BEFORE THE

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

REGULAR MEETING

LOCATION:	LUXE HOTEL 11461 SUNSET BOULEVARD LOS ANGELES, CALIFORNIA
DATE:	OCTOBER 27, 2009 4:30 P.M.
REPORTER:	BETH C. DRAIN, CSR CSR. NO. 7152
BRS FILE NO.:	84474

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LOS ANGELES, CALIFORNIA; TUESDAY, OCTOBER 27, 2009

4:30 P.M.

CHAIRMAN KLEIN: MELISSA KING, COULD YOU ADVISE THE CHAIR ON THE BOARD ON HOW WE'RE DOING IN THE TRANSIT PROGRESS OF BOARD MEMBERS?

MS. KING: WE HAVE 18 PEOPLE PRESENT RIGHT NOW, INCLUDING MARCY FEIT, WHO'S JOINING BY PHONE. QUICK CHECK. MARCY, CAN YOU HEAR ME? I UNDERSTOOD SHE WAS ON THE LINE. MAYBE SHE STEPPED AWAY FROM THE PHONE BRIEFLY. WE HAVE A COUPLE OF MEMBERS THAT I KNOW ARE ON THEIR WAY RIGHT NOW.

CHAIRMAN KLEIN: WITH THAT COUNT, I'M GOING TO PROCEED THROUGH THE BASIC INTRODUCTORY MATERIAL SO WE CAN MOVE THIS ALONG. WE DO UNDERSTAND THAT THE SANTA ANA WINDS HAVE EVIDENTLY WHIPPED UP THE WINDS AT THE AIRPORT AND MAY HAVE SLOWED DOWN SOME OF THE PEOPLE COMING IN FROM NORTHERN CALIFORNIA.

I'D LIKE TO WELCOME EVERYONE TO LOS ANGELES AND ASK IF MELISSA KING COULD LEAD US IN THE PLEDGE OF ALLEGIANCE.

(THE PLEDGE OF ALLEGIANCE.)

CHAIRMAN KLEIN: AND, MELISSA, IF YOU COULD PROCEED THROUGH THE ROLL CALL, PLEASE.

MS. KING: BEFORE I DO THAT, I JUST WANT TO LET EVERYBODY ON THE BOARD KNOW, BECAUSE I DID GET THIS QUESTION ASKED A COUPLE OF TIMES, YOU DO HAVE COPIES OF THE EXTRAORDINARY PETITIONS THERE IN THE LEFT FRONT COVER OF YOUR BINDER IN THE POCKET THERE. THEY'RE THE DOCUMENTS THAT ARE STAPLED TOGETHER, AND THERE ARE SIX OF THEM.

RICARDO AZZIZ. ROBERT PRICE FOR ROBERT BIRGENEAU.

DR. PRICE: PRESENT.

MS. KING: FLOYD BLOOM.

DR. BLOOM: HERE.

MS. KING: DAVID BRENNER. WILLIAM BRODY. JACOB LEVIN FOR SUSAN BRYANT.

DR. LEVIN: HERE.

MS. KING: MARCY FEIT.

MS. FEIT: HERE.

MS. KING: MICHAEL FRIEDMAN. LEEZA GIBBONS.

MS. GIBBONS: HERE.

MS. KING: MICHAEL GOLDBERG. SAM HAWGOOD. BOB KLEIN.

CHAIRMAN KLEIN: PRESENT.

MS. KING: SHERRY LANSING.

MS. LANSING: HERE.

MS. KING: GERALD LEVEY.
DR. LEVEY: HERE.
MS. KING: TED LOVE.
DR. LOVE: HERE.
MS. KING: ED PENHOET.
DR. PENHOET: HERE.
MS. KING: PHIL PIZZO. CLAIRE POMEROY.
DR. POMEROY: HERE.
MS. KING: FRANCISCO PRIETO.
DR. PRIETO: HERE.
MS. KING: CARMEN PULIAFITO. ROBERT QUINT. JEANNIE FONTANA FOR JOHN REED.
DR. FONTANA: HERE.
MS. KING: DUANE ROTH.
MR. ROTH: HERE.
MS. KING: JOAN SAMUELSON.
MS. SAMUELSON: HERE.
MS. KING: DAVID SERRANO-SEWELL. JEFF SHEEHY.
MR. SHEEHY: HERE.
MS. KING: JON SHESTACK. OSWALD STEWARD.
DR. STEWARD: HERE.
MS. KING: ART TORRES.
MR. TORRES: HERE.
CHAIRMAN KLEIN: THANK YOU VERY MUCH. IN

CALLING THIS TO ORDER HERE IN THE WEST SIDE OF LOS ANGELES, THANK DR. LEVEY FOR THE WEATHER.

MS. LANSING: HE'S TOTALLY RESPONSIBLE FOR THE WINDS. THAT'S IT.

CHAIRMAN KLEIN: WHEN YOU CONTROL THE GODS OF THE WINDS, YOU'RE UP THERE IN THE HIERARCHY. I'D LIKE TO THANK JENNIFER PRYNE AND MELISSA KING FOR GETTING THIS SESSION PUT TOGETHER LOGISTICALLY AND NICK WARSHAW FOR HIS HELP IN THAT EFFORT. WE HAVE ONE MEMBER JOINING BY PHONE TONIGHT AND TOMORROW, MARCY FEIT, WHO'S ON THE PHONE. AND COULD THE STAFF PLEASE, IF I'M NOT HEARING MARCY WHO WANTS TO MAKE A COMMENT, PLEASE STAND AND NOTIFY ME SO THAT I'M AWARE THAT SHE'S TRYING TO MAKE COMMENT IN DISCUSSION.

WE APPRECIATE, MARCY, THE SPECIAL EFFORT YOU'RE MAKING FOR THIS SESSION.

THE SESSION THAT WE'RE COMMENCING TODAY MARKS A CRITICAL, A HISTORIC BENCHMARK FOR THIS AGENCY AND THIS BOARD AS WE PROCEED TO MOVE DOWN THE PIPELINE TOWARDS PATIENTS AND PATIENT THERAPIES. IT IS A TREMENDOUS PRIVILEGE FOR US TO BE AT THIS POINT. IT IS A PRIVILEGE BECAUSE WE ON THE BOARD, AN EXTRAORDINARY BOARD OF EXCEPTIONAL INDIVIDUALS, ARE LIFTED BY THE WORK OF OUR WORKING GROUPS,

REPRESENTING PEOPLE THROUGHOUT CALIFORNIA AND THROUGHOUT THIS COUNTRY AND AROUND THE WORLD WHO HAVE CONTRIBUTED THEIR TIME, AND WE'RE ANCHORED BY AN INCREDIBLE STAFF OF PASSION AND COMMITMENT.

WE HAVE THE OPPORTUNITY TO HONOR IN AN UNPRECEDENTED FASHION THE VISION OF 7 MILLION CALIFORNIA VOTERS. IN THAT PROCESS IT'S IMPORTANT AS WE PROCEED TO RECOGNIZE AWARDS THAT ARE GIVEN TO INDIVIDUALS SERVING ON OUR WORKING GROUPS. ONE OF THOSE INDIVIDUALS IS DR. ALTA CHARO, WHO BEGAN HER INVOLVEMENT THROUGH THE NATIONAL ACADEMIES' TASK FORCE ON THE MEDICAL AND ETHICAL STANDARDS DEVELOPMENT. SHE PARTICIPATED AS A LEADER IN THE NATIONAL ACADEMY WORKSHOP AT THE BECKMAN CENTER IN IRVINE IN DECEMBER OF 2004 BEFORE OUR BOARD WAS EVEN FORMED. SHE LATER SERVED AS A MEDICAL AND ETHICAL STANDARDS ADVISOR TO OUR BOARD ITSELF IN THE FORMATION OF THE STANDARDS WORKING GROUP, AND SHE HAS SERVED WITH US FOR FIVE YEARS.

DR. CHARO IS NOW GOING TO TAKE A LEAVE BECAUSE SHE HAS BEEN MADE A SENIOR ADVISOR IN THE OFFICE OF THE COMMISSIONER AT THE FDA OVER THE NEXT YEAR, A TREMENDOUS ACCOMPLISHMENT AND POINT OF RECOGNITION.

IN ADDITION, I WOULD LIKE TO POINT OUT TWO

OTHER MEMBERS OF OUR STANDARDS WORKING GROUP WHO HAVE RECENTLY BEEN RECOGNIZED FOR THEIR EXCEPTIONAL SERVICE AND SCIENTIFIC ABILITY. DR. JANET ROWLEY WAS AWARDED THE GRUBER GENETICS PRIZE FOR CANCER RESEARCH, AND DR. ANN KIESSLING WAS AWARDED THE HESKEL GABBAY AWARD IN BIOTECHNOLOGY AND MEDICINE FOR SIGNIFICANT CONTRIBUTIONS IN THE FIELD OF ASSISTED HUMAN REPRODUCTION. SO WE SERVE WITH THE BENEFIT OF SOME EXTRAORDINARY INDIVIDUALS FOR WHOM WE HAVE TREMENDOUS RESPECT AND APPRECIATION.

IT IS ALSO VITAL TO RECOGNIZE AS WE GO FORWARD THAT WHILE THE 7 MILLION VOTES EMPOWERED THIS AGENCY WITH THE FINANCIAL AUTHORIZATION FROM THIS INITIATIVE, IT IS THE CONTINUING CONTRIBUTION AND COLLABORATIVE SUPPORT OF THE GOVERNOR'S OFFICE WITH MIKE GENEST AND HIS TEAM AT THE DEPARTMENT OF FINANCE AND TREASURER LOCKYEAR AND HIS STAFF THAT WE HAVE MOVED SO SUCCESSFULLY FORWARD TO MEET IN A TIMELY WAY OUR FINANCIAL NEEDS TO KEEP THE CONTINUITY OF OUR FUNDING AND TO PROVIDE THE ASSURANCES TO THE COMPLEX LARGEST INTERINSTITUTIONAL TEAMS THAT ARE PART OF THE DISEASE TEAM AWARDS, INCLUDING PARTICULARLY THE INTERNATIONAL COLLABORATIONS, THAT THE FUNDING IS THERE DESPITE A STRONG AND CONSTANT DRUMBEAT OF PUBLICITY ABOUT THE

CALIFORNIA ECONOMY AND THE CALIFORNIA BUDGET.

IT IS AN ARTICLE OF FAITH THAT SEVEN NATIONS HAVE JOINED TOGETHER WITH US IN BILATERAL AGREEMENTS GIVEN THE STATEMENTS THAT CALIFORNIA CANNOT MAKE THE COMMITMENTS FOR THE FUTURE THAT ARE SO CRITICAL TO ITS PEOPLE. CERTAINLY AT THIS POINT I'VE TALKED TO MEMBERS OF THE FINANCE AND/OR LEGAL TEAMS OF SIX OUT OF THOSE SEVEN NATIONS THAT HAVE JOINED WITH US IN BILATERAL AGREEMENTS AND PROVIDED, WITH THE ASSISTANCE OF JAMES HARRISON, A STATUTORY ANALYSIS, CONSTITUTIONAL ANALYSIS, BUDGET ANALYSIS, AND CONFIRMATIONS OUT OF OUR ABILITY TO FUND THIS RESEARCH.

IT IS VITAL TO CALIFORNIA TO BE ABLE TO LEVERAGE OUR RESEARCH OF OUR CALIFORNIA SCIENTISTS AND ALLOW THEM FROM A GROUND-UP BASIS TO JOIN WITH THE BEST MINDS IN THESE COUNTRIES TO ADVANCE THE RESEARCH BECAUSE IT LEVERAGES THE FUNDS OF CALIFORNIA VOTERS AND ACCELERATES THERAPIES FOR PATIENTS. BUT I WILL TELL YOU HAVING THE FUNDS IN THE BANK TO FUND THESE INTERNATIONAL COLLABORATIONS IS VERY PERSUASIVE. AND WITH THAT WE PARTICULARLY APPRECIATE THE GOVERNOR'S OFFICE, THE DEPARTMENT OF FINANCE'S SUPPORT, AND TREASURER LOCKYEAR AND HIS STAFF IN THE MOST RECENT BOND ISSUE WHERE WE

RECEIVED 118 MILLION OF NEW MONEY, WHICH GIVES US THE CAPACITY TO MOVE THROUGH TO OUR GOAL OF DECEMBER 2010 WITH A BUFFER.

NOW, AS WE GO FORWARD, BECAUSE THERE ARE OPPORTUNISTIC PROGRAMS AND ADDITIONAL APPLICATIONS WHICH AT TIMES MAY EXCEED THE TARGET FOR ANY PARTICULAR GRANT CYCLE, PART OF THAT BUFFER MAY BE USED. BUT WE CAN PROVIDE ASSURANCES TO OUR INSTITUTIONS WHO ARE STRAPPED AND CAN'T GET OUT ON A LIMB IF WE CAN'T FUND THESE GRANTS WE'RE APPROVING. WE CAN PROVIDE THEM REALLY STRONG COMFORT THAT WE HAVE THE FUNDS AVAILABLE TO MAKE THIS GRANT PROGRAM WORK AND DRIVE IT SMOOTHLY FORWARD IN A VERY ADVERSE ENVIRONMENT, BUT A CRITICAL, CRITICAL PROGRESS THAT HAS TO BE MAINTAINED IF OUR MANDATE FOR PATIENTS, OUR MISSION THAT 7 MILLION VOTERS DIRECTED US TO ACCOMPLISH IS TO BE FULFILLED.

SO IT IS WITH THE BENEFIT OF THOSE DOLLARS THAT WE MOVE FORWARD INTO THE DISEASE TEAM COMPETITION WHICH WILL BE A CENTRAL CORE OF OUR NEXT TWO DAYS. I WOULD LIKE TO SAY THAT IT IS IMPORTANT NOT TO LOOK AT THOSE GRANTS THAT HAVE LOWER RANKINGS AND BELIEVE THAT THE SCIENCE IS NOT GREAT SCIENCE. THAT LOWER RANKING MAY BE BECAUSE THE PEER REVIEW GROUP THOUGHT IT SHOULD BE A TRANSLATIONAL GRANT.

THE LOWER RANKING MAY BE BECAUSE THERE WAS A TIMING PROBLEM IN GETTING CRITICAL DATA IN UNDER OUR SYSTEM WHICH DOES NOT ALLOW FOR INTERIM SUBMISSIONS PRIOR TO THE PEER REVIEW WORKING GROUP DESPITE THE SIGNIFICANT TIME BETWEEN THE APPLICATION CUTOFF AND THE PEER REVIEW.

WE MIGHT, IN FACT, IN THE DECEMBER MEETING LOOK AT THAT BARRIER AND SEE IF, IN FACT, IT SHOULD BE AMENDED BECAUSE THESE TEAMS, SOMETIMES INVOLVING 50 OR 60 INDIVIDUALS, CAN PRODUCE SOME VERY CRITICAL DATA OVER FAIRLY SHORT PERIODS OF TIME. AND THE QUESTION IS DO WE WANT TO HAVE AN OPPORTUNITY FOR DATA TO COME IN PRIOR TO THE PEER REVIEW EVALUATION OCCURRING WITH ENOUGH TIME FOR THE OUTSIDE REVIEWERS TO PROPERLY ANALYZE THE DATA AND DO THE REVIEW.

IT MAY ALSO BE THAT A PARTICULAR PROPOSED AWARD WAS DOWNSTREAM ESSENTIALLY AT A CLINICAL TRIAL STAGE; AND, OF COURSE, THIS IS A ROUND WHERE WE'RE TRYING TO GET TO APPLICATIONS THAT WITHIN 48 MONTHS HAVE -- THE CONVINCING EVIDENCE THAT WITHIN 48 MONTHS THEY CAN GET TO A PHASE I APPROVAL. SO IF AN APPLICATION IS AT A CLINICAL TRIAL STAGE, FOR EXAMPLE, IN ANY OF THESE ROUNDS, IT WOULDN'T FIT INTO A DISEASE TEAM ROUND. IT WOULD BE APPROPRIATE FOR A CLINICAL TRIAL ROUND.

SO IT IS IMPORTANT TO RECOGNIZE THAT WE HAVE SOME GREAT SCIENCE AMONG SOME OF THESE OTHER APPLICATIONS. I THINK THE SCIENCE TEAM HAS BEEN VERY CLEAR THAT THAT GREAT SCIENCE IN SOME CASES WILL CERTAINLY BE PICKED UP IN LATER ROUNDS, WHETHER THE TRANSLATIONAL ROUNDS, WHETHER THE CLINICAL TRIAL ROUNDS, BUT WHAT WE'RE TRYING TO DO TODAY AND TOMORROW IS CAPTURE THOSE THAT ARE PREPARED TO MEET THE STANDARDS FOR THIS ROUND AT THIS TIME.

WITH THAT, I'D LIKE TO INVITE MELISSA KING TO MAKE A COMMENT.

MS. KING: I JUST WANTED TO STATE FOR THE RECORD THAT ICOC MEMBERS RICARDO AZZIZ AND ROBERT QUINT HAVE JOINED THE MEETING, AND WE DO HAVE A QUORUM.

CHAIRMAN KLEIN: THANK YOU VERY MUCH. DR. TROUNSON, IF YOU WILL TAKE THE PODIUM, PLEASE.

DR. TROUNSON: SO SORRY, MR. CHAIRMAN. THERE ARE A FEW FINGERS IN THE SLIDES THAT I'M GOING TO SHOW. SO GOOD AFTERNOON, BOARD. AND I WANT TO START WITH SOMETHING THAT'S A BIT UNUSUAL. ELIZABETH BLACKBURN HAS WON THE NOBEL PRIZE THIS YEAR FOR MEDICINE. AND I THINK IT'S AN OUTSTANDING ACHIEVEMENT. AND I HAVEN'T BROUGHT HER NAME FORWARD BECAUSE SHE'S AN AUSTRALIAN, BECAUSE SHE IS, BUT SHE

CLEARLY HAS AN APPOINTMENT AT THE UCSF. AND HER PRIMARY WORK DONE THERE ON TELOMERASE RESULTED IN HER GETTING AWARDED THE NOBEL PRIZE. BUT IT'S ALSO A VERY IMPORTANT DISCOVERY FOR STEM CELLS BECAUSE IT IS THE ADDITION OF THE TIPS, IF YOU LIKE, TO THE CHROMOSOMES THAT ALLOWS THE CELLS TO CONTINUE TO DIVIDE, AS FAR AS WE KNOW, IN AN IMMORTAL WAY.

SO WITH TELOMERASE YOU KEEP ADDING ON TO THE ENDS OF THE CHROMOSOMES, THE SO-CALLED TELOMERES, AND THEY ALLOW THE CELL TO CONTINUE DIVIDING. AS THE TELOMERES SHORTEN WHEN THERE IS NO TELOMERASE IN THE NORMAL CELLS OF YOUR BODY, THERE'S A CERTAIN LIFETIME TO THE CELL'S ABILITY TO DIVIDE.

AND SO THIS IS AN EXTREMELY IMPORTANT DEVELOPMENT NOT ONLY IN STEM CELLS, OF COURSE, IN CANCER AND MANY OTHER AREAS. AND I THINK WE OUGHT TO REJOICE IN LIZ WINNING THIS NOBEL PRIZE. IF YOU HAVEN'T MET HER, MAYBE WE SHOULD SOMETIME GET HER TO COME TO THE BOARD, CHAIR, BECAUSE SHE WOULD PROBABLY ENJOY MEETING ALL OF US. SHE STOOD UP FOR ALL OF US AT A TIME WHEN PRESIDENT BUSH WASN'T SO SUPPORTIVE, AND SHE GOT HERSELF LOST OFF THE ETHICS COMMITTEE. I THINK REALLY SHE REALLY DIDN'T EXPRESS THE RIGHT KIND OF SENTIMENTS, AS I UNDERSTOOD. SO SHE'S A VERY SPECIAL PERSON. AND AS I SAID, IT'S NOT ONLY

BECAUSE SHE'S AUSTRALIAN.

THE NEXT. SOMEBODY SAID AUSTRALIANS ARE TAKING OVER. NOT TRUE.

SO THE NEXT ONE YOU KNOW VERY WELL. AND, OF COURSE, I THINK WE ALSO NEED TO REJOICE IN BOB KLEIN WINNING THE GORDON AND LLURA GUND LEADERSHIP AWARD WHICH WAS JUST RECENTLY ANNOUNCED BY RESEARCH AMERICA.

(APPLAUSE.)

DR. TROUNSON: I THINK IT'S AS GOOD AS YOU GET, BOB, TO A NOBEL PRIZE. MAYBE THE PEACE PRIZE.

CHAIRMAN KLEIN: DR. TROUNSON, IN RECOGNIZING BOARD MEMBERS, I WAS GOING TO SAVE IT FOR A SPECIAL CELEBRATION, BUT I THINK IT'S A VERY HIGH HONOR IN THIS COUNTRY TO BE NAMED AS A SCIENTIFIC ADVISOR TO THE PRESIDENT. AND ON THAT SCIENTIFIC COUNCIL, DR. PENHOET HAS THAT HIGH HONOR, AND I THINK WE SHOULD GIVE HIM A ROUND OF APPLAUSE.

(APPLAUSE.)

DR. TROUNSON: THAT'S VERY IMPORTANT. AND I DIDN'T KNOW THAT IT HAD BEEN RATIFIED YET, ED. IT HAS, HAS IT? GOOD. GREAT. THAT'S FANTASTIC. WONDERFUL.

