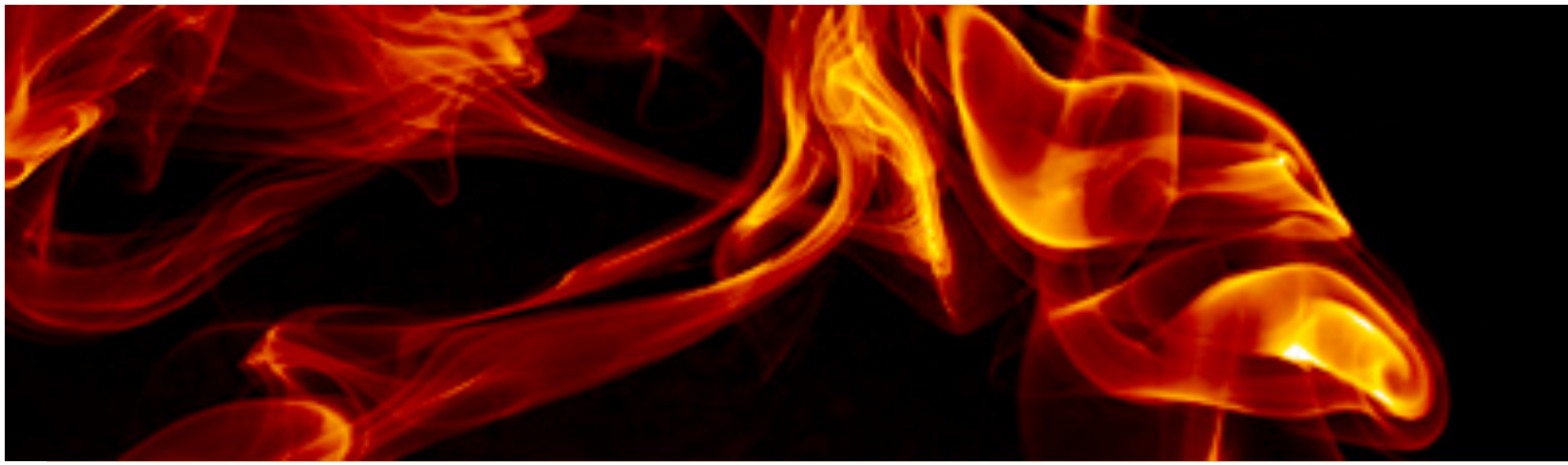

NIC002 & Theranos

Potential Applications and Benefits

[redacted], MD

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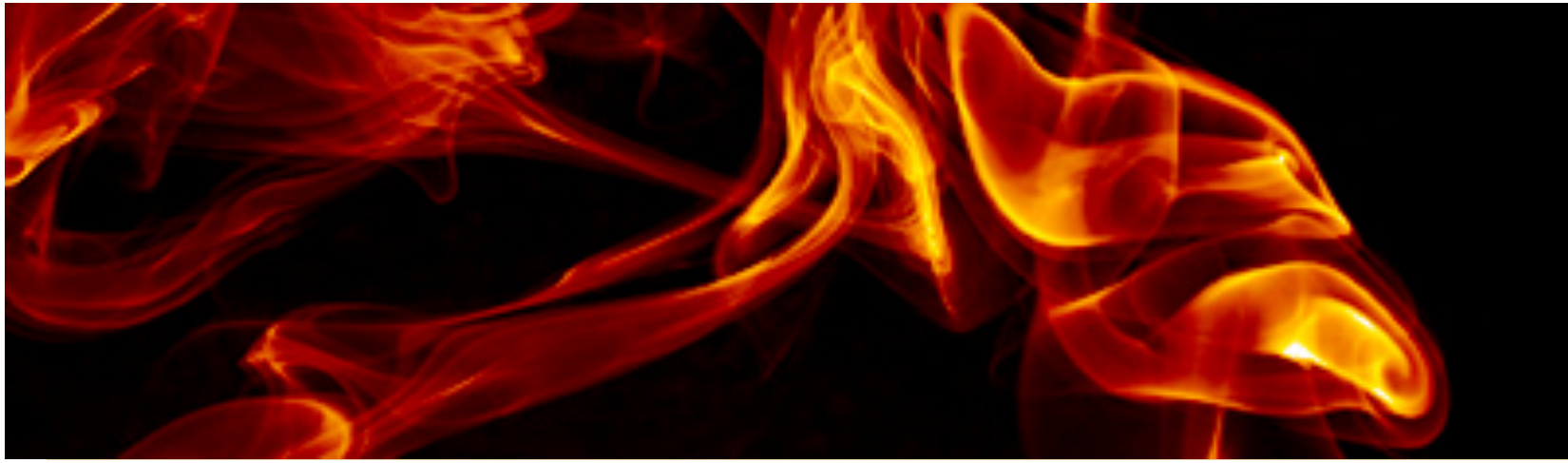


