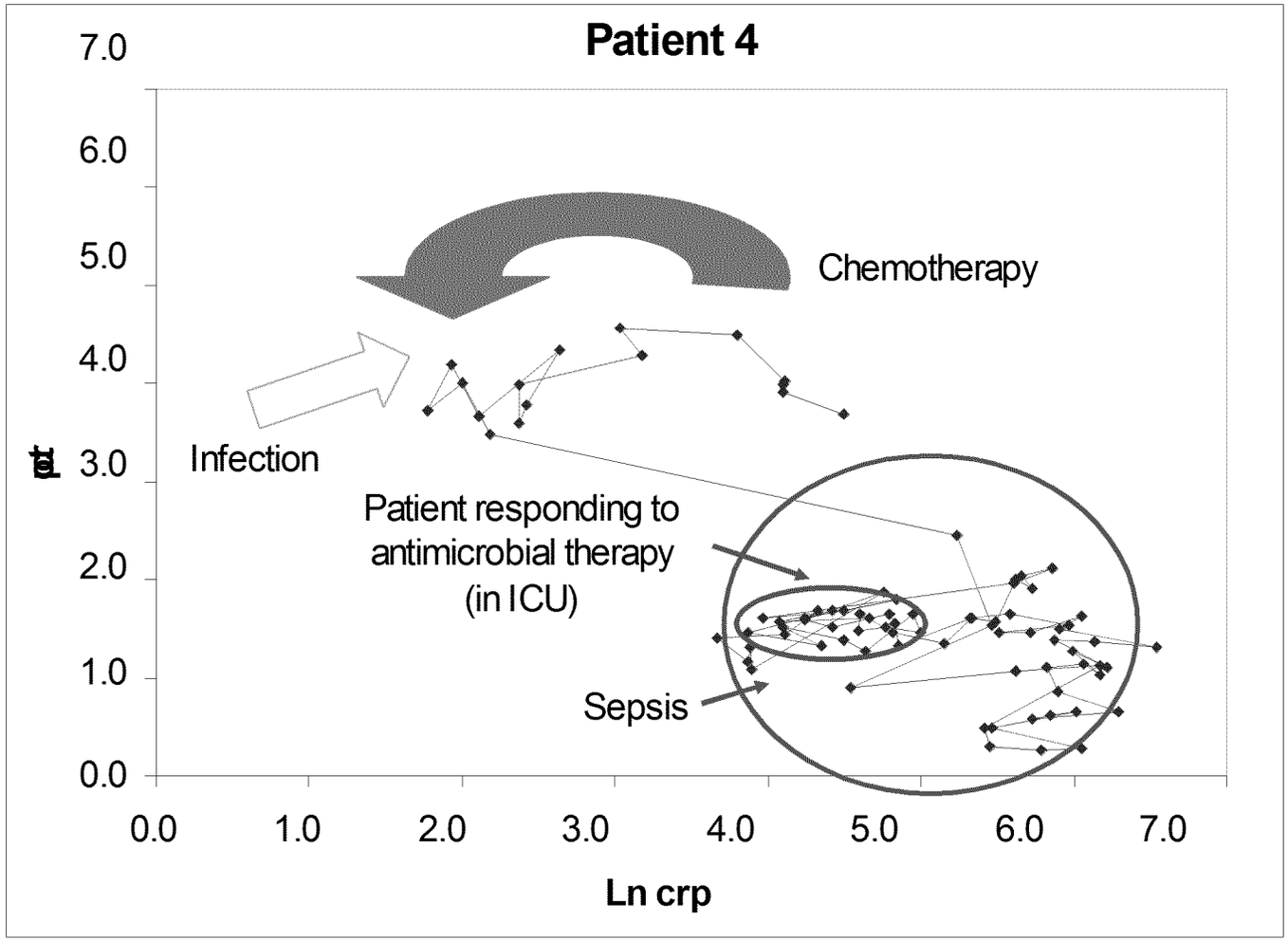
theranos



theranos
redefining healthcare

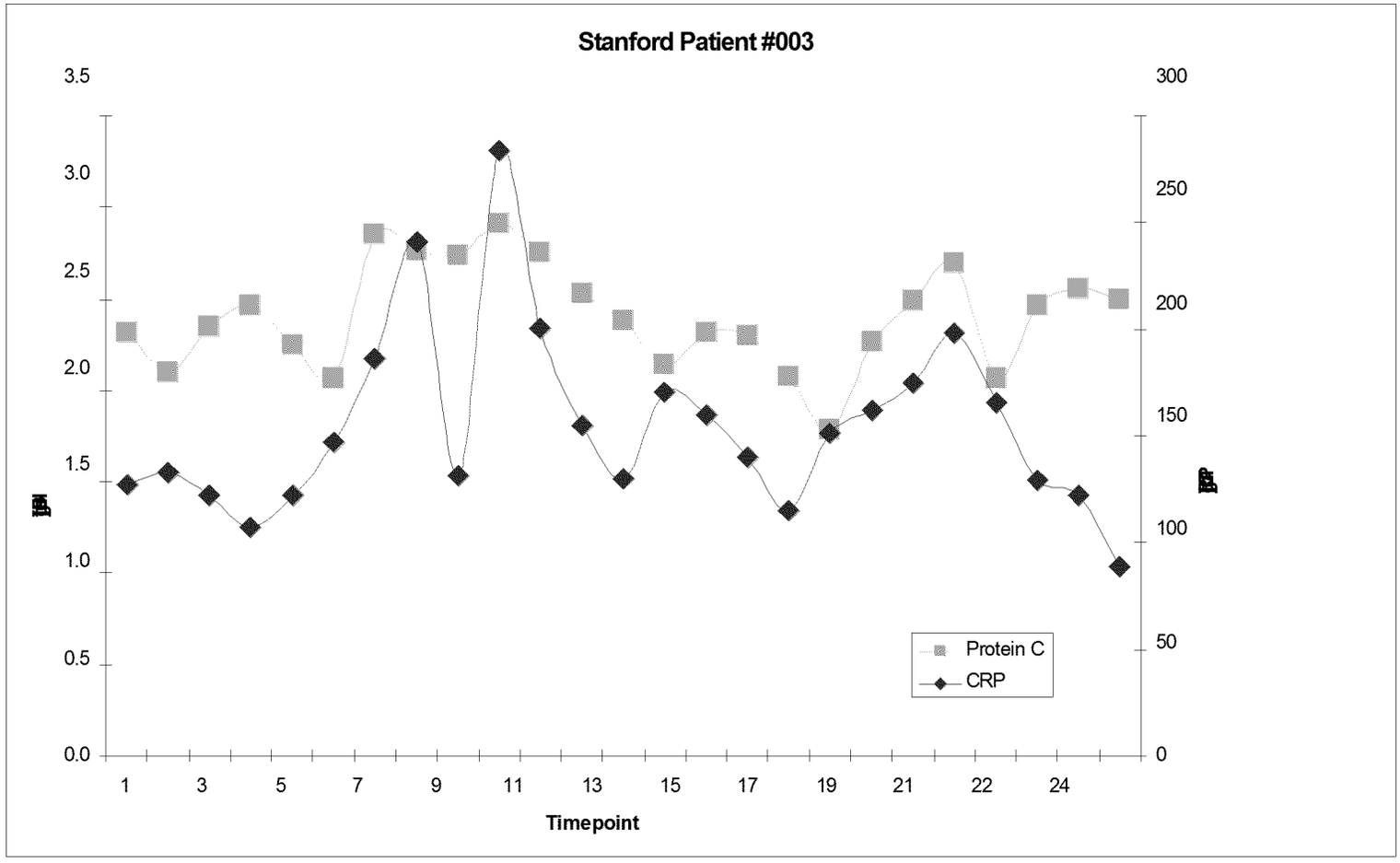
Multiple assays following disease and therapy
Trajectory to sepsis