SO THE NEXT SLIDE. NOW, BACK INTO THE SCIENCE. AND SO IN THIS FIRST ONE, FIRST SLIDE THAT

I WANTED TO SHOW YOU IS REALLY ABOUT PROSTATE CANCER STEM CELLS. THERE'S AN ARGUMENT, AS YOU KNOW, WHETHER SOLID TUMORS OR TUMORS AND CANCERS REALLY HAVE CANCER STEM CELLS. AND I THINK THIS IS A PAPER THAT WAS PUBLISHED IN *NATURE* IN SEPTEMBER ONLINE, THE 24TH OF SEPTEMBER. AND IT SHOWS THAT IN THE MOUSE THERE ARE RARE LUMINAL CELLS IN THE PROSTATE THAT EXPRESS A GENE CALLED NKX-3.1. IT'S A HOMEOBOX GENE, AND IN THE ABSENCE OF TESTICULAR ANDROGENS ARE BIOPOTENTIAL FOR SELF-RENEWAL SO THAT THEY PRODUCE -- THEY RENEW, BUT THEY ALSO PRODUCE OTHER CELLS, SO THEY'RE, IN FACT, A STEM CELL.

THESE CELLS ARE CAPABLE OF FORMING PROSTATE DUCTS IN RENAL GRAFTS USING SERIAL SINGLE TRANSPLANT ASSAYS. SO IF YOU TAKE A SINGLE CELL, YOU CAN ACTUALLY GET IT TO PRODUCE PROSTATE TISSUE WHICH GIVES YOU THE SENSE THAT THIS IS A GENUINE PROSTATE STEM CELL.

AND IF YOU DELETE IN A TARGETED WAY THE PTEN TUMOR SUPPRESSOR GENE IN THESE NKX-3.1 CELLS, YOU RAPIDLY INDUCE A CARCINOMA FORMATION AFTER ANDROGEN-MEDIATED REGENERATION. YOU ADD BACK THE ANDROGEN, AWAY IT GOES. SO IF YOU'VE GOT PROSTATE CANCER, OF COURSE, YOU TRY TO CUT DOWN THE ANDROGEN. THIS IS THE WAY THEY DISCOVERED THAT. SO THERE'S A

POPULATION OF LUMINAL CELLS THAT WERE SUSCEPTIBLE TO THE ONCOGENIC OR THE CANCER TRANSFORMATION. THEY'RE A POTENTIAL TARGET FOR CANCER STEM CELL THERAPIES.

AND I HAVEN'T GOT A POINTER HERE TO GET YOU TO IT, BUT THERE ARE SOME GREEN DOTS ON THE RIGHT-HAND SIDE WHICH ARE THE CELLS IN THE LUMEN. THEY'RE THE ONES UNDER ANDROGEN BLOCKADE THAT APPEAR. SO THESE ARE THE GREEN CELLS HERE. THIS IS -- IF YOU REMOVE ANDROGEN, YOU GET THE TUMOR TO REGRESS, AND YOU CAN SEE THESE CELLS VERY CLEARLY. AND THEN IF YOU THEN TARGET THIS DELETION AND THEN PUT THE ANDROGEN BACK, YOU GET A VERY AGGRESSIVE CARCINOMA.

SO I THINK IN A PROSTATE TISSUE THERE ARE DEFINITELY STEM CELLS THERE, SO THIS IS PROOF OF CONCEPT, IF YOU LIKE, OF HAVING THE CELLS THERE.

THE SECOND ONE IS ALSO A CANCER PAPER, AND I THINK IT WAS DRAWN TO MY ATTENTION BY THE STAFF. AND IT'S THE TREATMENT OF MEDULLOBLASTOMAS, SO WITH A HEDGEHOG PATHWAY INHIBITOR CALLED GDC-0449. AND THE INTEREST HERE IS THAT THE MEDULLOBLASTOMA IS THE MOST COMMON BRAIN TUMOR IN CHILDREN. IT'S THE MOST COMMON FORM OF BRAIN TUMOR IN CHILDREN. AND IT'S APPARENT THAT YOU SEE -- THIS IS A DRAWING OF HOW THESE VERY AGGRESSIVE MEDULLOBLASTOMAS FORM. THEY

CAN COME FROM THIS PARTICULAR ORIGINS, FROM THE VENTRICULAR ZONE, OR IT CAN COME FROM THE EGL PROGENITORS OR OTHER PATHWAYS.

BUT IT'S IN THIS PARTICULAR PATHWAY THAT THE HEDGEHOG ACTIVATION IS ONE WHICH LEADS YOU TOWARDS THE CONDITION OF THE MEDULLOBLASTOMA. AND SO IF YOU PUT IN A NORMAL HEDGEHOG INHIBITOR IN PATIENTS WHO HAVE GOT THIS FORM OF MEDULLOBLASTOMA, YOU GET A VERY RAPID TUMOR REGRESSION.

SO I THINK, AGAIN, THE HEDGEHOG MOLECULE IS A STEM CELL MOLECULE. IT'S PART OF THE STEM CELL REPERTOIRE, IF YOU LIKE, FOR THE DEVELOPING STEM CELL IN THE BRAIN. AND SO HERE IS ANOTHER EXAMPLE, I THINK, OF THE CONNECTION BETWEEN STEM CELLS AND SERIOUS CANCERS AND VERY COMMONLY SERIOUS CANCERS.

THE NEXT STUDY IS MOVING NOW TO THE NEED TO VIRALLY TRANSFECT ADULT CELLS TO PRODUCE IPS CELLS. THERE'S AN ENORMOUS ENERGY NOW IN THE SCIENTIFIC AREA ON IPS CELLS. AND THESE CELLS HAVE BEEN DIFFICULT TO GROW, RELATIVELY DIFFICULT TO GROW, AND IT'S NOW BEEN SHOWN BY A NUMBER OF LABS, AND TWO LABS IN PARTICULAR, THE ONE FROM KEVIN EGGAN'S LAB, WHO'S A WELL-KNOWN YOUNG RESEARCHER WHO'S DOING VERY, VERY GOOD WORK AT THE HARVARD STEM CELL INSTITUTE, PUBLISHED IN *CELL STEM CELLS*. HE'S

SHOWN THAT A SMALL MOLECULE INHIBITOR OF THE TGF-B, THE SIGNALING PATHWAY, AND THIS MOLECULE THEY'VE CALLED REPSOX. THIS IS THE MOLECULE HERE. IT'S BEEN IDENTIFIED THROUGH HIGH THROUGHPUT SCREENING THIS REPSOX MOLECULE.

IF YOU ADD THIS REPSOX MOLECULE TO THE CHEMICALS THAT YOU'RE DOING THE REPROGRAMMING, YOU CAN REPLACE TWO OF THE KEY GENES, THE SOX-2 GENE AND MYC GENE.

SHOWN ON THESE GRAPHS, HERE ARE THE CELLS WITHOUT THE MOLECULE IF YOU TAKE OUT MYC. AND IF YOU ADD THE MOLECULE BACK THERE, YOU PRODUCE A REAL RAPID DEVELOPMENT OF THESE IPS CELLS. SO IT VERY EFFECTIVELY REPLACES MYC, BUT ALSO VERY EFFECTIVELY REPLACES SOX, THE SOX GENE. AND SO YOU CAN THEN -- THESE FIGURES HERE DEMONSTRATE THAT YOU CAN THEN WHEN YOU REPROGRAM THESE CELLS, YOU CAN MAKE TERATOMAS AND YOU GET ALL OF THE CELLS THAT YOU IMAGINE THAT YOU NEED OUT OF IT, AND YOU CAN MAKE CHIMERIC MICE AND SO FORTH FROM THOSE CELLS.

SO HERE WE'RE MOVING THE IPS ALONG THE DEVELOPMENT PATHWAY. SO WE'RE GETTING BETTER AND BETTER AT FINDING THE MOLECULES THAT WILL BE ABLE TO REPLACE SOME OF THESE GENES THAT ARE INSERTED INTO THE CELLS.

THE NEXT PAPER IS A VERY SIMILAR ONE, AND IT'S COME OUT AT ALMOST THE SAME TIME SEPARATED BY JUST A FEW DAYS. AND IT, AGAIN, IS THE SAME TYPE OF THING. THERE'S A TGF-B, THE SIGNALING INHIBITOR, SO IT'S INHIBITING EXACTLY THE SAME PATHWAY. AND THIS IS A PAPER PUBLISHED BY KONRAD HOCHEDLINGER. SO HOCHEDLINGER AND EGGAN SEEM TO BE IN COMPETITION HERE, AND THEY'RE BOTH OUT OF THE HARVARD STEM CELL INSTITUTE. SO IT'S INTERESTING THAT BOTH THESE PAPERS APPEARED SIDE BY SIDE.

THEY SHOWED THAT, IN FACT, THE INHIBITOR -- THESE TWO SCIENTISTS, MAHERALL AND HOCHEDLINGER SHOWED THAT YOU CAN AGAIN REPLACE SOX-2 AND THE MYC-C, THE ONCOGENE, WITH THIS INHIBITOR. SO, AGAIN, YOU CAN SHOW IN THESE GRAPHICS HERE THAT YOU CAN REPLACE BOTH OF THESE GENES.

SO HERE'S TWO PAPERS FROM TWO RELATIVELY INDEPENDENT LABS GETTING THE SAME OUTCOME, WHICH WOULD MAKE YOU FEEL CONFIDENT IT'S A REAL EFFECT. AND, OF COURSE, THEY CAN MAKE CHIMERIC MICE, AND THEY CAN SHOW THAT YOU CAN MAKE ALL THE PRIMARY GERM CELLS THAT THE IPS CELLS FORM BY THIS, SO MAKE ALL THE PRIMARY STEM CELLS. AND IF YOU PUT THEM INTO A MOUSE EMBRYO, YOU CAN MAKE A CHIMERIC MOUSE. SO HERE WE ARE MOVING DOWN THE TRACK OF MAKING THESE

CELLS MORE AND MORE EFFECTIVELY.

THE NEXT SLIDE IS ONE FROM SHEN DING'S LAB. SO HERE ARE THESE THREE YOUNG TURKS, IF YOU LIKE, IN THE STEM CELL AREA. SHEN DING IS A VERY POWERFUL YOUNG SCIENTIST OUT OF THE SCRIPPS RESEARCH INSTITUTE, AND HE'S DOING MARVELOUS WORK I'D HAVE TO SAY. IN THIS PARTICULAR STUDY HE'S PICKED UP TWO OR THREE CHEMICALS THAT CAN ACCELERATE THE FORMATION OF THE IPS CELLS. SO IF YOU PUT THE FOUR GENES IN, YOU CAN GET A MASSIVE, 2 TO 2,000 TIMES EFFECTIVENESS OF YOUR MAKING THE IPS CELLS BY ADDING EITHER THE TWO NEW SMALL MOLECULES OR THE THREE. YOU CAN DO IT QUITE EFFECTIVELY WITH THE TWO, BUT IT'S EVEN MORE EFFECTIVE IF YOU USE THE THREE. AND YOU DON'T HAVE TO WAIT SO LONG TO MAKE THEM. WITHIN TWO WEEKS YOU'VE GOT EFFECTIVE COLONIES SPREADING OUT EVERYWHERE.

HERE, AGAIN, THESE SCIENTISTS HAVE SHOWN HOW TO GET THIS IN A MUCH MORE ECONOMICAL, EFFICIENT WAY. AND I THINK NOW, IT'S MY OWN VIEW, THAT THIS WORK IS GOING TO REALLY START TO ACCELERATE EVERYWHERE. THE OPPORTUNITY, I THINK, FOR CIRM TO BE PART OF THIS RESEARCH IS COMPELLING, AND I THINK DOWNSTREAM IT'S GOING TO BE VERY IMPORTANT. AND SO WE HAPPEN TO BE PART OF THE FRONT LINE OF THIS

RESEARCH, AND I THINK WE'LL BE REWARDED BY BEING THERE.

SO THE NEXT ONE IS QUITE A DIFFERENT STUDY, AND IT COMES FROM KEN CHIEN'S LAB AT, AGAIN, AT THE HARVARD STEM CELL INSTITUTE, BUT THEY PUBLISHED IN *SCIENCE* IN OCTOBER. AND HE IS ABLE TO SHOW FUNCTIONAL VENTRICULAR HEART MUSCLE CELLS IN THE MOUSE FROM VENTRICULAR PROGENITOR CELLS. SO THIS RED MARK AND THIS GREEN MARKER SHOW UP DIFFERENT PARTS OF THE DEVELOPING HEART IN THE EMBRYO.

THE GREEN IS A MARKER FOR WHAT'S KNOWN AS NKX-2.5, WHICH IS THE MOST COMMON MARKER FOR THE DEVELOPING HEART. IT ACTUALLY MARKS ALL OF THE DEVELOPING HEART IN THE EMBRYO. THE OTHER ONE, THE RED MARKER, IS A DIFFERENT MARKER. IT'S AN ISLET1-DEPENDENT ENHANCER. SO IT'S MARKING THIS PARTICULAR PATHWAY THAT'S CONNECTED TO THE MEF2C GENE.

NOW, I JUST WANT TO SHOW YOU THE COLORS FOR THE NEXT SLIDE, IF I MAY. WHEN YOU LOOK AT THIS, UNFORTUNATELY IT'S A BIT SMALL AT THIS DISTANCE, BUT YOU CAN SEE IN THESE BOTTOM GRAPHS, THESE ARE THE MORE EFFECTIVE WAY OF MAKING HEART MUSCLE CELLS AS SHOWN HERE ON THE BOTTOM. AND THESE

ARE THE CELLS THAT ARE MARKED IN GREEN ALONE OR GREEN AND RED. AND THIS HASN'T COME OUT VERY WELL, BUT WHAT THEY'VE DONE IS ESTABLISH EMBRYONIC STEM CELLS WITH THESE JEWEL MARKERS, THE RED AND GREEN FLUORESCENT MARKERS, AND THEY'VE SELECTED THE FLUORESCENT CELLS FROM THE EMBRYOID BODY THAT'S DIFFERENTIATING AND THEN GROWN THESE CARDIAC PROGENITORS ON MICROPATTERNS.

SO THEY MICROPATTERN THE SLIDE, AND THE SLIDE'S MICROPATTERNED IN A WAY THAT THEY'RE 25 MICROMETER WIDE LINES OF FIBRONECTIN, SO CELLS WILL STICK TO THE FIBRONECTIN. THAT'S A MATRIX MOLECULE THAT CELLS LIKE, AND THAT'S ALTERNATING WITH A 20 MICRON WIDE LINE OF PLURONIC F127. NOW, THAT ACTUALLY BLOCKS CELL ADHESION. SO YOU'VE GOT STRIPS WHERE YOU'VE GOT A CELL ADHESION MOLECULE AND THEN A STRIP WHERE THERE'S NONE.

IF YOU CAN SEE THIS, AND IT'S WORTH LOOKING AT AT SOME STAGE ONLINE, YOU WILL SEE THAT THE CARDIAC CELLS ARE LINED UP IN LINES. AND THEY FORM IN LINES AS THEY SHOULD DO, CONNECT ONE ANOTHER IN LINES. AND YOU CAN ACTUALLY PATTERN ON YOUR SLIDE, ON THE CULTURE SLIDE, TISSUE THAT'S ALL LINKED UP IN THE RIGHT DIRECTION. IF YOU DON'T DO THAT, IF YOU JUST USE FIBRONECTIN ON THE SLIDE, THEY

ALL LINE UP IN ALL DIFFERENT WAYS. SO THEY'RE QUITE CHAOTIC. THEY CAN ACTUALLY MOVE TOGETHER AND YOU SEE IT IN THOSE BEATING HEART MUSCLES. THEY CAN DO THAT, BUT THEY'RE NOT LINED UP IN THE PROPER WAY. SO IF YOU PUT THEM IN A HEART, THEY WOULD BE ALL OVER THE PLACE, TO BE HONEST. SO YOU REALLY NEED THE FIBERS LINED UP IN A PROPER DIMENSION.

SO THIS IS REALLY MOVING TOWARDS GETTING THE TISSUE INTO A PROPER FORMAT. SO WE LOOK AT THE NEXT ONE, JAMES. HERE THEY'VE TAKEN THESE PATTERN CELLS AND THEN THEY PUT THESE CELLS ONTO A MUSCULAR THIN FILM. SO THEY'VE CREATED A MUSCULAR THIN FILM ON A VERY THIN FILM OF POLYMER, AND THEY'VE GROWN THEM IN THAT SAME FASHION THAT I JUST EXPLAINED TO YOU.

YOU LOOK AT THESE, THIS IS THE RED PLUS THE GREEN CELLS, THESE CELLS ARE VERY EFFECTIVE IN BECOMING VENTRICULAR ACTION-LIKE POTENTIAL CELLS. SO YOU CAN SEE HERE THIS IS AN ACTION POTENTIAL FROM THE CELLS. AND THIS IS THE SYSTOLIC AND DIASTOLIC MOVEMENT OF THESE CELLS IN THIS FORMAT.

AND IF I GIVE YOU THE NEXT ONE, HOPEFULLY THE NEXT ONE WILL WORK, YOU NEED TO TOUCH THAT. SO HERE IS THE LITTLE TISSUE HERE. THIS IS THE SPONTANEOUS BEATING OF THAT TISSUE. IT'S CONNECTED

TO HERE ON THIS THIN FILM, AND HERE'S THIS HEART TISSUE STARTING TO BEAT. THAT'S SPONTANEOUS. IN A MOMENT WE'LL ADD SOME ELECTRICAL INPUT INTO THAT SO THAT WE'RE NOW PLAYING AT 1 HERTZ, AND YOU CAN SEE IT NOW PICKING UP. AND IF YOU BRING IT UP TO, I THINK IF YOU BRING IT UP TO THE 1 HERTZ OR THE 2 HERTZ, YOU GET THE SAME BEAT THAT YOU WOULD EXPECT IN A HUMAN HEART.

SO HERE WE HAVE EFFECTIVELY TISSUE WHICH IS NOW IN A VERY EFFECTIVE FORMAT. THAT, I THINK, IS THE KIND OF TISSUE THAT WE WANT TO REPLACE IN THE INFARCTED HEART. THIS HAS ALL BEEN DONE IN THE MOUSE, SO WE'VE STILL GOT A WAY TO GO TO DO THE SAME KIND OF WORK IN THE HUMAN. BUT I THINK IT'S REALLY A BEAUTIFUL PUBLICATION IN *SCIENCE*. IT'S JUST DONE A REALLY CLEAR-CUT JOB IN GETTING US SOME CELLS THERE IN THE RIGHT FORMAT DOING THE RIGHT THING CONNECTED IN A TISSUE FUNCTIONAL FORMAT. AND THESE MAY BE -- THIS MAY BE THE TISSUE TYPE THAT WE MAY NEED TO USE AS A TISSUE PATCH ON THE INFARCTED HEART TO MAKE IT FUNCTIONAL.

ON FROM THE SCIENCE NOW, WE HAVE TWO NEW MEMBERS OF STAFF THAT HAVE JOINED US. KAREN BERRY, WHO'S A SCIENCE OFFICER. SHE WAS FORMERLY WITH GENENTECH AS A SENIOR SCIENTIST GROUP LEADER IN THE

PHARMACODYNAMIC BIOMARKER DIVISION. AND TRANSLATIONAL MEDICINE AND IMMUNOLOGY IS HER SKILL SPACE. WE'RE BRINGING IN SCIENTISTS NOW, SCIENCE OFFICERS, WHO'VE GOT THE SKILL SPACE TO MOVE INTO THE TRANSLATIONAL PIPELINE.

INGRID CARAS, ANOTHER SCIENCE OFFICER, FORMERLY WITH PDL BIOPHARMA AS EXECUTIVE DIRECTOR OF PRECLINICAL AND CLINICAL DEVELOPMENT SCIENCE HAS ALSO JOINED US. AGAIN, ANOTHER REAL KEY APPOINTMENT BY PAT OLSON AND HER COLLEAGUES OF GETTING THE REALLY HIGH QUALITY YOUNG SCIENTISTS TO MOVE INTO THIS PART OF THE PIPELINE WITH US SO THAT WE'VE GOT SOME EXPERTISE DOWNSTREAM FROM THE BASIC SCIENCE.

MY PRIORITIES HAVE BEEN, IT SEEMS TO HAVE BEEN A STRESSFUL MONTH, I MUST ADMIT. THESE THINGS STRESS ME. THE CHAIR DOESN'T STRESS ME MUCH. COUPLE OF DAYS A WEEK HE STRESSES ME. BUT THE DISEASE TEAM GRANTS AND THE MEDIA AND COLLABORATIVE ISSUES AROUND THE DISEASE TEAM HAVE REALLY TAKEN A LOT OF TIME FROM US AND A LOT OF NEED TO TRY AND DO THIS IN THE BEST WAY POSSIBLE FOR THE INSTITUTE IN ORDER TO GET YOU THE INFORMATION THAT YOU NEED TO MAKE DECISIONS ABOUT THESE GRANTS. AND WE HAVE WORKED REALLY, REALLY HARD IN THAT REGARD. AND THE SCIENCE OFFICE HAS JUST DONE A MARVELOUS JOB. AND

BETTINA STEFFEN I WANTED TO SAY IN PARTICULAR, WHO'S LED THIS DISEASE TEAM PROGRAM, HAS KIND OF GIVEN UP HER LIFE OVER THE LAST WHATEVER IT IS, SIX MONTHS, TO DO THIS WHOLE THING. I'M SURE HER FAMILY IS GOING TO BE PLEASED WHEN THIS ENDS.

BUT PAT, OF COURSE, PAT OLSON IS ALWAYS THERE, ALWAYS HARD AT IT, AS ARE ALL THE OTHER SCIENTISTS. AND I THINK IT'S JUST A FANTASTIC TEAM, BUT THERE'S A LOT OF HARD WORK IN THERE.