Real Time Ambulatory ELISA Measurements

[redacted]

Measurement of Anti-Nicotine Antibodies

- More frequent ambulatory monitoring to obtain more comprehensive time-series
  - Enrichment of PK/PD modeling
    - More precise identification of optimal antibody-threshold for target quit date (enhancement of success of quitting)
    - More precise identification of optimal antibody-threshold for booster (relapse prevention)
  - Individualized Medicine
    - Need for additional dose and/or booster determined at patient level to bring everyone to high titer level and expand total user market
- Real time data integrated into clinical trial management system
  - Supportive for adaptive seamless design studies

Measurement of Nicotine in Blood

- Bound nicotine will remain in the blood much longer than free nicotine
  - Detection of Nicotine will cover a protracted period of time (the “HbA1c of smoking cessation”)
    - Harder and more convincing data relative to response
    - Reinforcement of patients compliance
  - No need for additional assessment technology (CO from exhaled air)
    - One drop of blood sufficient for all tests, which will be loaded on one cartridge
    - Harder data

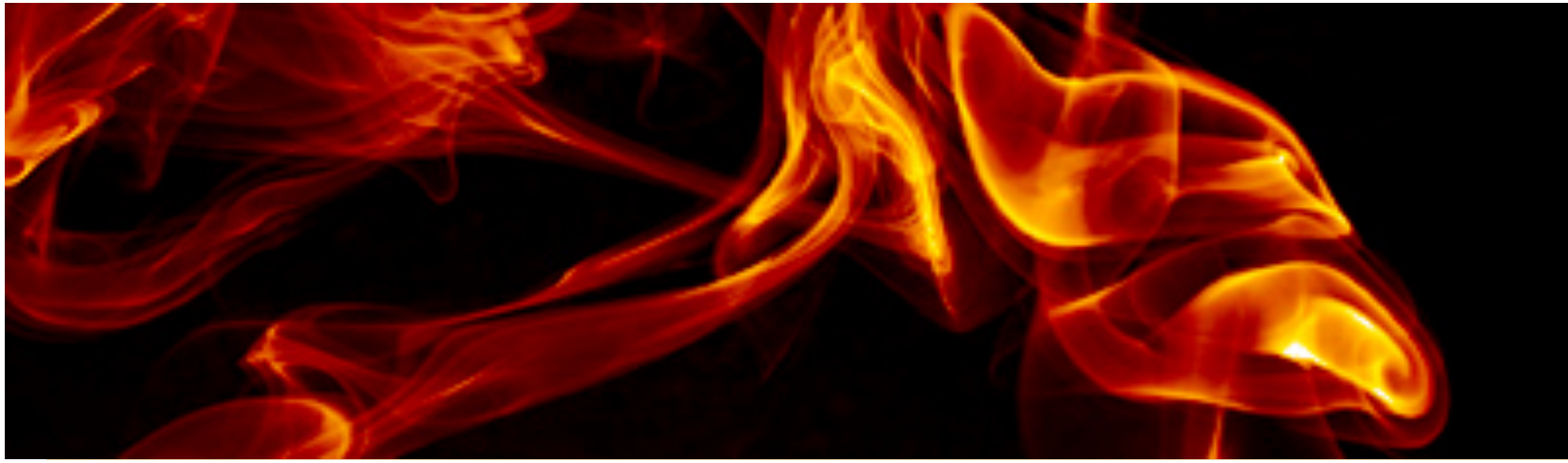
Real-time ambulatory measurement of key analyte (antibodies) concentrations simultaneously with other measurements

