BEFORE THE

INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
TO THE
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

A PUBLIC HEARING)
)
IN RE THE CIRM STRATEGIC)
PLAN UPDATE)
_____)

LOCATION: CITY OF HOPE
DUARTE, CALIFORNIA

DATE: MARCH 5, 2009
9:30 A.M.

REPORTER: BETH C. DRAIN, CSR
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I N D E X

DUARTE, CALIFORNIA; THURSDAY, MARCH 5, 2009

9:30 A.M.

DR. FRIEDMAN: LADIES AND GENTLEMEN, GOOD MORNING. IT'S A PLEASURE FOR ME TO WELCOME YOU HERE TO CITY OF HOPE FOR THIS PUBLIC DISCUSSION AS THE STRATEGIC PLAN FOR THE CALIFORNIA INSTITUTE OF REGENERATIVE MEDICINE STRATEGIC DIRECTION IS REVIEWED, REFRESHED, AND LAID OUT FOR THE NEXT SEVERAL YEARS. THIS IS AN IMPORTANT MEETING. WE APPRECIATE EVERYONE BEING HERE.

THIS EFFORT HAS BEEN A PRODUCT OF PUBLIC-PRIVATE PARTNERSHIPS ALL ACROSS THE STATE, AND CITIZENRY INVOLVEMENT IS CRUCIAL TO THE SUCCESS. HAVING YOUR INPUT HELPS THE STAFF OF THE CIRM DIRECT THE ORGANIZATION AT A TIME OF UNPRECEDENTED OPPORTUNITIES, A TIME OF REAL CONSTRAINTS, IN A TIME OF OBVIOUS RISKS. TO CHART THE RIGHT COURSE IS NO SIMPLE MATTER, BUT LUCKILY WE HAVE A VERY FINE STAFF UP TO THIS TASK AND EAGER TO MOVE FORWARD.

THE PROGRAM THIS MORNING WILL BE A PRESENTATION FIRST BY ALAN TROUNSON. HE WILL BE FOLLOWED BY DR. OWEN WITTE, AND THEN THERE WILL BE AN OPPORTUNITY FOR DISCUSSION, QUESTIONS, AND ANSWERS. ALL THE COMMENTS TODAY WILL BE TRANSCRIBED

AND RECORDED SO THAT WE WILL BE ABLE TO CAPTURE THE ADVICE, THE CRITIQUES, THE SUGGESTIONS THAT ARE MADE.

IT'S MY PLEASURE NOW TO INTRODUCE TO YOU DR. ALAN TROUNSON, EXTRAORDINARY SCIENTIST, SKILLED ADMINISTRATOR, AND A LEADER OF THIS EFFORT. DR. TROUNSON.

DR. TROUNSON: THANK YOU VERY MUCH, MICHAEL. THANK YOU FOR HOSTING THIS PUBLIC SESSION. IT'S VERY IMPORTANT FOR US TO GARNER SOME INPUT ON REVISIONS TO OUR STRATEGIC PLAN BECAUSE THE STRATEGIC PLAN WAS DEVELOPED IN 2006. IT'S A REAL DOCUMENT. IT'S MOVING IN REAL-TIME. THERE HAVE BEEN CHANGES THAT HAVE HAPPENED IN THE SCIENCE, THERE ARE CHANGES HAPPENING IN THE CLINICAL AREA, AND WE WANT TO TAKE THE OPPORTUNITY TO ENSURE THAT WE'RE SEEKING AN OPTIMUM PLAN TO BE ABLE TO DELIVER ON THE MISSION THAT WAS SET WHEN WE BEGAN.

SO JUST TO KEY YOU IN ON THE MISSION, IT REALLY VERY SPECIFICALLY ASKED US TO TAKE THOSE IMPORTANT DISCOVERIES AND BRING THEM TO THE CLINIC. AND I THINK IN MY OWN MIND, IF WE DON'T GET THESE IMPORTANT DEVELOPMENTS INTO THE CLINIC, WE WON'T HAVE SATISFIED THE INTEREST IN GETTING PROPOSITION 71 UP. SO IN MANY WAYS I SEE IT'S IMPORTANT FOR US

TO INDICATE TO OUR BASIC SCIENCE COLLEAGUES THAT WHATEVER THE NEW DEVELOPMENTS THEY'VE BEEN MAKING, AND THEY'RE EXTRAORDINARY, WHEN YOU LOOK UPSTREAM FOR OPPORTUNITIES SO THEY CAN GO FORWARD IN SOME WAY TOGETHER WITH OTHER DISCOVERY THAT AFFORD SOME WAY TO CLINICAL TREATMENTS AND, ONE HOPES, CURES IN DUE COURSE.

SO HAVING SPECIFIED THE MISSION STATEMENT, THERE ARE A NUMBER OF GOALS IN THOSE PAPERS THAT ARE AVAILABLE TO YOU. I'M NOT GOING TO GO THROUGH ALL THE GOALS, JUST TO IDENTIFY THAT THERE ARE GOALS THAT HAVE BEEN SET OUT IN OUR ORIGINAL PLAN. WE ACTUALLY AREN'T CHANGING ANY OF THEM SPECIFICALLY EXCEPT GOAL 5, THAT WE HAVE NOT TAKEN ANY STEPS TOWARDS FORMING A STEM CELL BANK. I THINK THAT'S ACTUALLY BEEN THE RIGHT DECISION AT THIS POINT IN TIME BECAUSE THERE'S BEEN SO MUCH MOVEMENT IN THE SPACE ABOUT WHAT IS IMPORTANT TO BANK. AND ANYWAY, THERE ARE BANKS AVAILABLE IN THIS COUNTRY AND, OF COURSE, INTERNATIONALLY THAT ARE ACCESSIBLE TO CALIFORNIA RESEARCHERS.

WE ARE HOPING TO MAKE MORE STEM CELLS, PARTICULARLY EMBRYONIC STEM CELLS THAT HAVE GENETIC MUTATIONS, MUCH MORE AVAILABLE TO CALIFORNIA SCIENTISTS. BUT MY FEELING, AND YOU CAN TELL ME IF

I'M WRONG, MY FEELING HERE IS AT THE MOMENT THAT YOU'VE GOT ADEQUATE ACCESS TO RESEARCH LINES.

THE OTHER ISSUE ABOUT WHETHER WE'VE GOT SUFFICIENT LINES OF EMBRYONIC STEM CELLS FOR CLINICAL APPLICATION IS ANOTHER MATTER ALTOGETHER, AND IT'S ONE THAT WE'VE BEEN EXAMINING CLOSELY TO OUR INTEREST IN SETTING UP GMP FACILITIES. WE ARE HERE AT THE HOME OF ONE OF THE MAJOR GMP FACILITIES HERE AT THIS INSTITUTION. SO WE'RE ADVISED ESSENTIALLY THAT THERE ARE REALLY SUFFICIENT GMP FACILITIES AVAILABLE TO CALIFORNIA RESEARCHERS AT THIS POINT IN TIME. WHETHER THAT'S TRUE IN THREE TO FIVE YEARS WE WOULDN'T LIKE TO PREDICT. IT DEPENDS REALLY ON WHAT SORT OF CELL LINES WE HAVE GOING FORTH CLINICALLY. BUT ESSENTIALLY WE HAVE SAID THAT THERE'S NOT A REAL DRIVE TO CREATING A SPECIFIC CIRM STEM CELL BANK.

THE OTHER GOALS, WE'VE BEEN MAKING SOME PROGRESS ON THEM AND, INDEED, WE FEEL CONFIDENT IN ALL THE GOALS WE WILL MAKE IN THE FIVE-YEAR TIMEFRAME. WE'RE SITTING HERE, ABOUT TWO YEARS, LITTLE OVER TWO YEARS, SO HALFWAY THROUGH THE FIRST FIVE YEARS. AND SO WE'VE GOT TIME, CERTAINLY ENOUGH TIME TO BE ABLE TO ADDRESS ALL OF THOSE ORIGINAL GOALS THAT ARE SET THERE. WHETHER THERE IS A NEED

TO REVISE SOME OF THE GOALS BEYOND WHAT WE'RE DOING, I THINK IT'S A MATTER FOR US TO GET INPUT FROM YOU.

THERE ARE TEN-YEAR GOALS. THEY EXIST AS WELL, AND I'M NOT GOING TO TRY AND ADDRESS THOSE, BUT THEY EXIST THERE. IF YOU LOOK CAREFULLY, YOU WILL SEE THOSE TEN-YEAR GOALS THAT WE'RE COMMITTED TO IN THE ORIGINAL PLAN.

SO WHAT I WANT TO DO IS SORT OF FOCUS YOU ON WHERE WE ARE. WE'RE SEEING CIRM RESEARCHERS AS A PIPELINE OF VALUE GOING FROM THE VERY BASIC END THROUGH TO THE CLINICAL END WHERE WE HAVE OCCUPATION, IF YOU LIKE, OF THE BASIC UNIVERSITIES, RESEARCH INSTITUTIONS, AND HOSPITALS, AND THE VENTURE COMPANIES THAT ARE THE MIDDLE PART OF THE TRANSLATION, THE EARLY CLINICAL PHASES AND, OF COURSE, BIG BIO AND BIOTECHNOLOGY AND THE PHARMACEUTICAL INDUSTRY WOULD OCCUPY THE OTHER CLINICAL END. SO THERE ARE DISCRETE ENTITIES IN THIS PIPELINE, AND ACTUALLY WE FEEL THAT WE WANT TO INTEGRATE THAT PIPELINE TO MAKE OUR MISSION FEASIBLE AND LOOK FORWARD TO BE GENUINELY ACHIEVABLE.

THERE ARE BIG ISSUES ABOUT THE AMOUNT OF MONEY THAT'S NECESSARY IN THAT VENTURE CLINICAL AREA BECAUSE THE COSTS OF -- AT LEAST THE DRUG INDUSTRY MODEL COSTS ARE VERY HIGH ON THE ORDER OF A BILLION

DOLLARS OR MAYBE MORE TO GET A DRUG SUCCESSFULLY INTO PRACTICE, INTO TREATMENT, ROUTINE TREATMENT FOR PATIENTS. IT MAY BE LESS COST TO GET CELL THERAPIES THROUGH THAT FRAMEWORK, BUT WE'RE VERY LIKELY TO BE DEALING WITH SMALL MOLECULES IN THE FIRST INSTANCE ANYWAY, SO VERY MUCH A ROUTINE DRUG MODEL THAT'S DEVELOPING OUT OF THE ASSAYS THAT THE SCIENTISTS HAVE WORKED THROUGH FOR THE STEM CELLS.

BUT WE'RE GOING TO NEED ADDITIONAL FINANCING HERE BECAUSE THE MODEL IS -- THE BUSINESS MODEL IS VERY HARD TO EXPLAIN TO INVESTORS, VENTURE CAPITALISTS, BECAUSE THE HIGH COSTS OF GOING THROUGH THE DEVELOPMENT AND THE CLINICAL STUDIES, AND IF YOU ARE DEALING WITH TREATMENT WHICH MIGHT BE RELATIVELY SIMPLE, A CURE WHERE A PATIENT, FOR EXAMPLE, GETS A DOSE OF CELLS, IT'S VERY HARD TO EQUATE BENEFITS IN A BUSINESS SENSE FROM WHAT YOU CAN CHARGE IN YOUR THERAPEUTIC MODE FOR THE COSTS OF THE INVESTMENT.

SO WE'RE LOOKING TO SEE IF WE CAN DEVELOP SOME NEW MODELS HERE. THEY WOULD BE LOOKING TO THE BENEFICIARIES OF THE CURES, IF YOU LIKE, AND THAT WOULD BE GOVERNMENT WHO END UP PAYING FOR A LOT OF PATIENT COST, HEALTH INSURANCE INDUSTRY, LOOKING TO SEE IF THERE ARE WAYS TO REFIT THE INVESTMENTS SO THAT IT MAKES A BETTER SENSE MODEL FOR INVESTORS AND

THE PHARMACEUTICAL INDUSTRY TO CONNECT WITH US.

AND SO THAT'S ONE OF THE ACTIVITIES THAT WE'RE LOOKING AT. IS THERE A DIFFERENT PARADIGM, IF YOU LIKE, TO ENABLE US TO GET THESE NUMEROUS TREATMENTS THAT ARE ARISING, PARTICULARLY THE CELL THERAPIES, TO BE ABLE TO GET THEM TO GO THROUGH TO CLINICAL TREATMENT.

WITH THE PIPELINE THAT WE CURRENTLY HAVE ADVANCED, THE GREEN IS THE VERY BASIC END OF IT. AND I'VE PUT THAT IN LARGE BLOCKS ON THE PIPELINE BECAUSE MOST OF OUR INVESTMENT HAS BEEN IN THE BASIC AREA. WE'VE SEEN COMPREHENSIVE GRANTS, NEW CELL LINES, AND BIOLOGY, BASIC BIOLOGY PROGRAMS. THE BLUE BAR IS WHERE WE'VE BEEN MOVING INTO TRANSLATION, AND YOU WILL SEE THERE IS ONLY -- WE'VE JUST ONLY GONE INTO A PURE TRANSLATION AND EARLY TRANSLATIONAL RFA. AND WE'VE NOW RELEASED THE DISEASE TEAM PROGRAM. SO WE'RE STARTING TO MOVE UP THAT PIPELINE TO GET PEOPLE TO THINK ABOUT JOINING TEAMS, TEAMS WHICH WILL TAKE THE RESEARCH THROUGH TO IND'S IN THE CASE OF DISEASE TEAMS. CAN YOU GET THE RESEARCH WITHIN A FOUR-YEAR TIMEFRAME TO ACTUALLY RESULT IN AN IND APPLICATION TO THE FDA.

WE HAVE OPPORTUNITIES, IT'S TRUE, FOR CO-INVESTING OR CLINICAL TRIALS THAT ARE CURRENTLY

UNDER WAY. WE HAVEN'T CHOSEN TO DO THAT AT THIS STAGE, BUT WE WOULD BE INTERESTED IN YOUR FEEDBACK. WE THINK THAT THERE IS A ROLE FOR US TO PLAY IN THE CLINICAL END, BUT THERE'S A LIMIT TO HOW MUCH FUNDING THAT WE'VE GOT AVAILABLE IF WE WANT TO DRIVE THE ENTIRE PIPELINE. AND IT REALLY HASN'T GOTTEN ITSELF TO THE POINT WHERE WE FELT A STRONG RECOMMENDATION TO GO TO THE ICOC, THE BOARD.

THE FUNDS AWARDED TO DATE BY THE ICOC IS AROUND $633 MILLION AS BEING TRAINING AND RESEARCH GRANTS AND SHARED LABORATORIES AND FACILITY AWARDS. AND SO THERE ARE THE DOLLARS THAT WE'VE ACTUALLY EXPENDED. YOU'D BE INTERESTED THAT THE ICOC HAS AGREED TO A THIRD OF THE TOTAL FUNDS, WHICH IS AROUND ONE BILLION. SO THEY'VE ACTUALLY MADE DECISIONS FOR US TO GO FORWARD ON A BILLION DOLLARS. THAT'S A THIRD OF THE PROGRAM. AND THAT'S WHY I THINK IT'S A VERY IMPORTANT MOMENT TO DISCUSS THE STATE OF THE STRATEGIC PLAN WITH YOU.

MOSTLY THAT'S TAKEN UP IN THE NEW PROGRAMS ON DISEASE TEAMS. THERE'S OVER $200 MILLION THAT THE BOARD HAS AWARDED US TO CONSIDER. IT'S ONLY A CONSIDERATION. WE'VE GOT TO FIND THE NUMBER OF REALLY PERSUASIVELY SUCCESSFUL PROGRAMS AMONGST THE DISEASE TEAMS COMING FORWARD, BUT WE'VE BEEN ALERTED

TO THE FACT THAT WE MAY RECEIVE UP TO A HUNDRED APPLICATIONS IN THIS AREA. SO THERE'S ALWAYS VIEWS OUT THERE IN THE RESEARCH AND THE BIOTECHNOLOGY COMMUNITY THAT THERE ARE STUDIES THAT COULD GET THROUGH TO THAT IND IN THAT TIME.

SO WE'VE BEEN ALLOCATED BY THE ICOC AROUND A THIRD OF OUR TOTAL $3 BILLION BUDGET. AND JUST TO SHOW YOU WHERE THOSE THINGS HAVE GONE, YOU CAN SEE THAT THE BLUE LINE IN TERMS OF RESEARCH FUNDING, THAT THE LARGE ALLOCATIONS GET TOWARDS THAT CLINICAL END FOR THE DISEASE TEAM ALLOCATION, WHICH IS THE DARK BLUE, AND THE TRANSLATION IS THE LIGHT BLUE, TWO BIG COST AREAS WE HAVE TO MOVE THE PROJECTS UP IN VALUE AS WE MOVE DOWN THE PIPELINE.

SO THERE IS A NECESSITY FOR US TO BE CAREFUL AND TO BE THOUGHTFUL ABOUT WHERE WE'RE INVESTING. THERE ARE SOME ISSUES, OF COURSE, WHICH YOU WILL BE AWARE OF IN TERMS OF THE CALIFORNIA BUDGET. AND AT THE MOMENT WE'RE STILL ON TRACK FOR OUR PROGRAM, BUT IT DOES REQUIRE US TO RAISE SOME ADDITIONAL MONEY THROUGH PRIVATE PLACEMENTS OF CALIFORNIA BONDS, AND THAT WE ARE PREPARED TO TAKE QUESTIONS ON THAT IF YOU WISH, BUT WE HAVE A DEGREE OF CONFIDENCE THAT THAT CAN BE ACHIEVED. AND THAT WHILE OUR PROGRAMS MIGHT BE CUT DOWN A BIT IN THE

SHORT TERM AS A CASH-FLOW PROBLEM, WE BELIEVE THAT WE WILL EITHER BE CLOSE ON TRACK, OR THERE WILL BE SOME MINOR ADJUSTMENTS TO ACCOMMODATE THE FUNDS THAT WILL BE AVAILABLE TO US IN THE NEXT TWO YEARS.