WE ARE WORKING VERY HARD ON THE VP, VICE PRESIDENT R & D, SEARCH. WE NOW HAVE TEN NAMES. I KNOW ONE OF THEM, BUT I HAVEN'T INTERVIEWED THE OTHER NINE. THESE ARE INCREDIBLY, INCREDIBLY WELL CREDENTIALED PEOPLE. THEY REALLY HAVE TAKEN MY BREATH AWAY, PEOPLE WHO ACTUALLY WANT TO WORK WITH US, WHO WANT TO SLIP INTO THIS SPACE, WHO WANT TO BE PART OF THE R & D, THE TRANSLATION, THE EARLY CLINICAL THROUGH TO THE CLINICAL. THEY ARE REALLY VERY KEEN TO BE PART OF IT, SO IT'S A VERY COMPETITIVE GROUP OF PEOPLE THAT WE HAVE. WE'LL BE GOING THROUGH THESE PEOPLE TO NARROW THEM DOWN TO HOPEFULLY JUST A FEW, TWO OR THREE AT THE MOST, BUT ON PAPER IT WILL BE VERY DIFFICULT TO MAKE DECISIONS BETWEEN THEM. AND THEY MOSTLY COME UP FROM THE TOP END OF THE PHARMACEUTICAL INDUSTRY, AND SOME ARE IN

THE BIOTECH, BUT IT'S PRIMARILY THE TOP END OF THE PHARMACEUTICAL INDUSTRY. I THINK THAT BODES WELL FOR WHERE WE'RE GOING. AND I HOPE YOU WILL AGREE WHEN WE EVENTUALLY BRING FORWARD A CANDIDATE.

THE TRANSPLANTATION AND IMMUNOLOGY RFA IS NEARLY READY TO GO. AND THAT'S TAKEN QUITE A LOT OF WORK BECAUSE THE IMMUNOLOGISTS HAVEN'T BEEN CONNECTED WITH THE STEM CELL FIELD. AND SO WE'VE BEEN OUT THERE TRYING TO GET THEM INTERESTED, GET THEM CONNECTED, GET THEM TO WANT TO BE PART OF WHAT WE'RE DOING. THAT'S ACTUALLY TAKEN A LOT OF LEGWORK AND A LOT OF EFFORT TO DO THAT, BUT I THINK WE'RE GETTING THERE. WE'VE GOT A LOT OF ATTENTION FROM THE INDUSTRY IN THE IMMUNOLOGY AREA, AND I HOPE WE'RE GOING TO GET A TERRIFIC RESPONSE FROM THAT.

GERMANY IS JOINING US IN THAT RFA AS IS THE STATE OF VICTORIA. SO AT LEAST COLLABORATIVE GRANTS MAY COME FORWARD WITH GERMAN AND AUSTRALIAN COLLABORATORS.

WE HAVE A STRATEGIC PLAN OPERATIONAL PLAN. HOPEFULLY WE CAN PUT THAT TO REST WITH YOU THIS MEETING SO THAT I CAN FOCUS ON THESE OTHER THINGS THAT ARE OCCUPYING A LOT OF TIME. ISSUES RAISED ON IP REGULATIONS AND LOANS FOR COMPANIES, AND I HAVE TO SAY WE'VE GOT A LOT OF WORK TO DO IN THAT AREA.

WE HAD ONE COMPANY PUT UP THEIR HAND FOR A LOAN. I DON'T THINK THAT'S A GOOD ENOUGH RESPONSE, AND WE'VE GOT A LOT OF WORK TO DO IN THAT SECTOR, AND WE REALIZE THAT IN MANAGEMENT, THAT THERE'S A NEED TO GET OUT THERE AND REALLY DEMONSTRATE TO THE COMPANIES THAT THIS IS IN THEIR FAVOR AND WE'RE NOT DOWN THE OTHER END OF THE SPECTRUM WHERE I'M AFRAID I THINK WE ARE AT THE MOMENT OF NOT BEING THE MOST DESIRABLE TO CONNECT WITH OVER LOANS. SO WE'VE GOT WORK TO DO, AND IT'S A REALITY GRAB AND ONE WHICH MANAGEMENT RECOGNIZES THAT WE HAVE TO DO LOTS OF REALLY HARD WORK IN THERE.

DEVELOPING NETWORKS IN U.S. SCIENCE AND INDUSTRY. THIS IS SOMETHING STRATEGICALLY THAT ELONA AND I HAVE BEEN WORKING ON, AND WE'RE PROGRESSING THAT. WE'VE HAD A LOT OF HELP FROM PEOPLE LIKE TED LOVE AND OTHER SENIOR MEMBERS OF MANAGEMENT, BUT WE'LL GO ABOUT THAT IN A WAY WE'LL HOPEFULLY BRING FORWARD TO YOU SOMETIME NEXT YEAR A NEW MODEL OF WORKING WITH THE BUSINESS END, PARTICULARLY THE PHARMACEUTICAL END OF BUSINESS BECAUSE THAT'S WHERE WE NEED TO CONNECT IF WE'RE GOING TO TAKE A LOT OF THESE THINGS THROUGH TO CLINICAL TRIAL.

A PROGRAM OF CIRM RESEARCH LEADERSHIP

AWARDS, NOW EVERYBODY WANTS ONE OF THESE, SO EIGHT IS NEVER GOING TO BE ENOUGH. SO THAT'S GOOD. THERE'S A LOT OF INTEREST AND A LOT OF COMPETITION FOR THOSE APPOINTMENTS, AND THAT'S TERRIFIC BECAUSE WE WILL DRAW SOME VERY GOOD PEOPLE, I'M SURE, IN THAT PROGRAM. I GET A LOT OF CONNECTION, AS DOES JOHN ROBSON FROM THE INDUSTRY AND FROM SCIENCE IN REGARD TO THAT.

AS I SAID, WE'VE ESTABLISHED A DIALOGUE WITH THE MAJOR PHARMACEUTICAL INDUSTRY, AND I THINK IT'S A VERY POSITIVE INTERACTION, I'D HAVE TO SAY, REPORTING TO YOU THAT THIS GROUP OF PEOPLE NOW WANT TO BE CONNECTED TO CIRM. AND SO I THINK THAT'S A TERRIFIC MOVE AND A GREAT OPPORTUNITY. AND WE'LL TAKE THIS FORWARD CAREFULLY AND KEEP YOU INFORMED AS WE DO.

THERE ARE DIVERSITY ISSUES THAT I'LL BRING TO YOUR ATTENTION JUST AT THIS MEETING BECAUSE WE HAVEN'T FOCUSED MUCH ON THAT. AND WE HAD A MEETING TODAY WITH THE CHARLES DREW UNIVERSITY AT LUNCHTIME. IT WAS CHAIRED BY ART TORRES AND DID A GREAT JOB AT THE CHAIRING, AND I THINK IT WAS A TERRIFIC MEETING. AND THANK YOU, ART, FOR THAT BECAUSE, YOU KNOW, THE SKILLS IN SORT OF HELPING PEOPLE FROM DISPARATE SIDES TO COME TOGETHER AND DO SOMETHING POSITIVE,

CLEARLY YOU HELPED THAT A GREAT DEAL. SO I FEEL THAT WE'VE MADE SOME STEPS IN THE RIGHT DIRECTION THERE.

AND WE ARE WORKING ON CIRM ECONOMIC STIMULUS ISSUES ON HOW WE CAN ACTUALLY HELP STIMULATE -- HOW WE ARE HELPING TO STIMULATE THE ECONOMY CLEARLY IN CALIFORNIA. IT'S A TOUGH TASK FOR THE PEOPLE OUT THERE, AND WE'RE DOING OUR JOB TO STIMULATE IT, SO WE'RE TRYING TO GET SOME QUANTITATIVE FIGURES AROUND THAT.

SO IN THE NATIONAL/INTERNATIONAL LINKAGES, WE'VE SIGNED THREE MOU'S WITH GERMANY. THEY'RE SET TO PARTICIPATE IN THE IMMUNOLOGY RFA WITH CHINA. AND WE DRAW YOUR ATTENTION TO THE QUOTES THERE, THAT THE AGREEMENT THAT WE HAVE WITH THE CHINESE IS TO WORK TOGETHER IN COMPLIANCE OF THE HIGHEST STANDARDS FOR ETHICAL CONDUCT AND SAFETY AT ALL STAGES OF RESEARCH, INCLUDING CLINICAL STUDY. I WANT TO EMPHASIZE THAT WE MADE THIS POINT VERY STRONGLY TO THE MINISTER AND HIS COLLEAGUES WHO VISITED WITH US. AND IT WAS INTERESTING THAT HE DEPARTED FROM THE SET SPEECH BY RECOGNIZING THIS AS AN IMPORTANT ISSUE THAT THEY WILL BE FURTHER ADDRESSING.

SO I THINK OUR NEGOTIATIONS WITH THESE KEY COUNTRIES IN PARTICULAR, BOTH IN GERMANY AND CHINA,

HAVE BEEN A VERY POSITIVE ELEMENT. I THINK WE'VE DONE THINGS THAT PERHAPS PEOPLE THOUGHT WE COULDN'T DO. I KNOW THE GOVERNOR HELPED IN THE CASE OF GERMANY, BUT WE WERE CONCERNED ABOUT SOME ISSUES IN GERMANY AND WERE ABLE TO GET THEM ON THE TABLE AND RECOGNIZED AND ISSUES DEALT WITH THERE. AND THE SAME IS THE CASE IN CHINA.

AND I THINK THE GENERAL COMMUNITY IN SCIENCE APPRECIATES WHAT WE'VE BEEN DOING IN THAT REGARD. I THANK VERY MUCH ELONA AND NANCY KOCH IN HELPING US DO ALL THESE THINGS. PARTICULARLY IN THE CASE OF CHINA, ELONA DID A VERY GOOD JOB IN BRINGING THAT TO THEIR ATTENTION IN A VERY DIPLOMATIC WAY.

WE HAVE A CONNECTION, WE HAVE AN AGREEMENT WITH MARYLAND WITH JOHNS HOPKINS, CLEARLY A MAJOR UNIVERSITY, UNIVERSITY OF MARYLAND AND HUGO MOSER RESEARCH INSTITUTE. SO THIS ENABLES THOSE SCIENTISTS TO LINK WITH CALIFORNIANS AND IN THIS CASE OF MARYLAND WILL FUND THEIR COMPONENT, AND, OF COURSE, WE FUND OUR COMPONENT, THE SAME MODEL, IF YOU LIKE, AS WE'VE HAD WITH THE COUNTRIES.

OUR ROLE IN DIVERSITY, IT IS A KEY VALUE AND I DREW THAT -- WE DREW THIS COMMENT FROM THE GUIDE AND IMBUE CIRM EFFORTS AND ACTIVITIES WHICH IS OUT OF THE STRATEGIC PLAN. IMPORTANT TO MAKE

SPECIAL EFFORTS TO ENCOURAGE THE TRAINING AND EDUCATION OF MINORITY SCIENTISTS. CIRM WILL ALSO NEED TO ENSURE THE CLINICAL TRIALS WITH THERAPIES RESULTING FROM STEM CELL RESEARCH INCLUDE MINORITY POPULATIONS. AND CIRM WILL MAKE SPECIAL EFFORTS TO MAINTAIN COMMUNICATION WITH THE DIVERSE PUBLIC CONSTITUENCIES. SO THAT'S EMBEDDED IN OUR PHILOSOPHY. WHAT WE'RE DOING NOW IS TAKING SOME STEPS TO ENSURE THAT WE DO, WE'RE DELIVERING ON THOSE, IMPLEMENTING THOSE COMPONENT PARTS OF THE PHILOSOPHY.

SO WE'VE HAD A REVIEW OF PRESENT POLICIES AND PROCESSES IN THE TRAINING PROGRAMS, THE CRITERIA THAT CIRM ENCOURAGES INSTITUTIONS TO MAKE SPECIAL EFFORTS CONSISTENT WITH THE LAW TO RECRUIT AND RETAIN INDIVIDUALS FROM MANY BACKGROUNDS, INCLUDING UNDERREPRESENTED MINORITIES AND TRAINEES AND MENTORS. AND WE'RE MEASURING THAT THROUGH THE PROGRESS REPORTS. SO WE'RE ACTUALLY GETTING A QUANTITATIVE MEASURE ON THAT IN OUR PROGRESS REPORTS, AND WE WILL REPORT THAT TO YOU.

THE BRIDGES PROGRAM REALLY BROADENS THE PARTICIPATION IN STEM CELL RESEARCH BY HAVING INDIVIDUALS REPRESENTING THE DIVERSITY OF THE POPULATION IN CALIFORNIA AND FACILITATES INVOLVEMENT

OF STUDENTS WHO DO NOT OTHERWISE HAVE OPPORTUNITIES TO TAKE PART IN RESEARCH FOCUSED ON REGENERATIVE MEDICINE.

AND THE GRANTS ADMINISTRATION POLICY REQUIRES THAT ALL CIRM-FUNDED CLINICAL RESEARCH WILL BE CARRIED OUT IN A MANNER SUFFICIENT TO ELUCIDATE INFORMATION ABOUT INDIVIDUALS OF BOTH SEXES, GENDERS, AND DIVERSE RACIAL AND ETHNIC GROUPS, AND IN PARTICULAR IN CLINICAL TRIALS TO EXAMINE DIFFERENTIAL EFFECTS ON SUCH GROUPS. SO WE'RE NOW TRYING TO GET IMPLEMENTATION OF THOSE.

SO THE NEXT ONE. THE PARTICIPATION IN CLINICAL TRIALS ARE BOTH CHALLENGES AND SUCCESSES. WE'VE COMMISSIONED A WHITE PAPER TO INTERVIEW CONSTITUENTS TO DETERMINE WHERE THE BARRIERS ARE TO PROVEN BRIDGES TO TRIAL PARTICIPATION. AND THAT'S DUE IN DECEMBER. SO DON GIBBONS IS MANAGING THAT PARTICULAR TASK, AND WE WANT TO BE WELL INFORMED ABOUT IT.

EDUCATION COMMUNICATION, SUPPORT THE SCIENCE PROGRAMS OF PUBLIC SCHOOLS IN CALIFORNIA. WE'RE DOING THAT. REVIEWING IDEAS OF HOW STATE UNIVERSITY FACULTY MEMBERS MIGHT PARTICIPATE IN CIRM TRAININGS. WE HAVE STEM CELL AWARENESS DAY EDUCATION PROGRAMS, AND WE'RE PLANNING TO BRING

TOGETHER THE BRIDGES PROGRAM APPLICANTS WITH THE TRAINING GRANT DIRECTORS AND REPRESENTATIVES WITH INDUSTRY. SO WE'RE DOING ALL OF THOSE THINGS IN THE EDUCATION COMMUNICATION.

WE WANT TO CONSIDER BEST PRACTICE IN RECRUITMENT TO TRAINEE PROGRAMS, SO WE'RE HOLDING A WORKSHOP TO DISCUSS BEST PRACTICES AT CIRM AT THE 2010 GRANTEE MEETING.

WE HAD A DISCUSSION, AS I SAID, ABOUT A PROPOSED WORKSHOP, THE ROLE OF CIRM IN ENHANCED DIVERSITY. THE GOAL THERE IS TO IDENTIFY HOW CIRM CAN ENHANCE DIVERSITY IN THE FIELD OF REGENERATIVE MEDICINE. SO WE PROPOSE THAT THIS BE HELD AT THE CHARLES DREW UNIVERSITY, BUT INCLUDES OTHER MEMBERS THAT WOULD REPRESENT DIVERSITY IN THE CALIFORNIA COMMUNITY COMING TOGETHER. AND THEN THE TOPICS WE PROPOSE, MEETING CLINICAL NEEDS OF THE COMMUNITY, ATTRACTING PATIENTS AND PHYSICIANS TO CLINICAL TRIALS, ATTRACTING STUDENTS TO STEM CELL RESEARCH, AND DEVELOPING CROSS-INSTITUTIONAL COOPERATION. AND IT WAS AGREED TO TODAY THAT WE WOULD MOVE FORWARD ON THAT. WE WOULD HAVE A WORKSHOP, AND WE WOULD WELCOME ANY BOARD MEMBERS INTERESTED IN PARTICIPATING IN THAT. I THINK IT SHOULD BE VERY INTERESTING AND RATHER DIFFERENT TO SOME OF THE

OTHER WORKSHOPS THAT WE'VE HAD. AND CHALLENGING, INDEED, BUT A VERY STRONG INPUT, IF YOU LIKE, FROM THE CHARLES DREW MEMBERSHIP, VERY STRONG, AND WANTING TO BE INVOLVED IN THIS PROGRAM.

SO UPCOMING GRANT REVIEWS, WE HAVE BASIC BIOLOGY II. WE RECEIVED 154 APPLICATIONS. WE'VE JUST HAD THE PREAP REVIEW ON OCTOBER 22D, AND WE'RE INVITING 57 OF THE 154 FORWARD. THE APPLICATION DEADLINE FOR THE PRIMARY APPLICATION WILL BE DECEMBER THE 8TH. AND THE GRANTS WORKING GROUP REVIEW WILL BE IN FEBRUARY OF NEXT YEAR.

AND THE BASIC BIOLOGY I AND II BROUGHT TOGETHER 289 APPLICATIONS, SO IT WOULD HAVE BEEN IMPOSSIBLE TO DEAL WITH THEM IN THE ONE TIME. AND I DON'T KNOW HOW YOU CAN DEAL WITH THIS NUMBER OF PROJECTS UNLESS YOU DO HAVE A PREAP REVIEW, BUT WE'RE COMING IN DECEMBER TO REPORT ON OUR EXPERIENCE OF THE PREAP PROCESS FOR YOUR CONSIDERATION AS TO WHETHER WE CAN CONTINUE THAT OR NOT.

UPCOMING RFA'S, THE STEM CELL TRANSPLANTATION IMMUNOLOGY, POSTING THE RFA EARLY NOVEMBER, SO PRETTY SOON. APPLICATION DEADLINE WILL BE IN JANUARY NEXT YEAR, THE REVIEW IN APRIL, AND THE ICOC IN JUNE NEXT YEAR. RESEARCH LEADERSHIP AWARDS, WE'LL BE POSTING THE RFA IN DECEMBER, THIS

YEAR, AND THE FIRST APPLICANT DEADLINE WILL BE IN FEBRUARY 2010. AND THEN OUR NEXT EARLY TRANSLATIONAL RFA II, THE CONCEPT CLEARANCE WILL BE COMING TO THE BOARD ON DECEMBER, AND WE'LL HOPEFULLY POST THE RFA IN FEBRUARY.

QUICK WORKSHOP REPORT, WE HAD A WORKSHOP TOGETHER WITH THE JAPANESE JST. WE HAD A WORKSHOP TOGETHER WITH THE SCIENCE AND TECHNOLOGY GROUP IN JAPAN WITH THEIR KEY SCIENTISTS IN IMMUNOLOGY TO EXCHANGE IDEAS AND FACILITATE DEVELOPMENT OF COLLABORATIVE PROJECTS BETWEEN THE CALIFORNIANS AND THE JAPANESE SCIENTISTS IN IMMUNOLOGY. WE HAD EIGHT CALIFORNIAN IMMUNOLOGISTS AND THERE WERE 14 JAPANESE IMMUNOLOGISTS. WE HAD A GREAT MEETING. IT WAS HOSTED BY THE JAPANESE, THE JST IN KYOTO IN AUGUST, END OF AUGUST, AND THE PRESENTATIONS, DISCUSSIONS WERE IN THE AREAS OF IMMUNOLOGICAL TOLERANCE, IMMUNE MANIPULATION STEM CELL THERAPY, AND STEM CELL DIFFERENTIATION, AND STEM CELL TRAFFICKING.

JAPAN HAD AN ELECTION WHILE WE WERE THERE. AND THEY GOT A NEW GOVERNMENT THAT THEY DIDN'T QUITE PREDICT. SO THAT'S THROWN LOTS OF THINGS IN THE AIR FOR THE MOMENT, SO THEY WERE UNABLE TO PARTICIPATE IN THE RFA, WHICH WAS A DISAPPOINTMENT BECAUSE THE SCIENTISTS HAD ACTUALLY CREATED REALLY LINKAGES,

THEY HAD DATA, AND THEY WERE GOING TO WORK TOGETHER, BUT WE WERE UNABLE TO GET THE JAPANESE TO COME ONTO THAT.

SO NOW I WONDER IF I CAN HAND OVER TO DON GIBBONS, JUST A COUPLE OF SLIDES ON THE STEM CELL AWARENESS DAY.

MR. GIBBONS: THANK YOU, ALAN, CHAIRMAN KLEIN, MEMBERS OF THE BOARD. IT WAS A VERY SUCCESSFUL DAY THIS YEAR. IT STARTED OUT VERY SMALL LAST YEAR AND IT GREW DRAMATICALLY THIS YEAR. WE WENT TO OUR GRANTEES AND SAID WE'D LOVE FOR YOU TO GO INTO A CLASSROOM THIS DAY WITH A LECTURE. WE'RE GOING TO GIVE YOU NOTES THAT WE'VE PREPARED AND TESTED IN CLASSROOMS IN THE BAY AREA SO WE KNOW THEY'RE AT THE RIGHT LEVEL. WE'LL MAKE IT EASY FOR YOU.

WE HAD RESEARCHERS IN 47 SCHOOLS, WHICH I THINK WAS GREAT. WE REACHED OVER 5,000 KIDS.

I WANT TO TALK ABOUT ONE COMPANY, NOVOCELL, GAVE THREE RESEARCHERS THE DAY OFF. THEY ALL THREE SPENT THE ENTIRE DAY IN SCHOOL DOING MULTIPLE CLASSES. ONE SCHOOL CALLED BACK-TO-BACK SCHOOL ASSEMBLIES WITH 200 KIDS FOR FOUR ASSEMBLIES. ONE NOVOCELL RESEARCHER REACHED 800 KIDS. ALTOGETHER OF THOSE 5,000, 1,000 WERE FROM THE

NOVOCELL RESEARCH TEAM. SO I DON'T WANT TO GUILT OUT ANY NONPROFITS IN THE ROOM, BUT I THINK THEY REALLY DID SHINE.

