Feinstein Kean Healthcare
caBIG® Bio IT World Presentations
Lecture by Sorena Nadaf
Thursday 2:00 p.m. Waterfront 1 track 7-8

Sorena Nadaf: Okay. Thank you all. This is my third Bio IT conference and I can say this is the best year so far for me. I think it's been a great conference. I'll start off with making this little statement. One of my favorite statements from a previous director of the NIH speaking specifically to the period of time that we are all in and the changes in biomedical sciences that has really brought us to where we are today. So I want to start off with a question, a complicated question that all of us in our institutions who are involved in translational sciences and research have to deal with. Bear with me because there are two slides that are wordy like this. You have a clinician who likes to perform a—likes to compare various types of cancer treated with a specific chemotherapeutic agent. These patients are involved in clinical trials where the study subjects live longer than two years post study and in order to find gene expression patterns that might be predictive of a positive outcome. The researcher has expression arrays and mass spec data for the patient population that live for less than two years and is very interested in performing proteomic analysis. In this case shotgun proyomic analysis on the same substantive patient samples and provide his colleagues blinded data sets for quality control experiments. Here is a complicated query. Site investigator needs to collect all available next generation sequencing data from lung cancer patients which are part of a clinical trial using Taxol as the agent within a period of time. Same investigator needs the data from available tissue samples localized within a ten millimeter within ten millimeter of the tumor site and the original tumor site on the same patient population, so that she can perform further analysis. Finally the need to identify all adverse events and serious adverse events for the patients that had a severity rating of four. And that are linked to Taxol administration.

This is nothing unusual. I think in this time and day in the era of molecular medicine the types of work that we are all trying and the answers we are trying to come up with. The description of these challenges really outlines a landscape of clinical basic science and translational research and it's showing the changes are enabled really by high throughput molecular science to various data communication and computing requirements that are cutting edge today and they're really driven by large national programs. The NIH's CTSA's. The NCI's caBIG® programs. The road map programs. The biomarker discovery programs. And like the spores and the specs. So what is it going to take for us in order to move forward, keeping up with all of this, basically translating this research into a practical environment? Why do we need to do this, how and of course, more importantly, with what? Here is the challenge: Filling this translational research gap. Over the past, in the past decade or so, our understanding of diseases has really gone through the roof at a large scale, but our management of patients has really not changed much, so filling this gap which translational research really fits in is our goals here. So in order to do this we are bridging the lab and clinic in both directions and not only at UCSF but at all centers, especially at Moffit and other academic institutions where we are dealing with accelerating the development of specific individual targeted agents revolving around small molecules, antibodies, sRNA's and leading toward downstream development of identified biomarkers that enable understanding, better understanding of the risk, of the tumor burden and predictive markers for response linking the molecular diagnostics and all these therapeutic

swimming lanes if you would in order to personalize patient care. You've seen this again in this same session.

What is personalized medicine? It is what it is today; current practice is one drug for each patient and, of course, the right treatment for the right person at the right time. Patients with the same diagnosis, we all know are not the same. A handful of patients here, predict good response to a drug or a combination of drugs with the same diagnosis, the same group of patients will predict poorly to the same drugs. What do we do? We change the drug. And again a subset of these patients, again, have an increased likelihood of adverse events or serious toxicities and what do we do again? We change the drugs. This is pretty much what personalized medicine has been about for the past decade or so - we're giving it, of course, a new direction. In cancer specifically we have to deal with heterogeneity of the disease. We know that cancer develops in hundreds of different sites and most are clonal and they rise from the progeny of a single cell and they accumulate at least five mutations and with over 100 oncogenes and tumor suppressor genes we have tens of billions of possible combinations and given that the differences, the genetic differences between patients and cancer are not identical, there is not a single cancer that is exactly alike.

What has really changed our thinking? Projects like the human genome project, the technologies that have led to the expanded analysis of RNA and proteins both leading to the better understanding of signaling pathways and biomarker discovery. This really has been a see change. And this comprehensive amount of omic data which is a result of all the different technologies that we see here today, presented, the companies that are providing solutions for this. The institutions are giving us standards to actually understand this the right way and this has really pushed us and, with the large number of patients and samples that we are studying today with the addition of the cutting edge biostatistical and computational analysis technologies, we are doubling our comprehension based on only on computing methods alone. We're doubling it every two years pretty much.