Data connected by time



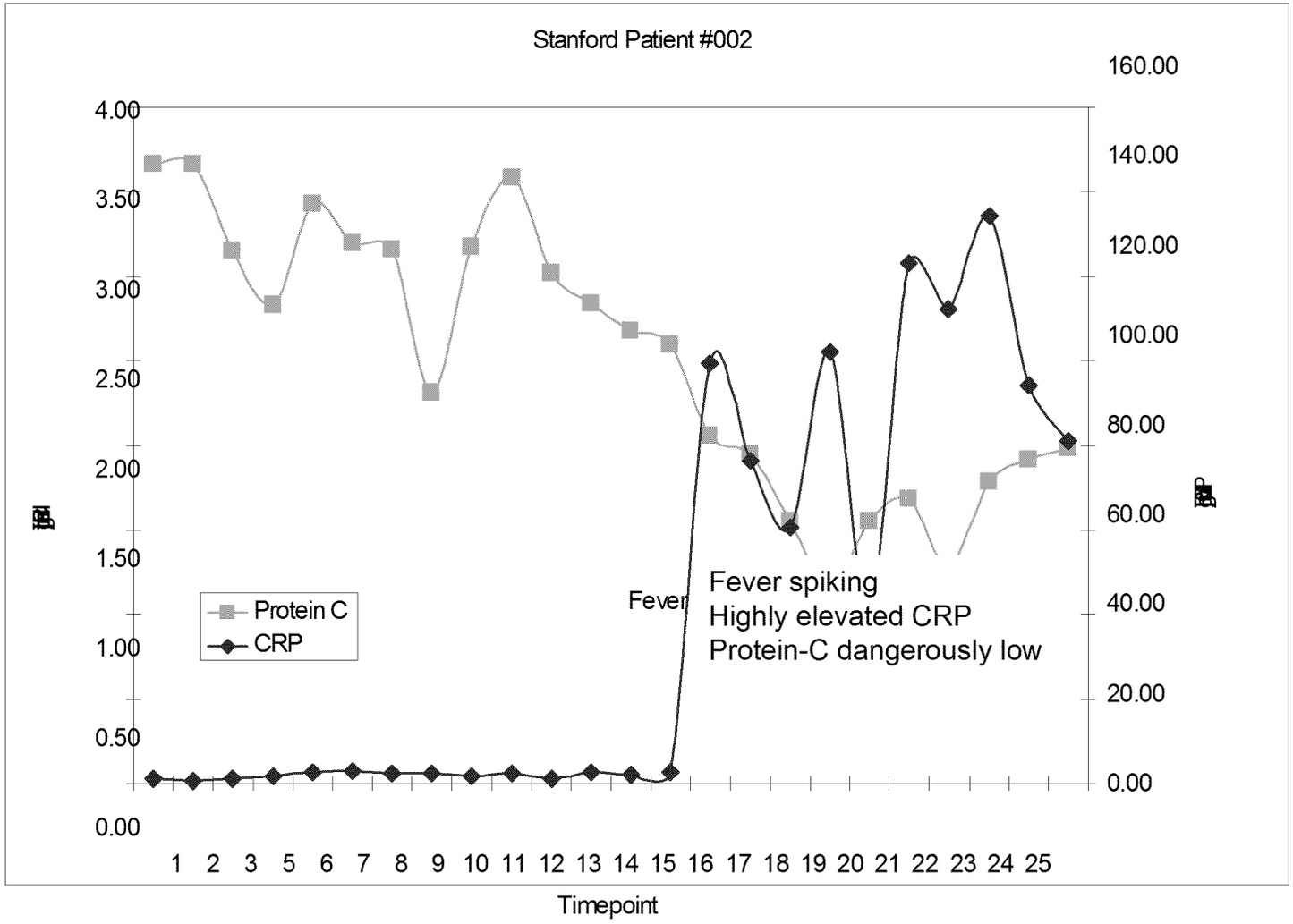
theranos
redefining healthcare

Patient 03AB
Patient did not get fever



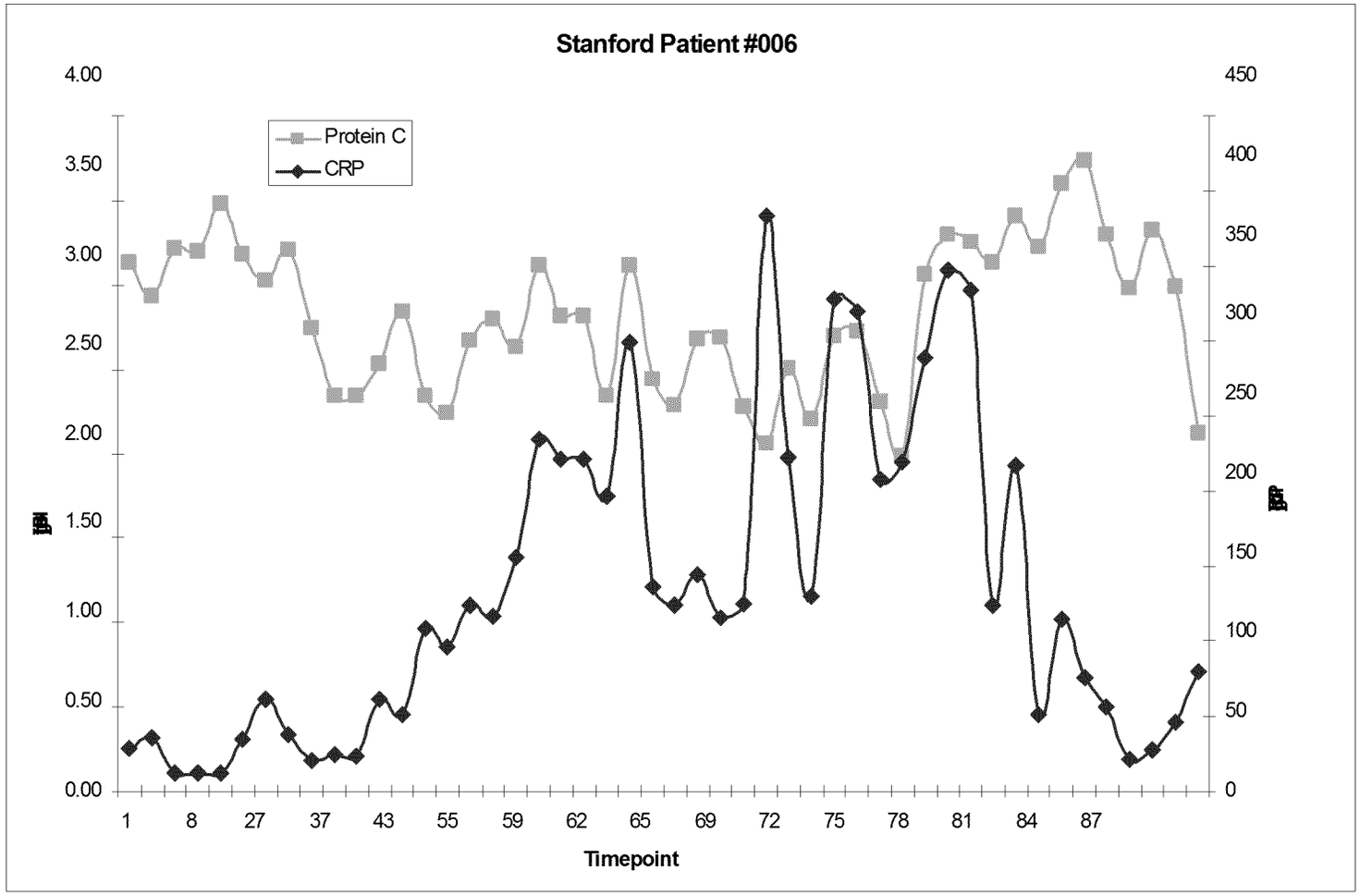
theranos
redefining healthcare

Patient 02AB