THERE WERE A NUMBER OF EVENTS AT OUR GRANTEE INSTITUTIONS. THERE WERE SEVEN. AND THEN THERE WERE EVENTS IN NEW YORK, MONASH IN AUSTRALIA, CANADA, PROCLAMATIONS FROM GOVERNORS IN WISCONSIN, MARYLAND, NEW YORK, AND CALIFORNIA, GOVERNOR SCHWARZENEGGER, AND PROCLAMATIONS FROM A NUMBER OF MAYORS UP AND DOWN THE COAST THAT SENATOR TORRES HELPED US ARRANGE.

MR. TORRES: AND VICE CHAIRMAN ROTH AS WELL.

MR. ROTH: THERE WERE A COUPLE REPUBLICANS OUT THERE.

MR. GIBBONS: WE'RE BIPARTISAN. OUR MEDIA COVERAGE GARNERED AROUND 260,000 VIEWER IMPRESSIONS. BUT I THINK THE REAL SUBSTANCE OF THE DAY IS CAPTURED IN THIS E-MAIL I GOT. ONE TEACHER ASKED EVERY STUDENT TO WRITE A THANK-YOU NOTE TO THE GRANTEE. I'M GOING TO READ ONE LINE FROM FOUR OR FIVE PAGES OF THESE. MY BIFOCALS BROKE, SO BEAR WITH ME WHILE TRADE GLASSES.

"I HAVE DEFINITELY TAKEN AN INTEREST IN THIS FIELD AND HOPE TO PURSUE A CAREER IN IT IN THE

FUTURE."

ANOTHER ONE, "MAYBE IN THE FUTURE I MIGHT ROLL INTO THIS PROFESSION."

"I WAS ESPECIALLY INTERESTED IN THE FACT THAT WE CAN BE HELPING OUT SO MANY PEOPLE IN THE FUTURE BY NOT JUST CURING ONE DISEASE OR ONE INJURY BUT MANY."

"THANK YOU FOR IMPLANTING THE SEEDS OF WONDER ABOUT THE TOPIC OF STEM CELLS INTO OUR BRAINS."

AND ONE LAST ONE, "NOW THAT I'VE LEARNED A LOT ABOUT STEM CELLS AND THE RESEARCH, THE CAREERS INVOLVED SEEM VERY INTERESTING. WHEN I HEARD THAT MILLIONS OF DOLLARS IS PUT INTO STEM CELL RESEARCH, I WAS QUITE SHOCKED. I THOUGHT THAT STEM CELL RESEARCH WAS NOT THAT BIG A DEAL TO PUT THAT MUCH MONEY INTO IT. HOWEVER, WHEN THE PRESENTATION WAS OVER, I NOW KNEW WHY STEM CELLS ARE SO IMPORTANT."

THANK YOU.

CHAIRMAN KLEIN: THANK YOU VERY MUCH. DR. TROUNSON, I THINK IT WOULD BE VALUABLE AS WELL IN THE COUNTRIES THAT YOU COVERED, SO THAT THE BOARD UNDERSTANDS THE LEVEL AT WHICH THESE DECISIONS ARE BEING MADE IN THESE COUNTRIES, TO REALIZE THAT WHEN THE MINISTER OF SCIENCE FROM CHINA CAME TO OUR

HEADQUARTERS OFFICES ON A SUNDAY WITH HIS TRAVELING PARTY OF ABOUT 14, INCLUDING THE HEAD OF THE EMBASSY SCIENCE TEAM IN WASHINGTON, D. C., THAT THE MINISTER OF SCIENCE IS THE VICE CHAIRMAN OF THE COMMUNIST PARTY AND A MEMBER OF THE EXECUTIVE COMMITTEE OF THE COMMUNIST PARTY THAT RUNS THE COUNTRY ON A DAY-TO-DAY BASIS.

THAT COMES FROM OUR VICE CHAIR ART TORRES, WHO IS OUR CHINESE TECHNICAL POLITICAL ADVISOR BECAUSE HE HAPPENS TO HAVE REPRESENTED A VERY LARGE CHINESE COMMUNITY FOR MANY YEARS IN LOS ANGELES.

BUT IT IS EXTRAORDINARY THE LEVEL AT WHICH THESE DECISIONS ARE BEING MADE, WHICH, OF COURSE, IN SOME COUNTRIES IS NECESSARY TO MAKE SURE THEY'RE ACTUALLY IMPLEMENTED. BUT IT IS A GREAT COMPLIMENT TO THE EFFORTS OF OUR SCIENTIFIC STAFF THAT WE ARE GETTING THE ATTENTION AT THESE LEVELS.

DR. TROUNSON: RIGHT. CHAIR, WE MOVE FROM THAT TO CULTURE. AND NOW THIS WAS A SHORT POEM THAT RECEIVED THE AWARD THAT WAS JUDGED BY AN EXPERT IN POETRY. AND IT STEMMED FROM HAIKU. "TIS A DAY TO PRAISE, THE BASE OF LIFE UNHAZED, THE WORLD IN ONE CELL." AND THAT WILL PROBABLY ENTER HISTORY AND BE REMEMBERED LONG AFTER WE'VE GONE, CHAIRMAN KLEIN.

SO JONATHAN LEE AT THE DREW SCHOOL, THE

DREW SCHOOL, WAS THE WINNER OF THAT POETRY AWARD. SO GOOD FOR JONATHAN AND HE RECEIVED THE PRIZE. I CAN'T RECALL WHAT THE PRIZE WAS.

SO IF I CAN INVITE PAT OLSON FORWARD ON THIS.

DR. OLSON: MR. CHAIRMAN, MEMBERS OF THE BOARD, PUBLIC, I JUST WANTED TO UPDATE YOU ON AN ACTION ITEM FROM OUR AUGUST BOARD MEETING. SO AS YOU MAY RECALL, AT THE AUGUST BOARD MEETING, THE ICOC APPROVED A TRANSLATIONAL AWARD TO DEVELOP STANDARDIZED, WELL-CHARACTERIZED MODELS OF DISEASE FOR THE TESTING OF STEM CELL-BASED THERAPIES.

CIRM AT THAT TIME COMMITTED TO THE BOARD TO UNDERTAKE A SURVEY OF CALIFORNIA SCIENTISTS TO ASCERTAIN THE UTILITY OF THE PROPOSED MODELS AND TO SOLICIT INPUT ON OTHER MODELS OF INTEREST FOR DEVELOPMENT. WE CONDUCTED A SURVEY OF MANY OF THE LEADING CALIFORNIA STEM CELL RESEARCHERS, THOSE WHO LEAD PROGRAMS IN THEIR INSTITUTION. THE RESPONSE RATE WAS 73 PERCENT. IT WAS GENERALLY POSITIVE FOR THE UTILITY OF THE PROPOSED MODELS.

SO THERE WAS ONE -- I THINK THERE WERE A COUPLE OF MODELS THAT ONE PERSON DIDN'T LIKE, BUT I THINK IT HAD TO DO WITH HOW COULD THESE BE ACTUALLY IMPLEMENTED. BUT MOST PEOPLE -- COMMENTS, LET ME

JUST READ YOU A COUPLE COMMENTS. "STANDARDIZED AND VALIDATED ANIMAL MODELS ARE EXTREMELY IMPORTANT, AND THEY WOULD BE QUITE USEFUL IF THEY WERE READILY AVAILABLE FOR INVESTIGATORS." "THERE'S GOOD REASON TO SUPPORT WELL-CHARACTERIZED DISEASE MODELS."

SO, IN GENERAL, PEOPLE WERE POSITIVE ABOUT ALL THESE MODELS THAT WERE DISCUSSED. THERE WAS ONE RESPONSE THAT, IN FACT, REFLECTED THE DEBATE THAT THE GRANTS WORKING GROUP HAD AND THAT I THINK THAT THIS BOARD WENT THROUGH TOO, WHICH IS THAT THERE ARE EXPERTISE IN PERFORMING THESE MODELS IN VARIOUS LABS IN CALIFORNIA. SO WHY DO WE NEED A SET OF STANDARDIZED MODELS? BUT AS I SAY, IN GENERAL, THE RESULTS WERE GOOD. THE SCIENCE OFFICER WHO IS IN CHARGE OF THIS PROGRAM WILL BE SHARING THE RESULTS OF THIS SURVEY ANONYMOUSLY WITH THE PI AT THE JACKSON LABS. WE'LL ALSO BE SHARING WITH THEM THE MODELS THAT WERE OF INTEREST TO DEVELOP AND JUST EXPLORE WITH THEM THOSE KINDS OF CONSIDERATIONS.

SO I DID WANT TO BRING TO YOU THE RESULTS OF THAT. THANK YOU.

CHAIRMAN KLEIN: THANK YOU VERY MUCH. DR. TROUNSON. DR. PENHOET.

DR. PENHOET: COULD I MAKE ONE COMMENT BECAUSE BOB PRICE DIDN'T, BUT LIZ BLACKBURN WAS BORN

IN AUSTRALIA AND NOW WORKS AT UCSF, BUT SHE DID HER NOBEL PRIZE WINNING WORK WHILE SHE WAS A FACULTY MEMBER AT UC BERKELEY.

DR. TROUNSON: I STAND CORRECTED. SO I WANTED GEOFF LOMAX TO REPORT TO YOU THE COMPLIANCE PROGRAM THAT WE'VE HAD IN PLACE BECAUSE I DON'T THINK YOU'VE HAD ANY DISCUSSION OF THE COMPLIANCE PROGRAM THAT IS IN PLACE. YOU MAKE THE AWARDS. WE ACTUALLY MAKE SURE THAT THE COMPLIANCE TO THOSE AWARDS IS HAPPENING. AND SO I ASKED GEOFF TO GIVE YOU A SUMMARY OF THAT COMPLIANCE PROGRAM.

DR. LOMAX: MR. CHAIRMAN, MEMBERS OF THE BOARD, DR. TROUNSON HAS ASKED ME TO GIVE YOU AN OVERVIEW OF A PROGRAM THAT'S APPROXIMATELY 16 MONTHS OLD AT THIS TIME. IT'S THE COMPLIANCE PROGRAM. THE PROGRAM REPRESENTS A SERIES OF CHECKUPS ON OUR GRANTEES. IT'S A FIELD-ORIENTED PROGRAM WHERE WE LOOK AT INSTITUTIONAL RESEARCH OVERSIGHT. WE LOOK AT SPECIFIC GRANTS TO VERIFY COMPLIANCE WITH VARIOUS CIRM STANDARDS, PARTICULARLY STANDARDS RELATING TO PUBLICATIONS, IP, AND THE MEDICAL AND ETHICAL STANDARDS. IN ADDITION, WE HAVE A BUDGET AND EXPENDITURE COMPONENT.

CHAIRMAN KLEIN: GEOFF, LET ME DO THIS. IN TERMS OF OUR TIMING TONIGHT, DR. TROUNSON, I'M

WONDERING IF WE CAN DEFER THIS PARTICULAR REPORT BECAUSE WE HAVE A NEED TIMEWISE TO GET INTO AN EXECUTIVE SESSION, AND THEN I'M GOING TO BRING THIS UP. IT'S EXTREMELY IMPORTANT THE WORK IS GOING ON, AND I WOULD LIKE TO AGAIN REINFORCE THE STATEMENT MADE PREVIOUSLY, THAT GEOFF WAS ABSOLUTELY VITAL IN THE NIH STANDARDS EFFORT, ABSOLUTELY VITAL, AND IN COORDINATING WITH THE OTHER STATES SO WE HAD A CONSISTENT POLICY. HIS LEADERSHIP HAS BEEN TREMENDOUS.

BUT I'D LIKE TO DEFER THIS. I'M ALSO GOING TO DEFER AN ITEM BY OUR VICE CHAIR THAT'S VERY IMPORTANT. ART TORRES IS GOING TO REPORT TO US ON INITIATIVES THAT ARE CRITICAL ISSUES FOR US TO BE AWARE OF IN THE 2010 ELECTION. BUT WE NEED TO MOVE FORWARD VERY QUICKLY HERE AT THIS MOMENT SO THAT WE CAN MAINTAIN MAXIMUM NUMBER OF MEMBERS WITHIN THE EXECUTIVE SESSION.

DR. LOMAX: I'LL LOOK FORWARD TO BRINGING THAT BACK.

DR. PRIETO: WILL WE GET TO TALK ABOUT THIS BEFORE GETTING INTO THE DISEASE TEAM AWARDS? BECAUSE I THINK THERE MAY BE SOME ISSUES THAT HAVE SOME APPLICABILITY.

CHAIRMAN KLEIN: LET ME VISIT WITH YOU

DURING THE BREAK, AND WE'LL MAKE SURE THAT THE TIMING IS RELEVANT TO YOUR CONCERNS.

DR. TROUNSON, ARE WE ALL RIGHT?

DR. TROUNSON: SURE.

CHAIRMAN KLEIN: OKAY. I WANT TO -- WHAT I'D LIKE TO DO IS MOVE ALL THE WAY DOWN TO THE AGENDA AND REALLY GO INTO AN EXECUTIVE SESSION; BUT BEFORE DOING THE EXECUTIVE SESSION, WHAT I'D LIKE TO DO HERE IS LOOK AT THE OVERALL PICTURE OF THE RECOMMENDATIONS FROM THE GRANTS WORKING GROUP TO FRAME FOR THE PUBLIC AND THE BOARD THE GRANTS THAT ARE UNDER CONSIDERATION FOR TONIGHT.

DR. STEFFEN: MR. CHAIRMAN, BOARD MEMBERS, MEMBERS OF THE AUDIENCE, AND GUESTS, TODAY I WOULD LIKE TO PRESENT THE RECOMMENDATIONS PUT FORTH BY THE GRANTS WORKING GROUP IN SEPTEMBER FOR THE DISEASE TEAM RESEARCH AWARDS. THIS IS AGENDA ITEM NO. 11 IN YOUR BINDER.

SO THE DISEASE TEAM INITIATIVE WILL HELP THIS INSTITUTE ACHIEVE ITS GOAL TO DEVELOP STEM CELL BASED-THERAPIES BY MOVING THERAPEUTIC CANDIDATES TOWARD THE CLINIC. AND IN ORDER TO DO THIS, WE SET SOME STEEP BUT ACHIEVABLE GOALS TO HAVE THESE TEAMS.

FIRST, TEAMS WHO RECEIVE THIS AWARD SHOULD BE ABLE TO FILE AN APPROVABLE INVESTIGATIONAL NEW

DRUG APPLICATION FOR IND WITHIN FOUR YEARS OF THE START OF THE AWARD. THE IND IS THE FINAL STEP BEFORE CLINICAL STUDIES CAN BEGIN IN HUMANS AND IS A MAJOR MILESTONE IN THE DEVELOPMENT OF THERAPEUTICS.

SECOND, TEAMS WHO RECEIVE THIS AWARD SHOULD BE ON A PATH TO DEVELOP CLINICALLY COMPETITIVE, NOVEL THERAPEUTICS FOR WHICH THERE IS AN UNMET MEDICAL NEED. AND WE BELIEVE OUR BEST CHANCES ARE THOSE PROJECTS WITH A STRONG SCIENTIFIC RATIONALE.

SO IN A FEW SLIDES WE WILL REVISIT THE REVIEW CRITERIA FOR THIS RFA, AND YOU WILL SEE THESE KEY CONCEPTS EMPHASIZED.

THE SCOPE OF THE RESEARCH AWARDS WAS CRAFTED TO ACHIEVE THE GOAL OF PRODUCING THE APPROVABLE IND'S WHILE ALSO HELPING PAVE THE PATH TO THE CLINIC FOR CLINICALLY COMPETITIVE THERAPIES. AND WE BELIEVE THAT DIVERSITY IN THE PORTFOLIO IS BENEFICIAL. SO FOR THIS REASON THE RFA WAS OPEN TO A BROAD SCOPE OF DISEASES AND CELL TYPES. WE WERE OPEN TO PROPOSALS IN ALL DISEASES AND INJURIES, AND CIRM WILL SUPPORT RESEARCH USING THE FULL SPECTRUM OF PLURIPOTENT CELLS WITH AN EMPHASIS ON EMBRYONIC STEM CELLS AND ALSO PROGENITOR AND CANCER STEM CELL TYPES.

CIRM WILL CONSIDER MANY ROLES OF THE STEM CELLS IN THESE PROJECTS, INCLUDING CELLS AS THE TARGETS OF THE THERAPEUTICS, SUCH AS THE CANCER STEM CELL, CELLS AS CRITICAL TOOLS FOR DISCOVERY, SUCH AS USING CELLS IN A PRIMARY SCREENING ASSAY FOR DRUG DISCOVERY, OR CELLS AS A THERAPEUTIC ITSELF.

AND THEN, FINALLY, CLINICAL TRIALS WITH THE PROPOSED THERAPEUTIC CANDIDATE ARE NOT WITHIN THE SCOPE OF THIS FIRST ROUND OF DISEASE TEAM RESEARCH AWARDS.

IN DECEMBER THIS BOARD APPROVED THE CONCEPT OF THE DISEASE TEAM RESEARCH AWARD INCLUDING THE CIRM FUNDING TARGETS LISTED ON THIS SLIDE. YOU APPROVED UP TO 10 TO 12 AWARDS, EACH OF UP TO FOUR YEARS WITH JUSTIFIABLE PROJECT COSTS OF UP TO $20 MILLION PER PROJECT AND TOTAL PROJECT COSTS ESTIMATED AT $210 MILLION FOR THE PROGRAM. THESE NUMBERS REPRESENT THE CIRM-FUNDED PORTION OF THE PROGRAM, AND WE WILL DISCUSS THE FUNDING PARTNER CONTRIBUTIONS SHORTLY.

AWARDS WILL BE MADE AS GRANTS TO NOT-FOR-PROFIT ORGANIZATIONS AND AS LOANS TO FOR-PROFIT ORGANIZATIONS.

NOW, IN ADDITION TO THE CIRM FUNDS AVAILABLE FOR THIS PROGRAM, ADDITIONAL FUNDS WERE

MADE AVAILABLE AND CONTRIBUTED BY OUR COLLABORATIVE FUNDING PARTNERS. IN THIS ROUND OF AWARDS, WE HAD ROBUST PARTICIPATION BY OUR FUNDING PARTNERS, INCLUDING THE CANCER STEM CELL CONSORTIUM OF CANADA, THE MEDICAL RESEARCH COUNCIL OF THE UNITED KINGDOM, AND THE SPANISH MINISTRY OF SCIENCE AND INNOVATION.

I'D LIKE TO MENTION THAT NANCY KOCH OF CIRM WAS INSTRUMENTAL IN DRAFTING, NEGOTIATING, AND BRINGING TO CLOSURE THE FUNDING AGREEMENTS THAT ARE MAKING THESE JOINT PROJECTS POSSIBLE. WITHOUT HER, WE WOULD NOT BE ABLE TO SAY WE HAVE THESE JOINT PROGRAMS.

FINALLY, WITH THESE AWARDS CIRM IS IMPLEMENTING THE CO-PRINCIPAL INVESTIGATORS AS ADOPTED BY THIS BOARD. WE HAVE EVIDENCE THAT THIS HAS ENCOURAGED COLLABORATIONS, NOT ONLY ACROSS THE SPECTRUM OF BASIC TO CLINICAL EXPERTISE, BUT ALSO ACROSS INSTITUTIONS AND BETWEEN ACADEMIA AND INDUSTRY.

THE REVIEW PROCESS FOR THESE AWARDS WAS A TWO-STEP ENDEAVOR. IN RESPONSE TO THE ICOC'S REQUEST TO NOT LIMIT THE APPLICATIONS, WE CAME UP WITH THE PRELIMINARY APPLICATION AND FULL APPLICATION CONCEPT THAT YOU'RE FAMILIAR WITH FROM THE BASIC BIOLOGY RESEARCH ROUNDS. SO THE

PRELIMINARY APPLICATIONS WHICH WERE RECEIVED IN MAY 2009 HAD NO INSTITUTIONAL LIMITS ON THE NUMBERS THAT COULD BE SUBMITTED, AND EACH PRELIMINARY APPLICATION UNDERWENT EVALUATION BOTH BY SCIENTIFIC EXPERTS FROM OUTSIDE CALIFORNIA AND CIRM SCIENTIFIC STAFF. THE FULL APPLICATIONS WERE REVIEWED BY THE GRANTS WORKING GROUP IN SEPTEMBER OF THIS YEAR.

JUST TO GIVE YOU A FEEL OF THE APPLICATIONS THAT WE RECEIVED, WE RECEIVED A TOTAL OF 73 PREAPPLICATIONS. THIRTY-TWO WERE IDENTIFIED THROUGH THAT PREAP PROCESS AS THE MOST PROMISING AND COMPETITIVE AND RESPONSIVE, AND 31 FULL APPLICATIONS WERE RECEIVED AND REVIEWED.

I'D LIKE TO BRIEFLY REMIND YOU OF THE REVIEW CRITERIA THAT WERE USED IN THE EVALUATION OF THESE AWARDS. THE SCIENTIFIC RATIONALE AND SIGNIFICANCE REALLY HAD TWO COMPONENTS IN THIS CASE. THE ONE IS THE WHY ARE WE DOING THE PROJECT? WHAT ARE THE SCIENTIFIC UNDERPINNINGS? AND WHY DO WE FEEL GOOD ABOUT GOING FORWARD WITH SUCH A PROJECT? AND THE SECOND, WE REALLY ASKED REVIEWERS TO SAY WILL IT BE COMPETITIVE? DOES IT OFFER SOME ADVANTAGE OVER THERAPIES THAT ARE IN PLACE TODAY OR POTENTIALLY IN THE DEVELOPMENT PIPELINE? SO TWO IMPORTANT COMPONENTS TO RATIONALE AND SIGNIFICANCE

IN THIS ROUND.