So the promise of molecular diagnostics, what does this really mean in helping achieve personalized healthcare? We estimate that the risk of developing various kinds of cancers really leads to specialized individualized plans for screening patients, very selective use of chemotherapeutic drugs and other recommendations like diet and lifestyle. We, molecular diagnostics, has enabled the detection of disease at a much earlier rate. We are making an impact and defining each cancer patient more precisely and allowing the predictive response of drugs and their modalities much more specifically.

The promise of molecular therapeutics is predicting, is helping us individualize patient care and personalizing medicine by allowing predictive toxicities for normal tissues with a much higher accuracy than we ever have before. We are developing effective treatment plans and we're really turning cancer into a chronic disease. All these treatments can be personalized in various ways.

So translational research and its community -- who is this made up of? Of course clinical oncologists deal directly with the heterogeneity of cancer every day and really have been personalizing cancer care as a disease for a very long time, but these really rapid advances in basic research has really helped us understand the individual patients and so we are treating the individual. Continued advances in medical education also are enabling us but highlighting that more computer based treatment planning is really becoming a downstream possibility. One day you may have the patient going into their doctor and I'm not saying tomorrow, but this is not too far along. We are using a lot of the computing models to help diagnose patients these days. So

we are accelerating personalization of patient care and integrating molecular diagnostics and therapeutics. Collaboration with multiple groups, academia, the NCI and pharmaceutical companies. And in order to really move this forward, we have established translational support teams and its infrastructure platforms are common informatics tools standards, which I will get into, is key to the success and our current success. Sustained architecture and interoperability between local and commercial partners is key here. So requirements for translational research supporting personalized healthcare, of course, is requiring long term investments and effective support teams made up of everything that's listed here but highlighting, more importantly, for people like me that are in the biomedical informatics field specialists in the clinical and bioinformatics, in order to support the physician scientists, the molecular imagers, the pathologists, the research nurses and the statisticians. We all work together as a team. Furthering the requirements for translational research, of course, is being able to study large patients in a uniform way -- standard treatment protocols, routine biopsies and novel trial designs and adaptive trials to test predictive markers for agents. The requirement and infrastructure for the collection, the management, the understanding, the breakdown, of clinical biomedical biospecimen data under compliant conditions is a very important requirement in order to move us forward in this field.

Unified infrastructure needs. We are leveraging integrative standards and platforms in all academic institutions. We are all made up of multiple collaborating investigators working as an investigative team to address all of these complicated issues. So at UCSF we, in our mission and our focus, is to support all that we have—all I have described, capturing managing clinical and biomedical research data, so we can merge it, integrate it, aggregate it with other data sets using the standards that the National Cancer Institute caBIG® program, CBIIT initiatives and the CTSA initiatives all collectively together we are focusing on trying to bring this together. So if you look at a number of scientific strategic goals and the corresponding platforms that we have. If you look at this in three tiers, building clinical and translational research capabilities correspond to specific informatics platforms that we have all invested in, for example: management of array data, next generation sequencing data, managing all biospecimens, being able to extract and integrate with registries, patient surveys are critical, managing the data that are collected in clinical trial collection systems, and understanding better large cooperative group trials and the management and the electronic data capturing tools that are necessary to enable proper uniform data collection. Enhancing the collaborations is key and one of our strategic goals at our academic institutions, specifically at UCSF where we are—where we can have electronic data interchange tools based on standards that exist. Data lab services, what we call databuses, being able to bring all this data uniformly together, EDW's, datamarts, etc. Of course, encouraging not just T1 but T2 and T3 research utilizing things like genome browsers that are available to us, GWAS processing and understanding the genome/phenomena data sets and analyzing them. Pathway analysis tools and overall interpretation tools. We're trying to bring it together one KB at a time.

Standards, operations and tools. Standards are key. The National Cancer Institute has helped UCSF over the past few years really put together the framework for our studies and we have a large number of studies including pharma, FDA, and some commercial partners have all worked together for us to really bring everything together including the infrastructure enabling our research informaticians, our high performance computing environments, enabling real change and impacting our day to day lives. So change is hard. It's good. Everyone says you go first. I think we're not the first; but however we are moving forward. We have hundreds of

active studies open to accrual. Both therapeutic and non-therapeutic, requiring translational infrastructure in support of personalized medicine. Dozens of studies bringing together genome/phenome data, adaptive protocols, multisite cooperative group style studies and I'll highlight one example. The I-SPY breast cancer study led by Dr. Laura Esserman at UCSF has brought together almost every bullet point in the slide I have presented. It really has made a tremendous difference in our direction and in supporting this type of multi-arm, multi-study multi-drug research environment. And with that, I'll answer any questions.

[Applause]

[End of Recording]