Patient 06AB Febrile but no sepsis

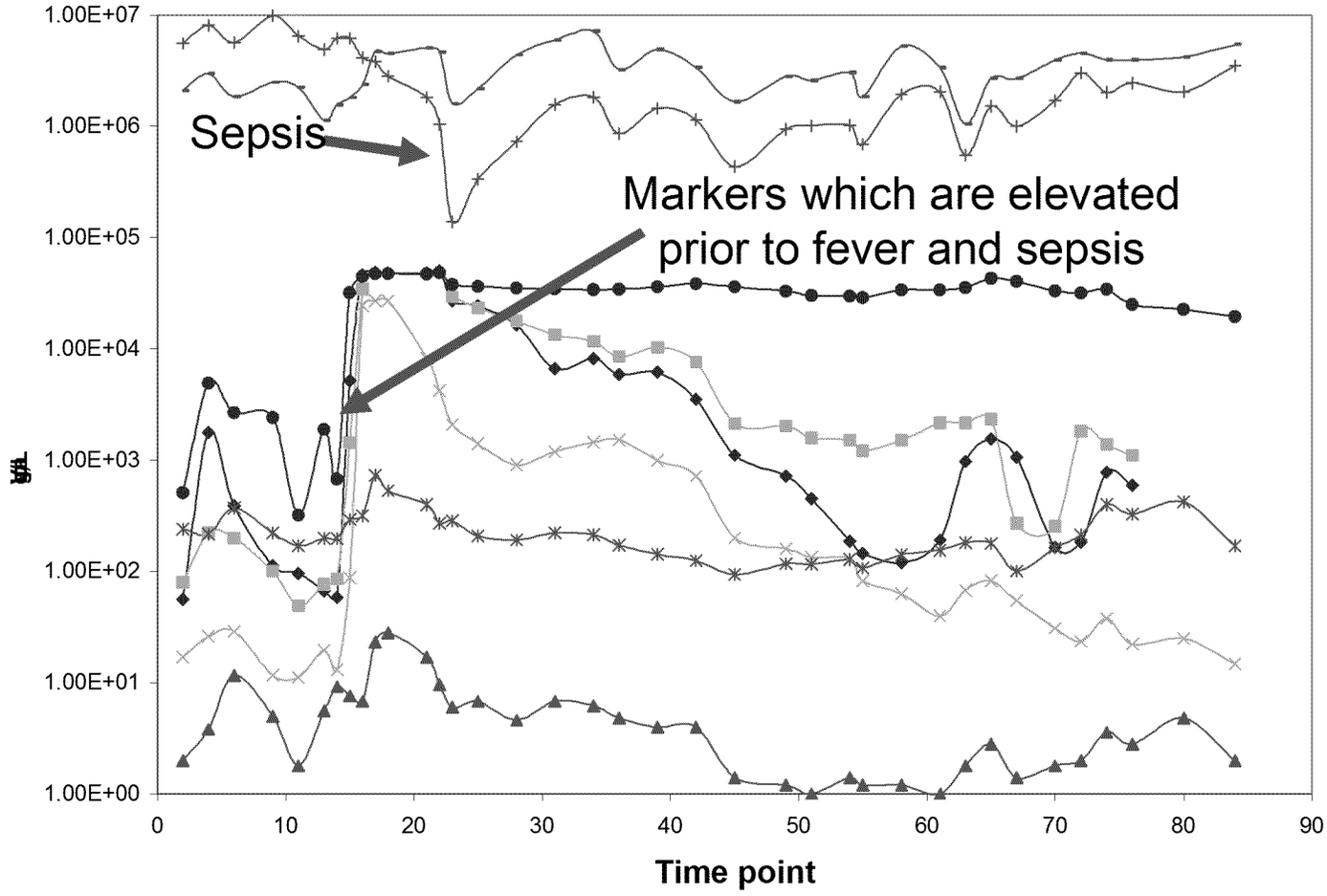
theranos
redefining healthcare



theranos
redefining healthcare

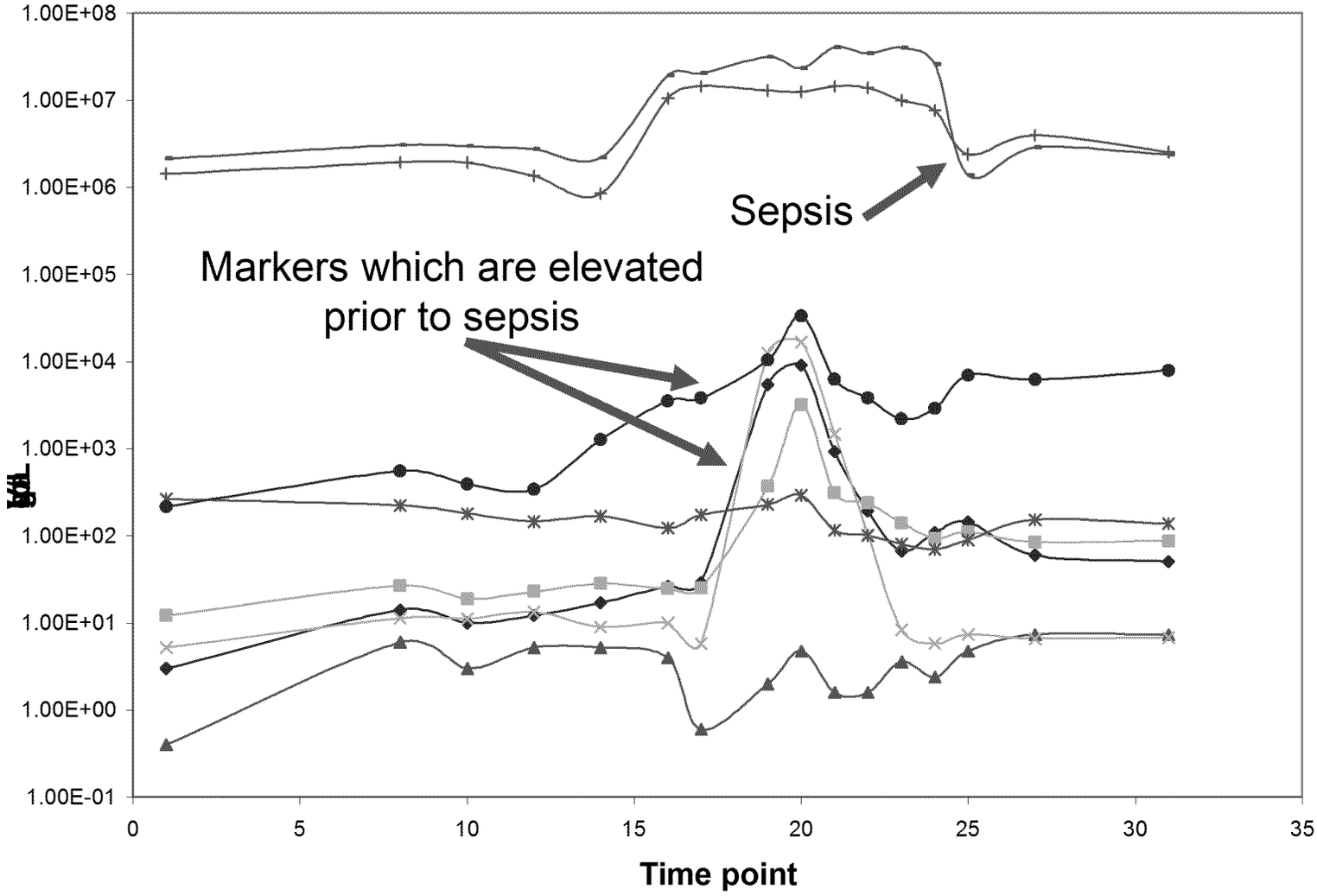
Profiling AML patients for onset of sepsis