IN THE FEASIBILITY OF THE PRECLINICAL RESEARCH AND DEVELOPMENT PLAN, WE ASKED REVIEWERS TO LOOK AT THREE MAJOR COMPONENTS. WHAT ARE THE PRELIMINARY DATA AND ARE THEY COMPELLING? SECOND, WE ASKED THEM TO LOOK AT COMPLETENESS OF THE RESEARCH AND DEVELOPMENT PLAN. AND HERE OUR SCIENTIFIC REVIEWERS OF THE GRANTS WORKING GROUP LOOKED AT THE TECHNICAL ASPECTS OF THE PROPOSAL. DID THE EXPERIMENTS MAKE SENSE? WERE THE READOUTS RIGHT AND SO FORTH?

NOW, WE INTRODUCED A NEW COMPONENT WHERE WE ASKED INDIVIDUALS WITH REGULATORY EXPERTISE WHO HAD AT PRIOR POINTS IN THEIR CAREERS EVALUATED SUCH PROGRAMS WITHIN CEBR AND CEDR. AND THEY EVALUATED THE PLAN FROM A REGULATORY PERSPECTIVE TO SEE IF ALL THE NECESSARY ACTIVITIES WERE PRESENT IN THE PROPOSAL TO REACH AN APPROVABLE IND.

AND THEN, FINALLY, UNDER THE FEASIBILITY, WE ASKED REVIEWERS TO COMMENT ON THE MILESTONES AND TIMELINES AS A REMINDER THAT WITH THESE LARGE AWARDS, WE WILL BE DOING MORE ACTIVE MANAGEMENT AND LOOKING TO RESEARCHERS TO REALLY MEET HARD MILESTONES DURING THESE PROJECTS.

THE THIRD REVIEW CRITERIA WAS THE

PRINCIPAL INVESTIGATOR AND THE RESEARCH TEAM LEADERSHIP. PREVIOUSLY YOU'VE ENCOUNTERED THIS AND WE'VE EVALUATED OUR PRINCIPAL INVESTIGATORS. UNDER THIS AWARD, WITH THE INCLUSION OF CO-PRINCIPAL INVESTIGATORS AND PARTNER PI'S, THEY WERE ALSO PART OF THIS EVALUATION. I SHOULD NOTE BRIEFLY THAT NEITHER CO-PI'S NOR PARTNER PI'S WERE A REQUIREMENT OF THIS RFA. AND IT WAS REALLY IF IT WAS JUSTIFIED BY THE PROJECT AND MADE SCIENTIFIC SENSE.

AND THEN, FINALLY, THE FOURTH REVIEW CRITERIA WERE THE COLLABORATIONS RESOURCES ENVIRONMENT, WHAT DID THESE TEAMS AND THEIR COLLABORATORS BRING TO THE TABLE TO ACHIEVE SUCCESSFUL COMPLETION OF THE PROJECT?

SO THIS GRAPHIC SHOWS THE DISTRIBUTION OF THE SCORES WHEN THE FULL APPLICATIONS WERE REVIEWED, AND THIS IS THE STARTING POINT WHERE THE GRANTS WORKING GROUP BEGAN THEIR PROGRAMMATIC DISCUSSION. THERE'S A GREEN LINE ON THE RIGHT OF YOUR SCREEN, AND APPLICATIONS TO THE RIGHT OF THAT GREEN LINE WERE JUDGED TO BE SCIENTIFICALLY MERITORIOUS AND WERE RECOMMENDED FOR FUNDING. APPLICATIONS TO THE LEFT OF THE RED LINE WERE LESS MERITORIOUS AND WERE NOT RECOMMENDED FOR FUNDING. THOSE APPLICATIONS IN BETWEEN WERE DESIGNATED BY THE GRANTS WORKING GROUP

PROVISIONALLY RECOMMENDED. ALL APPLICATIONS IN THE PROVISIONALLY FUNDED CATEGORY WERE INDIVIDUALLY DISCUSSED AND AFFIRMATIVELY PLACED INTO EITHER RECOMMENDED FOR FUNDING OR NOT RECOMMENDED FOR FUNDING CATEGORIES. AND THE RESULTS OF THE PROGRAMMATIC DISCUSSION ARE SUMMARIZED ON THE FOLLOWING SLIDE.

IN THE RECOMMENDED FOR FUNDING CATEGORY, THERE ARE A TOTAL OF 11 APPLICATIONS WITH A TOTAL FUNDS REQUESTED, $171.8 MILLION. THERE WERE NO APPLICATIONS IN THE PROVISIONALLY RECOMMENDED CATEGORY, AND THE BALANCE OF 20 APPLICATIONS ARE IN THE NOT RECOMMENDED CATEGORY.

THAT CONCLUDES THE PRESENTATION ON THE RECOMMENDATIONS FROM THE GRANTS WORKING GROUP.

CHAIRMAN KLEIN: LET ME ASK, JEFF SHEEHY, YOU CONDUCTED, AS THE VICE CHAIR OF THE PROGRAMMATIC REVIEW, THAT PART OF THE SESSION. WOULD YOU LIKE TO MAKE ANY STATEMENT BEFORE WE GO INTO EXECUTIVE SESSION, OR WOULD YOU LIKE TO RESERVE COMMENTS UNTIL AFTER EXECUTIVE SESSION?

MR. SHEEHY: JUST A COUPLE OF GENERIC COMMENTS. AND THIS IS JUST -- I DON'T KNOW IF THIS CORRELATES WITH ANYTHING, BUT JUST AN OBSERVATION. SINCE WE'VE GONE TO A PREAP PROCESS, WE HAVE

ACTUALLY TENDED TO FUND IN THE WORKING GROUP BELOW OUR FUNDING LINE, AND WE TEND TO FUND AT A 30-PERCENT RATE. SO WE HAD 31 APPLICATIONS AND WE HAD 11 RECOMMENDED. THERE IS A LITTLE BIT OF GRADING TO CURVE, SO TO SPEAK, THAT TAKES PLACE. AND I THINK PEOPLE SHOULD BE CONSCIOUS OF THAT.

THE OTHER THING TOO, BEFORE WE GO INTO SESSION, IS TO UNDERSTAND SOME OF THE RELATIONSHIPS BETWEEN THE SPECIALISTS' SCORES AND THEN TO BE THOUGHTFUL ABOUT THAT. AND I THINK THIS IS SOMETHING WE MAY BE ABLE TO DISCUSS IN CLOSED SESSION, BUT THE SPECIALIST SCORES ARE NOT SOMETHING THAT YOU ARE GOING TO SEE WHEN YOU LOOK AT THE SCORES AND WERE GIVEN SEPARATELY AND WERE INFORMATIVE, BUT WERE INTEGRATED INTO THE FINAL SCORES. YET THAT WAS KIND OF A GO/NO-GO METRIC BECAUSE IF YOU DIDN'T HAVE THE NECESSARY REGULATORY FRAMEWORK IN ORDER TO GET TO AN IND, I MEAN THIS WAS A FAIRLY HARD AND FAST STRUCTURAL THING. IF YOU DIDN'T SCORE WELL ON THAT, THERE WAS REALLY NO POINT IN BEING ABLE TO FULFILL THE RFA.

I THINK THAT THAT IS SOMETHING IN EXECUTIVE SESSION THAT PEOPLE SHOULD BE CONSIDERING. OBVIOUSLY, AS YOU ALL KNOW, YOU RECEIVED A GREAT MANY EXTRAORDINARY PETITIONS. IF THEY HAD THE

NECESSARY REGULATORY PATHWAY, AND THERE'S SCIENTIFIC EXPERIENCE AROUND THIS BOARD, I THINK PEOPLE SHOULD TAKE THOSE PETITIONS -- SHOULD BE ABLE TO EVALUATE SOME OF THE SCIENCE THAT'S BEING DISCUSSED.

MY FEELING WAS THAT DURING THE WORKING GROUP SESSION, WE PRETTY MUCH ADHERED TO THE NUMBERS. I THINK FOR THE KIND OF PROGRAMMATIC REVIEW THAT WE NEED TO DO, I THINK IT'S IMPORTANT THAT WE'RE CONSCIOUS OF THE DISEASE REPRESENTATION THAT WE HAVE IN THIS GRANT ROUND, BUT ALSO TO BE CONSCIOUS OF THE DISEASE REPRESENTATION WE HAD IN THE TRANSLATION ROUND BECAUSE THE TWO ARE REALLY A SET PIECE. THE SAME PI COULD NOT APPLY IN BOTH ROUNDS. WITH THOSE KIND OF CAVEATS, I THINK THAT'S THE ONLY THING I HAVE TO ADD.

CHAIRMAN KLEIN: VERY SPECIFICALLY, OF COURSE, JEFF'S COMMENTS ARE FOCUSED ON THE FACT THAT IN EXECUTIVE SESSION ANY COMMENT ON THE SPECIALISTS WILL BE IN THE TERMS OF THEIR PARTICULAR INPUT ON PROPRIETARY IP OR REGULATORY TECHNIQUE AND CONFIDENTIAL INNOVATIVE APPROACHES THAT THEY'VE MADE IN THE REGULATORY PROCESS AND OTHER PRIVILEGED INFORMATION.

DR. PRICE: COULD WE GET SOME EXPLANATION OF THIS NEW CONCEPT, PROVISIONALLY RECOMMENDED?

THIS IS THE FIRST TIME WE'RE USING IT.

CHAIRMAN KLEIN: THAT WOULD HAVE BEEN EQUIVALENT TO RECOMMENDED IF FUNDS WERE AVAILABLE. SO IN THE RECOMMENDED FOR FUNDS AVAILABLE, THEY CHOSE NOT TO LEAVE ANYTHING IN THAT CATEGORY.

DR. PRICE: I HAVE A FOLLOW-UP QUESTION. SINCE EVERY SINGLE ONE OF OUR RFA'S IN THE PAST HAVE HAD SOME GROUP THAT WERE IN THE IF FUNDS ARE AVAILABLE CATEGORY, I'M JUST WONDERING WHY WE'VE GOT A GOOSE EGG HERE THIS TIME. WHAT WAS SO DISTINCT?

CHAIRMAN KLEIN: I THINK THAT WHEN WE COME BACK INTO THE GENERAL SESSION, THIS WILL BE AN ITEM WE WILL DISCUSS. BUT, JEFF, IF YOU COULD JUST GIVE US A SUCCINCT.

MR. SHEEHY: WE ACTUALLY HAVE HAD BEFORE, WHEN THE WORKING GROUP DOES NOT FEEL LIKE ENOUGH APPLICATIONS MEET OUR FUNDING LINE, THEN IT DOESN'T MAKE SENSE TO SAY RECOMMENDED FOR FUNDING IF FUNDS ARE AVAILABLE BECAUSE YOU HAVEN'T FUNDED TO THE FUNDING LINE. SO THAT MIDDLE AREA HAS ONLY BEEN ONE THAT'S BEEN USED WHEN THERE HAVE BEEN AN EXCESS OF GRANTS THAT THEY CONSIDER WORTH FUNDING AND THEY'RE FUNDING BEYOND. OUR METRIC WAS 210 AND WE'RE OBVIOUSLY BELOW 210.

CHAIRMAN KLEIN: ALL RIGHT.

MR. SHESTACK: 210 WAS THE AMOUNT THAT WAS BUDGETED?

CHAIRMAN KLEIN: THAT WAS THE BUDGET. AND, IN FACT, BASED UPON OUR CASH-FLOW PROJECTIONS THAT WE WERE WORKING ON, WE HAD A CONTINGENCY IN OUR NUMBERS ON THE FUNDING SIDE EVEN ABOVE 210. IF THERE HAD BEEN SUFFICIENT APPLICATIONS THAT WERE MERITORIOUS, WE HAD A CONTINGENCY ACCOUNT TO ADDRESS THAT.

DR. POMEROY: IF I RECALL, THERE'S GOING TO BE ANOTHER ROUND OF THESE. CAN YOU REMIND US ABOUT THE AMOUNT OF MONEY THAT WAS SET ASIDE FOR THAT?

CHAIRMAN KLEIN: THE ADDITIONAL ROUND IS NOT SCHEDULED TO COME BACK TO THIS BOARD UNTIL 2011. BUT THE APPLICATIONS -- THE RFA IS EXPECTED TO BE APPROVED IN APPROXIMATELY OCTOBER OF 2010; IS THAT CORRECT, DR. TROUNSON?

DR. TROUNSON: I THINK IT'S PROBABLY A LITTLE LATER THAN THAT, BUT BASICALLY AS SOON AS IS REALLY POSSIBLE. PAT, DO YOU HAVE --

DR. OLSON: CONCEPT APPROVAL IS OCTOBER. AND I WOULD REMIND PEOPLE THAT WHAT WE ARE CONTEMPLATING FOR THE NEXT DISEASE TEAM AWARDS PROBABLY WOULD BE MORE LIKE THE PRECLINICAL

DEVELOPMENT CLINICAL STAGE. SO THEY WILL NOT BE STRICTLY EQUIVALENT IN THE OVERLAP WITH EARLY TRANSLATIONAL THAT EXISTED IN THIS ONE. SO PEOPLE WHO ARE RESEARCHERS WHO ARE INTERESTED IN GETTING THEIR DRUG DEVELOPMENT CANDIDATE IN, GETTING THE PRECLINICAL DATA TOGETHER, THE DISEASE MODIFYING ACTIVITY WOULD BE -- SHOULD BE LOOKING AT EARLY TRANSLATIONAL. AND WE WILL MAKE THAT CLEAR IN THE RFA. JUST TO CLARIFY THAT.

CHAIRMAN KLEIN: OKAY. THANK YOU. WHAT I'D LIKE TO DO, IF I CAN, HERE IS ADJOURN. I THINK WE'RE GOING TO BE IN THIS EXECUTIVE SESSION UP TO TWO HOURS, AND I BELIEVE THAT WE MAY BREAK THIS EXECUTIVE SESSION AND RECONVENE IT AS WELL SOMETIME TOMORROW MORNING, IF NECESSARY.

BUT, MR. HARRISON, IF YOU COULD READ THE QUALIFYING LANGUAGE FOR THE EXECUTIVE SESSION.

MS. SAMUELSON: MAY I ASK ONE MORE INFORMATIONAL QUESTION?

CHAIRMAN KLEIN: IF MR. HARRISON CAN READ THE SECTION, AND THEN I'M GOING TO TAKE THE QUESTION.

MR. HARRISON: SURE. THE BOARD WILL BE CONVENING IN CLOSED SESSION PURSUANT TO HEALTH AND SAFETY CODE SECTION 125290.30(D) TO CONSIDER

CONFIDENTIAL AND PROPRIETARY INTELLECTUAL PROPERTY OR WORK PRODUCT INFORMATION.

CHAIRMAN KLEIN: OKAY. AND, MELISSA KING, WOULD YOU TELL US WHERE WE'RE GOING TO CONVENE?

MS. KING: YES. WE'LL BE HAVING DINNER AND CLOSED SESSION IMMEDIATELY NEXT DOOR.

CHAIRMAN KLEIN: I'M GOING TO ASK THAT WE HEAR JOAN SAMUELSON'S QUESTION. AND THEN IF THE BOARD CAN ASSEMBLE VERY QUICKLY BECAUSE AT THE BEGINNING OF THIS EXECUTIVE SESSION, I'D LIKE TO COVER SOME MATERIALS OF GENERAL INTEREST EXCEPT FOR THOSE IN CONFLICT.

MS. SAMUELSON: HOW MANY APPLICATIONS WERE THERE THAT WERE DENIED AT THE PREAP LEVEL?

CHAIRMAN KLEIN: THERE WERE A TOTAL OF 72 OVERALL APPLICATIONS. SO THE 11 REPRESENTS ABOUT A 15-PERCENT SAMPLE OF THE GROSS APPLICATIONS AND ABOUT A 30-PERCENT SAMPLE OF THOSE QUALIFIED FOR THE FULL APPLICATION PROCESS. SO WE'RE DEALING WITH A DIMINISHED SAMPLE, I THINK, WAS JEFF'S POINT.

MS. SAMUELSON: SO 41 DIDN'T MAKE THE PREAP CUT?

CHAIRMAN KLEIN: YES. SO IF WE CAN ADJOURN AND IMMEDIATELY ASSEMBLE IN THE AREA NEXT DOOR. THANK YOU. THE PORTION OF YOUR BOOKS FOR

MATERIALS THAT DEALS WITH THE GRANT PROGRAM, TAB 11, YOU SHOULD TAKE.

(THE BOARD THEN RECESSED TO CLOSED SESSION, NOT REPORTED NOR HEREIN TRANSCRIBED.)

CHAIRMAN KLEIN: ALL RIGHT. THANK YOU VERY MUCH FOR YOUR PATIENCE. TONIGHT, IF WE COULD START TO REFRESH THE RECOLLECTION OF EVERYONE THAT'S PRESENT, IF WE COULD, IN FACT, SHOW ON THE SCREEN THE PRIOR LIST OF THE GRANTS DISCRIMINATING BETWEEN THE RECOMMENDED GRANTS AND THE NONRECOMMENDED GRANTS AND INDICATE WHERE THE CUTOFF LINE IS ON THE RECOMMENDED GRANTS AS A STARTING POINT. ALL RIGHT. I THINK WE HAVE SOMETHING CUT OFF THERE AT THE BOTTOM.

IT'S MY UNDERSTANDING AS WELL WE HAVE A COUPLE MORE BOARD MEMBERS, MELISSA, WHO WILL BE PRESENT TOMORROW MORNING. IS THAT A CORRECT STATEMENT?

MS. KING: THAT WE HAVE A QUORUM?

CHAIRMAN KLEIN: THAT WE HAVE A COUPLE MORE BOARD MEMBERS THAT WILL ALSO BE PRESENT TOMORROW MORNING.

MS. KING: I'M SORRY. CAN YOU REPEAT THE QUESTION FOR ME?

CHAIRMAN KLEIN: WILL THERE BE A COUPLE OF

ADDITIONAL BOARD MEMBERS WHO WILL BE PRESENT TOMORROW MORNING?

MS. KING: YES, THERE WILL, BUT WE ALSO HAVE TWO BOARD MEMBERS, I DON'T KNOW IF YOU ALREADY NOTED THIS, THAT JOINED US DURING THE CLOSED SESSION, MICHAEL GOLDBERG AND DAVID SERRANO-SEWELL.

MR. TORRES: WELCOME.

CHAIRMAN KLEIN: SO WHAT I WOULD PROPOSE IS THAT WE GO THROUGH THOSE APPLICATIONS THAT HAVE AN EXTRAORDINARY PETITION BEFORE WE GO THROUGH THE RECOMMENDED APPLICATIONS SO WE HAVE AN OVERVIEW OF THE ENTIRE FIELD OF APPLICATIONS AND THE INFORMATION THAT'S AVAILABLE FOR A DECISION.

DR. TROUNSON, IS THAT AN ACCEPTED APPROACH?

DR. TROUNSON: MR. CHAIR, I DON'T HAVE ANY OBJECTION TO THAT. IT'S NOT NECESSARILY THE COMMON WAY WE DO IT, BUT I DON'T HAVE AN OBJECTION.

CHAIRMAN KLEIN: JEFF SHEEHY.

MR. SHEEHY: I WAS JUST GOING TO SAY OUR POLICY HAS ALWAYS BEEN NOT TO BRING UP AN EXTRAORDINARY PETITION UNLESS A MEMBER BROUGHT IT -- UNLESS A MEMBER OF THE BOARD ASKS FOR THAT APPLICATION TO BE CONSIDERED BECAUSE WE -- PART OF THE POLICY IS THAT WHILE WE ACCEPT EXTRAORDINARY

PETITIONS, WE DON'T WANT TO CREATE A SITUATION WHERE PEOPLE FEEL LIKE THAT THEY CAN PUT ONE IN NO MATTER WHAT. PERSONALLY I WOULD PREFER THAT WE JUST ASK PEOPLE TO BRING UP APPLICATIONS -- THAT WE STATE OUR PROCESS, WE EITHER BRING APPLICATIONS UP THAT WE WANT TO BRING UP, OR APPLICATIONS DOWN THAT WE WANT TO BRING DOWN. BUT I THINK GIVING A HEARING TO SOMEONE JUST BECAUSE THEY SUBMITTED AN EXTRAORDINARY APPLICATION IS A VERY BAD PRECEDENT.

CHAIRMAN KLEIN: I'M IN CONCURRENCE. MY INTENT WAS TO GO THROUGH THEM BASED UPON THE ONES THAT THE BOARD WANTED TO DISCUSS.

MR. SHESTACK: WE ACTUALLY JUST AT THIS POINT GO DOWN THE LIST ONE BY ONE. IT'S NOT SUCH A LONG LIST.

CHAIRMAN KLEIN: THE POINT I THINK JEFF IS MAKING IS AS WE GO DOWN THE LIST, WE WILL ASK IF ANY BOARD MEMBER WANTS TO DISCUSS A SPECIFIC APPLICATION.

MR. SHESTACK: BUT WE WILL VOTE EN BLOC?

CHAIRMAN KLEIN: INDIVIDUALLY BECAUSE WE WANT TO MINIMIZE CONFLICTS AND MAXIMIZE THE POTENTIAL TO HAVE DISCUSSION.