AVERAGE AWARD AMOUNTS SHOWN IN THE SEED, COMPREHENSIVE, NEW CELL LINES, TOOLS AND TECHNOLOGIES, NEW FACULTY. THEY'RE ON THE OTHER SIDE OF THE SCALE FOR NIH FUNDING. NIH TENDS TO AWARD A LITTLE LESS THAN THAT, BUT WE'RE NOT THAT FAR AWAY FROM THE NIH FUNDING. SO THOSE PEOPLE WHO ARE INTERESTED IN HOW MUCH THE AWARDS ARE, THIS GIVES YOU SOME IDEA OF WHAT THE YEARLY AWARDS THAT HAVE BEEN MADE.

IN THE CASE OF THE TRANSLATIONAL STUDIES, WE'RE PREPARED TO AWARD UP TO SIX MILLION. AND IN THE CASE OF THE DISEASE TEAMS, WE'RE PREPARED TO AWARD UP TO 20 MILLION. THAT DOESN'T MEAN WE WILL DO THAT, BUT WE HAVE THE VIEW THAT IF THE STUDIES ARE GOOD ENOUGH, SOUND ENOUGH, AND PERSUASIVE, THEN WE WOULD GO THAT DISTANCE TO ENSURE THAT WE GET TO THE CLINIC ON TIME.

THE STEM CELL PATHWAYS ARE SET OUT HERE. WE HAVE A LOT OF OPTIONS. THE CELL THERAPIES, INCLUDING TRANSPLANTATION, DO INCLUDE THE PROBLEM WE HAVE WITH TRANSPLANTING ALLOGENEIC CELLS. THIS IS A

REAL ISSUE WHICH THE REVIEWERS HAVE CONFRONTED US WITH IN REVIEWING THE GRANTS AT THE PRESENT TIME. WE WILL GO TO AN IMMUNOLOGY RFA PROGRAM TO TRY AND SEE IF WE CAN DRAW THE BASIC IMMUNOLOGISTS AND THE CLINICAL IMMUNOLOGISTS INTO EITHER THE PROGRAM WITH US IN STEM CELLS. THE ISSUE OF TOLERANCE, I THINK, IS A VERY IMPORTANT ONE IF YOU'RE GOING TO START PUTTING ALLOGENEIC CELLS INTO PATIENTS. AND THAT IS SOMETHING YOU NEED TO ADDRESS, OTHERWISE WE MAY HAVE A STALL IN SOME OF THE CELL THERAPIES UP AT THE APPLICATION END.

DRUG DISCOVERY AND ENVIRONMENT, TOXICOLOGY, BOTH OF THOSE ARE IMPORTANT. I THINK THE DRUG DISCOVERY IN THE SMALL MOLECULES IS GOING TO BE THE FAST RUN SECTOR OF THE WORK WE FUND TO THE CLINIC. YOU'VE GOT GENE THERAPY AS AN OPTION HERE. IT REALLY HASN'T DRAWN SUCH A LOT OF ATTENTION, BUT THE CELLS THAT WE GET TRANSFERRED TO THE PATIENTS THAT ARE BETTER TARGETED TO SPECIFIC ORGANS COULD CONTAIN PRODUCTS THAT WOULD REVERSE THE GENETIC DISEASE. AND, OF COURSE, THE WHOLE AREA OF TISSUE ENGINEERING IS A VERY STRONG AND IMPORTANT AREA FOR CELLULAR TRANSPLANTATION. AND IT'S LIKELY THAT A LOT OF THE CELLS THAT WE'LL TRANSPLANT WILL HAVE TO HAVE SOME DEGREE OF ENGINEERING.

ONE OF THE PRIMARY TARGETS SET FOR CIRM, THESE ARE THE ONES THAT WE UNDERSTAND ARE REALLY HIGHEST ON OUR RADAR. THE BASIC DISCOVERIES OF STEM CELL BIOLOGY, WE BELIEVE, ARE THE IMPORTANT THINGS EMANATING FROM THE BASIC SCIENCE ALL THE TIME. TOOLS AND TECHNOLOGIES, VERY IMPORTANT TO HELP THE SCIENTISTS BOTH AT THE BASIC AND TRANSLATIONAL LEVEL TO GARNER THE DATA NECESSARY. NEW MOLECULES AND THERAPY APPLICATIONS BASED ON STEM CELL RESEARCH AND MOBILIZATION OF ENDOGENOUS STEM CELL TISSUE IS STILL AN IMPORTANT PART OF WHAT WE CONSIDER.

IDENTIFICATION OF ABERRANT STEM CELLS THAT COME AS CANCER STEM CELLS IS REALLY QUITE AN IMPORTANT PART OF OUR PORTFOLIO AT THE MOMENT. AND WHILE I RECOGNIZE THERE ARE ARGUMENTS ABOUT WHAT IS A CANCER STEM CELL, IT IS IMPORTANT, IT HAS BEEN INDICATED STRONGLY THROUGH THE COMMUNITIES AS AN IMPORTANT TARGET FOR OUR WORK, SO THERAPIES, OF COURSE, GENE THERAPIES AND TISSUE RECONSTRUCTION.

I THINK THE IMPORTANT PART OF THINKING ABOUT THIS IS THAT THERE ARE A NUMBER OF REAL GENUINE OPPORTUNITIES APART FROM THE OBVIOUS CELL THERAPIES. STEM CELL MOBILIZATION IS LIKELY TO FLOW FROM A BETTER UNDERSTANDING OF STEM CELL TYPE AND WHAT HOLDS THEM IN THE TISSUE AND WHAT RELEASES THEM

INTO MOBILIZATION IS BECOMING MORE AND MORE IMPORTANT. AND IPS CELLS ARE PRETTY IMPORTANT IN THAT PARTICULAR AREA ALONG WITH PERSONALIZED MEDICINE.

AND THE SMALL MOLECULE WORK, WHICH IS DRIVING VERY RAPIDLY OUT OF SOME OF THE BIG HIGH THROUGHPUT CAPACITY INSTITUTES IS BRINGING FORWARD MANY, MANY CANDIDATES THAT COULD BE VERY EFFECTIVE IN TISSUE REGENERATION. AND THE AWARENESS OF THESE AREAS WHICH ARE MOVING, I THINK, IS SOMETHING THAT WE NEED TO RECOGNIZE.

IN TERMS OF THE WAY WE SEE THE RELEASE OF OUR RFA'S, I PUT SOME BLUES ON SOME OF THEM THAT WE SEE EVOLVING. THAT IS, WE WOULD TAKE EVERY 12 TO 18 MONTHS AND HAVE IT AS A CORE. THAT WOULD BE THE EARLY TRANSLATIONAL RESEARCH, DISEASE TEAMS, AND BASIC SCIENCE INNOVATION STUDIES. BUT ALONG WITH THAT THERE ARE TRAINING GRANTS AND TOOLS AND TECHNOLOGIES WHICH WE WOULD DO IN A MULTIPLICATIVE WAY IN RESPONSE TO THE COMMUNITY'S VIEWS ABOUT HOW OFTEN WE SHOULD RUN THOSE. WE DON'T NECESSARILY SEE THAT THOSE SHOULD BE YEARLY, BUT THEY SHOULD BE MADE AVAILABLE IN RESPONSE TO THE NEEDS.

WE SEE THE HARD CORE, IF YOU LIKE, BEING IN TRANSLATION, DISEASE TEAMS, AND THE BASIC

SCIENCE. AND THAT'S THE WAY WE'RE FORMATTING IT. WE HOPE YOU UNDERSTAND THAT BETTER AND GIVE YOU A BETTER IDEA OF WHAT'S COMING FORWARD. IT WILL ENABLE SCIENTISTS WHO DON'T GET THE GRANTS TO TAKE THE REVIEWS AND REEXAMINE THEM FOR BEING ABLE TO IMPROVE THEM FOR THE NEXT TIME.

THE CLINICAL PROGRAMS SIT THERE AS AN OPPORTUNITY. I THINK WE NEED TO RECOGNIZE WHEN WE SHOULD GO TO THE CLINIC, AND IMMUNOLOGY IS A ONE-OFF AT THIS STAGE, TO SEE IF WE CAN STIMULATE THAT AREA.

WHERE ARE WE IS A GOOD QUESTION NOW THAT NIH HAS ENTERED THE FIELD WITH A CHANGE IN THE ADMINISTRATION SORT OF VIEW TOWARDS EMBRYONIC STEM CELL RESEARCH. WE THINK THAT THERE WILL BE A LOT MORE MONEY COMING TO BASIC FROM NIH. WE ALSO BELIEVE THAT BIG PHARMA IS BACKING UP TO THIS AREA. THEY'RE TAKING THE OPPORTUNITY TO LOOK AT PARTNERSHIPS. I THINK THEY WILL BE INVOLVED IN TRADES, BUY-INS, MERGERS, AND SO FORTH TO TAKE SUCCESSFUL BIOTECH COMPANIES AND DRAW THEM INTO THEIR OWN PROGRAMS.

SO WE SIT IN THIS NICHE. IS IT A REALLY APPROPRIATE NICHE FOR US TO HAVE IN THE SO-CALLED VALLEY OF DEATH OR VALLEY OF OPPORTUNITY? IT'S JUST A MATTER OF WHICH WAY YOU THINK ABOUT IT. I THINK

THERE IS A NICHE THERE, BUT I DON'T SEE WHY WE SHOULD EXIT FROM EITHER THE BASIC OR THE CLINICAL END UNNECESSARILY UNLESS THERE'S SUFFICIENT SUPPORT IN BOTH THOSE SECTORS. BUT AN IDEAL NICHE FOR CIRM MAY WELL BE IN THIS AREA BETWEEN THOSE TWO WHERE MANY THINGS FAIL FOR ALL SORTS OF REASONS AND GOOD IDEAS GO AGROUND OR NOT DEVELOPED AT THE RATE THAT WE WOULD HOPE.

GLOBAL PARTNERSHIPS WITH COLLABORATION WITH VICTORIA WHICH SORT OF CAME INTO OUR TRANSLATIONAL PROGRAMS. WE HAVE THE UK, SPAIN, AND JAPAN, AND CANADA. CANADA THROUGH CANCER, THE CANCER STEM CELL CONSORTIUM, AND THE JDRF HAVE ALL COME TOGETHER. THEY WILL PROVIDE, IF THE SCIENTISTS MAKE APPLICATIONS TOGETHER FOR FUNDING WITHIN THE RFA'S AND THOSE PROJECTS ARE AWARDED AT THE TOP LEVEL, WE'LL PAY FOR THE CALIFORNIA PART AND THE OTHERS WILL PAY FOR THE BRITISH PART OR THE CANADIAN PART.

HERE'S A WAY OF ACTUALLY BUILDING CAPACITY WITHOUT REALLY INTERFERING WITH THE WAY THE SCIENCE IS DONE IN THESE DIFFERENT AREAS. SO AN OPPORTUNITY, IF YOU LIKE, FOR CALIFORNIA TO TAKE EVEN MORE LEADERSHIP, BUT ALSO BE ABLE TO UTILIZE THE VERY SPECIAL CAPACITY THAT SITS OUTSIDE

CALIFORNIA. WE BELIEVE WE MAY HAVE ABOUT TEN OF THESE MOU'S OR AGREEMENTS TO WORK TOGETHER. AND WE ARE RESPONDING TO THE SCIENTISTS BECAUSE IT ONLY WORKS IF THE SCIENTISTS ARE PREPARED TO COME TOGETHER AND MAKE AN APPLICATION.

SO THAT'S THE KIND OF FRAMEWORK THAT WE'RE WORKING. WE WOULD LIKE SOME FEEDBACK ON WHAT YOU THINK ABOUT THESE THINGS, AND WE HOPE THAT THERE WILL BE SUFFICIENT TO THINK ABOUT WHAT I'VE SAID AND SOME QUESTIONS THAT MICHAEL HAS. I WANT TO PASS OVER TO OWEN WITTE. OWEN WE'VE ASKED TO COME ALONG BECAUSE HE'S ACTUALLY BEEN AT THIS BUSINESS OF GOING FROM THE BENCH TO THE BEDSIDE. HE'S A SCIENTIST WHO'S BEEN VERY SUCCESSFUL IN THIS. HE'S SOMEBODY WHO KNOWS THE TRACK, HAS BEEN UP AND DOWN THIS TRACK, AND THIS IS A PLACE WHERE WE WANT TO BE. AND WE WOULD LIKE TO HEAR FROM HIM HOW HE SEES THIS SPACE BETWEEN THE BASIC SCIENCE AND THE CLINIC AND HOW WE SHOULD SORT OF POPULATE THAT AND MAYBE GIVE US SOME EXAMPLES FROM HIS OWN WORK. OWEN.

DR. WITTE: MORNING, EVERYONE. ALAN, THANK YOU FOR THE INVITATION TO SPEAK. I HAD TO INFORM ALAN THAT DUARTE IS NOT GENERALLY CLOSE TO WEST LOS ANGELES, BUT I MADE IT HERE ANYWAY.

WITH THAT OVERVIEW THAT ALAN PROVIDED,

THERE ARE SOME MAJOR ISSUES TO THINK ABOUT AND THEY HAVE TO DO WITH TRANSITIONS. AND AS A BASIC SCIENTIST WITH A MEDICAL DEGREE, I'VE ALWAYS BEEN INTERESTED IN APPLYING WHAT WE LEARN IN THE LABORATORY INTO THE CLINIC. WHAT I WANT TO DO TODAY IS SHOW YOU THREE EXAMPLES FROM MY OWN WORK, WHICH IS CLEARLY I HAVE AN INTIMATE INVOLVEMENT WITH ALL THE THINGS I'LL TELL YOU ABOUT IN WHICH WE HAVE PROVIDED INFORMATION OR SPECIFIC TECHNOLOGY OR EXPERTISE THAT HAS CONNECTED THE BENCH TO THE BEDSIDE.

WHAT'S INTERESTING TO ME, AS I SAT DOWN TO PREPARE THIS, I HADN'T REALLY CONTEMPLATED HOW DIFFERENT EACH OF THE EXAMPLES WERE, BOTH IN THEIR TIMING, AND THEY ALL TAKE A LONG TIME, AND THE WAY THAT THINGS WERE FINANCED FOR THESE TRANSITIONS.

SINCE I'M GOING TO TALK ABOUT THINGS THAT INVOLVE ME AND THEY INVOLVE EVENTUALLY COMPANIES AND ACCESS TO THE PUBLIC, I NEED TO SHOW YOU ALL OF MY POTENTIAL CONFLICTS, AND THEY'RE LISTED HERE. AND THE BASIC IDEA IS THAT WHEN WE HAVE SOMETHING THAT MIGHT BE CLINICALLY VALUABLE, I THINK IT'S VERY IMPORTANT TO FILE PATENTS ON IT BECAUSE OTHERWISE NO ONE WILL BE INTERESTED IN DEVELOPING IT TO THE STAGE OF BRINGING IT TO THE PUBLIC. AND I PARTICIPATED IN

THE BIOTECHNOLOGY INDUSTRY, AND I HOPE TO PARTICIPATE AGAIN FOR SOME OF THE LATTER WORK I'LL SHOW YOU.

FIRST CASE, THIS GOES BACK A WAYS. IT HAS TO DO WITH DEFINING THE ENZYME TARGET FOR THE MOLECULAR PATH OF CERTAIN LEUKEMIAS. WE STARTED ACTUALLY BACK IN THE 1970S, LATE '70S. I WAS A POSTDOCTORAL FELLOW WITH DAVID BALTIMORE. SOME OF YOU MAY REMEMBER THE WAR ON CANCER WHICH FUNDED A LOT OF VERY GOOD BASIC WORK ON GENES THAT MIGHT REGULATE A CANCER PHENOTYPE.

ONE OF THOSE GENES IS CALLED ABL, A-B-L, NAMED AFTER A PEDIATRIC ONCOLOGIST HERB ABELSON, WHO DISCOVERED THE VIRUS, GAVE IT HIS OWN NAME, AND THEN GENE FROM THAT VIRUS TURNED OUT TO BE OBVIOUS NAME CALLED ABL. IT WAS SOMETHING I STUDIED AS A POSTDOCTORAL FELLOW, CAME TO UCLA, AND ONE OF MY FIRST GRADUATE STUDENTS, JEAN KONOPKA, MADE THIS AT THE TIME REALLY STARTLING OBSERVATION, HERE SHOWN IN PANEL B FROM THIS PAPER AND THIS FIGURE, THAT THERE WAS AN UNUSUALLY LARGE FORM OF THE ABL ONCOGENE, A SPECIFIC CELL LINE K562 THAT HAD A VERY, VERY HIGH LEVEL OF AT THAT TIME SOMEWHAT UNIQUE AND POORLY UNDERSTOOD ENZYME CALLED TYROSINE KINASE.

THIS PARTICULAR OBSERVATION UNIFIED QUITE

A WIDE VARIETY OF OBSERVATIONS IN THE FIELD IN THE EARLY 1980S THAT EXPLAINED HOW A SPECIFIC CHROMOSOME TRANSLOCATION COULD CREATE WHAT'S CALLED A CHIMERIC GENE PRODUCT THAT HAS AN ACTIVATED TYROSINE KINASE AND IS ASSOCIATED WITH A VERY SPECIFIC TYPE OF LEUKEMIA.

ONE IMMEDIATELY KNEW THAT THIS WAS THE TARGET THAT YOU WANTED TO GO AFTER FOR THIS DISEASE, AND A WHOLE LOT OF WORK FROM A LOT OF LABORATORIES, MY OWN INCLUDED, SHOWED THAT THIS GENE PRODUCT CAUSED THIS DISEASE IN A VARIETY OF ANIMAL MODELS, ALL SUPPORTED IN THEIR WORK BY NIH AND EVENTUALLY BY HOWARD HUGHES MEDICAL INSTITUTE.