Patient 4

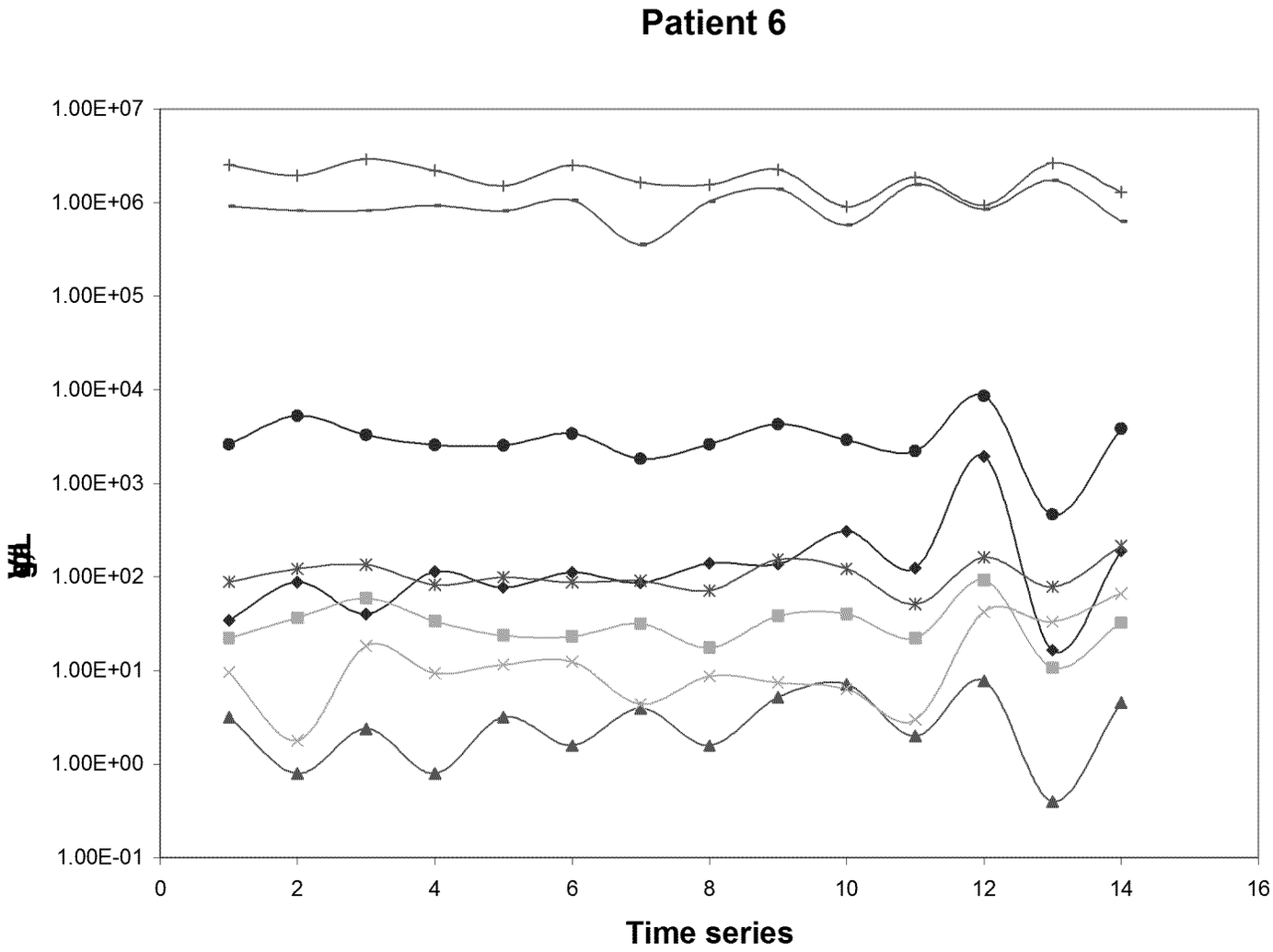


theranos
redefining healthcare

Patient 1



Patient who did not become septic



theranos
redefining healthcare

PSA time-points are not effective endpoints:

- Focus on **MOA**
- Measure panels of **mechanism AND disease specific markers** over time to progression against control populations
- Progression as defined as:
  " - Clinical progression, defined as treatment with chemotherapy, radiotherapy or surgery (excluding transurethral resection (TUR) with negative histology) or a new dose of hormone based therapy
  - Requirement for opiate analgesia
  - Objective progression of malignant soft tissue (RECIST Criteria)
  - Death prior to progression "

theranos
redefining healthcare

Targeting the mechanism ..Not the tumor

- Leverage optimal sampling capabilities (frequency of monitoring and multiplex of markers monitored) to map MOA and through doing so, better map compound efficacy and disease progression
- Whereas previous infrastructure allowed only for isolated time-point measurements, TheranOS allows for protein trend analyses to be mapped in the context of the pathophysiology of a disease on an individual basis, resulting in far more effective analytics when mathematical tools are applied
- 'Maps' are rapidly generated through 4-7 x / week time-points and data analyses which are compared to control populations throughout collection process (as permissible by the study protocol)

theranos
redefining healthcare

Theranos 'Optimal Sampling': Prostate Cancer

- Longitudinal time-series measurements of mechanism and disease specific panel
- Multiplexed panels serve as better indicators of disease progression than single proteins alone
- Change in rate of a panel correlates to clinical and surrogate endpoints, not necessarily value of single protein at any isolated time-point

theranos
redefining healthcare

Approach

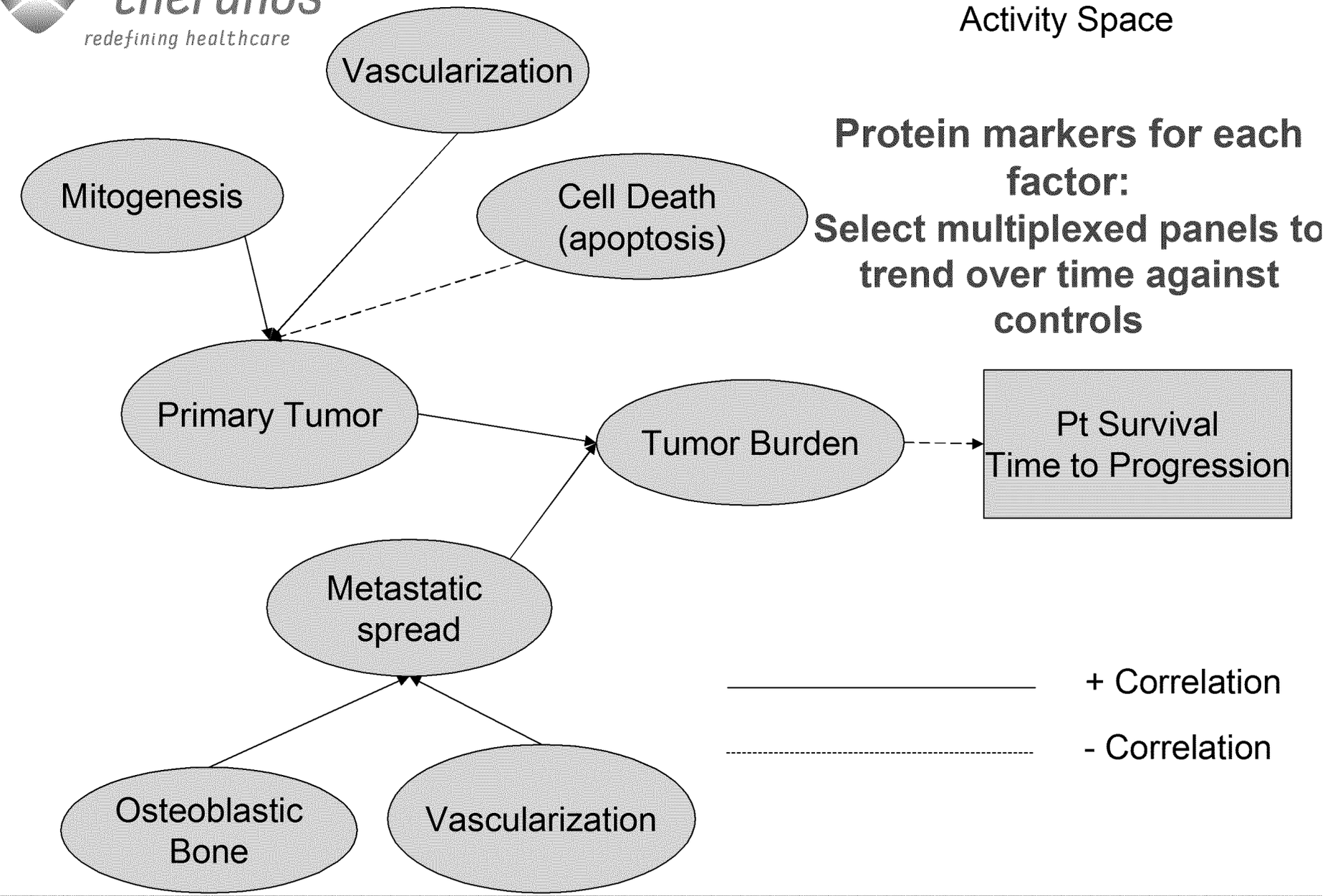
Rapidly map correlations through better longitudinal time series measurements across dosed populations and controls