DR. AZZIZ: LET ME ASK A POINT OF CLARIFICATION AGAIN BECAUSE WE'RE DEVIATING A LITTLE

BIT, AND I'M FULLY UNDERSTANDING. BUT WE DO HAVE A TIER I AND A TIER III, WE HAVE A NUMBER OF EXTRAORDINARY PETITIONS THAT WE COULD DISCUSS, BUT I DON'T THINK ANY OF THE EXTRAORDINARY PETITIONS ACTUALLY APPLY TO TIER I.

MR. SHESTACK: THEY DO.

DR. AZZIZ: THEY DO IN TIER I?

DR. TROUNSON: NO.

DR. AZZIZ: IF I DID, I MISSED THAT ONE. THERE'S A COUPLE OF LETTERS OF SUPPORT ENCOURAGING US TO SUPPORT SOME AREAS OF RESEARCH, BUT I DON'T THINK THERE'S ANY EXTRAORDINARY PETITION FOR A TIER I APPLICATION. I MAY BE WRONG.

MR. SHESTACK: NO, BUT I THINK THERE'S INFORMATION IN AN EXTRAORDINARY PETITION FOR A YELLOW GRANT THAT WAS PERTINENT TO THE DECISION IN A TIER I RANKED GRANT.

CHAIRMAN KLEIN: I THINK THAT THIS IS A CORRECT STATEMENT. AND THE INTENT WAS TO GO THROUGH THOSE PETITIONS THAT INDIVIDUALS WANTED TO DISCUSS TO SEE AND THEN GO BACK AND TAKE A VOTE. NOW, IT'S ALSO TRUE THAT I WAS TRYING TO INCLUDE IN THE VOTE TOMORROW MORNING THE ADDITIONAL MEMBERS WHO WOULD BE HERE SO WE HAD THE BROADEST VOTE OF THE BOARD MEMBERS POSSIBLE. AND BY HAVING THE DISCUSSION AT

THIS POINT RATHER THAN VOTING ON TIER I, WE HAVE THE OPPORTUNITY TO HAVE A BROADER PARTICIPATION. I'M OPEN TO ANY APPROACH, BUT I'M TRYING TO MAXIMIZE PARTICIPATION.

MR. SHEEHY: CAN I MAKE A SUGGESTION? I THINK IT WOULD REALLY BE HELPFUL IF WE STAYED REALLY PRETTY MUCH -- I MEAN I TOTALLY AGREE THAT WE CAN WAIT FOR THE FINAL VOTE UNTIL TOMORROW, BUT OUR TYPICAL MODE OF PROCEEDING IS TO LOOK INTO, FOR INSTANCE, THE BOTTOM TIER, ASK THE QUESTION IS THERE A MOTION TO MOVE AN APPLICATION INTO TIER I, TAKE THOSE MOTIONS, MAKE THOSE VOTES, THOSE ARE NOT DEFINITIVE OR FINAL, AND THEN ALSO AT SOME POINT WE NEED TO ASK THE QUESTION IS THERE ANY APPLICATION IN TIER I THAT PEOPLE WANT TO MOVE OUT OF TIER I, AND JUST GO THROUGH THAT. WE MAY NOT EVEN NECESSARILY GET THROUGH ALL THAT TONIGHT, BUT WE'LL HAVE THAT PREPARED AND ALREADY DONE.

WHAT I DON'T THINK WOULD BE HELPFUL IS THAT WE HAVE A DISCUSSION OF THE GRANTS WITHOUT VOTES BECAUSE THAT GETS VERY HARD TO SUSTAIN AND WE END UP TALKING ABOUT IT TWICE.

MR. SHESTACK: WHY WOULDN'T YOU WANT TO VOTE ON WHAT YOU CAN VOTE ON NOW? WHY WOULD YOU WANT TO POSTPONE ANY VOTING?

MR. SHEEHY: FOR THE FINAL VOTES, WE MAY WANT TO WAIT UNTIL TOMORROW. WE MAY NOT GET THROUGH ALL THIS TONIGHT.

CHAIRMAN KLEIN: WHAT JEFF IS PROPOSING COMBINES BOTH BEST CASES.

MR. SHESTACK: PLEASE EXPLAIN THE TERM "FINAL VOTE."

CHAIRMAN KLEIN: THERE'S A PROVISIONAL VOTE AT THIS POINT TO MOVE SOMETHING UP INTO TIER I. UNTIL WE APPROVE ALL THE TIER II'S, IT IS NOT A FINAL VOTE. RIGHT. THERE'S A PROVISIONAL VOTE THAT WILL BE TAKEN ON SOMETHING THAT'S NOT IN TIER I. IF IT GETS MOVED UP INTO TIER I, WE STILL HAVE TO HAVE THE VOTE ON ALL THE TIER I APPLICATIONS.

DR. PRIETO: WE VOTE IN A LUMP SUM EXCEPT FOR THOSE APPLICATIONS FOR WHICH I AM CONFLICTED.

MR. SHESTACK: I'M JUST SAYING DO WE HAVE TO? THERE AREN'T SO MANY. THEY'RE A LARGER AMOUNT THAN WE USUALLY VOTE FOR.

CHAIRMAN KLEIN: LET ME DO THIS. THE ADVANTAGE OF -- FIRST OF ALL, WHAT JEFF IS PROPOSING IS VERY CONSISTENT WITH THE APPROACH I WAS TAKING, WHICH IS GO THROUGH THEM ONE AT A TIME, SEE IF ANYONE WANTS TO MAKE A MOTION ON THEM. IF THEY DO, THEN WE DISCUSS IT. IF THEY DON'T, WE GO TO THE

NEXT ONE. AND WE'LL SYSTEMATICALLY GO THROUGH THEM TO THE EXTENT THAT ANYONE WANTS TO MAKE A MOTION TO MOVE THEM. ONCE WE HAVE DONE THAT, WE WILL THEN GO TO TIER I AND SEE IF ANYONE WANTS TO MAKE A MOTION TO MOVE ANY OF THOSE. ALL RIGHT. SO WITH THAT --

MS. SAMUELSON: MR. CHAIRMAN, I DON'T WANT TO BE A BAD APPLE, BUT THIS IS THE MOST IMPORTANT GRANT CYCLE WE'VE HAD. IT'S THE CLOSEST TO OUR CORE MISSION. AND THERE AREN'T THAT MANY GRANTS. I'M THINKING WE SHOULD HAVE A DISCUSSION ON ALL OF THEM, NOT THAT ALL OF THEM WOULD TAKE A LONG TIME.

CHAIRMAN KLEIN: JOAN, THAT'S AVAILABLE TO THE BOARD. AS WE GO THROUGH THE TIER III, IF WE HAVE A MOTION AND A SECOND, WE WILL DISCUSS EACH OF THOSE GRANTS ON WHICH WE HAVE A MOTION AND A SECOND TO MOVE UP TO TIER I. SO WITH THAT, I'D LIKE TO KNOW --

MS. SAMUELSON: IS THERE AN ASSUMPTION THAT WE WOULDN'T DISCUSS TIER I ALTHOUGH IT'S ONLY A RECOMMENDATION TO THE BOARD AS WELL?

CHAIRMAN KLEIN: WE WILL GO BACK AND DISCUSS TIER I AFTER TIER III AND SEE IF ANYONE WANTS TO MOVE ANY DOWN.

MS. SAMUELSON: I'M NOT NECESSARILY SUGGESTING WE DO THAT.

CHAIRMAN KLEIN: WE ARE GOING TO DO THAT.

MS. SAMUELSON: I JUST ASSUMED THAT WE WOULD WANT TO.

CHAIRMAN KLEIN: WE WILL. SO THE FIRST GRANT IN TIER III IS 1485. COULD THE COUNSEL STATE THE CONFLICTS?

MR. HARRISON: THE CONFLICT IS MICHAEL GOLDBERG.

CHAIRMAN KLEIN: ALL RIGHT. ON 1485 IF WE COULD HAVE -- IS THERE A MOTION THAT WE MOVE 1485 INTO TIER I?

MR. SHESTACK: IS THERE A MOTION TO --

CHAIRMAN KLEIN: TO MOVE 1485 INTO TIER I.

MR. SHEEHY: I'LL MAKE THAT MOTION.

CHAIRMAN KLEIN: ALL RIGHT. WE NEED A SECOND. I WILL SECOND THAT MOTION. DISCUSSION? WE NEED THE -- IF WE COULD HAVE THE SCIENCE OFFICER.

DR. TROUNSON: MICHAEL YAFFE WILL LEAD THE DISCUSSION FOR YOU, CHAIR.

DR. YAFFE: WOULD YOU LIKE A SYNOPSIS OF IT, MR. CHAIRMAN?

CHAIRMAN KLEIN: PLEASE IF YOU COULD DO A SHORT SYNOPSIS.

DR. YAFFE: THIS IS PROPOSAL FOCUSED ON THE DEVELOPMENT OF A NOVEL TREATMENT FOR ACUTE

MYELOID LEUKEMIA, AML. THE TREATMENT'S BASED ON A THERAPEUTIC MONOCLONAL ANTIBODY THAT TARGETS THE CELL SURFACE MOLECULE CD 47 PREFERENTIALLY EXPRESSED ON LEUKEMIA STEM CELLS.

THESE CELLS ARE THOUGHT TO DRIVE THE LEUKEMIA AND TO DISPLAY ELEVATED RESISTANCE TO CONVENTIONAL CHEMOTHERAPY AGENTS. ANTIBODY BINDING TO CD 47 OR TO ADDITIONAL CELL SURFACE MOLECULES IS EXPECTED TO FACILITATE MACROPHAGE-MEDIATED PHAGOCYTOSIS AND REMOVE THE LEUKEMIC STEM CELLS. THAT'S THE BASIS FOR THE THERAPY, THE PROPOSED THERAPY.

THE APPLICANT WILL DEVELOP A HUMANIZED BLOCKING ANTIBODY AND TEST ITS EFFICACY IN A MOUSE XENOTRANSPLANTATION MODEL AND ALSO IDENTIFY ADDITIONAL POTENTIAL CELL SURFACE TARGETS ON AML LEUKEMIC STEM CELLS. THEY'LL EVALUATE THE THERAPEUTIC VALUE OF SUCH ANTIBODIES AND IN LATER STAGES OF THE STUDY DEVELOP GMP-GRADE PRODUCTION OF PROMISING ANTIBODIES FOLLOWED BY EFFICACY AND SAFETY TESTING AND APPROPRIATE IN VIVO MODELS AND PROCEED WITH PREPARATION OF AN IND.

THIS PROPOSAL WAS EVALUATED BY THE GRANTS REVIEW GROUP WHICH RECOGNIZED A NUMBER OF IMPORTANT STRENGTHS AND CRITICIZED THE PROPOSAL BASED ON SOME

PERCEIVED WEAKNESSES. KEY STRENGTHS OF THIS PROPOSAL WERE THE PI AND PARTNER PI WHO ARE RECOGNIZED AS OUTSTANDING WORLD LEADERS IN THEIR FIELDS, COMPLEMENTARY AND WELL-ESTABLISHED COLLABORATIONS, AND THE MEDICAL NEED FOR BETTER TREATMENTS OF AML. THE SIGNIFICANCE WAS VIEWED AS EXTREMELY HIGH.

WEAKNESSES PERCEIVED BY THE GRANTS WORKING GROUP INCLUDED SERIOUS CONCERNS ABOUT THE VALIDITY OF THE PROPOSED THERAPEUTIC TARGET AND OTHER ISSUES CONCERNING THE PROJECT'S FEASIBILITY.

I'M HAPPY TO ELABORATE OR ANSWER ADDITIONAL QUESTIONS.

MR. SHESTACK: WHAT WAS THE SCORE?

CHAIRMAN KLEIN: WHAT WAS THE SCORE ON THIS GRANT?

DR. YAFFE: THE SCORE ON THIS GRANT WAS 65.

CHAIRMAN KLEIN: AND COULD YOU INDICATE THE STAFF'S POSITION ON THE REBUTTAL OF THE POINTS? SPECIFICALLY I BELIEVE THIS GRANT WAS CENTRALLY -- ONE OF THE CENTRAL FIGURES IN GRADING THIS DOWN WAS AN ASSERTION THAT YOU COULDN'T HAVE A THERAPY IF YOU ONLY HAD A TWO TIMES OVEREXPRESSION. I BELIEVE THAT THE STAFF HAS ANALYZED WHETHER, IN FACT, THAT YOU

CAN'T HAVE AN EFFECTIVE THERAPY WHEN THE OVEREXPRESSION IS IN THAT RANGE.

DR. YAFFE: WELL, THIS WAS A CONTENTION OF THE APPLICANT IN THE EXTRAORDINARY PETITION ABOUT A TWOFOLD DIFFERENCE IN THE EXPRESSION LEVEL OF THIS TARGET MOLECULE. THE APPLICANT FELT THAT THIS WOULD BE SUFFICIENT TO PROVIDE A THERAPEUTIC WINDOW. THE REVIEWERS FELT THIS WOULD NOT BE SUFFICIENT.

CHAIRMAN KLEIN: OKAY.

DR. YAFFE: WE VIEW THIS AS A DIFFERENCE IN SCIENTIFIC OPINION BETWEEN THE REVIEWERS AND THE APPLICANT.

CHAIRMAN KLEIN: ALL RIGHT. I THINK THAT THE REBUTTAL WENT SUBSTANTIALLY BEYOND THAT IN PROVIDING EVIDENCE THAT, IN FACT, THERE WERE TWO THERAPIES AT LEAST THAT WERE WELL-KNOWN THAT, IN FACT, WERE EFFECTIVE WITH TWO TIMES OVEREXPRESSION; IS THAT RIGHT?

DR. YAFFE: IT WASN'T TWO TIMES. THERE WAS A POINT MADE THAT THERE HAVE BEEN EFFECTIVE THERAPIES IN THE CASE WHEN THERE'S BEEN SMALL DIFFERENCE IN EXPRESSION LEVELS.

DR. TROUNSON: MR. CHAIR, THE ISSUE THAT YOU ARE TRYING TO DRAW ON IS THAT THERE'S A TWO TIMES DIFFERENCE, WHICH IS LOW IN THIS CASE. IT

WOULD BE THOUGHT TO BE A LOW DIFFERENCE, A MINOR DIFFERENCE. AND THERE'S ALSO EXPRESSION OF THE CD 47 ANTIGEN WIDELY IN THE BODY, THAT THAT COULD ACT AS ANTIGEN SINK, TAKE OUT THE ANTIBODY. IN FACT, THE APPLICANTS HAVE SHOWN SOME EFFECTIVE TREATMENT OF THEIR ANIMAL MODEL.

SO THE SENSE OF IT IS THAT IF YOU'VE GOT AN EFFECTIVE TREATMENT, AND EVEN IT IS ONLY A TWO TIMES DIFFERENCE AND THERE'S NOT AN ANTIGEN SINK WHICH IS STOPPING THE EFFECT, THEN YOU'VE STILL GOT AN EFFECTIVE TREATMENT. SO THERE IS SOME VERY NOVEL COMPONENT PARTS OF THIS. THEY CALL IT A DON'T-EAT-ME ANTIGEN. IF IT IS WIDESPREAD, IF IT'S EFFECTIVE AND YOU CAN BLOCK IT, YOU MIGHT VERY WELL HAVE QUITE A MAJOR DIFFERENCE IN CANCER MORE BROADLY THAN EVEN THE CONDITION THAT IT'S FOCUSED ON.

SO I THINK WHERE WE'RE AT IS WE'RE NOT REALLY DISAGREEING WITH THE REVIEWERS, AND I DON'T THINK WE'RE DISAGREEING WITH THE PI. I THINK IT'S GENUINELY A PROJECT THAT'S IN THAT AREA WHERE YOU CAN MAKE A DECISION ON, AND I DON'T THINK ANY OF US WOULD BE REALLY TOO UNCOMFORTABLE ABOUT WHATEVER DECISION THAT YOU MAKE.

CHAIRMAN KLEIN: OKAY. DR. LOVE, YOU WERE SERVING AS THE ACTING SCIENTIFIC OFFICER DURING THIS

REVIEW. WOULD YOU LIKE TO MAKE A COMMENT?

DR. LOVE: I WAS JUST GOING TO REEMPHASIZE, I THINK, WHAT ALAN JUST SAID. I DON'T THINK ANYBODY WOULD SUGGEST THAT THE TWOFOLD DIFFERENCE IS A STRENGTH. IT WOULD BE MUCH MORE DESIRABLE, I THINK EVERYONE WOULD ADMIT, FOR THERE TO BE ABSOLUTE PERFECTION IN TERMS OF IT ONLY EXISTING ON THE TARGET AND NOT EXISTING ON ANY OTHER CELL. THAT CLEARLY DOESN'T EXIST. BUT AS ALAN SAID, THE GRANT APPLICANT PROVIDED INFORMATION THAT SHOWS IN HIS MODEL THAT IT SEEMS TO WORK. AND AS YOU SAID, THERE ARE THERAPIES ON THE MARKET WHERE THERE'S ACTUALLY NOT A GREAT DEAL OF DIFFERENCE OF EXPRESSION OF THE ANTIGEN, PARTICULARLY THE EGFR RECEPTOR ANTAGONIST. THERE'S NOT A GREAT DEAL OF DIFFERENCE BETWEEN THE EXPRESSION ON THE TUMORS AND ON MANY OTHER CELLS, AND YET THESE THERAPIES STILL WORK. ACTUALLY TO MAKE IT EVEN MORE INTERESTING, THERE'S A TOTAL LACK OF CORRELATION BETWEEN OVEREXPRESSION OF THE ANTIGEN AND EFFICACY OF THE THERAPY.

SO I THINK AT THE END OF THE DAY, THERE ARE A LOT OF OUTSTANDING ISSUES HERE, AND THAT'S WHY I DO THINK THAT IT'S OPEN FOR DEBATE SCIENTIFICALLY. AND I THINK THE BOARD SHOULD FEEL, AT LEAST IN MY

VIEW, COMFORTABLE COMING DOWN ON EITHER SIDE OF THIS. I DEFINITELY DON'T THINK THERE'S ANYTHING TO SUGGEST IT WOULD BE UNSAFE OR UNWISE OR IRRESPONSIBLE TO FUND THIS GRANT.

CHAIRMAN KLEIN: ALL RIGHT. ADDITIONAL COMMENTS FROM BOARD MEMBERS ON THIS?

MS. SAMUELSON: YEAH. IN THAT EVENT, GIVEN THE HIGH IMPACT OF A POSSIBLE SUCCESS OF THIS APPROACH ON A POPULATION OF CALIFORNIANS AND AMERICANS, WHY WOULD WE NOT WANT TO FUND IT, I GUESS, IS MY QUESTION?

CHAIRMAN KLEIN: IT DEFINITELY IS A HIGH IMPACT WHICH THE REVIEWERS DID TAKE NOTE OF. I WOULD JUST LIKE TO SAY THAT THIS IS A TEAM THAT WAS NOTED FOR SUBSTANTIAL STRENGTH, I BELIEVE, BOTH IN THE U.S. COMPONENT AND IN THE BRITISH COMPONENT. IS THAT A CORRECT STATEMENT?

DR. YAFFE: THAT'S CORRECT.

CHAIRMAN KLEIN: AND THERE IS AN EXTRAORDINARY DEPTH TO THIS TEAM THAT WAS ACKNOWLEDGED. IN THAT CONTEXT I THINK IT IS ALSO IMPORTANT TO NOTE THAT AMONG THE REVIEWERS WERE A NUMBER OF PEOPLE WHO DON'T BELIEVE THAT CANCER STEM CELLS EXIST AT ALL. VERY STRONG IDEOLOGICAL POSITION.

MR. SHESTACK: DON'T BELIEVE WHAT?

CHAIRMAN KLEIN: THAT CANCER STEM CELLS EXIST AT ALL. THERE'S A SUBSTANTIAL -- THERE ARE MAJOR SCHOOLS IN CALIFORNIA AS A DOMINANT AREA WHERE THERE'S A LOT OF PEOPLE WHO BELIEVE IN CANCER STEM CELLS, THERE'S A LOT OF PUBLISHED INFORMATION THAT CANCER STEM CELLS EXIST IN VARIOUS DIFFERENT CANCER TYPES. IN THE UK THERE'S SOME SUBSTANTIAL SUPPORT FOR CANCER STEM CELLS AS WELL AS IN CANADA AND SOME OTHER COUNTRIES.

BUT MY PERSONAL IMPRESSION IS THAT THIS GRANT COULD EASILY HAVE BEEN AFFECTED IN THAT REVIEW BY THE FACT THAT THERE IS THIS VERY STRONG REPRESENTATION OF INDIVIDUALS THAT DIDN'T BELIEVE IN CANCER STEM CELLS IN THAT REVIEW. I THINK THEY WOULD MAKE A VERY SINCERE EFFORT TO BE OBJECTIVE, AND I'M SURE THEY MADE A FULL EFFORT TO BE OBJECTIVE. THE ISSUE HERE IS I FIND IT DIFFICULT FOR SOMEONE WHO IS PASSIONATELY COMMITTED TO ONE OF THESE SCHOOLS OR ANOTHER TO HAVE A COMPLETELY OBJECTIVE EVALUATION ON THIS ALTHOUGH CERTAINLY THEY MAY HAVE. I THINK THAT'S ANOTHER ISSUE.

DR. TROUNSON: CHAIR, RESPECTFULLY I DISAGREE WITH YOU. I ACTUALLY THINK THERE WAS VERY LITTLE VARIANCE IN THE MARK GIVEN TO THIS GRANT. SO

WHILE THERE IS, AS YOU SAY, A VARIANCE IN THE COMMUNITY, THE SCIENTIFIC COMMUNITY, ON THIS MATTER, I DON'T THINK THIS NECESSARILY PREJUDICED THIS PARTICULAR GRANT.