I WENT TO EVERY MAJOR PHARMACEUTICAL COMPANY I COULD GET ACCESS TO, AND I TOLD THEM THIS MOLECULE IS WHAT YOU WANT TO HIT WITH AN INHIBITOR. THEY ALL SAID THE SAME THING. IT'S NOT OUR PATIENT WITH THIS DISEASE, AND WE CAN'T MAKE INHIBITORS FOR THIS FAMILY OF ENZYMES. VERY NEGATIVE. VERY POLITE, BUT VERY NEGATIVE. SO I THINK THE KEY HERE IS THAT IT TOOK SOME OTHER EVENTS TO OCCUR BEFORE A FAMILY OF DRUGS DEVELOPED FIRST BY NOVARTIS AND NOW BY VARIOUS PHARMACEUTICAL COMPANIES SO THESE TYROSINE KINASES COULD BECOME AVAILABLE TO THE PUBLIC.

THIS PROCESS FROM PRIMARY DISCOVERY, THE CLASS OF ENZYMES AROUND THE LATE 1970S, EARLY 1980 UNTIL THE USE OF THIS CLASS OF COMPOUNDS IN PEOPLE, FOR EXAMPLE, GLEEVEC IN THE FIRST CLINICAL TRIAL BY BRIAN DRUKER AND CHARLES SAWYERS TOOK ABOUT 20 PLUS YEARS AND WANTED TO TRY TO SHORTEN THAT TIME SCALE. HOW COULD WE DO THAT? PERHAPS THAT'S GOOD FOR THE QUESTIONS.

SO THAT'S THE FIRST STORY. TWENTY YEARS, BASIC SCIENCE OBSERVATION, NOT MUCH INTEREST FROM THE PHARMACEUTICAL INDUSTRY UNTIL OTHER EVENTS TOOK OVER SOME HAPPENSTANCE AND GOOD LUCK AND SOME GOOD PEOPLE SEEING SOMETHING AND EVENTUALLY PUT IT INTO CLINICAL TRIALS.

IN THE MID-1990S I GOT INTERESTED FOR PERSONAL FAMILY REASONS IN PROSTATE CANCER AND SWITCHED A LARGE PORTION OF MY EFFORTS TO STUDY THAT DISEASE. ONE OF THE FIRST THINGS WE DID WAS A FEW OF US AT UCLA, CHARLES SAWYERS, MYSELF, ROB REITER, AND OTHERS GOT TOGETHER AND DECIDED WHAT WE WOULD LOOK FOR WOULD BE TARGETS FOR MONOCLONAL ANTIBODY THERAPY. IT SEEMS TRIVIAL NOW TO THINK ABOUT THAT STRATEGY, BUT IN THE MID-1990S, THAT WAS NOT SO POPULAR. WE FELT THAT THE RESURGENCE OF MONOCLONAL ANTIBODY WORK, THAT THIS WOULD BE A REASONABLE THING

TO DO.

IT WAS ALSO NOT AVAILABLE IN THAT FIELD AT THE TIME VERY GOOD BIOLOGICAL MODELS FOR STUDYING THIS DISEASE AND ITS PROGRESSION. SO IN A COLLABORATIVE WITH CHARLES SAWYERS AND ROB REITER, WE PRODUCED A SERIES OF BIOLOGICAL MODELS WHICH WE COULD OBSERVE THE DIFFERENT STAGES OF PROSTATE CANCER. WE USED THOSE MODELS AND OTHER TOOLS THAT WERE AVAILABLE AT THE TIME TO ISOLATE A SERIES OF ANTIGENS THAT WERE PREFERENTIALLY EXPRESSED AT HIGH LEVEL ON PROSTATE CANCER, PARTICULARLY AS IT PROGRESSED, BUT ONE OF THEM, WHICH WE CALL PSCA, THE PROSTATE STEM CELL ANTIGEN, IS A CLOSE RELATIVE OF A STEM CELL FOUND ON HEMATOPOETIC STEM CELLS AND A VARIETY OF OTHER CELL TYPES.

NOW, THIS WORK WAS ALL FUNDED BY NIH AND HOWARD HUGHES MEDICAL INSTITUTE AND OTHER SOURCES. IT WAS VERY ACADEMIC; BUT WE KNEW THAT IN ORDER TO GET IT FURTHER, WE WOULD HAVE TO TAKE IT INTO A CORPORATE SETTING BECAUSE THE AMOUNT OF MONEY NEEDED TO BOTH PRODUCE THE REAGENT AND TEST IT WERE WELL BEYOND WHAT WE COULD DO IN OUR CLINICAL SETTING AT UCLA EVEN WITH LOTS OF PEOPLE INTERESTED IN HELPING.

SO I'VE SUMMARIZED HERE A TIMELINE OF A COMPANY WHICH I WAS A CO-FOUNDER AND CHAIRMAN OF THE

SCIENTIFIC ADVISORY BOARD CALLED AGENSYS. THE ORIGINAL NAME WAS AGENSYS. IT WAS FOUNDED IN 1997 BY GROUP OF UCLA FACULTY AND A VERY EXPERIENCED BUSINESS EXECUTIVE. THE COMPANY HAS GROWN. WE NOW HAVE OVER A HUNDRED EMPLOYEES. ONE OF THE IMPORTANT THINGS HERE IS FOR THE ECONOMICS OF CALIFORNIA, IT'S GOOD TO FORM COMPANIES AND PRODUCE THINGS AND EMPLOY PEOPLE. AND I THINK A VERY IMPORTANT DECISION WAS MADE TO HAVE ITS OWN GMP PRODUCTION FACILITY FOR THIS COMPANY. NOT MANY YOUNG COMPANIES MAKE SUCH A DECISION BECAUSE IT'S QUITE EXPENSIVE.

OVER THE COURSE OF TIME, THERE HAVE BEEN SIX MAJOR RESEARCH AND DEVELOPMENT DEALS WITH MAJOR PHARMA COMPANIES OVER THE LAST DECADE OR SO. AND THE COMPANY MAINTAINED A PRIVATELY HELD STATUS, I WENT THROUGH ALL THE PRESS RELEASES, WELL OVER $100 MILLION IN TOTAL INVESTMENT IN A TEN-YEAR PERIOD. IT WAS RECENTLY ACQUIRED BY A JAPANESE PHARMACEUTICAL COMPANY, ASTELLAS, FOR ABOUT $400 MILLION, AND CERTAINLY A GOOD ECONOMIC OUTCOME FOR ALL THE INVESTORS AND PARTICIPANTS.

AND ITS FIRST IDENTIFIED TARGET INTELLECTUAL PROPERTY THAT ENABLED A COMPANY TO BEGIN DEVELOPMENT IS IN EARLY PHASE CLINICAL TESTING. SO HERE'S TEN YEARS, $100 MILLION IN

INVESTMENT, EVENTUALLY PROFITABLE INVESTMENT, BUT YET NOT EVEN BRINGING THE FIRST INTELLECTUAL PIECE OF PROPERTY THROUGH THE CLINIC AND INTO HUMAN USE AND CARE. THEY HAVE MANY OTHER DISCOVERIES. THEY HAVE A DISCOVERY PIPELINE AND SO ON. IT'S NOT AN ADVERTISEMENT FOR THEM.

AT THIS POINT SOMETHING HAS HAPPENED WHICH, I THINK, ANYBODY IN THE AUDIENCE WHO HAS BEEN INVOLVED IN THE BIOTECH INDUSTRY WILL APPRECIATE, AT THIS POINT THEY DON'T NEED THE FOUNDERS ANYMORE. SO I HAVE ALMOST NOTHING TO DO WITH THE COMPANY. I ONLY LEARN ABOUT IT BY LOOKING FOR PRESS RELEASES AND SEEING WHAT'S HAPPENING ON THE WEBSITE. ALTHOUGH THAT WAS IN A SENSE MY DISCOVERY, I NO LONGER CONTROL THAT DISCOVERY BECAUSE IT HAD TO BE PASSED OFF TO THE BIOTECH INDUSTRY TO SEE WHAT WOULD HAPPEN. SO I WISH THEM WELL. THE PSCA ANTIBODIES WILL FIND A PLACE IN CANCER THERAPY FOR PROSTATE, PANCREAS, AND OTHER DISEASES.

THE THIRD TYPE OF CASE STUDY THAT WE'RE CURRENTLY INVOLVED WITH, AND THIS IS WORK THAT'S EVOLVING AND INVOLVES LOTS OF OTHER PEOPLE, IT'S TO TRY TO DEVELOP WHAT WE CONSIDER TO BE A VERY BROAD CONCEPT OF HOW TO TREAT CANCER USING IMMUNOTHERAPY OF A CELLULAR VARIETY. AND THIS IS SOMETHING THAT'S

RUN OVER THE LAST THREE OR FOUR YEARS WITH A GROUP OF COLLEAGUES HERE. AND WE'RE TAKING ACTUALLY SORT OF SOMEWHAT NARROWER ROLE IN TERMS OF BEING INTERESTED IN HOW WE IMAGE THE IMMUNE SYSTEM, BUT IT INVOLVES PEOPLE AT UCLA, CALTECH, USC, PIN WANG IS ACTUALLY HERE IN THE AUDIENCE TODAY, AND ONE COLLEAGUE FROM THE UNIVERSITY OF CONNECTICUT.

AND THIS PROGRAM BRINGS TOGETHER EXPERTISE FROM A WIDE VARIETY OF LABORATORIES AND IS BASED AROUND THE FOLLOWING PROBLEM, WHICH IS THAT IF YOU TAKE A DISEASE LIKE HUMAN MELANOMA, THE INCIDENCE SEEMS TO BE INCREASING, BUT THE SUCCESS IN THERAPY AS TRADITIONAL CHEMOTHERAPY MODES IS NOT. THIS IS ABOUT STAGE 4, STAGE 3 MELANOMA THAT IS NOT VERY RESPONSIVE TO CHEMOTHERAPY THAT WE CURRENTLY HAVE IN OUR COLLECTION OF TOOLS.

SO THE OBJECTIVE WAS TO CHANGE THAT AND TAKE ADVANTAGE OF THE BIOLOGICAL OBSERVATION THAT SOME MELANOMA PATIENTS, IF THEY'RE STIMULATED IN THEIR IMMUNE SYSTEM IN CERTAIN WAYS, CAN UNDERGO VERY DRAMATIC REGRESSION OF THEIR TUMOR AND QUITE STABLE IN THEIR DISEASE-FREE TIME. BUT THE PROBLEM IS THAT IT'S A VERY RARE EVENT, 4 OR 5 PERCENT IN MOST OF THE STUDIES. WHAT WE'D LIKE TO DO IS CAPTURE THE PRINCIPLE BY WHICH THE PATIENTS CAN

REGRESS THEIR TUMORS AND STAY STABLE, WHICH IS THE T-CELL, KILL THE T-CELL BASED ON THE SPECIFIC T-CELL RECEPTORS.

A TREMENDOUS AMOUNT OF WORK HAS ALREADY BEEN ACCOMPLISHED BY THIS GROUP IN THE FIELD, AND SUCH T-CELL RECEPTORS HAVE BEEN IDENTIFIED IN MELANOMA SPECIFIC KILLERS. THEY'VE BEEN ABLE TO BE CLONED BY WORK BY DAVID BALTIMORE AND ASSOCIATES, AND ABLE TO TRANSPLANT THOSE INTO VARIOUS MODEL SYSTEMS TO DEMONSTRATE THAT THAT IS THE ACTIVE PRINCIPLE. AND THE IDEA WOULD BE THAT IF YOU CAN GIVE EVERY PATIENT THE RIGHT T-CELL RECEPTOR AT A HIGH ENOUGH AMOUNT, YOU'LL BE ABLE TO CHANGE THE BALANCE BETWEEN THE IMMUNE SYSTEM OF THE TUMOR.

IN ORDER TO DO THAT YOU'VE TAKEN THIS FROM BASIC SCIENCE STUDIES ALL THE WAY UP TO RIGHT NOW CLINICAL TRIALS AT UCLA WHICH WE'RE USING OUR EXTENSIVE GMP FACILITY PARTIALLY SUPPORTED AND RENOVATED RECENTLY WITH MONEY FROM CIRM TO DO THIS. AND THE OVERALL STRATEGY WOULD BE TO TAKE EITHER PERIPHERAL BLOOD T-CELLS, WHICH ARE THE FIRST TRIALS WE HAVE TO DO TO DEMONSTRATE SAFETY BECAUSE THAT'S THE STANDARD OF THE FIELD CURRENTLY.

BUT OUR NEXT MOVE IS TO TAKE BLOOD STEM CELLS OR STEM CELLS, BLOOD STEM CELLS DERIVED FROM

IPS CELLS, FOR EXAMPLE, AND TRANSPLANT INTO THEM BY GENETIC MEANS USING MOST LIKELY BLENDING VECTORS INTO THOSE CELLS, THE SPECIFIC MELANOMA REACTIVE TCR WHICH HAVE TO BE SPECIALLY BLENDED, IF YOU WILL, TO THE IMMUNE STRUCTURE OF THE PATIENT TO THEIR OWN COMPATIBILITY LEVELS. AND THEN USE A VARIETY OF TECHNIQUES CALLED PET, POSITRON EMISSION TOMOGRAPHY, TO FOLLOW THOSE CELLS. AND THIS IS ONE OF THE MOST IMPORTANT THINGS I CAN SAY TO YOU TODAY IS THAT IF YOU DO SUCH THERAPIES AND YOU DO NOT AT THE SAME TIME DEVELOP ANALYTICAL PROCEDURES TO ASSESS THE OUTCOME, THEN YOU NEVER UNDERSTAND WHY AN EXPERIMENT FAILS AND, HENCE, YOU CANNOT MAKE IT BETTER.

I THINK IT'S VERY GOOD THAT THE TOOLS AND TECHNOLOGY COMPETITION FUNDED A VARIETY OF GRANTS THAT ARE AIMED AT EXACTLY THIS SORT OF DEMONSTRATION AND FOLLOWING OF THE CELLS USED IN SUCH TRANSPLANTATION MODALITIES. VERY STRONGLY, YOU HAVE TO HAVE THAT IN PARALLEL.

THESE STUDIES ARE ACTUALLY JUST UNDER WAY AND ACTUALLY HAVE AN IND THAT WAS FILED ON IT. THE REGULATORY PHASE IS COMPLETE TO DO THIS TRANSPLANT, NOT INTO BLOOD STEM CELLS, BUT CONVERT T-CELLS FROM THOSE PATIENTS WE'VE RECRUITED CURRENTLY.

IN ORDER TO DO THIS IN THE SETTING OF AN

ACADEMIC MEDICAL CENTER, YOU HAVE TO A GMP-QUALIFIED CELL PROCESSING FACILITY. THERE ARE NOT ENOUGH OF THOSE FACILITIES, IN MY MIND, IN THE STATE OF CALIFORNIA TO DO MANY SUCH TRIALS. THERE ARE SOME EXCELLENT ONES. THERE'S SOME EXCELLENT ONES HERE. WE HAVE RECENTLY RENOVATED AND UPGRADED OUR FACILITIES TO ABOUT 5,000 SQUARE FEET OF SPACE, MULTIPLE ROOMS FOR MULTIPLE TRIALS SIMULTANEOUSLY, AND ALSO BUILT OUR IPS AND ES FACILITIES WITHIN THIS STRUCTURE WHERE, AS WE BEGIN TO DEVELOP IPS LINES AND ES LINES UNDER THIS FACILITY, IT WILL BE DONE IN A GMP-COMPATIBLE MANNER.

IN THE PROCESS OF THINKING ABOUT THIS IMMUNE THERAPY, WE ALSO BEGAN TO THINK ABOUT HOW TO TAKE INFORMATION WE WERE INTERESTED IN CONCERNING MONITORING AND MEASURING THE IMMUNE SYSTEM TO JOIN UP WITH THESE CLINICAL TRIALS. AND THIS IS A PAPER THAT WAS RECENTLY PUBLISHED FROM AN ACADEMIC COLLABORATION IN MY LAB WITH MIKE PHELPS AND C.G. RADU, WHO'S AN ASSISTANT PROFESSOR FELLOW WITH ME AND NOW IS INDEPENDENTLY WORKING IN SOME GROUP, ON A NEW CLASS OF POSITRON EMISSION TOMOGRAPHY.

HOW WE GOT THERE IS AN INTERESTING STORY. WE DON'T HAVE TIME FOR IT TODAY, BUT THE IMPORTANT POINT IS THAT THIS PROBE IS NOT TOTALLY SELECTIVE

FOR SEEING IMMUNE CELLS. IT SEE OTHER CELLS AS WELL, BUT IT'S ENHANCED IN IMMUNE SITES. FOR EXAMPLE, THIS IS A MOUSE. THAT'S THE IMAGE HERE. THERE'S A TUMOR, THE TU IS MARKED. THE TUMOR TAKES UP THIS PROBE LARGELY BECAUSE IT'S INFILTRATED WITH LYMPHOCYTES AND MACROPHAGES AS PART OF THE IMMUNE RESPONSE. THEY'RE TRAILING THE LYMPH NODE FROM THE SHOULDER DOWN TO THE AXILLARY AREA. IT'S DRAMATICALLY ACTIVATED AND PICKS UP A LOT OF THE PROBE, AND THERE'S DISTANT STIMULATION OF ANTIGEN TO SITES LIKE THE SPLEEN AND THE GUT LINING AS SHOWN HERE.

SO WE THINK THAT THIS TYPE OF PROBE COULD BE VERY USEFUL IN MONITORING SOME NEW THERAPY THAT WE'RE GOING TO DO IN PATIENTS, BUT THAT NEEDS TO BE TESTED, AND WE THINK IT MIGHT HAVE GREAT VALUE ALSO FOR MONITORING OTHER AUTOIMMUNE DISEASES.