- Identify optimal dose – Monitor more frequently to obtain more comprehensive time-series measurements
  - Database automatically integrates time-series measurements with other data points (patient record, patient diary, etc.) to provide better ‘map’ of efficacy than isolated “snapshot” blood measurements.
  - Graphical portrayal of integrated data set allows for better extraction of actionable information
- Strengthen efficacy monitoring through measurement of nicotine (or cotinine) levels simultaneously with main assessment (antibodies)

[redacted]

Summary

- Measure the titer of individual sera to determine the effect of the vaccine and ensure an individual has properly been inoculated.
- Monitor the effect of free nicotine in test subjects in real-time before it is cleared by the kidneys - thus proving efficacy of the treatment directly
- Screen subjects to aid in selecting responders (high titer levels) for trial
- Same systems works for any user of tobacco products (smokeless tobacco …)



Remote Interaction with Patients

[redacted]

Portal to Enhance Remote Interactions with Patients

- Engage patients in managing their dependence
  - Integration of customized smoking cessation programs
- 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 for support of adaptive seamless design studies
  - Link to monitoring data allows for enhanced compliance and clinical success
    - Reinforcement of patient compliance to aid in the management of their own disease
  - Direct interaction between physician and patient (two ways) during drug development and post-marketing

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

[redacted]

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 survey feedback
  - Patient classes are identified at program initiation
  - 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, and is derived from Theranos Human Centered Design team with a link to the Nicotine Dependence Center at Mayo Clinic
  - It represents leading psychological approaches to smoking cessation motivation and therapy, delivered in small, memorable chunks.