THE ONLY OTHER THING THAT I THINK I SHOULD DRAW TO THE ATTENTION OF THE BOARD IS THAT THE MEDICAL RESEARCH COUNCIL, WHICH IS RESPONSIBLE FOR THE BRITISH PART OF IT, EXAMINED THE ISSUE AND HAD THEIR SCIENTIFIC TEAM LOOK AT THE ISSUE, AND THEY CAME OUT ADVICE TO US THAT IF THE BOARD WAS WILLING TO SUPPORT THIS PROJECT, THEN THE MRC WOULD BE.

CHAIRMAN KLEIN: ALL RIGHT. DR. LEVIN.

DR. LEVIN: MY QUESTION WAS JUST THAT, WHAT WAS THE VARIANCE IN THE SCORES? WERE THEY ALL 65S OR DID THEY BREAK INTO TWO CAMPS?

DR. TROUNSON: SPECIFICALLY --

DR. YAFFE: STANDARD DEVIATION WAS VERY SMALL.

DR. TROUNSON: VERY SMALL HERE. I ASKED ABOUT SOME OF THESE PROJECTS. THERE ARE SOME DIFFERENCES, AND THIS WAS NOT ONE OF THEM.

CHAIRMAN KLEIN: WHAT WE'RE DEALING WITH HERE IS A DIFFERENCE OF FIVE POINTS, WHETHER IT'S WITHIN THE 70-POINT CUTOFF THEY USED OR NOT. SO IT DOESN'T TAKE MUCH VARIANCE.

DR. LOVE: I WOULD JUST SAY AND THERE WAS ACTUALLY A ROBUST DISCUSSION IN THE GRANTS WORKING GROUP ABOUT WHETHER OR NOT THIS GRANT SHOULD GO UP OR DOWN IN TERMS OF THE FUNDING. SO THERE WERE PEOPLE ON THE COMMITTEE WHO MADE, I THINK, A CASE THAT THIS GRANT COULD BE FUNDED, AND THERE WERE PEOPLE OF THE OTHER OPINION.

MR. TORRES: I VOTED AYE THEN, AND I WANT TO VOTE AYE AGAIN.

DR. POMEROY: BOB, I HAVE A COUPLE OF QUESTIONS HERE ON SOME OTHER ISSUES. THE REVIEW TALKS ABOUT A SIGNIFICANT CONCERN BECAUSE THE TREATMENT WOULD DEPEND UPON MACROPHAGE PHAGOCYTOSIS, AND THE REVIEWERS FELT THAT IT WAS UNLIKELY THAT SOMEONE WHO HAD RECEIVED CHEMOTHERAPY OR HAD LEUKEMIA WOULD HAVE ROBUST MACROPHAGE ACTIVITY.

AND IT SPECIFICALLY SAYS THAT THE APPLICANT DIDN'T ADDRESS THAT POTENTIAL COMPLICATION. AND THE REVIEW ALSO GOES ON TO SAY THAT THE PROPOSAL LACKED ADEQUATE DISCUSSION OF POTENTIAL PITFALLS AND ALTERNATE PLANS SHOULD ROADBLOCKS BE ENCOUNTERED. I THINK WE HEARD A NUMBER OF THINGS WHICH SUGGEST THERE COULD BE ROADBLOCKS BECAUSE OF THESE CONCERNS.

DO YOU HAVE ANY ADDITIONAL INFORMATION

THAT PERTAINS TO THOSE TWO POINTS?

DR. YAFFE: WITH REGARD TO THE MACROPHAGE ACTIVITY, THE APPLICANT IN HIS EXTRAORDINARY PETITION SUGGESTED THAT, BASED ON CLINICAL PRACTICE AND EXPERIENCE FROM CLINICAL PRACTICE, IN AML MANY PATIENTS DO NOT HAVE A DECREASED LEVEL OF MACROPHAGE FUNCTION. BUT THERE WAS NO SUCH DATA SUPPLIED WITH THE APPLICATION, SO THE CRITICISM STANDS, AND WE'RE LEFT WITH A DIFFERENCE OF OPINION BETWEEN THE APPLICANT AND THE COMMITTEE.

THE OTHER THING THAT THE GRANTS REVIEW GROUP POINTED OUT IN THIS REGARD IS THAT THE INITIAL TARGET POPULATION PROBABLY WHICH THE COMMITTEE FELT WOULD BE USED TO TEST THIS THERAPY WOULD BE PATIENTS WHO HAD ALREADY UNDERGONE SOME CONSIDERABLE CHEMOTHERAPY. AND THAT'S GOING TO BE A DIFFERENT POPULATION FROM THE NAIVE NEW CANCER PATIENT WHO HAD NEVER EXPERIENCED CHEMOTHERAPY. UNFORTUNATELY WE'RE LEFT WITHOUT DATA HERE.

CHAIRMAN KLEIN: I'M NOT SURE THAT THAT'S CORRECT.

DR. PRIETO: CAN I RESPOND TO THAT? I THINK CLINICALLY THAT THERE'S AMPLE EVIDENCE THAT THAT ISN'T CORRECT. AND ONE OF THE OTHER THAT THOSE PATIENTS DON'T HAVE WHO HAVE HAD CHEMOTHERAPY DON'T

SHOW SIGNS OF THE TYPE OF INFECTIONS YOU WOULD EXPECT IF THEY DIDN'T HAVE ADEQUATE MACROPHAGE FUNCTION.

AND THE OTHER ISSUE THAT'S SORT OF TANGENT TO THIS, BUT THAT ANOTHER ONE OF THE EXTRAORDINARY APPLICATIONS BROUGHT UP, WAS THAT WE ONLY ALLOW FOUR PAGES OF PRELIMINARY DATA IN THE APPLICATION, AND THEY MENTIONED THAT THEY MIGHT HAVE MENTIONED THIS IF THEY HAD NOT BEEN SPACE CONSTRAINED. SO IT'S JUST A POINT.

CHAIRMAN KLEIN: AND, DR. LOVE, I BELIEVE THERE WAS A SPECIFIC REBUTTAL OF THIS ANALOGIZING TO A SITUATION WHERE THERE'S BEEN TESTING TO SHOW THAT MACROPHAGES, IN FACT, DO SURVIVE IN A SIMILAR --

DR. LOVE: I THINK THERE WERE TWO LINES, AND PROBABLY ONE IS VERY CLEAR. THAT IS THAT CLINICALLY THESE PATIENTS DON'T GET SOME OF THE INFECTIONS THAT YOU WOULD EXPECT FROM PEOPLE WHO HAVE NO MACROPHAGE FUNCTION. SO, IN FACT, THEY PROBABLY DO HAVE SOME MACROPHAGE FUNCTION. HOW THAT WILL TRANSLATE IN TERMS OF THE DEGREE OF EFFECTIVENESS ON THIS THERAPY, WE DON'T KNOW, BUT IT'S CLEAR THAT THERE IS SOME MACROPHAGE ACTIVITY LEFT.

THE OTHER EXAMPLE THAT WAS REFERRED TO WAS

THE USE OF RITUXIMAB. AND, AGAIN, IT'S CLEARLY WORKING THROUGH MACROPHAGE ACTIVITY IN SOME OF THESE PATIENTS.

DR. YAFFE: WITH ALL DUE RESPECT, DR. LOVE, I HAVE TO SAY THAT THE RITUXAN IS NOT AN ADEQUATE ANALOGY BECAUSE RITUXAN'S MODE OF ACTION DOES NOT DEPEND ON MACROPHAGE FUNCTION.

DR. LOVE: I KNOW RITUXAN B-CELLS, BUT I THOUGHT THE REFERENCE WAS THAT SOME OF THE ACTIVITY OF THE RITUXIMAB IS, IN FACT, BEING MEDIATED THROUGH MACROPHAGE --

DR. YAFFE: THAT'S THE SUGGESTION IN THE PETITION. BUT, IN FACT, THE DATA FROM THE SCIENTIFIC LITERATURE INDICATES THE RITUXAN KILLS BY THREE MECHANISMS THAT'S NOT DEPENDENT ON MACROPHAGE. IT'S DEPENDENT -- IT INDUCES APOPTOSIS AND IT RECRUITS KILLER T-CELLS. SO THAT PARTICULAR -- I THINK THAT YOUR FIRST ARGUMENT ABSOLUTELY IS ONE THAT WE SHOULD CONSIDER AND HAS VALIDITY. THE SECOND WHICH THE APPLICANT RAISED IS PROBABLY NOT SUPPORTED BY THE SCIENTIFIC AND MEDICAL LITERATURE.

DR. LOVE: I'LL REST WITH MY FIRST ARGUMENT THEN.

CHAIRMAN KLEIN: THANK YOU VERY MUCH. ANY ADDITIONAL QUESTIONS BY MEMBERS?

MR. SHESTACK: COULD YOU, ALAN, TALK ABOUT THIS IN TERMS OF THE GO/NO-GO RUBRIC THAT WE'RE USING FOR THESE AWARDS?

DR. TROUNSON: I'LL TAKE THAT, JON. THE GRANTS ARE GOING TO BE SUBJECT TO MILESTONE EVALUATION AS YOU WOULD IN COMMERCIAL GRANTS. THEY'RE VERY CLOSELY SUPERVISED WITH RESPECT TO MEETING MILESTONES. IN THE FIRST YEAR WE WILL HAVE MILESTONES, AND THEY WILL BE CONNECTED TO GO/NO-GO DECISIONS. WE'LL BE NEGOTIATING WITH THE APPLICANTS TO ENSURE THAT THERE IS POINTS IN THE PROJECT, IF THEY DON'T MAKE SUITABLE PROGRESS IN THE PROJECT IN MEETING SOME OF THE DEMANDS THAT ARE APPLIED, THAT WE WILL FOREGO FUNDING IF IT WAS A GO/NO-GO DECISION IF THEY FAILED TO MAKE THAT MILESTONE IF THEY HAD REASONABLE OPPORTUNITY TO DO THAT.

SO THAT'S GOING TO BE A MAJOR ACTIVITY OF OUR NEW VICE PRESIDENT R & D TO BE WITH THESE GRANTS WORKING WITH THEIR STEERING COMMITTEES, BUT ALSO WITH OUR OWN ADVISORY COMMITTEE TO MAKE SURE THAT THE PROGRESS OF THE GRANTS IS CONTINUOUS AND ON TARGET TO GET TO THE IND. SO IF THEY DON'T, WE WILL TERMINATE THEM AND WE'LL RETURN THE MONEY TO THE POOL. IF THEY DO, IF THERE'S REASON TO BELIEVE SOME ADJUSTMENT WOULD ENABLE IT TO HAPPEN, AND WE WOULD

BE GUIDED BY THE COMMITTEE AND BY OUR NEW SENIOR STAFF MEMBER, THEN WE MAY CONTINUE, PROBABLY CONTINUE THE PROJECT TILL THE NEXT POINT. IF THEY DIDN'T MAKE THAT, WE WOULD CERTAINLY CLOSE IT DOWN.

SO ALL OF THESE PROJECTS ARE GOING TO BE SUBJECT TO THOSE GO/NO-GO DECISIONS BECAUSE THESE ARE BIG PROJECTS, THEY'RE $20 MILLION, OFTEN UP TO $20 MILLION OR EVEN FURTHER IN THE CASE OF SOME OF THE CANADIAN AND THE UK GRANTS. THIS PARTICULAR GRANT IS BIGGER THAN 20 MILLION. IT WILL BE INCLUDING, I THINK, $4.3 MILLION FROM THE MRC IN ENGLAND FUNDING THE OXFORD COMPONENT. AND WE'VE NOW COME TO AGREEMENT WITH THE MRC THAT WE WILL DUALLY EXAMINE THESE PROJECTS ON THEIR PROGRESS GOING FORWARD. SO I HOPE YOU FEEL THAT WE WILL PUT IN THAT EFFORT TO SUPPORT WHATEVER DECISIONS THAT YOU MAKE.

MR. SHESTACK: THE REASON I BRING IT UP IS I JUST WANT TO MAKE CLEAR THAT IF WE DECIDE AS A GROUP TO FUND THIS GRANT, IT'S NOT BECAUSE THEY HAD A SUCCESSFUL EXTRAORDINARY PETITION THAT THEY PRESENTED. THEIR EXTRAORDINARY PETITION COMPLAINED ABOUT THEIR SCORE. AND THEY MIGHT HAVE BEEN VALID, BUT IT'S BECAUSE THE GROUP HAS DECIDED THAT THIS IS EXCELLENT, THE AUSPICES ARE EXCELLENT, THE WORK IS

PROBABLY GOOD, AND TO EXTEND THE PAYLINE BECAUSE THERE MAY BE DOWN THE ROAD GRANTS THAT ACTUALLY WHERE TRULY NEW INFORMATION IS PRESENTED TO THE GROUP. AND I REALLY WANT US TO MAKE THE DISTINCTION BECAUSE THIS IS A NEW PROCEDURE, THE EXTRAORDINARY PETITION, AND I DON'T WANT IT TO BE INTERPRETED FOR THE FUTURE, FOR FUTURE APPLICANTS, AS A CHANCE TO JUST GET REREVIEWED. IT'S NOT WHAT IT'S MEANT FOR. BUT OFTEN THIS GROUP HAS DECIDED TO EXTEND -- HAS DECIDED TO FUND THINGS IF FUNDING WAS AVAILABLE, AND AS IT HAPPENS THERE IS FUNDING AVAILABLE. I JUST WANT TO FRAME --

CHAIRMAN KLEIN: IT IS ALSO AN OPPORTUNITY TO CORRECT MISTAKES OR FACTUAL ERRORS IN THE PROCESS THAT CAN BE DISCOVERED. AND THAT, IN FACT, THE WHOLE PROCESS IS A SAFEGUARD AND AN ABILITY FOR US TO MAKE AN INDEPENDENT JUDGMENT.

I'D LIKE TO, DR. LOVE, YOU WERE THE ACTING SCIENTIFIC OFFICER AT THE TIME OF THIS. SO LOOKING AND HEARING ALL OF THESE DISCUSSIONS, WHAT IS YOUR OPINION AS TO WHETHER THIS WOULD BE REASONABLE TO FUND HAVING CERTAINLY THE VERY IMPORTANT POINT THAT MR. SHESTACK HAS MADE --

MR. ROTH: HOW FAR ARE WE GOING TO GO FROM THIS?

CHAIRMAN KLEIN: -- MR. SHESTACK HAD MADE WHICH IS WE HAVE MILESTONE FUNDING POINTS.

MR. ROTH: WE LOBBIED THIS ONE. I THINK WE'VE HAD ENOUGH DISCUSSION.

CHAIRMAN KLEIN: CALL THE QUESTION. AND I WILL --

MR. ROTH: LEEZA HAS HAD A QUESTION.

MS. GIBBONS: I WAS JUST GOING TO SAY TO YOUR POINT THAT REGARDLESS OF THE EXTRAORDINARY PETITION PROCESS, EVEN IF YOU JUST TAKE WHAT THE SCIENCE TEAM HAS GIVEN US HERE, WE'VE GOT A FAIRLY HIGH SCORE, WE'VE GOT A LOT OF MERIT FOR THIS PROPOSAL, WE'VE GOT A LOT OF RESPECT FOR THE PI AND FOR THE TEAM, AND I THINK WE HEARD DR. TROUNSON AND OTHERS SAY THERE WAS RESPECT FOR SCIENTIFIC DISAGREEMENT ON SOME OF THESE ISSUES, AND THEY WOULD BE COMFORTABLE WITH US GOING EITHER WAY. IS THAT NOT CORRECT?

CHAIRMAN KLEIN: THAT'S RIGHT. SUCCINCTLY PUT. PUBLIC COMMENT ON THIS GRANT?

MR. REED: THIS APPLIES ALSO TO THE GENERAL FEELING I'M GETTING. THERE'S A SUPPOSEDLY TRUE STORY ABOUT A SETTLER WHO WAS FOUND DEAD AFTER AN INDIAN ATTACK, AND HE HAD ARROWS ALL THROUGH HIS BODY. AND IS HIS HAND WAS A RIFLE WHICH HELD A

SINGLE SHOT UNFIRED. I HATE THE THOUGHT OF THAT. IF IT WAS ME, I WOULD FIRE THE SHOT, I WOULD THROW THE RIFLE, I WOULD PICK UP A ROCK. I THINK THAT SHOULD BE OUR APPROACH TOWARD THIS MONEY THAT WE HAVE.

WE'RE FIGHTING THE MOST HORRIBLE DISEASES ON EARTH. IF THIS IS ONE THAT'S CLOSE, MY FEELING IS WE SHOULD GO FOR IT.

CHAIRMAN KLEIN: I THINK IT'S AN IMPORTANT POINT, THAT WE HAVE TO BE DEALING WITH SCIENTIFIC MERIT HERE. IF WE COULD CALL THE ROLL ON THIS. AND, AGAIN, IT'S MICHAEL GOLDBERG WHO IS IN CONFLICT; IS THAT CORRECT?

MS. KING: THAT IS CORRECT.

CHAIRMAN KLEIN: THIS IS A MOTION TO MOVE THIS INTO TIER I.

MS. KING: RICARDO AZZIZ.

DR. AZZIZ: ABSTAIN.

MS. KING: ROBERT PRICE.

DR. PRICE: YES.

MS. KING: FLOYD BLOOM.

DR. BLOOM: YES.

MS. KING: JACOB LEVIN.

DR. LEVIN: YES.

MS. KING: LEEZA GIBBONS.

MS. GIBBONS: YES.
MS. KING: BOB KLEIN.
CHAIRMAN KLEIN: YES.
MS. KING: GERALD LEVEY.
DR. LEVEY: YES.
MS. KING: TED LOVE.
DR. LOVE: YES.
MS. KING: ED PENHOET.
DR. PENHOET: YES.
MS. KING: CLAIRE POMEROY.
DR. POMEROY: YES.
MS. KING: FRANCISCO PRIETO.
DR. PRIETO: YES.
MS. KING: ROBERT QUINT.
DR. QUINT: YES.
MS. KING: DUANE ROTH.
MR. ROTH: NO.
MS. KING: JOAN SAMUELSON.
MS. SAMUELSON: YES.
MS. KING: DAVID SERRANO-SEWELL.
MR. SERRANO-SEWELL: YES.
MS. KING: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. KING: JON SHESTACK.
MR. SHESTACK: NO.

MS. KING: OSWALD STEWARD.
DR. STEWARD: ABSTAIN.
MS. KING: ART TORRES.
MR. TORRES: AYE.
CHAIRMAN KLEIN: THANK YOU. THE NEXT ITEM IS --
MS. KING: FOR THE RECORD, I'D JUST LIKE TO STATE THAT THAT MOTION CARRIES. I WAS GIVING COUNSEL TIME TO COUNT, BUT I THINK I CAN MAKE THAT STATEMENT.
CHAIRMAN KLEIN: THANK YOU. THE NEXT ITEM IS 1480. THE CONFLICTS, PLEASE.
MR. HARRISON: THE CONFLICTS ARE AZZIZ, GOLDBERG, LEVEY, LEVIN, AND STEWARD.
CHAIRMAN KLEIN: COULD YOU REPEAT THOSE, PLEASE?
MR. HARRISON: AZZIZ, GOLDBERG, LEVEY, LEVIN, AND STEWARD.
DR. LOVE: MR. CHAIRMAN, I'D LIKE TO MOVE THAT WE MOVE GRANT 1480 UP TO TIER I.
CHAIRMAN KLEIN: IS THERE A SECOND?
DR. PRIETO: SECOND.
CHAIRMAN KLEIN: SECOND BY DR. PRIETO.
DR. OLSON, COULD YOU SUMMARIZE THE POSITIONS AND POTENTIALLY THE HIGH POINTS ON THE

PETITIONS AS WELL AS STAFF'S RESPONSE.

DR. OLSON: SO WHAT THIS APPLICATION PROPOSES TO TREAT ARE THE MOTOR SEQUELAE FOLLOWING SUBCORTICAL STROKE. AND THEY PROPOSE TO DO THIS BY USING AN ALLOGENEIC NEURAL STEM CELL LINE DERIVED FROM HUMAN EMBRYONIC STEM CELLS THAT WILL BE EITHER DELIVERED ALONE OR IN COMBINATION WITH MATRIX MATERIAL INTO THE INFARCTED AREA OF THE BRAIN. AND THEY'VE, OF COURSE, SINCE THIS IS AN ALLOGENEIC THERAPY, WILL USE CONCOMITANT IMMUNOSUPPRESSION.

SO IT'S BASED ON THE HYPOTHESIS THAT THE TRANSPLANTED CELLS WILL STIMULATE ENDOGENOUS REPAIR MECHANISMS AND THAT THE SURVIVAL AND DURATION OF THE NEURAL RESTORATIVE ACTIVITY OF THESE CELLS WILL BE ENHANCED THROUGH COMBINATION WITH THE MATRIX MATERIAL. SO THOSE ARE THE HYPOTHESES.

THE APPLICANT WILL CONDUCT THE PRECLINICAL EXPERIMENTS EVALUATING GRAPH TARGETING EITHER WITH OR WITHOUT MATRIX MATERIAL, WILL LOOK AT THE OPTIMAL TIMING FOR TRANSPLANTATION, THE DOSE, TUMOROGENICITY, AND FUNCTIONAL RECOVERY IN RODENT MODELS. AND THEY ALSO OUTLINE PLANS FOR GMP MANUFACTURING AND EARLY PRE-PRE-IND MEETING AND OTHER APPROPRIATE IND ENABLING ACTIVITIES.