WHAT'S THE SENSITIVITY? WHAT'S THE LIMITATION? ALL THESE THINGS NEED TO BE FIGURED OUT, AND THE GAME PLAN IS TO FIRST SEE IF IT HAS ANY UTILITY IN HUMANS BECAUSE THAT VALLEY OF DEATH THAT ALAN TALKED ABOUT, IF YOU GO TALK TO VENTURE CAPITALISTS OR PHARMACEUTICAL COMPANIES, THEY ALWAYS ASK YOU THE SAME QUESTION. DOES IT WORK IN PEOPLE BECAUSE A MOUSE IS NOT A PERSON. A MOUSE IS WHAT WE

USE TO THINK ABOUT SOMETHING TO GET TO TEACHING US SOMETHING ABOUT HOW IT MIGHT WORK IN PEOPLE.

WITH RADIOACTIVE PROBES FOR PET SCAN, IT WAS QUITE INTERESTING. THERE'S A VERY NICE MECHANISM TO TAKE SUCH PROBES AND TO QUALIFY THEM FOR GMP-CERTIFIED PRODUCTION AND THEN TEST THEM THROUGH A PHYSICIAN IND AT THE LOCAL LEVEL TO FIRST ASSESS THEIR GENERAL QUALITY. THIS IS WORK DONE BY JOHANNES CZERNIN. HE'S THE HEAD OF OUR NUCLEAR MEDICINE DEPARTMENT. USING THIS FAC-TYPE PROBE, IT'S AN INTERESTING CASE BECAUSE WE COULDN'T REALLY DETERMINE WHAT KINDS OF PATIENTS YOU WOULD USE IT ON INITIALLY BECAUSE WE DIDN'T HAVE A TRIAL IN MIND. WE HAD AN IDEA TO ASCERTAIN IF THE PROBE HAD ANY VALUE. BUT IT TURNED OUT THAT THE DAY THAT THIS PROBE MANUFACTURER, IT'S NOT EVERY DAY, A PATIENT CAME IN WITH PANCREATITIS, WITH A DIFFERENTIAL DIAGNOSIS OF PANCREATITIS IN A 56-YEAR-OLD SMOKER. IT'S USUALLY, UNTIL PROVEN OTHERWISE, CANCER. AND SO ONE OF THE THINGS YOU WOULD DO FOR SUCH A PATIENT IS YOU WOULD DO AN FDG SCAN FOR PANCREATIC OR EPITHELIAL CANCERS.

THAT FDG SCAN, HOWEVER, WAS NEGATIVE IN THIS PATIENT. AND THE PROCESS FAC WAS AVAILABLE AND ALREADY AUTHORIZED FOR USE. PATIENT CONSENTED TO

HAVING AN FAC SCAN, AND HERE THE HEAD OF THE PANCREAS TURNS UP QUITE BRIGHTLY. AND LATER, BECAUSE OF THIS COMBINATION DATA AND CONFUSION AS TO WHAT THE PATIENT MIGHT HAVE, THE PATIENT WENT TO BIOPSY WHERE THE DIAGNOSIS WAS MADE OF AUTOIMMUNE PANCREATITIS.

NOW, THIS IS A PERSON, THE BEST EXAMPLE, WORST EXAMPLE, THERE ARE PLENTY OF OTHER PATIENTS THAT HAVE BEEN EVALUATED WHERE WE CAN'T REALLY DISCERN MUCH WITH THIS PROBE, BUT THIS GIVES US HOPE THAT THIS WILL, IN FACT, BE SOMETHING THAT WE CAN MOVE ON TO THE CLINIC IN A VARIETY OF SETTINGS. IT MAY ALSO LEAD TO DESCRIBING PATIENTS WHICH CAN RESPOND TO CERTAIN CLASSES OF CHEMOTHERAPY WHICH ARE CLOSELY RELATED TO THE STRUCTURE OF THIS PROBE.

SO JUST IN SUMMARY, LET ME SAY, AND, AGAIN, THIS SORT OF A MESSAGE TO THOSE OF YOU WHO HAVE A BIG DECISION ABOUT WHERE TO PUT THESE RESOURCES, THAT IT'S NOT CLEAR THAT THERE'S ANY SINGLE PATHWAY OR SET OF GOALS ONE CAN EVER ESTABLISH FOR MOVING SOMETHING FROM THE BENCH TO THE BEDSIDE AND INTO COMMERCIALIZATION SO IT'S BROADLY AVAILABLE.

I THINK YOU HAVE TO KIND OF MOVE FLUIDLY AND CONSIDER THERE'S A VARIETY OF OPTIONS.

CERTAINLY MICE BRINGS, IT'S VERY TIME-CONSUMING AND VERY EXPENSIVE. AND SO I DON'T THINK CIRM SHOULD BE IN A POSITION OF PUTTING UP ROADBLOCKS TO PREVENT PEOPLE FROM TRYING NEW METHODS FOR PUTTING UP THINGS THAT HELP THEM TRY TO DO ALTERNATIVES.

FIRST, DIFFERENT PATHWAYS, ACADEMIC BASIC RESEARCH TO CONNECT TO THE CLINIC AND ON TO COMMERCIALIZATION. AND ONE OF THE THINGS THAT I NOTICE AT UCLA AND OTHER CENTERS IS THAT THERE REALLY ARE SUCH DRAMATIC IMPROVEMENTS IN THE TECHNOLOGIES FOR SMALL MOLECULE SCREENING, HUMANIZED MONOCLONAL ANTIBODIES, DIAGNOSTIC IMAGING, AND GMP CELL PROCESSING IN A VARIETY OF ACADEMIC CENTERS THAT CERTAIN THINGS WE USED TO THINK YOU HAD TO DO WITH AN INDUSTRIAL PARTNER ARE NOW ACTUALLY QUITE DOABLE IN ACADEMIA, BUT PERHAPS NOT ON THE SCALE TO GET ALL THE WAY TO THE FINISH LINE, BUT MAYBE MOVE A LITTLE FURTHER THROUGH THAT PIPELINE.

FINALLY, THERE'S NO DOUBT THAT TO GET TO THE POINT OF HAVING CLINICAL DEMONSTRATION OF EFFICACY THAT YOU WILL THEN NEED TO TURN TO MUCH LARGER SOURCES OF CAPITAL TO MAKE THIS HAPPEN FOR THE POPULATION. HOWEVER, IF YOU CAN GET IT TO THE POINT WHERE YOU'RE SURE IT'S GOING TO WORK, THEN THERE'S A REASONABLE CHANCE AND PEOPLE WILL BEGIN TO

THINK ABOUT IT, THEN I REALLY DON'T THINK THERE'S GOING TO BE MUCH OF A SHORTAGE OF INTEREST FROM THE PHARMACEUTICAL COMPANY. BUT WHAT THEY ALWAYS ASK IS WILL IT WORK IN PEOPLE? IF WE CAN USE OUR FUNDS TO GET THAT FAR, THEN I THINK THE INTEREST LEVEL GOES UP DRAMATICALLY.

SO I'M DONE WITH MY PRESENTATION. AND I DON'T KNOW, ALAN, IF YOU WANT ME TO ANSWER QUESTIONS. BUT I JUST WILL SAY I TOLD ALAN I HAVE TO LEAVE PROBABLY AROUND 10:45, SO PLEASE DON'T THINK I'M IMPOLITE WHEN I ZOOM OUT OF HERE. I HAVE TO GET BACK TO UCLA FOR A MEETING ABOUT COMPETING FOR A CIRM GRANT.

DR. FRIEDMAN: WHAT I WOULD SUGGEST AT THIS POINT IS, ALAN, FOR OWEN TO HAVE THE OPPORTUNITY TO ENGAGE IN A PUBLIC DISCUSSION. THE GOAL HERE, JUST TO REITERATE, IS TO HAVE AS MUCH GUIDANCE AND SUGGESTION ABOUT WHERE THE STRATEGIC INITIATIVES FOR THE CIRM SHOULD GO OVER THE NEXT PERIOD OF TIME. AND YOU'VE HAD TWO OVERVIEW DISCUSSIONS THIS MORNING. THIS COUPLED WITH THAT AND A PREEXISTING KNOWLEDGE YOU HAVE ABOUT THE INITIATIVES AND ORGANIZATION SHOULD STIMULATE SOME QUESTIONS AND SOME COMMENTS.

YOU HAVE BEFORE YOU A SERIES OF CARDS

WHICH YOU'RE WELCOME TO FILL OUT IF YOU'D LIKE TO HAVE QUESTIONS WRITTEN DOWN TO ADDRESS. OBVIOUSLY IF YOU HAVE COMMENTS OR IF YOU WISH TO ASK THE QUESTIONS VOCALLY, PLEASE FEEL FREE TO DO SO. THERE ARE MICROPHONES AT THE BACK OF THE AUDITORIUM, AND WE CERTAINLY WELCOME A BROAD PARTICIPATION. AGAIN, FOR THOSE OF YOU WHO THINK YOU MAY HAVE QUESTIONS FOR OWEN, SINCE HE IS ON A SHORT TIME SCHEDULE, WE OUGHT TO PAY SPECIAL ATTENTION NOW.

DR. IVERSON: LINDA IVERSON. I READ THE STRATEGIC PLAN ON THE CIRM WEBSITE, AND I WAS TROUBLED BY THE FACT, WHICH I DON'T THINK IT WAS MADE IT HERE, THAT CIRM PLANS TO DOUBLE THE AMOUNT OF MONEY FOR DISEASE PLANNING OR EARLY TRANSLATIONAL. I'M AWARE OF THE FACT THAT CALIFORNIA TAXPAYERS DEMAND OR WOULD LIKE TO SEE SOME TRANSLATIONAL STEM CELL RESEARCH INTO THE CLINIC OF SOME DEMONSTRABLE THERAPEUTIC BENEFIT, BUT A LOT OF THIS RESEARCH IS NOT QUITE READY FOR PRIME TIME.

AND SINCE THIS MEETING IS AT THE CITY OF HOPE, I WOULD LIKE TO USE CITY OF HOPE AS A SPECIFIC EXAMPLE, IF I MAY. CITY OF HOPE IS SPONSORING RESEARCH OF A KNOWN ONCOGENE MYC TO IMMORTALIZE NEURAL STEM CELLS TO USE TO TREAT PATIENTS WITH

BRAIN TUMORS. A PAPER WAS PUBLISHED IN *PLOS MEDICINE* THREE WEEKS AGO, DEMONSTRATING THE FETAL NEURAL STEM CELLS GAVE RISE TO BRAIN AND SPINAL CORD TUMORS IN THE PATIENT. A CAREFUL CYTOGENETIC ANALYSIS DEMONSTRATED THAT IT WAS THE DONOR CELLS WHICH WERE DERIVED FROM FEMALES THAT PRODUCED THE TUMORS. THE PATIENT WAS MALE.

SO I AM CONCERNED ABOUT CIRM'S, IT SEEMS LIKE, A RADICAL DEPARTURE ON THE PART OF CIRM TO SHIFT MONEY THAT IS IN SHORT SUPPLY FROM WHAT MAY BE BASIC RESEARCH THAT IS REQUIRED AND IS ESSENTIAL FOR UNDERSTANDING WHAT THESE STEM CELLS CAN DO BEFORE THIS MONEY IS SPENT IN CLINICAL TRIALS THAT MAY PERHAPS BE ILL-ADVISED, ILL-CONCEIVED, AND PERHAPS EVEN DANGEROUS.

SECONDLY --

DR. FRIEDMAN: CAN WE SEE IF WE CAN FIELD ONE QUESTION.

DR. IVERSON: LET ME FINISH HERE. SO MY FIRST QUESTION IS WHAT SCIENTIFIC STANDARDS.

DR. FRIEDMAN: LET'S ADDRESS THAT ONE, THEN YOU'RE WELCOME TO ASK YOUR SECOND.

DR. IVERSON: I NEED TO LEAVE TO GO TO A MEETING ALSO. MY FIRST QUESTION IS WHAT SCIENTIFIC STANDARDS CIRM WILL ENACT IN ORDER TO ADDRESS THIS

NEW REVELATION IN THE FIELD OF STEM CELL RESEARCH.

I'M ALSO CONCERNED ABOUT GOVERNANCE AND ETHICAL STANDARDS. I UNDERSTAND THAT CITY OF HOPE EXECUTIVE IS A MEMBER OF THE -- CHAIR OF THE CIRM MAJOR FACILITIES SUBCOMMITTEE. AND SINCE CITY OF HOPE INVESTED A GREAT DEAL OF FUNDS IN A GMP FACILITY AND THERE'S A NEED FOR MORE GMP PRODUCTION CAPACITY, I'M WONDERING WHAT ETHICAL STANDARDS CIRM HAS ENACTED TO PREVENT ANY OR THE APPEARANCE OF A CONFLICT OF INTEREST FOR ANY CELL -- POTENTIALLY CELL HEALING TRANSACTIONS.

FINALLY, AND THEN I WILL FINISH, THERE WAS AN ARTICLE PUBLISHED IN THE *L.A. TIMES* THIS MORNING. THE U.S. SUPREME COURT RULED THAT THE FDA SEAL OF APPROVAL DOES NOT PROTECT A COMPANY FROM LAWSUITS ARISING FROM DANGEROUS DRUGS OR THERAPIES. DID YOU READ THE ARTICLE? IT WAS A SIX/THREE RULING THAT CAME OUT YESTERDAY.

SO AS SOMEONE WHO ALSO HAS EXPERIENCE IN THE BIOTECH INDUSTRY, I ALSO KNOW INVESTORS ARE, OF COURSE, INTERESTED IN THE BOTTOM LINE, BUT THEY'RE ALSO INTERESTED IN LIABILITY. LIABILITY CUTS INTO THE BOTTOM LINE.

IF CIRM IS NOW GOING TO PARTNER WITH THE BIOTECH INDUSTRY, WHAT LIABILITY ISSUES DOES THIS

HAVE FOR CIRM AS THE INSTITUTE AS A GRANTING AGENCY OR AS CIRM GRANTEES, INSTITUTIONS RECEIVING CIRM MONEY? OKAY? NOW I'M FINISHED.

DR. CSETE: SO FOR THE FEW PEOPLE IN THE ROOM I HAVEN'T MET, I'M MARIE CSETE. I'M THE CHIEF SCIENTIFIC OFFICER OF CIRM. AND I FIRST WANT TO ADDRESS YOUR QUESTION ABOUT THE VERY DISTURBING REPORT OF THE CHILD WHO RECEIVED SUPPOSEDLY FETAL SOURCE NEURAL STEM CELLS AND THEN DEVELOPED TUMORS IN THE BRAIN FROM AT LEAST TWO DONOR SOURCES.

SO WE HAVE NO WAY OF KNOWING WHAT THOSE CELLS WERE. AND, IN FACT, THROUGH THE SCIENTIFIC COMMUNITY, IT'S PRETTY CLEAR THAT OTHER CHILDREN HAVE BEEN IDENTIFIED WHO DEVELOPED TUMORS AFTER BEING TREATED AT THAT CLINIC. AND THE TUMOR TYPES SUGGEST THAT THE CELLS WERE NOT NEURAL STEM CELLS AT ALL. THERE HAVE BEEN SOME EFFORTS APPARENTLY TO INVESTIGATE WHAT THE PRECISE CELL SOURCE IS, BUT THAT INFORMATION JUST HASN'T BEEN MADE AVAILABLE BY THE CLINIC.

SO CERTAINLY THERE'S BEEN -- THERE ARE NEURAL STEM CELLS FROM FETAL SOURCES CURRENTLY BEING USED IN PHASE I TRIALS FOR TWO DIFFERENT DISEASES IN CHILDREN, AND THERE ARE PROBABLY OTHER NEURAL STEM CELL TRIALS GOING ON FROM FETAL SOURCES IN EUROPE.

I THINK THE ASSUMPTION THAT THOSE CELLS WERE WHAT THE CLINICIANS SAID THEY WERE IS JUST NOT TO BE BELIEVED.

CERTAINLY WE NEED TO EXAMINE THOSE KINDS OF CASES EXTREMELY CAREFULLY FOR ANY POTENTIAL PROBLEMS THAT THEY MAY HOLD FOR SIMILAR CELL THERAPIES, BUT GETTING TO THE SOURCE MATERIAL WILL BE DIFFICULT.

AS WE ANTICIPATE THE DISEASE TEAMS AND CELLULAR THERAPIES, OBVIOUSLY SAFETY IS THE FIRST CONCERN. AND IT'S NOT ONLY OUR INTERNAL EXAMINATION OF WHAT THE BEST STANDARDS ARE FOR SAFETY FOR CELLULAR THERAPIES, BUT WORKING WITH THE RECOGNIZED EXPERTS OUTSIDE THE STATE, WORKING CLOSELY WITH REGULATORY AGENCIES. WE'VE BEEN TRYING VERY HARD TO MAKE RECOMMENDATIONS ABOUT HOW SAFETY CAN BE ADDRESSED, AND WE JUST STARTED TO DO THAT INTERNALLY. NOBODY WANTS TO PROCEED WITH AN UNSAFE THERAPY. AND WE WILL JUST TAKE THE BEST ADVICE OF THE SCIENTISTS IN THIS FIELD AND NOT MAKE THESE DECISIONS BY OURSELVES.

YOUR SECOND QUESTION HAD TO DO --

DR. IVERSON: THE APPEARANCE OF CONFLICT OF INTEREST.