Based on the hypothesized MOA, the following biological activity space would be sampled

- **Biological activity space surrounding Time to event measures (Time to Disease progression and All Cause mortality).**
  - **Included is the advent and spread of bone metastases as a contributor to overall tumor burden and eventual survival**

theranos
redefining healthcare

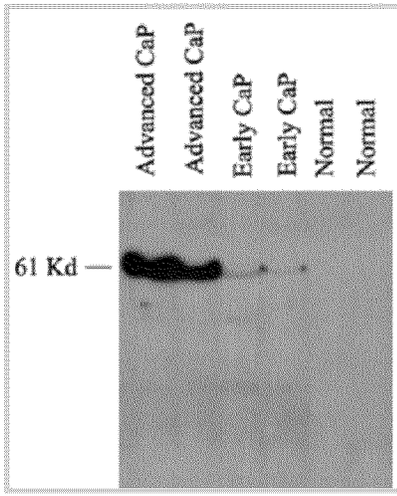
Figure 1: Biological Activity Space



theranos
redefining healthcare

Data Integration

- Drug, marker, and data from patient record integrated into single profile to map efficacy and safety against a threshold:
- Combination of multiple parameters serve as better indicators of disease progression



Performance of marker panels

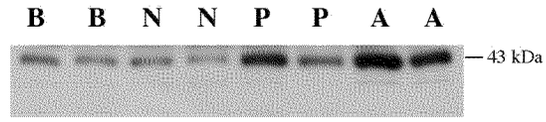


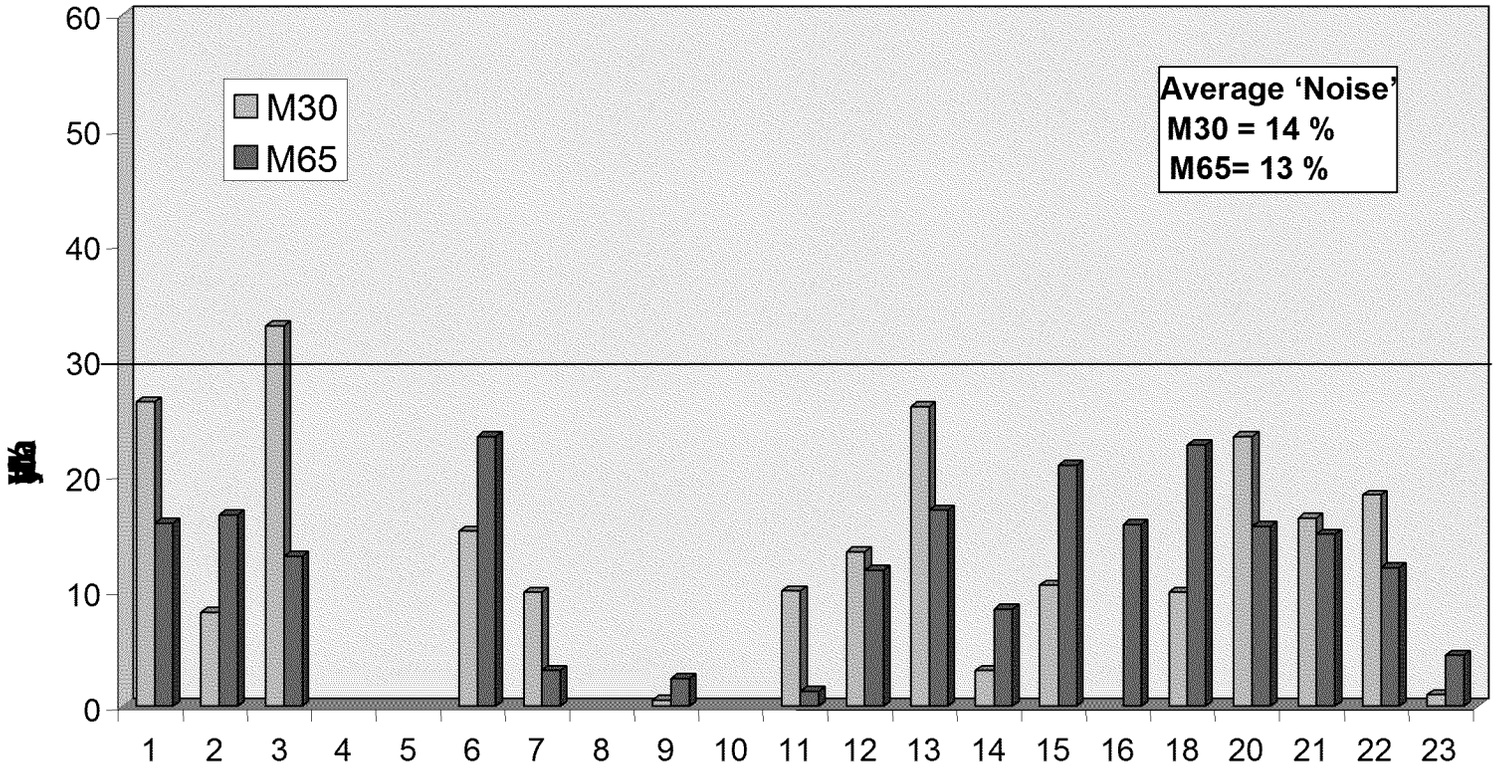
Table: Positive detection rate of different tests			
	PAMP_mab test	PSA test	Combination test
Advanced CaP	50	70	100
Early stage Cap	50	0	50
normal	0	0	0

Leroy Hood, Institute for Systems Biology

theranos
redefining healthcare

The Bacon and Eggs Expt
M30/ M65 Biomarker Qualification
Establishing Significance in Patients at the 2:1 Signal to Noise Ratio

Variability in M30 and M65 Pre-dose Levels
(5-7 day gap between 2 pre-dose samples)



Ongoing Analysis Strategy in Evolution

We currently work on the basis that a 2 x Noise i.e 30% increase of drug-treated over basal is significant for M30 and M65