Next generation GUI based patient programs

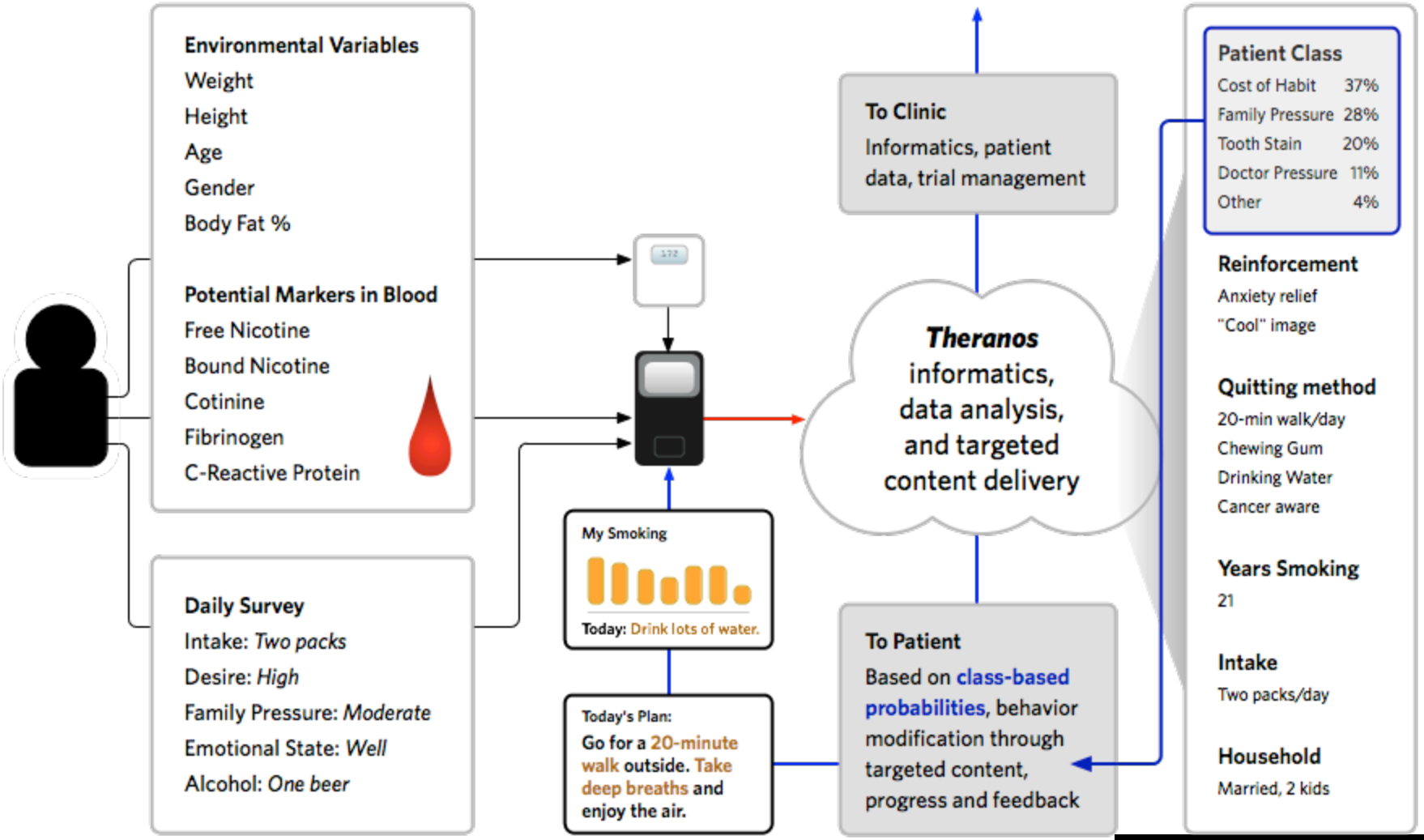
- Increased Compliance with a Program
  - Ease of Use - a graphical touch-screen uses simple symbolic input
  - Cognitive demand is reduced giving patients a higher level of satisfaction
  - Theranos readers can be used at home where patients are most comfortable
  - Programs are individualized

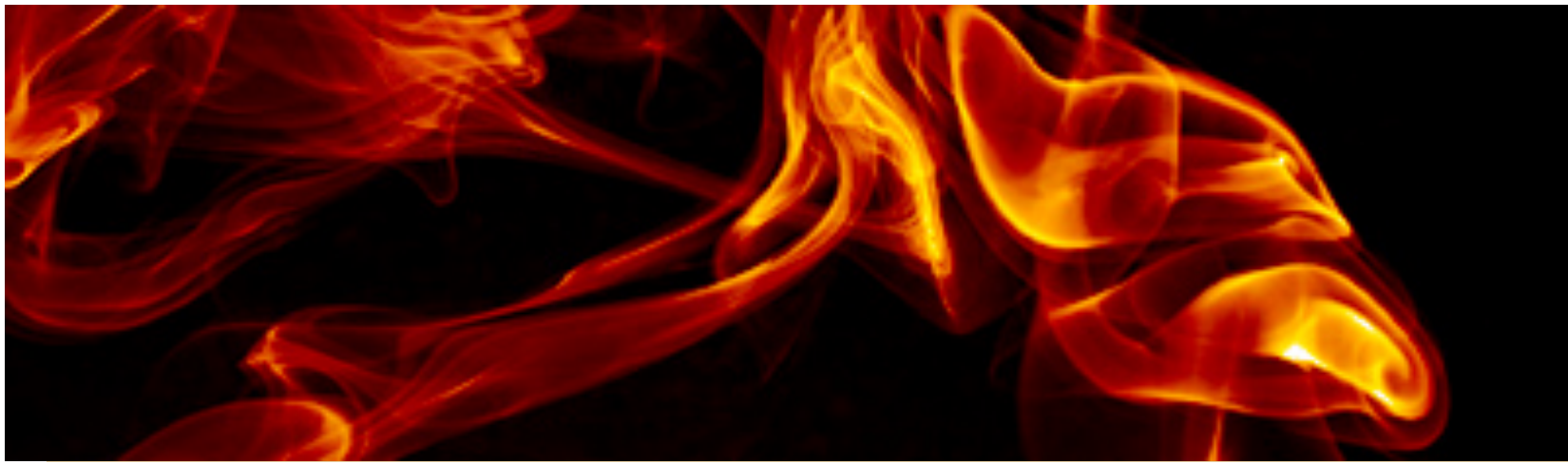
[redacted]