DR. CSETE: WELL, I GUESS I SHOULD HAVE

THE LAWYERS COME UP AND TALK ABOUT THIS, BUT WE CERTAINLY HAVE VERY CLEAR-CUT CONFLICT OF INTEREST POLICIES, BOTH FINANCIAL AND SCIENTIFIC, IN OUR INTERACTIONS WITH OUR GRANTEES, AND OUR IP POLICIES HAVE ALSO BEEN REFINED RECENTLY. AND CIRM DOESN'T HOLD INTELLECTUAL PROPERTY, FOR EXAMPLE. IF WE HAVE SPECIFIC QUESTIONS ABOUT THE CONFLICTS ARE HANDLED, WE WORK WITH OUR LAWYERS ON THAT. SO IAN SWEEDLER.

MR. SWEEDLER: GOOD MORNING. IAN SWEEDLER. I'M THE INTERIM GENERAL COUNSEL OF CIRM. WE HAVE VERY STRICT CONFLICT OF INTEREST RULES AND PROCEDURES. THEY APPLY IN A VARIETY OF WAYS IN DIFFERENT CIRCUMSTANCES, BUT FUNDAMENTALLY NOBODY WHO IS AFFILIATED WITH AN INSTITUTION GETTING INCOME FROM THAT INSTITUTION OR HAS AN ECONOMIC INTEREST IN THAT INSTITUTION HAS ANY ROLE IN DECIDING WHETHER OR NOT FUNDING GOES TO THAT PARTICULAR INSTITUTION. THEY DON'T VOTE ON THAT. THEY HAVE NO ROLE IN EVALUATING THE SCIENTIFIC MERIT OF A PROPOSAL.

SO THAT'S SOMETHING THAT WE HAVE ADDRESSED CAREFULLY. OUR STANDARDS HAVE BEEN REVIEWED AND FOUND TO BE STRICTER THAN THOSE USED BY THE NIH AND MEET OR EXCEED WHAT'S REQUIRED BY CALIFORNIA LAW.

DR. FRIEDMAN: IF IT'S OKAY, I'LL TRY TO ADDRESS THE THIRD QUESTION SINCE I WAS ACTUALLY AT

THE AGENCY WHEN SOME OF THE PREEMPTION LAWSUITS WERE FIRST BROUGHT. I HAVE NOT READ THE DETAILED JUDGMENT, AND SO I'VE ONLY READ THE NEWS BRIEF AS YOU HAVE, DR. IVERSON. SO I DON'T KNOW HOW BROADLY OR HOW NARROWLY IT'S DRAWN, AND I APOLOGIZE FOR NOT KNOWING MORE.

THAT SAID, THE ISSUE OF NATIONAL PREEMPTION IS EXTREMELY IMPORTANT AND WILL AFFECT NOT ONLY BIOPHARMACEUTICALS, BUT DEVICE MANUFACTURERS AND MANY, MANY OTHER AREAS AS WELL. IT WILL MEAN GREATER AMOUNT OF SCRUTINY WILL FALL UPON THE INDIVIDUAL INDUSTRIES AND COMPANIES THAT MAKE THESE PRODUCTS. AND WE WILL HAVE TO BE VERY CAREFUL. THAT SAID, I DON'T THINK IT CHANGES THE ESSENTIAL BALANCE THAT EXISTS, AT LEAST WITH CIRM, AND LET ME TELL YOU WHY.

OUR CONCERN IS FUNDAMENTALLY NOT A LEGAL CONCERN, A FINANCIAL CONCERN. OUR CONCERN IS A HUMAN CONCERN. AND AS DR. CSETE AND DR. TROUNSON AND DR. WITTE HAVE STATED, OUR INTENTION IS TO DO THE VERY BEST WE CAN FOR THE PATIENTS AND MINIMIZE RISK WHERE WE CAN SEE IT, BUT WE RECOGNIZE THE LIMITS OF OUR BIOLOGIC INSIGHTS. THERE MAY BE SOME THINGS THAT WE WILL MISS, BUT THERE'S EXTRAORDINARY EFFORTS THAT WILL BE SPENT AND ARE BEING SPENT TO

MAKE SURE THAT SAFE, UNDERSTANDABLE EXPERIMENTS ARE PERFORMED WHERE THE SUBJECTS ARE FULLY, FULLY VERSED IN ALL THE THINGS THAT WE KNOW RIGHT NOW. WE THINK IT'S A TREMENDOUS RESPONSIBILITY, AND THIS IS A HUGE BURDEN. IT'S ALSO A HUGE OPPORTUNITY FOR US. SO THANK YOU FOR THOSE QUESTIONS. DR. JONES.

DR. JONES: RICH JONES, CITY OF HOPE. DR. TROUNSON AND DR. WITTE BOTH MENTIONED THE IMPORTANT ROLE OF HIGH THROUGHPUT SCREENING AND SMALL MOLECULES IN STEM CELL-BASED THERAPEUTICS. I WONDER IF YOU COULD PLEASE ELABORATE A LITTLE BIT MORE ABOUT WHERE YOU SEE THAT HAVING THE GREATEST IMPACT AT LEAST EARLY ON IN THIS FIELD.

DR. WITTE: I CAN GIVE MY ANSWER TO THAT, WHICH IS SCIENTISTS HAVE NEVER REALLY HAD AT ACADEMIC CENTERS THE TOOLS TO DO SMALL MOLECULE SCREENING TILL CERTAINLY THE LAST FIVE YEARS OR SO. SO GIVE SCIENTISTS A NEW TOOL, THE BEST THING TO DO IS NOT TO TRY TO RESTRICT THEM OR GUIDE THEM TOO MUCH IN TERMS OF WHAT THEY USE THE TOOL FOR.

SO I'VE SEEN MARVELOUS BASIC SCIENCE STUDIES LOOKING FOR SMALL MOLECULES THAT WILL INHIBIT THE DEVELOPMENT OF SPECIFIC CELL TYPES USING ZEBRAFISH USING THE ENTIRE FISH AS THE ASSAY SYSTEM. I'VE SEEN WONDERFUL THINGS IN YEAST, E. COLI.

THEY'RE FINDING NEW PATHWAYS IN GENE REGULATION AND LOTS OF THINGS INVOLVED IN CANCER. I THINK WHERE IT'S GOING IS EXACTLY WHAT HAPPENS IN SCIENCE IS THINGS WE HAVEN'T THOUGHT OF IS THE MOST EXCITING.

STEM CELLS, I SEE TWO OR THREE STEM CELL CENTER DIRECTORS HERE, EVERY ONE OF US HAS PEOPLE WHO ARE SCREENING STEM CELLS, BETA TISSUE STEM CELLS, EMBRYONIC STEM CELL, IPS-DERIVED, ETC., WITH THESE SMALL MOLECULE LIBRARIES. WE HAVE A VERY NICE FACILITY AT UCLA, AND MORE AND MORE RESOURCES BEING PUT INTO IT.

WHEN IT COMES OUT, A SECOND TOOL, WHICH IS SMALL MOLECULES TO INTERROGATE BIOLOGY. AT THAT STAGE IT'S ALL VERY BASIC. I DON'T THINK ANYBODY SHOULD CONFUSE A SMALL MOLECULE SCREENING CENTER WITH A PHARMACEUTICAL COMPANY. THERE IS SO MUCH MORE TO IT THAN FINDING AN INITIAL HIT IN AN ASSAY. THAT REQUIRES MEDICINAL CHEMISTRY, STRUCTURE ACTIVITY RELATIONSHIP, AND REAL PHARMACOLOGY TO TAKE IT TO THE NEXT STAGE. WITHOUT THOSE TOOLS, YOU CAN'T UNDERSTAND BIOLOGY; AND WITHOUT UNDERSTANDING BIOLOGY, YOU CAN'T DEVELOP THE THERAPEUTIC. THAT'S MY FEELING ABOUT THE SCREENING CENTER.

DR. CSETE: WE HAVE A PERFECT STORM BECAUSE THE OPPORTUNITY TO HAVE NEW DISEASE MODELS

IN A DISH FOR WHICH WE CAN DO HIGH THROUGHPUT SCREENING JUST OPENS THE DOOR IN A TOTALLY UNANTICIPATED WAY FOR STEM CELLS BEING IMPORTANT FOR DRUG DISCOVERY. I THINK THAT'S REALLY CRITICAL.

MR. SIMPSON: JOHN SIMPSON, CONSUMER WATCHDOG. I'M THE DIRECTOR OF OUR STEM CELL OVERSIGHT ACCOUNTABILITY PROJECT. AND I HAVE READ THE FULL REPORT SEVERAL TIMES, AND I THINK THE STAFF ARE TO BE COMMENDED FOR TAKING THIS STEP TO UPDATE WHAT WAS A VERY GOOD PLAN, WHICH HAS OBVIOUSLY BEEN OUT OF DATE AND INDEED UPDATE IT.

AND ALSO I THINK IT'S GREAT THAT YOU'RE HAVING THESE PUBLIC HEARINGS TO DO THIS. AND THAT GIVES US AN OPPORTUNITY MAYBE TO SAY A FEW THINGS THAT CONCERN US IN THE PLAN, AND THAT'S WHAT I AM GOING TO DO. I UNDERSTAND THE NEED TO HAVE A CLOSER PARTNERSHIP WITH BUSINESS, BUT I'M TROUBLED BY THE SUGGESTION THAT A BIOTECH ADVISORY COMMITTEE WOULD BE FORMED. I DON'T UNDERSTAND HOW THAT WOULD WORK IN A TRANSPARENT SORT OF WAY.

YOU ALREADY HAVE MEMBERS OF THE OVERSIGHT COMMITTEE WHO HAVE SEATS SPECIFICALLY BECAUSE THEY REPRESENT INDUSTRY, SO I THINK IT WOULD BE VERY TROUBLING TO HAVE ANOTHER SPECIAL GROUP WITH A SPECIAL ADVISORY PANEL FOR BUSINESS. I THINK

BUSINESS PEOPLE WHO WEREN'T ON IT WOULD BE RIGHTFULLY UPSET. I DON'T THINK IT'S IN KEEPING WITH THE OVERALL ICOC. DUANE ROTH, FOR INSTANCE, IS ONE OF THE MEMBERS OF THE BOARD WHO REPRESENTS THE LIFE SCIENCE INDUSTRY AND DOES IT VERY WELL.

THE OTHER THING, IN THAT BUSINESS SECTION THERE ARE SOME AREAS I THINK WHERE YOU MAY BE GOING BEYOND WHAT YOUR MISSION SHOULD BE. YOU ARE TALKING ABOUT COMING UP WITH POLICIES ON EUROPEAN PATENTS. NOW, I FIND THAT A LITTLE INTERESTING AND TROUBLING BECAUSE WHEN OUR ORGANIZATION TOOK ON WHAT MOST SCIENTISTS IN THE UNITED STATES THINK WERE OVERREACHING STEM CELL PATENTS HELD BY WARF, WE FILED CHALLENGES TO THOSE PATENTS. CIRM'S POSITION WAS THAT THEY REALLY DIDN'T WANT TO GET INVOLVED IN IT. I DON'T KNOW WHY THIS PLAN FORESEES GOING OFF TO EUROPE.

FINALLY, I UNDERSTAND --

DR. FRIEDMAN: TODAY IS THE DAY FOR THREE-PART QUESTIONS OBVIOUSLY.

MR. SIMPSON: -- YOU CONSOLIDATED YOUR RFA'S INTO A MORE REALISTIC NUMBER, AND THAT I THINK MAKES SENSE BY EXPERIENCE. I DON'T UNDERSTAND WHY IN 2010 YOU ONLY SEEM TO BE FORESEEING PRESENTING TWO ROUNDS OF RFA'S FOR APPROVAL. THAT SEEMS TO BE

A LOWER NUMBER. MAYBE I'M READING THE CHART WRONG. I DON'T KNOW.

DR. FRIEDMAN: SO, ALAN, MAY I ASK YOU PLEASE TO ADDRESS THOSE THREE POINTS.

DR. TROUNSON: ONE OF THE THINGS THAT IS VERY IMPORTANT TO UNDERSTAND IN THIS SECTOR IS REALLY WHAT IS HAPPENING WITH RESPECT TO THE BIOTECH INDUSTRY AND THE PHARMACEUTICAL INDUSTRY AND THE WAY IN WHICH PEOPLE ARE THINKING. THERE'S A NEED FOR US TO BE ABLE TO UNDERSTAND WHAT'S GOING ON. AND IF YOU DON'T, YOU KNOW, YOU HAVE TO WAIT FOR SOMETHING TO HAPPEN IN A PUBLIC WAY. WHEN YOU'RE DEALING WITH THESE MAJOR INTERNATIONAL COMPANIES, THAT CAN BE TOO LATE AND UNFORTUNATE.

WE MEAN TO BE CHAPERONING CALIFORNIA STATE MONEY APPROPRIATELY. FOR EXAMPLE, IF THE PHARMACEUTICAL INDUSTRY WAS BACKING UP INTO AREAS WHERE IT WOULD BE HELPFUL TO US OR WHERE IT WOULD BE HELPFUL TO THE DELIVERY OF THE PROGRAMS AND THERE'S AN OPPORTUNITY TO EMBRACE THAT CONNECTION, WE SHOULD DO IT. THE THING ABOUT BIG BUSINESS, OF COURSE, IS IT GENERALLY DOESN'T LIKE TO SPEAK MUCH IN PUBLIC. IT'S A COMPETITIVE -- HAS THIS COMPETITIVE ATTITUDE WHETHER WHAT THEY SAY WILL BE TAKEN UP BY SOMEBODY ELSE.

SO THE WHOLE IDEA, JOHN, IS TO SEE IF WE CAN UNDERSTAND WHAT'S GOING ON IN THAT SPACE. ALL THE DECISIONS AND ALL OF THE ARGUMENTS THAT WOULD UNDERPIN ANY CHANGES IN WHAT WE DO OR ANY RELATIONSHIPS WE WOULD BEGIN WOULD ALL COME BACK INTO THE PUBLIC. BUT IT WOULD ENABLE US TO KNOW WHAT IS SOUND IN THE SENSE OF COMPOSING WHAT WE DO IN THE INTERSECTION BETWEEN NIH AND THE BASIC AND THE CLINICAL. SO I NEED TO TALK TO NIH AND SOMETIMES NEED TO TALK TO THEM OFF THE RECORD IN ORDER TO UNDERSTAND THAT. AND OCCASIONALLY WE TALK OFF THE RECORD SO YOU GET SOME BETTER UNDERSTANDING. THIS IS JUST PART OF THE PROCESS OF BEING BETTER INFORMED. IN THE END, WHATEVER DECISIONS WOULD COME OUT OF THAT WOULD BE ONES WHICH WOULD COME THROUGH THE PUBLIC FORUMS AND BE SUBSTANTIATED BY APPROPRIATE LITERATURE OR CASE IN THE SENSE OF THE ARGUMENTS.

SO I ACTUALLY THINK IT'S A SMART IDEA TO DO THAT, AND I'M NOT AFRAID OF IT. I THINK IT'S THE WAY TO UNDERSTAND WHAT'S GOING ON THERE THAT YOU WOULDN'T GET IF YOU JUST WAIT FOR THE NEWSPAPERS TO PRINT IT.

THE EUROPEAN PATENTS, WE AREN'T INVOLVED IN ANY EUROPEAN PATENTS, THAT'S FOR SURE. I'M NOT

SURE WHAT IS MEANT SPECIFICALLY, BUT THE RELATIONSHIP THAT WE HAVE WITH OTHER BODIES WOULD MEAN THAT COLLABORATIONS WOULD BE INTENDED TO MOVE THE FIELD FORWARD. IF THAT HAPPENED TO HAVE A COMPONENT OF A CLINICAL PROGRAM FOR WHICH THE UK WANTED TO -- THEIR SIDE WANTED TO ACTUALLY LOOK AT CLINICAL APPLICATIONS, THAT WOULD BE ENTIRELY A MATTER FOR THAT FUNDING BODY FROM, SAY, THE UK. WE ACTUALLY DON'T GET INVOLVED SPECIFICALLY IN PATENTS ARISING FROM OTHER PLACES.

WHILE IT'S INTERESTING TO KNOW ABOUT IT AND IMPORTANT FOR US TO RECOGNIZE IT, IT'S NOT GOING TO CHANGE WHAT WE DO BECAUSE WE'RE REQUIRED TO SPEND ALL OUR MONEY OR THE GREAT PART OF IT IN CALIFORNIA AND CERTAINLY, YOU KNOW, THE CALIFORNIA PATIENTS ARE THE TARGET FOR THE BENEFITS.

SO I DON'T KNOW IF I ANSWERED THAT QUESTION FOR YOU APPROPRIATELY, BUT I HAVEN'T BEEN LOOKING MYSELF AT THE PATENTS AT ALL EXCEPT AS A GENERAL INTEREST.

I THINK IF YOU NEED A LEGAL RESPONSE, WE CAN PROVIDE THAT, BUT I DON'T THINK IT'S OF SUBSTANCE TO ME AT THE MOMENT UNLESS THERE'S SOMETHING PARTICULAR THAT --

MR. SIMPSON: ON PAGE 28 IT SUGGESTS THAT

ONE OF THE FUNCTIONS OF CIRM WOULD BE HELPING BOTH MONITORING BLOCKERS TO INDUSTRY PARTICIPATION AND THE USE OF CIRM RESOURCES AND INFLUENCE JUDICIOUSLY TO RESOLVE LOGJAMS. EXAMPLES MIGHT INCLUDE REVIEWING THE EUROPEAN UNION'S VIEWS ON PATENTABILITY OF STEM CELL INVENTIONS AND THEIR IMPACT ON THE COMMERCIAL SECTOR.