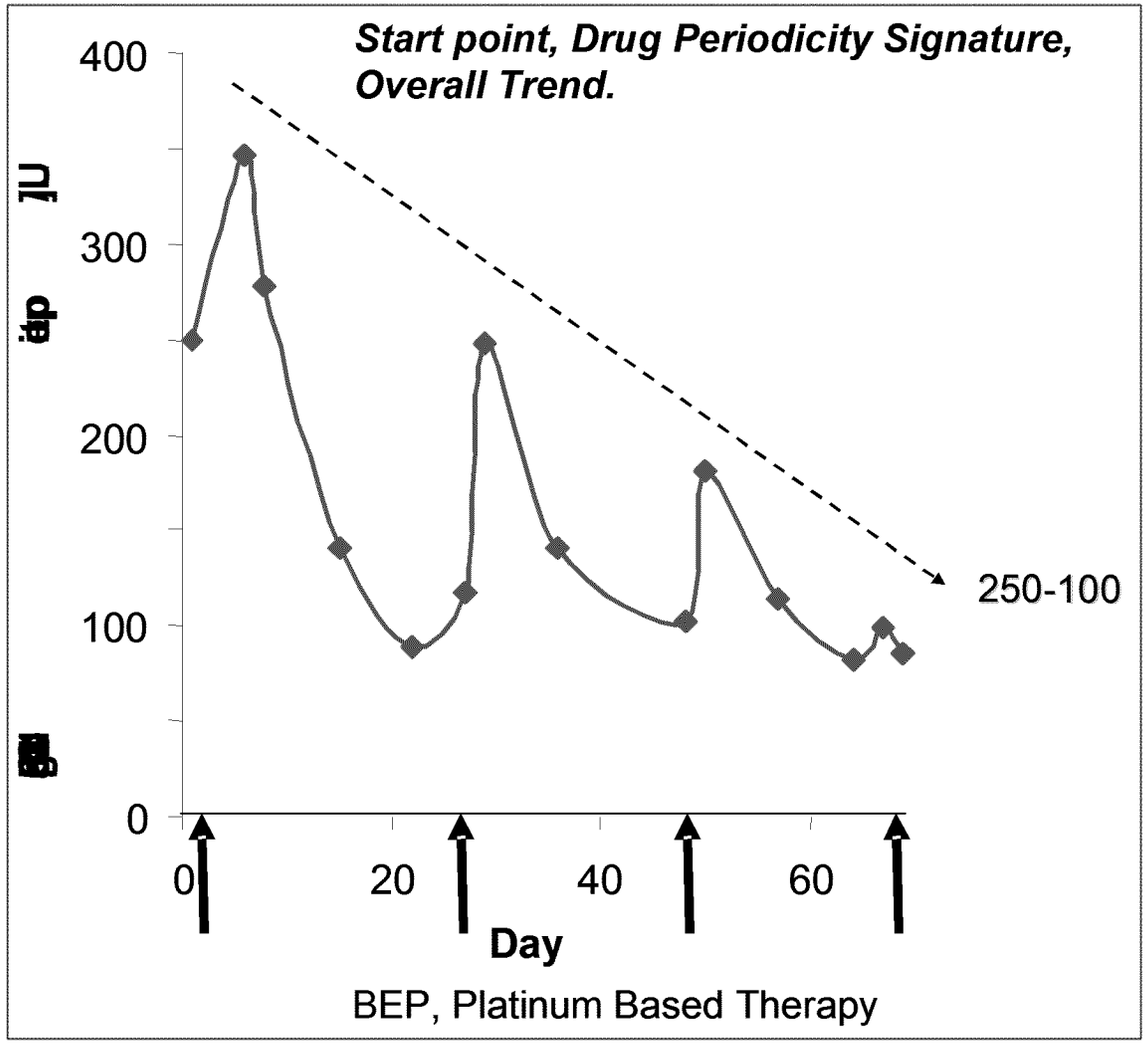
Jeff Cummings, Gordon Jayson

Ovarian Cancer study –same for other tumours?

theranos
redefining healthcare

Time series: chemosensitive solid tumour and M30 & M65 trends

Ongoing Study
of Testicular Cancer
(40 patients so far)



PICR/CEP/041

K Taylor, S De Jong, J Gietma (Groningen)

theranos
redefining healthcare

Mapping Efficacy Dynamics Faster and More Accurately than Possible Using a Conventional Lab

- Angiogenesis: (VEGF, VEGFR2, PlGF)
- Apoptosis: (nDNA, M30, M65)
- Bone: (Osteopontin, CTX, nTX, Osteocalcin, PINP, BAP)
- Inflammation: (CRP, IL-6, IL-1b, TNF-a)
  - Safety

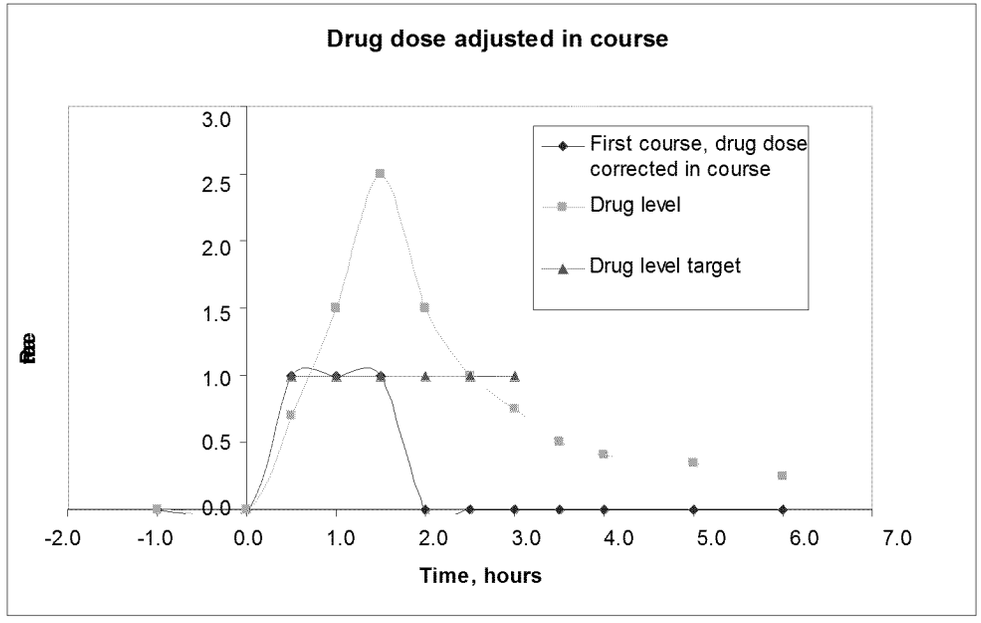
theranos
redefining healthcare

Case Study –Phase II Application

- Pharmaceutical Company has drug with clear efficacy signals but with dose related safety concern.
- Before moving into Phase III studies, Company has desire to understand correlation between dose and the safety signal.
- Solution:
  - Develop an antibody to the company's drug
  - The drug antibody will be incorporated into the Theranos Cartridge together with markers that are directly linked to the drug's activity.
  - Real-time drug level monitoring after infusion to reduce AE and account for differences in individual metabolism
    - Dose adjustment to maximize efficacy
    - Enable combination therapy
    - Study - Monitor 14 time points in first 48 hours after infusion
    - Drug marker enables dose adjustment based on efficacy and safety