The Theranos System: Benefits

- The Theranos approach allows patients to manage their own disease and gives targeted feedback about their progress
  - Targeted, class-based content engages patients in managing their own dependence
- 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
  - 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

The Theranos System: Case Study





Applications – Initial Thoughts

[redacted]

Drug Development

- Optimization of dose regimen
  - Enriched PK/PD model
    - Identification of key antibody thresholds for smoking cessation and for relapse prevention
      - Could number of initial injections be reduced in individual patients/subgroups?
      - Identification of TQD with enhanced PoS
      - Identification of optimal time point for booster
  - Supportive of adaptive seamless design
- [More] Robust clinical efficacy assessments
  - Direct Nicotine levels assessments
- Full integration of smoking cessation programs
  - Delivered directly through portal associated with the device
    - Less dependence on site specific interactions

[redacted]

Post-Marketing

- Unique integrated drug-program combo
  - Competitive advantage
    - Basic smoking cessation program won't be replaced by silver bullet drug and will remain key component of any quitting attempt

    → [redacted] **to deliver <u>full</u> package**
      - » Consumer point of care system has ability to serve as a companion to the vaccine pre and post-approval to serve as definitive differentiator from competition
  - Personalized medicine
    - Optimized regimen
      - Administration of most appropriate number of injections and optimized timing
    - Enhanced clinical outcome
      - Better reimbursement from payers?
  - Enhanced reproducibility of clinical studies data in real world
    - Less dependence on physician background
      - Less experienced physicians would still be able to administer both injection and smoking cessation program

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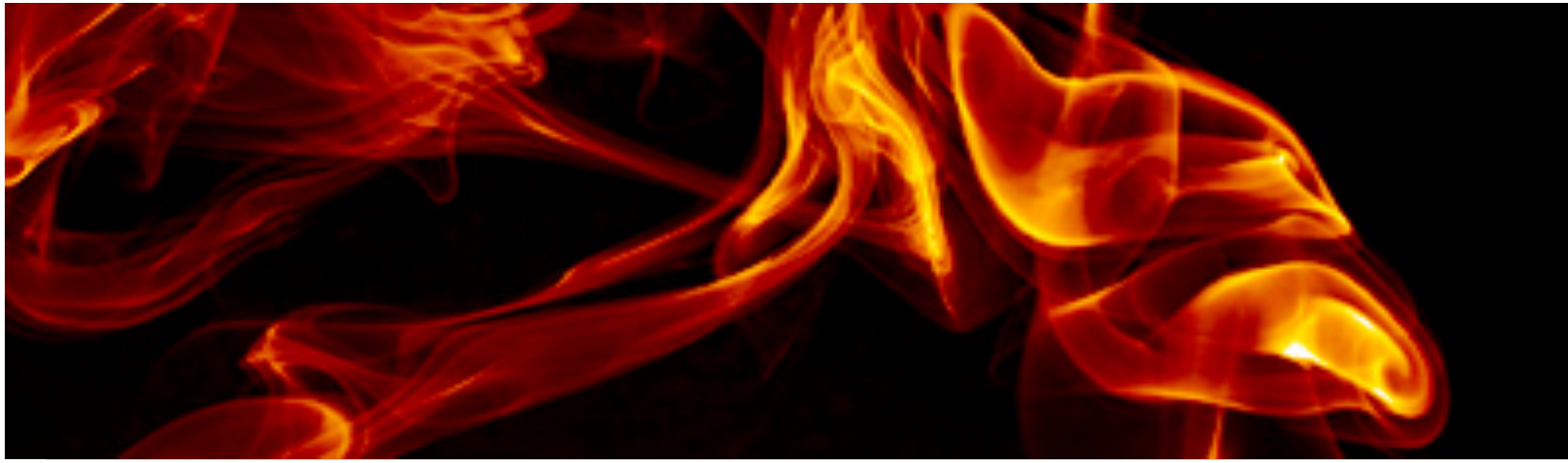