DR. TROUNSON: IN UNDERSTANDING THAT, IT HAS SOME RELEVANCE TO THE PATENT SITUATION HERE IN THE U.S.A. THAT IS RELEVANT; BUT UNLESS THE U.S. PATENT SYSTEM CHANGES TO EMBRACE IN SOME WAY EUROPEAN STANDARDS IN THE AREA, I DON'T THINK IT'S THAT RELEVANT TO US. BUT THE RELEVANCE IS, AS I SAID, IF WE'RE DOING A COLLABORATIVE RESEARCH PROGRAM FOR WHICH THE OTHER ARM IS DOING A CLINICAL STUDY, THAT WOULD HAVE RESPECT WHATEVER PATENTS EXIST IN EUROPE THAT MIGHT BE DIFFERENT FROM THE U.S., BUT LIKEWISE WE WOULD HAVE RESPECT FOR THE PATENTS THAT ARE REWARDED HERE IN THE U.S. WITH RESPECT TO PATENT PLACE AS ANYONE WOULD IN THIS DAY.

SO, AGAIN, I DON'T THINK IT'S A CRITICAL COMPONENT TO ME AT THE MOMENT UNLESS THINGS CHANGE AND IT BECOMES IMPORTANT AND RELEVANT TO BECOME PART OF THE DISCUSSION. YOU KNOW, I'M A PART OF PERSONALLY SUPPORTING THE CHALLENGE AND BATTLE ON

THAT FRONT. WHAT I PERSONALLY THINK AND WHAT I THINK ON BEHALF OF CIRM ARE TWO THINGS. I RESPECT THE PATENT. THAT IS THE LAW. IT IS WHAT IT IS; AND WHILE WE, YOU AND I, HAD A DIFFERENCE OF AGREEMENT WITH OTHER PEOPLE ON THAT, WE'RE ON THE SAME SIDE. WE DIDN'T WIN THE DAY, BUT I THINK WE MADE THE CASE. AND SO THE BOARD, I THINK, AND SENIOR MANAGEMENT AND PARTICULAR MEMBERS OF THE BOARD FEEL THAT THE U.S. PATENT SYSTEM IS ONE WHICH SHOULD LOOK AFTER ITSELF. AND WHILE WE MIGHT HAVE PERSONAL DIFFERENCES OF VIEWS THERE, I THINK WE WOULD RESPECT WHAT THE BOARD THINKS IN THIS MATTER. WELL, I HAVE TO ANYWAY.

DR. FRIEDMAN: OTHER QUESTIONS, PLEASE.

DR. ZAIA: I HAVE A QUESTION ABOUT THE DETAILS OF HOW THE EVENTUAL CLINICAL TRIALS THAT DERIVE FROM THE DISEASE TEAM RFA WILL BE FUNDED. I NOTICE IN YOUR SLIDE, YOU HAD A VENTURE CAPITAL ARROW, BUT HOW MUCH VENTURE CAPITAL DO YOU ANTICIPATE BECAUSE IT WAS NOT A REQUIREMENT BUILT INTO THE DISEASE TEAM RFA THAT YOU COME IN WITH VENTURE CAPITAL. AND WHEN YOU'RE DOING AN IND, YOU ALREADY KNOW WHAT'S GOING TO FUND THE STUDY IN MOST CASES WHERE YOU'RE GOING TO PROCEED DOWN THE PATH TOWARDS THE COMPLETION AND SUBMISSION OF THAT IND.

SO WHAT'S THE THINKING AND WHAT ARE THE DETAILS FOR WHERE THE MONEY WILL COME FROM FOR THOSE CLINICAL TRIALS?

DR. TROUNSON: I THINK IN SOME RESPECTS, RELATED TO AN EARLIER QUESTION, WE WANT TO BE IN THE SPACE WHERE WE WOULD BE LOOKING AT ASSISTING TEAMS TO LOOK AT WHAT THE SAFETY AND EFFICACY WAS. SO THIS PRE-IND PHASE TO PUT AS MUCH WE COULD INTO QUALITY STUDIES, REALLY HIGH QUALITY STUDIES, THAT FELT THEY COULD GET TO AN IND WITHIN FOUR YEARS. SO WE WANTED TO FOCUS ON THAT PARTICULAR COMPONENT, GIVE SOME STRENGTH TO THE SAFETY AND EFFICACY. AND SO THAT THERE WAS AN ENABLING, IF YOU LIKE, OF THE IND TO HAVE A MORE SUBSTANTIVE CAPACITY TO BE AWARDED WHEN IT WAS APPLIED FOR.

I THINK THE NEXT PHASE IS IMPORTANT THAT WE, FIRST OF ALL, JUST MAKE A JUDGMENT ON WHAT IS AVAILABLE IN THE SENSE OF REALLY HIGH QUALITY STUDIES THAT ARE PROGRESSING TO IND. WE HAVE SOME KNOWLEDGE OF THAT CURRENTLY IN THE ADULT STEM CELL AREA. AND TO MAKE A DECISION -- OR SORRY -- TO BRING A RECOMMENDATION TO THE BOARD AT SOME STAGE THAT WE WOULD CONVERT OUR HOPE TO THE PHASE I OR EARLY PHASE II CLINICAL STUDIES.

WE ARE AWARE THAT THE COSTS ACCELERATE

VERY DRAMATICALLY IN THAT PHASE, SO OUR CAPACITY WOULD BE DRAMATICALLY DIMINISHED IN TERMS OF THE NUMBERS OF STUDIES WE COULD HELP WITH. SO WHILE IT'S IMPORTANT, IT'S A BALANCE, AND IT'S A BALANCE THAT WE TRY TO CREATE AND THEN MAKE RECOMMENDATIONS TO THE BOARD, AND THE BOARD THEN MAKES FINAL DECISIONS ON IT. WHETHER WE SUPPORT A CLINICAL STUDY OR NOT HAS REALLY NOT GOT TO A SITUATION WHERE WE FELT THAT IT WAS A GOOD THING AT THIS POINT IN TIME TO RECOMMEND TO THE BOARD.

SO WE HAVEN'T STEPPED ACROSS THAT LINE, IF YOU LIKE. BUT IF THE WORK THAT WE FUND OUT OF THE DISEASE TEAMS, TEAMS WHICH GET TO AN IND WITHIN TWO OR THREE YEARS, I THINK IT MIGHT BE PERSUASIVE THAT WE MIGHT GO ON AND HELP THEM. BUT ESSENTIALLY I THINK WE NEED TO HAVE A GOOD HARD LOOK AT WHAT REALLY HIGH QUALITY WORK IS AVAILABLE TO US THAT WE WOULD THINK WAS VERY MUCH APPROPRIATE TO GET THE BOARD TO SUPPORT.

DR. ZAIA: DR. JOHN ZAIA, Z-A-I-A.

DR. FRIEDMAN: I'M GOING TO USE THE MODERATOR PREROGATIVE, NOT TO MAKE A POINT MYSELF, BUT TO REITERATE, BECAUSE DR. WITTE HAD TO LEAVE, A POINT THAT HE MADE, I THINK, THAT REALLY SPEAKS TO JOHN'S POINT, WHICH IS NOT ONLY IS IT IMPORTANT TO

DO GOOD CLINICAL STUDIES, BUT IT'S IMPORTANT TO UNDERSTAND WHY THOSE STUDIES FAIL TO SUCCEED. HE MADE THAT POINT VERY, VERY CLEARLY. AND I THINK THERE'S SUCH AN ENORMOUS INVESTMENT OF DOLLARS, OF TIME, OF HOPE IN EACH OF THESE CLINICAL EXPERIMENTS, THAT VERY LIKELY, WHEN THESE STUDIES ARE REVIEWED, CAREFUL ANALYSIS OF WHAT WE LEARN FROM THOSE STUDIES, WHETHER THEY'RE SUCCESSFUL OR NOT IN A CLINICAL SENSE, I THINK IS THE POINT DR. WITTE WOULD LIKE TO REITERATE WERE HE HERE.

OTHER QUESTIONS, PLEASE.

DR. CHIU: ARLENE CHIU, CITY OF HOPE. I HAVE THREE QUESTIONS REGARDING THE FUTURE STRATEGIES EMPLOYED BY CIRM. ONE IS THAT ONE OF THE MAJOR CHANGES IS A TREMENDOUS INFLUX OF MONEY TO FUND DISEASE TEAMS, $200 MILLION FOR THIS FIRST ROUND. I WONDER WHAT PLAN CIRM HAS TO MONITOR THE PROGRESS OF DISEASE TEAMS AND PERHAPS TO CURTAIL THOSE THAT ARE NOT SUCCESSFUL SO THAT MONEY COULD BE ROLLED INTO FUTURE OFFERS OF MORE TIMELY DISEASE TEAMS. THAT'S THE FIRST QUESTION. THE SECOND, WHETHER YOU SEE YOURSELF OFFERING MORE DISEASE TEAMS WITH THE FOLLOWING YEARS AS EVERYBODY HOPES.

THE SECOND QUESTION HAS TO DO WITH PART OF THE MISSION OF CIRM AS EXPRESSED IN PROP 71 AND A

QUESTION THAT MANY PEOPLE HAVE ASKED. THAT IS, THAT CIRM WAS BUILT TO FUND STEM CELL RESEARCH THAT COULD NOT BE FUNDED BY THE NIH IN A TIMELY FASHION, NOT NECESSARILY THAT IT ABSOLUTELY IS NOT FUNDABLE BY NIH. SO MANY PEOPLE ARE CURIOUS WHETHER STEM CELLS OTHER THAN HUMAN EMBRYONIC STEM CELL RESEARCH WOULD BE CONSIDERED WELCOME AT CIRM. AND PARTICULARLY TODAY IN ONE OF THE SLIDES IT WAS MENTIONED THAT ENDOGENOUS CELL GENESIS AS WELL AS CANCER STEM CELLS, TWO AREAS THAT ARE FUNDABLE IF NIH HAD THE MONEY, IS ALSO ON YOUR HORIZON. AND I WANTED TO KNOW WHAT YOUR THOUGHTS ARE IN FUNDING ADULT STEM CELLS AND OTHER STEM CELL APPROACHES. AND I'LL HOLD OFF ON MY THIRD QUESTION.

DR. TROUNSON: LET ME ASK MARIE TO ADDRESS THE MONITORING.

DR. CSETE: SO NOT ONLY DO WE MONITOR PERFORMANCE IN THIS WAY IN ANTICIPATORY FASHION ON DISEASE TEAMS, BUT WE DO THAT FOR ALL OF OUR GRANTS. NONPERFORMERS DO NOT CONTINUE. AND THAT'S BEEN SORT OF A DIFFICULT REALIZATION IN THE COMMUNITY. BUT THERE'S VERY DISCRETE PLANS FOR SAFETY MONITORING BOARDS ATTACHED TO DISEASE TEAMS AS WELL AS AN OVERSIGHT COMMITTEE THAT WILL MEET AT CRITICAL TIMES AT THE MILESTONES AND YEARLY, AND THOSE MEETINGS

WILL BE SUPERVISED BY THE SCIENCE OFFICE.

AND WE ABSOLUTELY UNDERSTAND THAT THERE WILL BE SOME RISKY GRANTS IN TERMS OF SUCCESS OUT THERE THAT WILL NOT GO THE WHOLE WAY, AND THAT MONEY, OF COURSE, WILL BE AVAILABLE FOR FUTURE DISEASE TEAMS. WE DON'T KNOW THE NUMBERS OF DISEASE TEAMS THAT WILL BE FUNDED IN THE SECOND ROUND OR THE FIRST ROUND, FOR THAT MATTER, AT THIS POINT. TIMES ARE HARD FOR EVERYONE. BUT WE'RE AIMING FOR SIX TO TEN THE FIRST ROUND, AND WE ANTICIPATE POSTING THE SECOND ROUND OF DISEASE TEAMS 18 MONTHS DOWN THE ROAD.

I JUST WANT TO SAY ONE THING ABOUT THE OVERLAP WITH NIH. IT IS STILL A REVIEW CRITERIA FOR OUR REVIEWERS THAT WE SHOULD PRIORITIZE WORK THAT COULD NOT BE FUNDED ELSEWHERE. THAT INCLUDES NIH AND ANY OTHER AGENCY, EITHER BECAUSE OF THE NATURE OF THE WORK OR BECAUSE OF LEGISLATIVE RESTRICTIONS.

DR. TROUNSON: I GUESS, ARLENE, YOU SHOULD KNOW BETTER THAN ANYONE THAT WHEN WE ANALYZE THE PROJECTS, THERE WERE SOMETHING LIKE 15 PERCENT OF THEM IN CANCER BEFORE YOU LEFT, SO YOU SHOULD BE ABLE TO ANSWER YOUR OWN QUESTION IN THAT RESPECT.

I SENSE THAT, YOU KNOW, UNDER THE PROPOSITION, WE'RE ABLE TO FUND PLURIPOTENTIAL STEM

CELLS THROUGH THE PROGENITOR CELLS, AND THAT'S A PRETTY WIDE SPECTRUM UNDER ANY KIND OF DEFINITION. IN A SENSE I THINK HERE THE EMBRYONIC STEM CELL WORK STILL MAY NOT BE VERY WELL FUNDED. WE'LL HAVE TO WAIT AND SEE. BUT WE HAVE ACTUALLY MOVED ALONG THE TRACK OF BRINGING IN IPS CELLS, THE INDUCED PLURIPOTENTIAL STEM CELLS. I THINK THEY HAVE A VERY REMARKABLE AND IMPORTANT ROLE TO PLAY IN REGENERATIVE MEDICINE AND ANALYSIS OF DATA AND UNDERSTANDING DISEASE.

I THINK ADULT STEM CELLS ARE IMPORTANT IN THE CLINIC. ARGUABLY MORE SHOULD BE DONE IN THE CLINIC, BUT I THINK THAT'S ARGUABLE. BONE MARROW WORK IS REASONABLY WELL FUNDED. THERE'S A LOT OF MESENCHYMAL STEM CELL WORK GOING ON. AGAIN, REASONABLE STUDIES, REASONABLE SCIENCE STUDIES BEING UNDERTAKEN, AND WE NEED TO MAKE JUDGMENT OF WHETHER HOW EFFECTIVE THEY ARE. AND THEN ON THAT BASIS, DO WE HAVE A BETTER CELL TYPE TO IMPROVE ON THE OUTCOMES, I THINK THAT MAKES GOOD SENSE.

SO I THINK THE CANCER STEM CELL AREA IS ONE WHICH IS UNDER DEBATE ABOUT WHETHER A STEM CELL TYPE ACTUALLY EXISTS, BUT THE PARALLELS BETWEEN EMBRYONIC STEM CELLS, PARTICULARLY IN CANCER CELLS, IS NOT ARGUED. THEY EXPRESS MANY OF THE SAME GENES.

ANYTHING THAT WE CAN LEARN FROM OUR PLURIPOTENTIAL STEM CELLS THAT WE COULD TARGET TO REDUCING OR CURING CANCER, I THINK WOULD BE ABSOLUTELY WELCOME BY THE COMMUNITY.

SO I HAVE HIGH HOPES THAT THE SCIENTISTS IN THIS SPACE IN CALIFORNIA WILL BENEFIT FROM WORK WHICH LINKS THE TWO, WHETHER THE ASSAYS AND DEVELOPMENTS THAT ARE COMING OUT OF THE PLURIPOTENTIAL STEM CELL AREA WILL INFORM ON THE NATURE OF THE CANCER AND HOW WE MIGHT BE ABLE TO ATTACK THAT CANCER IN INNOVATIVE WAYS. AND I THINK OWEN WITTE AND HIS COLLEAGUES AND MANY OTHERS HERE IN CALIFORNIA HAVE ALREADY DEMONSTRATED.

WE HAD A WORKSHOP WITH THE THOUGHT LEADERS IN CANCER IN CALIFORNIA, AND THEY WERE UNANIMOUS ON THE BASIS THAT WE SHOULD MOVE FORWARD WITH SUPPORT OF WORK IN THIS AREA AND TO INCLUDE OUR CANADIAN COLLEAGUES. SO I THINK IT IS WELL AND TRULY EMBEDDED IN THE STRUCTURE OF OUR THINKING THAT WE SHOULD SUPPORT THAT. THERE ARE DIFFERENT KINDS OF ADULT STEM CELLS AVAILABLE TO US. PLACENTAL STEM CELLS ARE STILL BEING EXAMINED. CORD BLOOD CELLS HAVE AN INCREASED SPECTRUM OF USEFULNESS. WHERE WE THINK THAT THERE IS INSUFFICIENT FUNDING, GENERALLY INSUFFICIENT FUNDING, WE WOULD CERTAINLY POINT THAT

OUT TO OUR REVIEWERS BECAUSE IT'S PART OF THE PROPOSITION AND THAT THAT OUGHT TO BE A FACTOR TAKEN INTO CONSIDERATION IN THOSE PROJECTS.

DR. CHIU: THANK YOU. MY LAST QUESTION IS CLEARLY THERE IS MORE EMPHASIS ON TRANSLATIONAL AND CLINICAL RESEARCH AS CIRM CONTINUES ON ITS PATH. I WONDER WHAT WILL HAPPEN WITH BASIC FUNDING OF BASIC RESEARCH. ONE OF THE ELEMENTS IN THE ORIGINAL STRATEGIC PLAN ARE RESEARCH TEAMS THAT ARE NOT NECESSARILY COALESCING AROUND A DISEASE CONCEPT. AND I DON'T KNOW IF THIS IS NOW LESS IMPORTANT AS WE MOVE FORWARD OR WHETHER THERE WILL BE TEAMS THAT COULD BUILD NEW TOOLS OR OTHER THINGS THAT WOULD BOOST THE ENTERPRISE.

DR. TROUNSON: I THINK I'LL LET MARIE MAKE SOME COMMENTS ON THIS, BUT ONE OF THE THINKINGS THAT WE HAVE WITH OUR INTERNATIONAL COLLEAGUES AND, WE HOPE, INTERSTATE COLLEAGUES COMING TOGETHER WAS THAT WE WOULD BE BUILDING TEAMS WITHIN AND EXTERNAL TO CALIFORNIA IN THE BASIC AREA AS WELL AS TRANSLATIONAL AREAS. AND WE EXPECT THAT TO HAPPEN. WE'VE ALWAYS BEEN VERY STRONG ABOUT HAVING TEAM APPROACHES IN CALIFORNIA ANYWAY.