theranos
redefining healthcare

Dose Customization



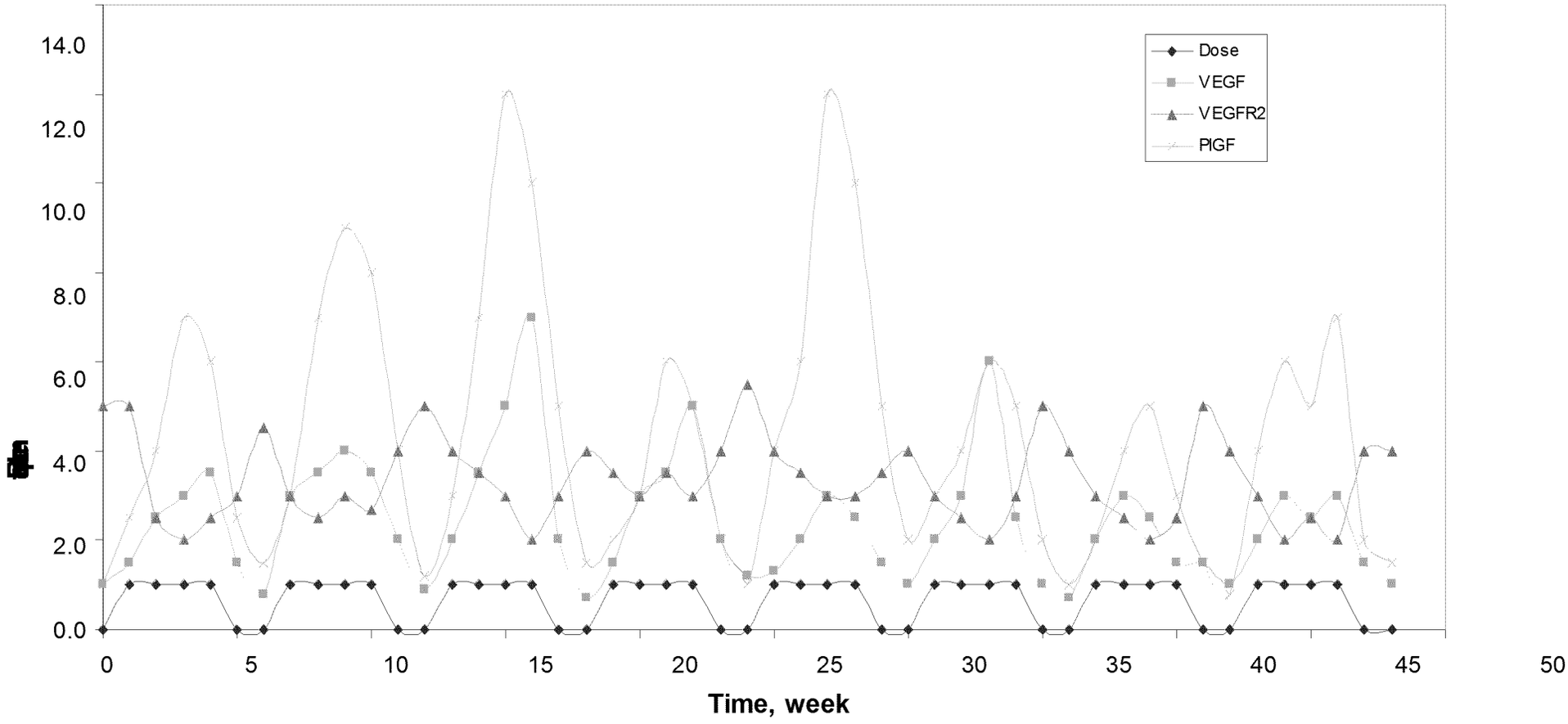
In the first course rapid (within one hour) feedback from Theranos monitor leads to a decision to stop infusion. Drug level drops from toxic to target.

theranos
redefining healthcare

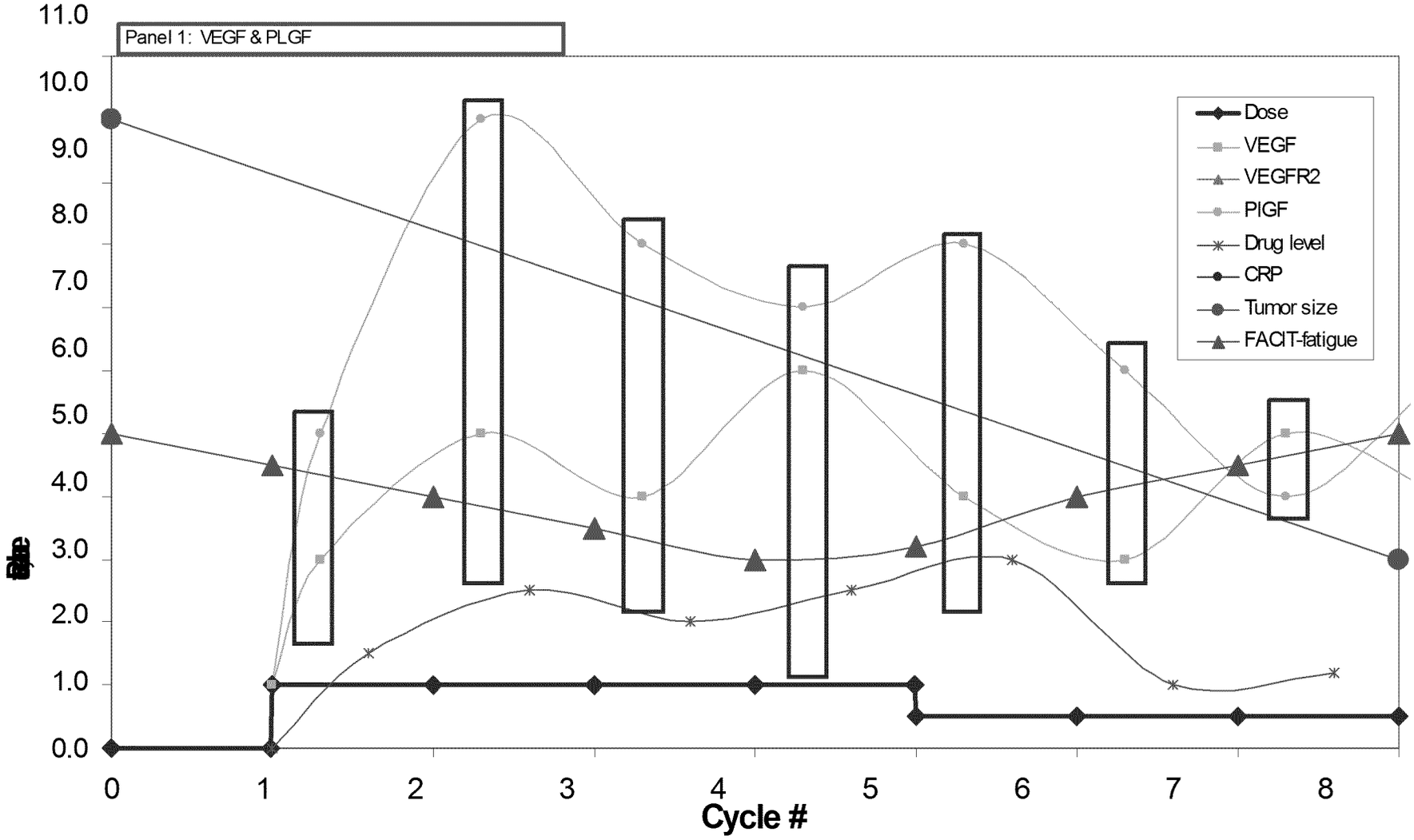
Case Study –Label Expansion

- Cancer Drug is Approved as 3rd line therapy resulting in limited target population
- Objective is to get Proof of Concept in other tumor types
  - Publication to add to compendia demonstrating efficacy and safety in earlier lines of treatment
- Solution
  - Utilize Theranos System with Investigator Sponsored Trial in two clinical studies; one with drug utilized as 2nd line therapy and one incorporating adaptive dosing where both proof of activity and alternative dosing can be rapidly evaluated.
    - Compare with trends and/or imaging from pivotal trials