Next Steps

Validation

- Theranos to develop and validate assays
  - MSA incorporates MTA
    - MSA signature
    - Theranos SOW for Phase A includes detailed material request
    - Material transfer desired by 12/31/07 – latest 1/15/08 for desired development lead time
- [redacted] to determine best opportunities for validation
  - E.g. PoC patients (subgroup)
    - Blood samples to be provided to Theranos prior to June study initiation
  - June study run with at home monitoring and in clinic testing
- Discussions on partnership
  - January meeting

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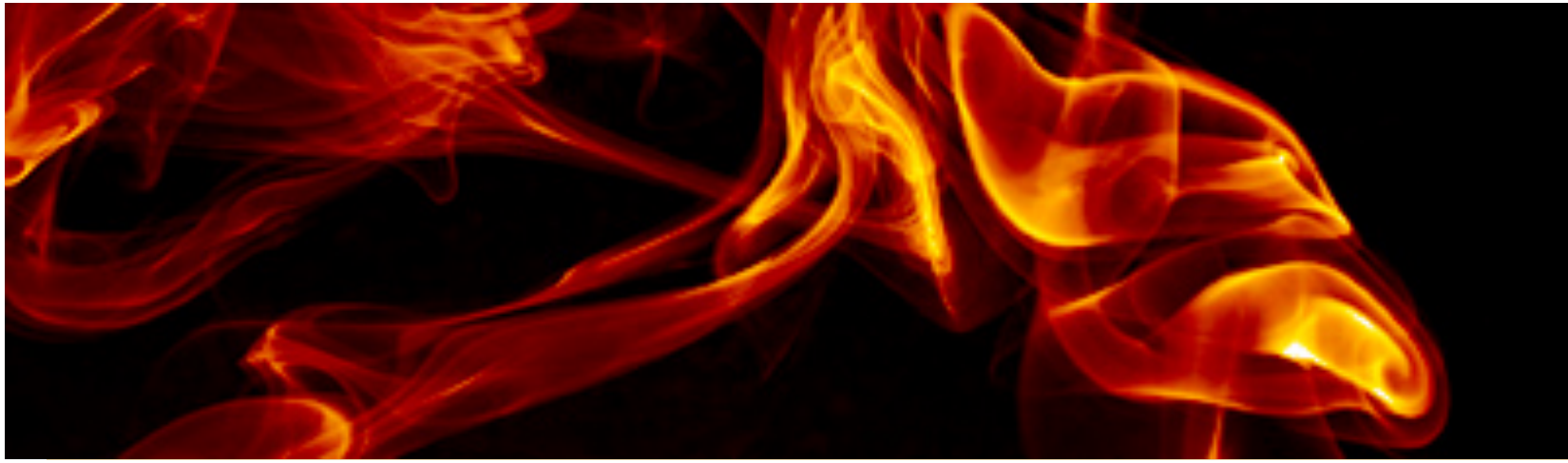

Back Up

[redacted]

Development of Nicotine Assay

1) **Measuring the titer of human anti-nicotine.**
   a. **A supply of nicotine that is used as the vaccine. 5 to 10 mgs**
   b. **A larger supply of nicotine conjugated to another protein to be used as the capture. 10 to 20 mgs to start with.**
   c. **As many human anti-vaccine samples as we can get. (25 + samples and several mls of each for Positive controls.**
   d. **If there exist a Monoclonal or Polyclonal sera to the conjugate.**
2) **Measuring nicotine levels in sera.**
   a. **Monoclonal or Polyclonal purified IgG specific for Nicotine,**
   b. **Nicotine conjugated to different carrier than vaccine in order to be conjugated to AP.**

[redacted]