I THINK THERE'S AN ARGUMENT SOMETIMES THAT BASIC SCIENTISTS DO BETTER BY THEMSELVES AND OTHERS

SAYING THAT THEY DO VERY MUCH BETTER WHEN THEY'RE IN TEAM RELATIONSHIPS. BUT I THINK THERE'S A MIXTURE, AND I THINK WE JUST OUGHT TO PERSUADE THE REVIEWERS, YOU KNOW, THAT THE TEAM APPROACH IS BETTER THAN THE INDIVIDUAL BRILLIANT IDEA THAT A SCIENTIST WANTS TO SORT OF EXPLORE. I THINK IT'S UP TO THE REVIEWERS.

DR. CSETE: SO WE HAVE NO INTENTION OF ABANDONING BASIC SCIENCE, AND THE REASON TO GO TO THE CORE THREE, IN PART ALSO ANSWERS JOHN SIMPSON'S QUESTION, IS THAT COVERING THAT VALLEY OF DEATH WITH REPEATING CYCLES OF BASIC BIOLOGY, EARLY TRANSLATION, AND DISEASE TEAMS ALLOWS US TO COME OUT IN A TIMELY FASHION AND CHANGE THE PRIORITIES, PLUG AND PLAY A LITTLE BIT WITHIN THOSE GRANTS FOR WHAT WE SEE IS NEEDED IN THE COMMUNITY. SO WE MAY HAVE LITTLE BITS OF DIFFERENT EMPHASIS ON EACH OF THOSE REPEATING PROGRAMS, BUT THEY COVER THE FULL SPECTRUM, RECOGNIZING THAT BASIC BIOLOGY IS ESSENTIAL TO BE ONGOING.

WE DO A LOT OF INFORMAL AND FORMAL MATCHMAKING AS WE'RE SEEING RESULTS COME BACK NOW, AND PEOPLE WHO SHOULD BE TALKING TO EACH OTHER ON THE BASIC SCIENCE LEVEL. AND WE HAVE PLANS TO DO THAT EVEN MORE FORMALLY BY BRINGING PEOPLE TOGETHER INTO THE OFFICE IN CIRM IN GROUPS SO THAT THEY CAN

HEAR MORE ABOUT WHAT'S BEING DONE AT INSTITUTIONS WHERE THEY'RE NOT FAMILIAR.

DR. FRIEDMAN: THANK YOU. OTHER QUESTIONS PLEASE OR COMMENTS.

I THINK ONE OF THE THINGS THAT THE ORGANIZATION IS LOOKING TO DO FROM THIS AND OTHERS IS SPECIFIC ADVICE. YOU'VE ASKED SOME VERY GOOD, PROVOCATIVE, AND HELPFUL QUESTIONS. IS THERE ANY ADDITIONAL GUIDANCE THAT YOU WOULD LIKE TO OFFER TO THEM, US, ALL CITIZENS?

DR. TIZIANO: SHORT QUESTION REGARDING THE BASIC BIOLOGY. SO AS A GRANTEE, I COULDN'T APPLY ON THE BASIC BIOLOGY I. WILL IT BE THE SAME FOR THE NEXT CYCLES? I'M MORE OF A BASIC RESEARCHER THAN A TRANSLATIONAL RESEARCHER, SO IT MEANS THAT WITH CIRM I'M DONE UNLESS I MOVE TO MORE TRANSLATIONAL STUDY?

DR. CSETE: WE HAVEN'T MADE A POLICY ABOUT THAT. RIGHT NOW IT WAS REALLY A MATTER OF SPREADING THE WEALTH. I MEAN THERE'S ONLY SO MUCH TO GO AROUND, AND WE THINK OUR NEW FACULTY AWARDS ARE QUITE GENEROUS AND WE REALLY WANTED TO FOCUS ON THEM. AND YOU ALSO NOTICED PROBABLY THAT THERE CAN BE OVERLAP OF PI'S WITH EARLY TRANSLATION AND DISEASE TEAMS, AGAIN, BECAUSE WE WANTED TO BRING DIVERSITY INTO THE SCIENTIFIC COMMUNITY. THESE ARE

MADE AS EACH RFA IS ISSUED AND WE LOOK AT OUR PORTFOLIO. SO THERE'S NO SET POLICY ABOUT THAT.

DR. TIZIANO: BARBERI TIZIANO FROM CITY OF HOPE.

DR. FRIEDMAN: OTHER QUESTIONS?

DR. IVERSON: I'VE HEARD A NUMBER OF COMMENTS NOW THAT GO BACK TO THE ORIGINAL ISSUE, AND THAT IS THE RADICAL SHIFT IN STRATEGY OF CIRM TO SPEND MORE MONEY ON TRANSLATIONAL, CLINICAL, AND DISEASE TEAM RESEARCH. NOW, I KNOW THAT THE NUMBER OF GRANTS MAY BE VERY SMALL, WHAT DID YOU SAY, SIX TO TEN DISEASE TEAMS, BUT THE DOLLAR AMOUNT IS SUBSTANTIAL. AND IF YOU LOOK AT ONE OF YOUR PIE CHARTS THAT ADDS UP THE TOTAL NUMBER OF CIRM DOLLARS SPENT ON DISEASE TEAM GRANTS, TRANSLATIONAL GRANTS, AND DISEASE TEAM PLANNING GRANTS, IT AMOUNTS TO ALMOST HALF OF THE CIRM MONEY SPENT. THAT MONEY MAY BE SPENT MORE WISELY FOCUSING ON BASIC RESEARCH.

I THINK YOU'VE HEARD THIS A NUMBER OF TIMES AT THIS MEETING THAT IT'S SOMETHING THAT CIRM REALLY NEEDS TO CONSIDER SERIOUSLY.

DR. CSETE: SO TO DATE THERE'S BEEN ABOUT $600 MILLION DISTRIBUTED IN BASIC RESEARCH BY CIRM, PLUS THE BUILDING FUNDS WERE 280 OR SO MILLION DOLLARS. WE THINK ABOUT THIS CONSTANTLY AND

EVALUATE THIS CONSTANTLY, AND RIGHT NOW WE THINK THIS BALANCE OF GETTING THE DISEASE TEAMS STARTED, EARLY TRANSLATION, AND REPEATED BASIC BIOLOGY AWARDS IS THE RIGHT MECHANISM TO GET TO OUR END GAME TO FULFILL THE GOALS OF THE STRATEGIC MISSION. WE WILL ALWAYS EVALUATE WHAT THAT BALANCE IS, BUT IT DEPENDS ON THE RESULTS AS WE GO ALONG.

DR. TROUNSON: I THINK MARIE'S ANSWERED THE QUESTION VERY WELL. WE TAKE THIS AS INPUT, SO WE UNDERSTAND THE POINT YOU ARE MAKING. AND I HAVE -- I'M A BASIC SCIENTIST MYSELF, SO I CLEARLY UNDERSTAND THE MERITS AND THE ADVISORIES OF REMAINING IN BASIC SCIENCE, BUT I THINK YOU ALSO HAVE TO RECOGNIZE THAT THE STATE OF CALIFORNIA GAVE $3 BILLION TO THE INITIATIVE TO GET THE WORK NOT TO THE SCIENTIFIC JOURNALS, BUT TO GET THEM TO MOVE ALONG TO THE CLINIC. AND I THINK THAT'S REALLY THE END OF THE TIME.

THE WAY CALIFORNIA'S COMMUNITY WILL ASSESS WHETHER THIS HAS BEEN A GOOD EXPERIMENT OR NOT IS WHETHER THE WORK HAS ACTUALLY TRANSFERRED SOME BENEFIT FOR THE PATIENTS OF CALIFORNIA.

AND THAT'S NOT -- THE REASON, AS I SAID AND MARIE SAID, THE REASON WHY WE'RE IN TRANSLATION AT THE PRESENT TIME AND IN THE DISEASE TEAMS IS TO

ENSURE THAT THE EFFICACY AND THE SAFETY IS AS STRONG AS POSSIBLE. WE DON'T ACTUALLY KNOW HOW MANY GRANTS WE WILL FUND BECAUSE IN THE DISEASE TEAMS BECAUSE WE HAVEN'T RECEIVED THEM. AND IN DUE COURSE IT MAY BE THAT THERE'S ONLY THREE OR FOUR WORTH SUPPORTING; BUT IF THERE ARE TEN OR TWELVE, IF THEY HAVE MERIT TO BE SUPPORTED THERE, THE REFEREES DECIDE THAT THEY'RE GREAT PROJECTS THAT MERIT, THEN AT LEAST THE BOARD WILL CONSIDER THAT AS A POSSIBILITY.

SO I THINK BOTH THE BOARD AND MANAGEMENT FEEL THAT IT'S THE RIGHT TIME TO EXPLORE THIS TRANSLATIONAL AREA IN ORDER TO START TO UNDERPIN THE SAFETY AND EFFICACY OF THE STUDIES WHICH ARE ALREADY GOING FORWARD.

SPEAKER: (NAME INDISCERNIBLE), UNIVERSITY OF CALIFORNIA RIVERSIDE. MY QUESTION IS A SCIENTIFIC QUESTION. I SAW IN ONE OF YOUR SLIDES THAT YOU MENTION IMMUNOLOGY RIGHT THERE IN THE RIGHT CORNER ALMOST OFF THE SLIDE. AND YOU ALSO MENTIONED THAT YOU ARE LOOKING FOR WAYS TO UNDERSTAND THE TOLERANCE OF THESE CELLS.

WELL, MY QUESTION IS, AS YOU ALSO CONSIDER THAT, ONE OF THE VERY KEY ASPECTS HERE IS THAT MOST DISEASES TODAY, WE KNOW, HAVE A VERY IMPORTANT KEY COMPONENT OF INFLAMMATION. SO USING A STEM CELL

TRANSPLANT WITHOUT CONTROLLING THAT ENVIRONMENT IS GOING TO BE PROBLEMATIC IN MY VIEW. SO I WONDER WHY THAT WASN'T ADDRESSED.

DR. CSETE: WE JUST HAD A WORKSHOP ON IMMUNOLOGY FOR THIS REASON, AND I THINK IT WAS REALLY TERRIFIC BECAUSE WE BROUGHT IN THE SOLID ORGAN TRANSPLANT COMMUNITY WHICH HAS, YOU KNOW, A HUGE EXPERIENCE IN IMMUNOLOGY, WITH OUR BASIC SCIENTISTS IN IMMUNOLOGY FROM AROUND THE WORLD, THESE WERE EXPERTS, TO REALLY UPDATE US ON WHAT THE BEST WAY TO DEVELOP A RESEARCH AGENDA TO ATTACK THIS ABSOLUTELY ESSENTIAL PROBLEM IN CELL THERAPIES IS.

SO WE'RE TAKING THE RESULTS OF THAT WORKSHOP AS WELL AS OTHER INFORMATION TO CONSTRUCT A SPECIFIC RFA TO ADDRESS THESE ISSUES.

DR. FRIEDMAN: PLEASE.

DR. HUGHES: KAREN HUGHES, CITY OF HOPE. I JUST WANT TO SAY THAT FOR ME AND MY TEAM MEMBERS WE'RE VERY APPRECIATIVE OF HOW CLEARLY YOU RECOGNIZE THAT VALLEY OF DEATH BETWEEN THE NIH-FUNDED MORE BASIC SCIENCE AND INDUSTRY FUNDING AFTER IT'S ALREADY IN PATIENT TRIALS.

I WANT TO ASK YOU A LITTLE BIT MORE. YOU STILL HAVE THIS REVIEW CRITERIA SPECIFICALLY PICKING GRANTS THAT ARE NOT FUNDABLE BY OTHER SOURCES.

HOWEVER, THE MAGNITUDE OF $20 MILLION FOR FOUR YEARS FOR A COMPREHENSIVE TEAM, EITHER IF SOME OF THIS STUFF IS FUNDABLE BY NIH OR PRIVATE SOURCES A HUNDRED THOUSAND AT A TIME, 50,000 AT A TIME, THERE'S NO COMPARISON OVER THE 15 TO 20 YEARS IT WOULD TAKE THAT WAY AS OPPOSED TO WHAT YOU ARE OFFERING. THERE'S VERY FEW SOURCES OF $20 MILLION IN A FOUR-YEAR PERIOD, SO ARE YOU CONSIDERING --

DR. CSETE: I THINK MY RESPONSE TO ARLENE CAPTURES EXACTLY THAT, THE NATURE OF THE WORK OR THE ABILITY TO GET FUNDING ELSEWHERE. WE UNDERSTAND THAT THE NATURE OF THE WORK AND ITS EXPENSE IS IMPOSSIBLE TO GET FUNDED ELSEWHERE DEPENDING ON THE PROJECT.

DR. TROUNSON: WE SAY FUNDING UP TO 20 MILLION, SO THESE STUDIES MIGHT COME IN A LOT LESS. AND IN MANY CIRCUMSTANCES THE MATURITY OF SOME OF THESE STUDIES MAY BE SUCH THAT IT REALLY ONLY TAKES A FEW MILLION DOLLARS TO GET THEM THERE IN A MUCH SHORTER TIME THAN FOUR YEARS. SO WE ARE JUST SAYING IT'S NOT $20-MILLION PROJECTS, BUT WE'RE GOING TO FUND UP TO 20 MILLION IF IT'S PERSUASIVE THAT THE ELEMENTS OF COST ARE GENUINE AND THE OPPORTUNITY WILL COME.

DR. IVERSON: CAN I ADDRESS HIS COMMENT,

PLEASE? $20 MILLION IS NOTHING TO A VENTURE CAPITALIST. IT'S EASY TO RAISE $20 MILLION. IT'S A LOT OF WORK AND HAS TO GO OUT AND BEAT THE PAVEMENT. BUT TO USE CIRM MONEY, TO USE TAXPAYERS' MONEY, ESSENTIALLY AS VENTURE CAPITAL MONEY, I THINK, IS BEYOND THE PALE. REALLY NEED TO RECONSIDER THIS. I'M NOT CERTAIN THAT PROPOSITION 71 EXPECTED CALIFORNIA TAXPAYERS TO FUND CLINICAL TRIALS. DID IT?

MR. ROTH: I'M DUANE ROTH. I'M A MEMBER OF THE ICOC AND REPRESENT INDUSTRY. I WOULDN'T WANT TO DEBATE YOU ABOUT THE STATUS OF VENTURE CAPITAL FOR ANY GIVEN PARTICULAR REASON. BUT I THINK YOU HEARD WHAT DR. WITTE TALKED ABOUT, THE VERY DIFFICULT TIME EVEN, IN AN ECONOMY THAT WAS FAR DIFFERENT YEARS AGO, JUST TO GET MONOCLONAL ANTIBODIES TO THE POINT WHERE WE COULD ACTUALLY GET PEOPLE TO INVEST IN THEM WAS YEARS AND YEARS. AND YOU SEE A DRUG LIKE THE LEUKEMIA DRUG THAT ACTUALLY CURED DISEASE, THAT WAS IMPOSSIBLE TO GET FUNDED FOR A LONG PERIOD OF TIME.

SO MY VIEW IS THAT THE RESEARCH THAT WE CAN THINK OF, BASIC RESEARCH, AS ALAN SAYS, YOU PUBLISH PAPERS. I'VE NEVER READ A PAPER THAT CURED A PATIENT, BUT PRODUCTS DO. AND THAT'S, I THINK,

WHAT WE HAVE TO KEEP IN MIND HERE. YOU NEED THE RESEARCH. WE NEED TO GO FORWARD, BUT EVENTUALLY YOU HAVE TO MOVE INTO HUMAN CLINICAL TRIALS, AND SOMETIMES YOU HAVE TO GO BACK. AND I'LL REMIND YOU, PEOPLE IN THIS ROOM KNOW FAR AS BETTER THAN ME, BUT THE FIRST ATTEMPT AT POLIO VACCINE BY JONAS SALK WAS A DISASTER. IT SET US BACK TEN YEARS, BUT EVENTUALLY WE GOT THERE, AND WE CURED THE DISEASE THAT HAD WE NOT DONE THAT, THE CONSEQUENCES WOULD BE DIRE.

SO WHILE THERE WILL BE RISK AND THERE ARE THINGS WE NEED TO DO TO MOVE THIS FORWARD, THERE HAS TO BE THAT BALANCE BACK AND FORTH. I THINK TODAY THERE'S A LOT MORE TRANSPARENCY SO THAT WE CAN LOOK AND STUDY EVERYTHING.

AND MAYBE THE FINAL COMMENT I'LL MAKE IS ABOUT GETTING INDUSTRY INVOLVED. INDUSTRY IS GOING TO BE NECESSARY TO COMMERCIALIZE THESE PRODUCTS. WHEN I SAY COMMERCIALIZE, GETTING THEM TO THE PATIENTS THAT NEED THEM. AND THEY ARE GOING TO BE VERY RELUCTANT TO INVEST HEAVILY UNTIL THEY CAN SEE THAT THERE'S ACTUALLY A SCIENCE HERE THAT WILL ALLOW THAT TO GO FORWARD. SO TODAY I THINK FUNDING RESEARCH INSTITUTES, WE'RE MOVING FURTHER THAN THEY EVER HAVE IN THE PAST, TO EXPLORE THESE VERY EARLY

STAGES IS IMPORTANT.