Typical time course

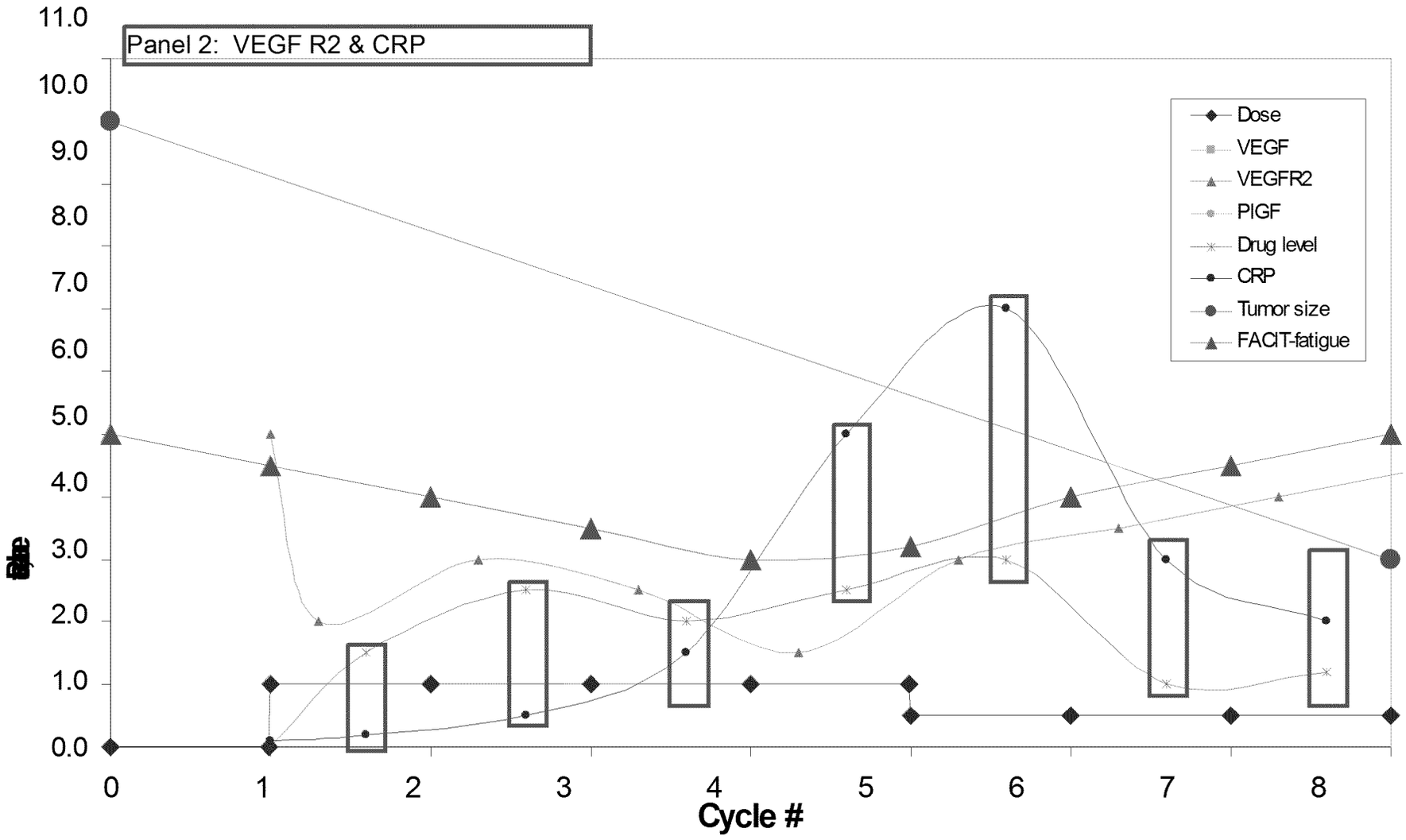


Dose modification at cycle 6



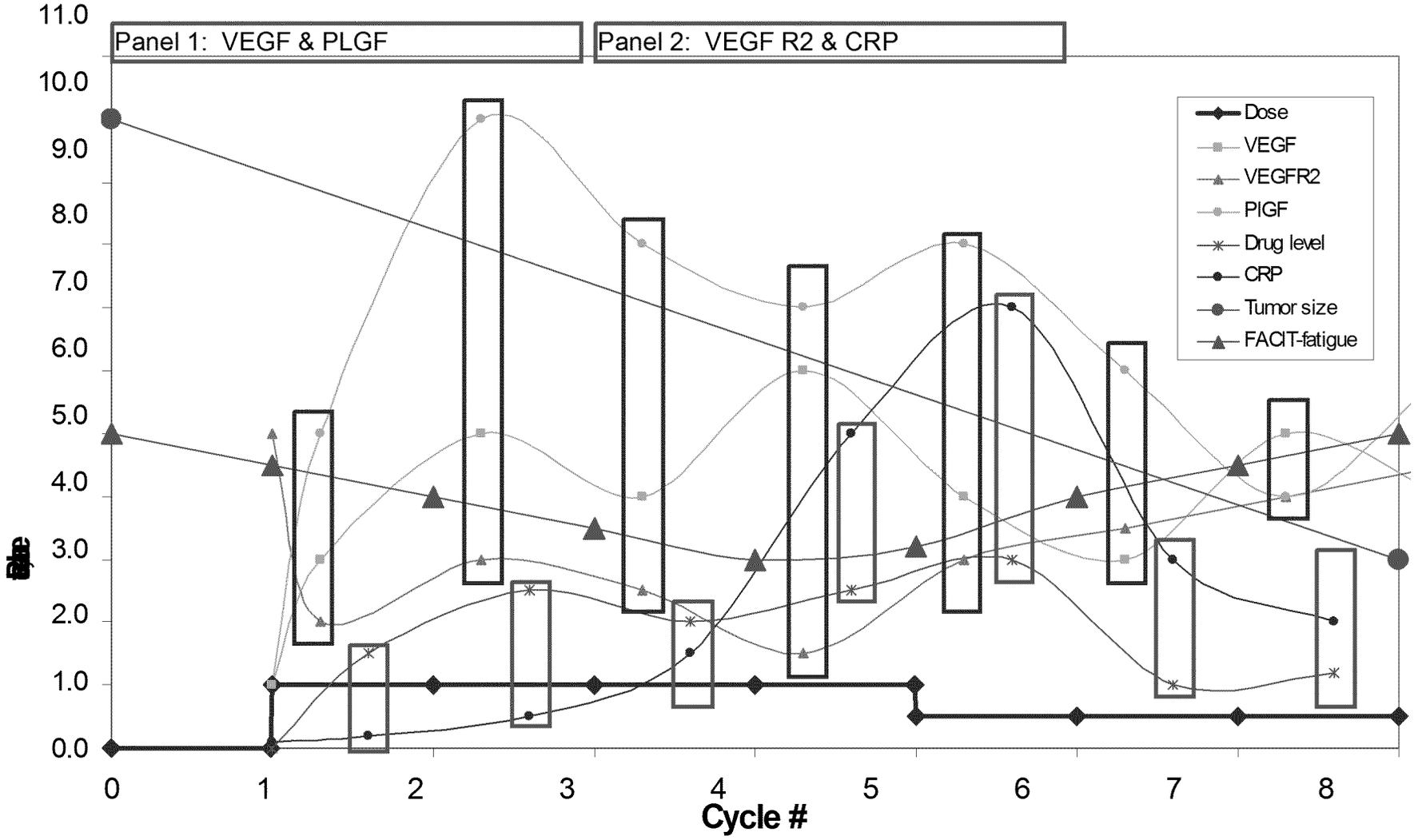
theranos Dose modification at cycle 6

redefining healthcare



Dose modification at cycle 6

theranos
redefining healthcare



theranos
redefining healthcare

Overarching Value Proposition to Pharma

- **Introduction of Theranos system across therapeutic areas to radically optimize Pharma's:**
  - Ability to fast-track growth through integration of dynamic systems designed to complement and enhance the value of Pharma's drugs
  - Ability to rapidly show efficacy and safety of drugs in multiple indications for multiple patient populations in a fraction of the time required today
    - Post-marketing, risk management and pre-approval
  - Ability to extract meaningful correlations from clinical data across pipeline