AND THE FINAL THING I'LL SAY IS ALMOST ALL OF THE FUNDING YOU SEE GOING ON HERE IS TOO EARLY TO FORM A BIOTECH COMPANY AND DO BIOTECH. IN SAN DIEGO THAT'S WHAT I DO EVERY DAY. WE AREN'T STARTING ANY THERAPEUTIC COMPANIES. AND THERAPEUTIC COMPANIES, WE CAN'T FUND THEM. IT'S TOO EARLY FOR REAL MONEY. IT'S TOO EARLY FOR A MANAGEMENT TEAM; AND, THEREFORE, WE LIVE IN THAT VALLEY OF DEATH. AND IT'S HEARTBREAKING TO SEE THESE PEOPLE THAT HAVE REALLY GREAT IDEAS AND A POTENTIAL TO MOVE THINGS FORWARD, AND THE VENTURE CAPITALISTS TO SAY, BUT, DUANE, THEY NEED $2 MILLION OR $3 MILLION. WE DON'T INVEST THAT SMALL AMOUNT OF MONEY. AND SECOND, WE CAN'T ATTRACT A MANAGEMENT TEAM AT THIS POINT. WHAT WOULD THEY DO? SIT AND WAIT FOR DATA.

HOW WE GET PEOPLE THROUGH THAT IS VERY IMPORTANT. AND IF WE'RE SUCCESSFUL, I HOPE INVESTORS MAKE MONEY. I HOPE PEOPLE WHO GET INVOLVED PARTICIPATE IN THAT. BUT THE FAR GREATER BENEFIT WILL BE TO SOCIETY BECAUSE IF YOU CURE DISEASE OR WE DO THINGS LIKE THAT, THE BIGGEST, BIGGEST REWARDS HAPPEN FOR ALL OF US WHO MIGHT GET SICK OR HAVE A DISEASE LIKE THAT.

I THINK WE'VE JUST GOT TO STAY IN THIS

TOGETHER. THERE NEEDS TO BE CHECKS AND BALANCES. WE NEED TO LOOK CONSTANTLY BACK AND FORTH WHERE WE'RE SPENDING THE MONEY. I THINK YOUR INPUT, ALL OF IT TODAY, HAS BEEN VERY HELPFUL TO HAVE. THANK YOU FOR LETTING ME COMMENT.

DR. TROUNSON: I THINK THERE SHOULDN'T BE ANY DOUBT THAT UNDER PROPOSITION 71 WE'RE ABLE TO SUPPORT CLINICAL STUDIES, CLINICAL TRIALS. I THINK IF MY LEGAL PARTNERS AND EVERYBODY AT CIRM IS THAT WE ABSOLUTELY UNDERSTAND THAT WE CAN BE SUPPORTIVE OF CLINICAL TRIALS. IN MY VIEW WE SHOULD DO WHAT'S NECESSARY TO HELP THIS PROCESS GET STARTED TO THE PATIENT.

DR. FRIEDMAN: PLEASE, YOU HAVE A QUESTION OR COMMENT?

SPEAKER: (NAME INDISCERNIBLE), CITY OF HOPE. I ACTUALLY HAVE MORE OF A REQUEST THAN A COMMENT. IT HAS TO DO WITH STEM CELL RESEARCH AND OVERSIGHT COMMITTEES. WE ARE REQUIRED TO HAVE ONE OF THESE TO OVERSEE THE STEM CELL WORK WE DO ON CAMPUS, YET AT LEAST IN OUR EXPERIENCE THE IMPLEMENTATION OF THIS BODY HAS BEEN THROUGH OUR OWN READING OF THE HEALTH CODES AND COLLABORATION WITH OTHER INSTITUTIONS. NOW WE'RE ALL TALKING TO EACH OTHER, I THINK IT WOULD BE REALLY GOOD IF CIRM COULD

GIVE MORE CLEAR GUIDANCE OF THE ROLE AND THE SCOPE OF THESE BODIES AS THE SCIENCE EVOLVES AND MOVES FORWARD.

DR. CSETE: SO WE DO HAVE A SCIENCE OFFICER WHO IS REALLY EXPERT IN THIS AREA, GEOFF LOMAX, AND HE'S BEEN GOING AROUND SYSTEMATICALLY TRYING TO VISIT THE SCRO'S -- I GUESS HE HASN'T BEEN DOWN HERE YET -- TO HELP YOU WITH YOUR PROCESSES AND STREAMLINING THINGS AND REALLY JUST FACILITATING YOUR WORK BECAUSE WE KNOW IT'S QUITE A BURDEN ADMINISTRATIVELY.

AFTER THE LAST STANDARDS WORKING GROUP MEETING, WE SAT DOWN WITH TWO OF THE PEOPLE WHO RUN SCRO COMMITTEES AT OTHER LARGE INSTITUTIONS AND DEVELOPED A PLAN TO BRING UP THE SCRO LEADERS TO ALL SIT DOWN TOGETHER IN THE CIRM OFFICES SOMETIME SOON SO THAT THEY CAN EXCHANGE BEST PRACTICES, SO THAT'S ON THE BOOKS.

DR. FRIEDMAN: YES, PLEASE.

MR. SIMPSON: JOHN SIMPSON, CONSUMER WATCHDOG. WE'VE BEEN TALKING A LITTLE BIT ABOUT FUNDING, AND I'M JUST WONDERING IF WE CAN GET AN UPDATE RIGHT NOW ON WHERE THAT STANDS. UNLESS -- AS I UNDERSTAND IT, UNLESS EITHER THE STATE SELLS BONDS OR THEY GET PRIVATELY PLACED, YOU WILL RUN OUT OF

MONEY FOR YOUR CURRENT COMMITMENTS PROBABLY IN SEPTEMBER. SO NONE OF US WANTS TO SEE THAT HAPPEN. I'M JUST CURIOUS WHERE WE STAND WITH THAT.

DR. TROUNSON: WELL, WE HAVE IN PROGRESS, IN TERMS OF HAVING MORE MONEY IN THE BANK AT THIS POINT, JOHN. WE HAVE A PLAN TO CUT DOWN OUR PROGRAM, NOT -- IN ORDER TO BRING IT DOWN INTO A MORE CUT-DOWN BASIS. AND IF WE'RE ABLE TO RAISE $200 MILLION IN TWO TRANCHES THIS YEAR IN A CUT-DOWN FRAMEWORK, WHICH WE WOULDN'T ALTER OUR RFA'S, BUT WOULD REDUCE THE AMOUNT THAT WE'RE GOING TO BE PASSING OUT, WE WOULD STAY ON TRACK.

NOW, IF YOU'RE ASKING ME MY ECONOMIC ANALYSIS ADVICE ON THAT, YOU HAVE TO TAKE THAT WITH A LARGE GRAIN OF SALT. BUT UNDERSTAND THAT THE AVAILABILITY OF PRIVATE BONDS GUARANTEED BY THE STATE THREE YEARS WITH A REASONABLE PERCENTAGE INTEREST IS ATTRACTIVE. AND SO I HAVE A FEELING PERSONALLY, WHICH MEANS NOTHING MORE THAN THAT, THAT WE WILL BE ABLE TO DO THE 200 MILLION.

NOW, IN ORDER TO BE ABLE TO COME BACK ON OUR NORMAL BOND PROGRAM, WE'RE ENVISAGING THAT IT MIGHT TAKE TWO YEARS IN ORDER NOT TO PUSH OUR WAY INTO THE LINE AND PUSH THE UNFORTUNATE MENTAL HEALTH PATIENTS, TEACHERS, ETC., OUT OF THE WAY.

SO ON THAT BASIS, TO HAVE THAT PROGRAM OPERATE AT THE REALLY HIGH RATE WE'RE OPERATING, WE WOULD NEED ANOTHER $150 MILLION NEXT YEAR, BUT I'M NOT COUNTING THAT AT THIS STAGE. I'D LIKE TO SEE HOW WE GO WITH THE BOND RAISING THIS YEAR ON A CUT-DOWN PROGRAM. I THINK WE'LL BE ABLE TO DO IT. MY FEELING IS OF SOME CONFIDENCE, BUT I AM NO EXPERT IN THE ECONOMIC MATTER. BUT MYSELF, AND PARTICULARLY JOHN ROBSON, WHO IS HERE, HAS BEEN WORKING ON THIS TO SEE WHAT WOULD BE THE BEST SET OF OPPORTUNITIES FOR RECOMMENDATIONS TO GO TO THE UPCOMING BOARD ABOUT WHAT WE SEE AS PRIORITIES IN ORDER TO DO THIS CUT-DOWN PROGRAM.

THERE WILL -- OF COURSE, WHATEVER CUT-DOWN COMPONENT THERE IS WILL CAUSE SOME PAIN, NO DOUBT; BUT THE WHOLE COMMUNITY IS SUFFERING, SO WE RECOGNIZE THAT THERE'S GOING TO BE SOME DIFFICULTY IN MAKING IT THROUGH THESE NEXT TWO YEARS FOR EVERYBODY AND WISH IT WASN'T LIKE THAT. BUT WE HOPE THAT WHAT WE RECOMMEND WILL BE ADOPTED OR SOMETHING LIKE THAT WILL BE ADOPTED BY THE ICOC, AND WE'LL BE ABLE TO CONTINUE OUR PROGRAMS.

DR. FRIEDMAN: YES.

DR. IVERSON: WHAT IS THE CURRENT INTEREST RATE CIRM IS PAYING ON ITS BOND DEBT?

DR. TROUNSON: I'M NOT AN EXPERT AT THAT. SO YOU CAN ASK OUR LEGAL PERSON.

MR. SWEEDLER: I DON'T KNOW THE INTEREST RATE FOR THE BONDS THAT HAVE ALREADY BEEN SOLD. THAT'S DETERMINED BY THE TREASURER'S OFFICE, WHICH DOES THAT FOR ALL STATE BONDS. AND THE TREASURER'S OFFICE WILL BE DETERMINING THE INTEREST RATE FOR THE BONDS THAT ARE CURRENTLY IN THE WORKS FOR PRIVATE PLACEMENT, SO THAT'S NOT SOMETHING THAT CIRM CONTROLS. THE STATE TREASURER DOES THAT FOR ALL STATE FUNDING.

DR. IVERSON: A RANGE, IS IT 2 PERCENT, 5 PERCENT.

MR. SWEEDLER: I DON'T KNOW.

DR. TROUNSON: WE THINK IT'S AROUND 5 PERCENT; BUT, AGAIN, IT'S NOT OUR DECISION, SO THAT'S WHAT WE THINK IT WILL BE.

MR. GIBBONS: TALKING ABOUT 3 TO 5 PERCENT IN CURRENT DISCUSSIONS, TAXABLE.

MR. SIMPSON: AND THE CURRENT ONES --

DR. FRIEDMAN: IF I COULD ASK PEOPLE TO USE THE MICROPHONE, PLEASE, TO CAPTURE ALL THESE COMMENTS.

DR. TROUNSON: I THINK DON GIBBONS MADE THE POINT THAT IN THE CURRENT DISCUSSIONS IT'S

AROUND 4 TO 5 PERCENT.

MR. GIBBONS: CORRECT.

DR. FRIEDMAN: OTHER COMMENTS OR QUESTIONS, PLEASE.

DR. TROUNSON: WE REALLY APPRECIATE ALL OF THE INPUTS. JUST BECAUSE WE'RE ANSWERING THEM, DON'T THINK WE'RE DEFENSIVE, BECAUSE I THINK IN THE SENSE THAT WE WANT THE INPUTS, AND SO I THINK THAT HELPS US. THIS MEETING IS TRANSCRIBED, AND THANKS VERY MUCH. IT'S A DIFFICULT JOB OF DOING THAT. SO THERE WILL BE A PERMANENT RECORD OF IT, SO YOUR VIEWS WILL BE KEPT AS RECORD FOR THOSE MEMBERS OF THE BOARD WHO ARE NOT HERE. AND WE HAVE A NUMBER OF OUR COLLEAGUES FROM THE BOARD, AND IT'S GREAT TO HAVE THEM HERE. THEY WILL OBVIOUSLY TAKE THIS MESSAGE BACK, BUT THE OTHER BOARD MEMBERS WILL BE ABLE TO READ THIS.

OUR CHAIRMAN OF THE BOARD, BOB KLEIN, WILL BE READING IT. HE TOLD ME THAT HE APOLOGIZES FOR NOT BEING HERE; BUT BECAUSE OF THE TRANSCRIPT, HE'LL BE ABLE TO READ THE COMMENTS.

SO IF THERE ARE OTHER COMMENTS AND OTHER INPUTS THAT YOU WANT TO MAKE, THE NATURE OF CIRM IS TO BE OPEN AND TO ACCEPT THEM AND TO RECEIVE THEM. SO THE BEST WAY OF DOING IT, I THINK, AT THIS POINT

IS IF YOU ADDRESS YOUR QUERIES TO DON GIBBONS AT THE INSTITUTE, AND HE THEN FARMS THEM OUT TO THE PEOPLE WHO WILL RESPOND APPROPRIATELY SO THAT WE ENSURE THAT SOMEBODY WHO HAS THE EXPERTISE TO ANSWER THE QUESTIONS WILL ANSWER THEM.

THIS IS PART OF THE PROCESS FOR US TO UNDERSTAND WHAT WE SHOULD DO IN TERMS OF REVISION OF OUR STRATEGIC PLAN. IT IS A PLAN WHICH WORKS IN REAL TIME, SO IT IS ALREADY DIFFERENT TO WHAT WAS WRITTEN IN 2006, BUT WE WANTED TO GET YOUR VIEWS, YOUR FEELINGS, AND YOUR CRITICISMS ABOUT THE DIRECTION THAT WE WOULD HOPE THAT WE MIGHT BE ABLE TO TAKE IN ORDER TO FURTHER OUR MISSION. AND OUR MISSION IS THE PRIMARY TASK THAT DRIVES US. SO PLEASE FEEL FREE TO CONTACT US. AND DO THAT, IF YOU WILL, THROUGH DON GIBBONS AT CIRM, AND YOU WILL FIND HIS OFFICE VERY RESPONSIVE TO YOUR QUESTIONS OR YOUR CRITICISMS OR YOUR ADVICE. AND WE THANK YOU FOR ALL YOUR INPUTS. AND, MICHAEL, THANK YOU FOR PROVIDING THIS FORUM FOR US.

(APPLAUSE.)

DR. FRIEDMAN: YOU'RE VERY WELCOME. LET ME JUST CLOSE THE MEETING, IF I CAN, BY THANKING THE CIRM STAFF FOR HAVING THIS MEETING HERE, TO ALL THE PARTICIPANTS IN THE AUDIENCE FOR YOUR THOUGHTFUL

QUESTIONS AND COMMENTS. TO REITERATE ALAN'S POINT, THIS IS A PROCESS OF PROGRESSIVE REVELATION WHERE IDEAS, SUGGESTIONS, COMMENTS, NEW SCIENCE DRIVES HOW THIS ORGANIZATION ACTUALLY SPENDS OUR COLLECTIVE MONEY. AND THAT THIS IS A VERY IMPORTANT ACTIVITY. YOUR PARTICIPATION HERE TODAY IS VERY MUCH APPRECIATED AND VERY MUCH RECOGNIZED.

I THINK WHAT WE SAW HERE TODAY IS WHAT I HOPED WE WOULD SEE, WHICH IS A TENSION BETWEEN COMPETING OPPORTUNITIES, NEEDS, AND CONCERNS. AND THIS IS A TENSION WHICH DAILY DRIVES THE CIRM STAFF AND, IN FACT, DRIVES THE SCIENTISTS TO PURSUE THESE WONDERFUL IDEAS.

YOU'VE HEARD DISCUSSION TODAY HOW MUCH EMPHASIS BASIC SINCE VERSUS HOW MUCH EMPHASIS ON TRANSLATIONAL OR CLINICAL SCIENCE. IT'S A WONDERFULLY IMPORTANT TOPIC. THERE'S NOT A SIMPLE ANSWER. IT REQUIRES ONGOING ATTENTION AND CONSIDERATION. YOU'VE HEARD VARIOUS COMPETITIONS BETWEEN PARTICULAR DISCIPLINES, THE IMPORTANCE OF IMMUNOLOGY, THE IMPORTANCE OF SMALL MOLECULE HIGH THROUGHPUT SCREENING. IT'S NOT THAT ONE IS GOOD AND ONE IS BAD. THESE ARE EXCELLENT IDEAS, AND IT'S NOT JUST TWO THAT ARE COMPETING, BUT LITERALLY DOZENS. AND THIS IS THE CHALLENGE THAT ALAN AND MARIE AND

OTHERS ARE LOOKING AT TO SEE HOW DO WE TAKE THE PRECIOUS DOLLARS THAT HAVE BEEN INVESTED BY THE CITIZENS OF CALIFORNIA IN THIS DIFFICULT ECONOMIC TIME, HOW DO WE TAKE THE HOPES AND ASPIRATIONS OF PATIENTS, THEIR FAMILIES, THEIR ADVOCATES WHO WANT BETTER OPTIONS, AND HOW DO WE TAKE THE RESPONSIBILITIES OF THE SCIENTISTS WHO ARE GENUINELY LOOKING FOR WHAT IS THE BEST WAY TO DISCOVER NEW KNOWLEDGE AND MAKE THAT KNOWLEDGE MEANINGFUL FOR ITS OWN SAKE FOR FUNDABLE APPLICATIONS.

THESE ARE VERY DIFFICULT, VERY DEMANDING TENSIONS THAT FORTUNATELY WE HAVE SOME OF THE BEST SCIENTISTS IN THE WORLD AND SOME OF THE MOST SKILLED AND THOUGHTFUL LEADERS OF THIS ORGANIZATION. IT'S A PRIVILEGE FOR ME TO SERVE ON THE INDEPENDENT CITIZENS OVERSIGHT COMMITTEE, AND I APPRECIATE YOUR PARTICIPATION TODAY. SO ON BEHALF OF EVERYONE THANK YOU VERY MUCH.

(APPLAUSE.)

(THE MEETING WAS THEN CONCLUDED AT 11:28 A.M.)

REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE PROCEEDINGS BEFORE THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF A PUBLIC HEARING IN RE PUBLIC COMMENT ON THE UPDATED STRATEGIC PLAN HELD AT THE LOCATION INDICATED BELOW

THE CITY OF HOPE
DUARTE, CALIFORNIA
ON
MARCH 5, 2009

WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

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