REVIEWERS FELT THE RATIONALE FOR THIS

PROPOSAL, THE SCIENTIFIC RATIONALE WAS SOLID. THERE'S ACTUALLY A LOT OF PUBLISHED EVIDENCE THAT NEURAL STEM CELLS ARE HELPFUL IN NEUROLOGICAL INJURY. THERE ARE PUBLISHED EXAMPLES OF NEURAL STEM CELLS IN STROKE MODELS WHERE A RETURN OF MOTOR FUNCTION IS IDENTIFIED. THERE HAS BEEN SOME DATA ON THE MECHANISMS OF THIS, AND IT IS BELIEVED THERE'S A NUMBER OF MECHANISMS THAT COULD COME IN.

THE SIGNIFICANCE OF THIS PROPOSED STRATEGY IS ACTUALLY QUITE HIGH. AS MANY OF YOU MAY KNOW, THE ONLY APPROVED THERAPIES FOR STROKE ARE THROMBOLYTIC AGENTS WHICH MUST BE GIVEN WITHIN THE FIRST FEW HOURS OF THE STROKE, OTHERWISE THEY ARE INEFFECTIVE. SO WHAT THIS THERAPEUTIC STRATEGY WOULD PROPOSE IS BEING ABLE TO GIVE ONE UP TO SEVERAL WEEKS AFTER THE EVENT, AFTER THE INSULT, AFTER THE STROKE. SO IN THAT SENSE, IT WOULD BE -- THERE'S NOTHING LIKE THAT THAT'S APPROVED. THERE'S NOTHING LIKE THAT THAT'S AVAILABLE.

SO REVIEWERS CONSIDERED THE PRELIMINARY DATA TO BE SUPPORTIVE OF THE MATURITY OF THE PROPOSED CANDIDATE, BUT THEY DID HAVE SOME CONCERNS. THEY NOTED THAT THE APPLICANT PRESENTS EVIDENCE FOR THE PROPOSED -- THAT THE PROPOSED CELL THERAPY IMPROVES MOTOR FUNCTION IN RODENT STROKE MODELS, BUT

THEY WERE REMINDED OF THE FACT THAT THESE MODELS ARE NOT PREDICTIVE OF THE HUMAN STROKE SITUATION. ESSENTIALLY NONE OF THE MODELS HAVE AN ATHEROSCLEROTIC OR ATHEROSCLEROTIC ANIMALS, WHICH IS ACTUALLY USUALLY THE CONDITION WITH THE HUMAN STROKE. THOSE ARE THE MODELS THAT ARE AVAILABLE, SO THAT JUST IS A FACT.

THEY WERE CONCERNED THAT THE EFFICACY READOUT, SO THERE ARE A NUMBER OF EFFICACY READOUTS THAT YOU CAN USE FOR THESE MODELS, AT LEAST THE EFFICACY READOUT THAT WAS PRESENTED IN THE DATA WAS CONSIDERED TO BE A MILD ONE. AND THEY WOULD HAVE LIKED TO SEE THE MORE COMPLEX READOUTS THAT ARE PERHAPS MORE STRINGENT EFFICACY MODELS.

THEY DID NOT -- THEY NOTED THAT ALTHOUGH THERE WAS PRECLINICAL STUDIES THAT SUGGEST THE STABILITY OF THE CELLS IN THE MODEL, THAT THEY WERE THERE FOR UP TO TWO MONTHS, THEY DIDN'T THINK THERE WAS ENOUGH INFORMATION ON THE PHENOTYPIC FATE. SO REALIZE THIS IS A PROGENITOR, A PRECURSOR POPULATION. WHAT THEY WANTED TO KNOW WAS WHAT DID THOSE CELLS BECOME IN THE BRAIN. AND THAT WAS NOT ADEQUATELY DESCRIBED IN THE APPLICATION AFTER TRANSPLANTATION IN THE ISCHEMIC BRAIN. SO THE FATE AND WHERE THOSE CELLS WENT, THERE WAS NO PRELIMINARY

DATA TO THAT EFFECT THAT WAS PRESENTED.

SO AS I SAID, THEY WERE PARTICULARLY INTERESTED IN THE FATE DETERMINATION BECAUSE THERE IS EVIDENCE THAT IN VIVO GLIAL CELLS, WHICH IS ONE OF THE TYPES OF CELLS THAT YOU CAN GET FROM DIFFERENTIATION OF NEURAL PROGENITORS, THAT THOSE ARE ACTUALLY THE CELL TYPE THAT PROVIDES TROPHIC SUPPORT, ONE OF THE PRESUMPTIVE MECHANISMS THAT'S OPERATING HERE. SO THEY WOULD HAVE LIKED TO SEE THAT. THERE WAS NO DATA FOR THE MATRIX MATERIAL WHATSOEVER, OF CELLS IN THE MATRIX MATERIAL, SO THEY WOULD HAVE LIKED TO SEE THAT.

SOME REVIEWERS COMMENTED THAT A MORE PHYSIOLOGICALLY RELEVANT ANIMAL MODEL WOULD HAVE BEEN DESIRABLE, AND THAT'S JUST SOMETHING THAT HASN'T BEEN DONE YET. THE APPLICANT DOES MENTION THAT THERE MAY BE A NEED TO DO SUCH STUDIES, BUT THERE'S NO INFORMATION ON HOW TO EXECUTE IT.

THEY WERE ALSO CONCERNED ABOUT THE POSSIBILITY OF INFLAMMATION IN A STROKE BRAIN. THE BLOOD BRAIN BARRIER WOULD BE DISRUPTED AND INFLAMMATORY RESPONSE MIGHT EXACERBATE THE SITUATION. SO THEY WERE CONCERNED ABOUT THAT.

THEY WERE GENERALLY POSITIVE ABOUT THE DEVELOPMENT PLAN ALTHOUGH THEY DID CONSIDER IT

INCOMPLETELY DEVELOPED IN LIGHT OF THOSE POINTS THAT THEY RAISED. THEY DID, HOWEVER, NOTE THAT THE APPLICANT'S PLANNED A PRE-PRE-IND MEETING TO DISCUSS ESSENTIALLY THEIR PROPOSED DEVELOPMENT STRATEGY. AND SO THESE ARE QUESTIONS THAT THEY COULD RAISE. MILESTONES WERE CLEAR AND WELL ARTICULATED, AND THE REVIEWERS ACTUALLY BELIEVE THAT, PARTICULARLY IF THEY STUCK WITH THE CELL THERAPY AS OPPOSED TO THE CELL IN MATRIX THERAPY, THAT AN IND IN FOUR YEARS WAS ACHIEVABLE.

THEY DID BELIEVE THAT IF THEY CHOSE TO GO WITH THE MATRIX MATERIAL, THAT ACTUALLY ADDS A LOT OF COMPLEXITY IN TERMS OF GMP PRODUCTION AND, THEREFORE, IT WAS LESS LIKELY.

THE STRENGTH OF THE PRINCIPAL INVESTIGATOR, THE CO-PI, AND THE TEAM WAS UNANIMOUSLY ACKNOWLEDGED. THE PI AND THE CO-PI NOT ONLY HAVE EXTENSIVE EXPERIENCE IN STEM CELL BIOLOGY, BUT THEY HAVE PARTICIPATED IN STROKE CLINICAL TRIALS. THEY HAD A VERY GOOD LEADERSHIP TEAM. THEY COMMENTED ON THE SELECTION OF CONSULTANTS WHO WOULD BE WORKING WITH THEM IN THE GMP PRODUCTION AND REGULATORY STRATEGIES.

OVERALL THEY AGREED THIS WAS A CRITICAL UNMET NEED AND THAT THE THERAPY FOR STROKE PATIENTS

AND THAT THE KNOWLEDGE AND EXPERIENCE OF THE INVESTIGATORS WERE HIGHLY TOUTED, BUT THE THING THAT REALLY RESULTED IN THIS SCORING WAS ESSENTIALLY THE BENEFIT AS EXEMPLIFIED BY THE DATA THAT WAS PRESENTED GIVEN THE RISK OF A HUMAN EMBRYONIC STEM CELL-DERIVED THERAPY IN THE BRAIN OF A STROKE PATIENT. SO THAT'S WHERE THEY CAME DOWN ON THAT.

NOW, THIS WAS THE SUBJECT OF AN EXTRAORDINARY PETITION. IN THE EXTRAORDINARY PETITION, IT REFERENCES INFORMATION THAT WAS NOT PREVIOUSLY PROVIDED IN THE APPLICATION, INCLUDING FINDINGS OF EFFICACY ATTRIBUTED TO A THIRD GROUP. THIS INFORMATION DOES NOT HAVE THE BENEFIT OF EXPERT REVIEW BY THE GRANTS WORKING GROUP AND ACTUALLY DOES NOT ADDRESS THE REVIEWERS' PRIMARY CONCERN ABOUT THE EFFICACY -- ABOUT THE ESSENTIALLY BENEFIT VERSUS RISK.

SO OVERALL WE BELIEVE THAT THE REVIEWERS DID CAREFULLY CONSIDER THE NOTABLE STRENGTHS OF THIS PROPOSAL AND CONCLUDED THAT, DESPITE NOTED MERITS, IT SHOULD NOT BE RECOMMENDED. I MEAN SPECIFIC POINTS THAT ARE NOT -- I MEAN THEY POINT OUT THAT THERE IS NO ATHEROSCLEROTIC STROKE MODEL, AND THAT IS JUST TRUE. THAT SIMPLY INCREASES THE RISK OF THE PREDICTABILITY OF THE MODELS. SO THAT IS A FACT.

THEY POINT OUT THAT ONE OF THE CRITICISMS WAS THE OUTPUT MEASURE. AND THEY HAVE -- IN FACT, THEY HAVE DONE A -- THEIR OUTPUT MEASURE IS MILD. THEY PROPOSE TO DO THE MORE STRINGENT OUTPUT MEASURES IN EFFICACY EXPERIMENTS GOING FORWARD. THAT WAS IN THE APPLICATION.

CHAIRMAN KLEIN: OKAY. I THINK THAT'S PROBABLY A GOOD SUMMARY. JEFF SHEEHY.

MR. SHEEHY: I WOULD JUST, HAVING SAT IN THE REVIEW, I THOUGHT THAT A MAJOR FACTOR WAS THE LACK OF AN APPROPRIATE ANIMAL MODEL, BUT I WOULD LIKE TO NOTE TWO POINTS ABOUT THAT. NO. 1, THIS IS THE ANIMAL MODEL THAT WOULD BE NECESSARY -- THIS ANIMAL MODEL THEY HAVE PROPOSED IS ADEQUATE FOR OBTAINING AN IND WITH THE FDA. THEY SAID IN THEIR REBUTTAL, AND AS DR. OLSON HAS MENTIONED, THERE IS NO ATHEROSCLEROTIC ANIMAL MODEL.

THE OTHER THING THAT THEY HAD SUGGESTED THAT THIS BE TESTED IN NONHUMAN PRIMATES; HOWEVER, BASED ON NATIONAL ACADEMY GUIDELINES AND OUR OWN ETHICAL STANDARDS, WE'RE NOT PERMITTED TO PUT EMBRYONIC STEM CELLS INTO NONHUMAN PRIMATE BRAINS AT THIS TIME. WHAT I THINK THAT THIS PARTICULAR APPLICATION GOES TO, AND I KNOW IT FELL -- CAN I MENTION THE SCORE, WHICH I BELIEVE WAS 65, IT BARELY

MISSED FUNDABILITY.

IF WE'RE GOING TO STRETCH OURSELVES, I THINK WHERE WE HAVE THOSE APPLICATIONS THAT ARE UNIQUE TO OUR MISSION, IPS, EMBRYONIC STEM CELLS, WHERE WE CAN MOVE THE FIELD FORWARD, WE CAN'T ACCURATELY PREDICT WHAT THE REGULATORY FRAMEWORK IS FOR PUTTING EMBRYONIC STEM CELLS INTO THE BRAIN. AND BY USING THIS --

DR. OLSON: NEURAL STEM CELLS, BUT IT'S THE SAME ISSUE.

CHAIRMAN KLEIN: DERIVED.

MR. SHEEHY: EXACTLY. SO BY FUNDING THIS, WE'RE MOVING THE FIELD FORWARD WITH THE TYPE OF MILESTONE DRIVEN -- THE WAY IN WHICH THIS PARTICULAR APPLICATION ROUND IS MILESTONE DRIVEN, IF THEY FAIL, THE MONEY WILL COME BACK TO US. BUT FOR ME I THINK THIS IS A PLACE WHERE IT'S CENTRAL TO OUR CORE MISSION TO EXERT OURSELVES TO PUSH AN EMBRYONIC STEM CELL APPLICATION DOWN THE REGULATORY PATHWAY AND SEE HOW FAR WE CAN GET. IT MAY BE A LITTLE MORE HIGH RISK THAN SOME OF THE OTHER APPLICATIONS. IN FACT, THEY SUGGESTED A DIFFERENT SET OF CELLS. MESENCHYMAL STEM CELLS MIGHT HAVE BEEN MORE FAVORABLY RECEIVED; BUT, FRANKLY, WE'RE AN EMBRYONIC STEM CELL FUNDING AGENCY, AND THIS IS OUR CHANCE TO

FULFILL OUR CORE MISSION. SO I WOULD URGE US TO APPROVE THIS.

CHAIRMAN KLEIN: LET ME JUST, DR. LOVE, DID YOU HAVE A COMMENT BEFORE I GO TO DR. PRIETO?

DR. PRIETO: I WAS ALSO IN THIS REVIEW, AND I'D LIKE TO TALK ABOUT THE ANIMAL MODEL ISSUE ALSO. I THOUGHT ABOUT THIS ONE QUITE A BIT SINCE THE REVIEW BECAUSE I THOUGHT, OKAY, MAYBE THAT'S A VALID DEFICIENCY. BUT WHEN I CONSIDERED IT, I THINK IT'S PROBABLY IMPOSSIBLE FOR THERE TO BE AN ATHEROSCLEROTIC ANIMAL MODEL OF STROKE THAT WOULD BE CONSISTENT AND PREDICTABLE ENOUGH THAT YOU COULD STUDY IT, HAVE A CONSISTENT MOTOR DEFICIT THAT YOU WOULD THEN ADDRESS THE RESPONSIVE TREATMENT TO. THAT'S ONE ISSUE.

BUT THE OTHER IS THAT THEY ARE NOT TRYING TO ADDRESS THE ATHEROSCLEROSIS, AND THIS IS NOT A TREATMENT FOR THE ATHEROSCLEROSIS. IT'S A TREATMENT FOR THE NEUROLOGIC SEQUELAE OF THE STROKE. FOR THAT, TYING OFF THE ARTERY IS A PERFECTLY CONSISTENT OR PERFECTLY ADEQUATE MODEL.

DR. OLSON: MAY I MAKE IT CLEAR THAT THE ISSUE WAS NOT THAT THERE WASN'T A MODEL OF -- ONE WOULD LIKE THAT. I THINK THE ISSUE WAS THE LACK OF PREDICTABILITY OF THE MODELS IN THE STROKE SETTING,

AND THAT ONE HAD TO CONSIDER THE RISK OF THOSE MODELS AND THE CONTEXT OF THE DATA THAT WAS GIVEN THOSE IN MOVING SOMETHING FORWARD. SO I THINK THAT'S REALLY --

DR. PRIETO: I THINK WHAT SOME OF THEM AT LEAST ARE SAYING IS THAT THE MECHANISM OF INJURY IS DIFFERENT. THAT'S CLEARLY TRUE, BUT THAT DOESN'T MEAN THAT THE RESULT OF THE INJURY IS DIFFERENT. AND THEY'RE LOOKING AT THE INJURY, AND CAN YOU THEN TREAT THE SUBSEQUENT INJURY, WHATEVER THE MECHANISM OF INJURY IS.

DR. OLSON: THAT'S WHERE YOU GET TO THE OUTPUT MEASURES.

MR. SHEEHY: THE OTHER POINT TO THIS IN TERMS OF THE ANIMAL MODEL IS WHAT DOES THE FDA REQUIRE BECAUSE THE END POINT HERE IS AN IND. AND THE FDA -- THE REGULATORY SPECIALISTS INVOLVED IN THIS SAID THAT THIS COULD PROCEED TO AN IND. SO THE ANIMAL MODELS PROVIDED DID NOT PRESENT AN INSUPERABLE BARRIER TO GETTING AN IND OR ELSE THEY WOULDN'T HAVE GIVEN IT --

DR. OLSON: I THINK I HAVE TO POINT OUT SOMETHING. THE FDA ALLOWS A LOT OF THINGS TO GO INTO THE CLINIC. IF YOU SHOW ADEQUATE SAFETY AND IF YOU HAVE SOME DEGREE OF EFFICACY DATA, THEY IN MANY

CASES DO NOT SPECIFY. IT'S ACTUALLY NOT A LEGAL REQUIREMENT THAT YOU HAVE EFFICACY DATA. WHAT THEY DO DEMAND IS SAFETY.

NOW, YOU CAN LOOK AT THE -- ANYBODY HERE WHO'S BEEN IN INDUSTRY OR BEEN INVOLVED WITH IT KNOWS THERE'S A LOT OF FAILED TRIALS. I GUESS MY POINT IS WHAT I THINK THE REVIEWERS WERE SAYING IS GIVEN WHAT THEY PERCEIVE, AND IT IS YOUR -- CERTAINLY YOUR RIGHT AS THE BOARD TO CHOOSE TO TAKE MORE RISK, BUT WHAT THEY PERCEIVED AS A POTENTIAL RISKY THERAPY FOR PATIENTS WHO MAY RESOLVE SPONTANEOUSLY IN THE FEW WEEKS AFTER THE STROKE TO DO AN EMBRYONIC STEM CELL THERAPY. IT'S A RISK BENEFIT ARGUMENT. THEY WOULD HAVE LIKED TO SEE MORE DATA GIVEN THAT. THAT IS WHAT THEY WANTED.

DR. TROUNSON: MR. CHAIR, JUST IN THE SENSE OF THE ARGUMENT, THE CELLS THAT HAVE BEEN PUT INTO RODENT BRAINS THAT HAVE BEEN DRIVEN INTO THE GLIAL LINEAGE, I DON'T THINK THERE REALLY IS ANY CASES OF TERATOMA FORMATION. SO IT DEPENDS ON -- THAT'S THE ONLY WAY YOU CAN TEST IT OUT, BY PUTTING THE CELLS INTO THE BRAINS OF RODENTS. AND THEY'RE DOING THOSE IN VERY LARGE NUMBERS AT THAT UNIVERSITY AND MANY OTHER UNIVERSITIES. SO I THINK AT SOME POINT IN TIME, WE'LL HAVE TO ACCEPT THAT THE

DIFFERENTIATION OF THESE CELLS IS A RELATIVELY LOW RISK TO FORM A TERATOMA, BUT YOU MIGHT GET SOMETHING YOU DIDN'T EXPECT WHEN YOU WORK IN THE HUMAN. THAT REMAINS AN ISSUE, BUT THAT'S WHY YOU DO PHASE I STUDIES. THAT'S ABOUT RISK. THAT'S ABOUT IS THERE DAMAGE.

THESE PATIENTS, THE LARGER EFFECT OF THESE PATIENTS IS A DREADFUL -- IS REALLY A DREADFUL OUTCOME, IF NOT DEATH. AND THE CHOICE HERE FOR THE NEUROSURGEONS IN THIS AREA IS TO DO SOMETHING WITHIN THE FIRST TWO WEEKS OR FIRST THREE WEEKS OR DO NOTHING BECAUSE THERE WOULD PROBABLY NOT BE ANY OPTION IF YOU WENT OUT TO FOUR TO SIX WEEKS BECAUSE I DON'T THINK THERE'S ANY EVIDENCE THAT YOU CAN IMPROVE THE SITUATION FOUR TO SIX WEEKS OR SIX WEEKS OUT FROM A STROKE. YOU HAVE TO TAKE A CHANCE. YOU HAVE TO GIVE THE PATIENT A CHANCE. YES, THERE IS A RISK, BUT THERE'S A CONSIDERABLE RISK IN THESE PATIENTS THAT THEY WILL BE DECIMATED. THEIR LIVES WILL BE DECIMATED ANYWAY, AND HOPEFULLY IN THE TWO WEEKS YOU GET A CHANCE FOR THOSE THAT ARE GOING TO SPONTANEOUSLY RESOLVE TO GIVE SOME INDICATION THAT SOMETHING IS HAPPENING THAT MIGHT BE SAY, WELL, IT'S TOO RISKY TO DO IT.

BUT THE BULK OF THE PATIENTS WON'T BE IN

THAT CATEGORY. SO I DO THINK THERE'S AN ISSUE HERE. THIS IS A DISEASE WHERE THERE'S NOT A LOT OF OPTIONS. AND MSC'S I DON'T THINK OFFER THE SAME PROSPECT OF AN OPTION HERE. SO I DO THINK IT NEEDS TO BE TAKEN IN BALANCE. I THINK THE REVIEWERS GOT IT RIGHT. IT'S ABOUT A 65 PROJECT. SO IT'S RIGHT ON THE BORDER FOR YOU. I THINK THIS IS ONE OF THOSE CONDITIONS THAT YOU ARE GOING TO HAVE TO TAKE SOME RISK. IT'S GOING TO BE PRE-IND, PRE, PRE, AND PRE-IND MEETINGS. SOMEBODY MIGHT SAY THAT YOU HAVE TO DO A MONKEY. IF THAT'S THE CASE AND WE CAN'T DO IT, THAT'S A PROBLEM AND WE'LL HAVE TO HAVE A GO/NO-GO DECISION ASSOCIATED WITH IT.

BUT I THINK IT'S RIGHT THERE. I THINK PAT'S LABELED IT EXACTLY CORRECTLY. THE REVIEWERS ARE PROBABLY ON THE MARK, BUT HERE'S A CHANCE TO DO SOMETHING WITH A TERRIBLE -- GENERALLY A TERRIBLE OUTCOME, AND IT JUST MIGHT BE EFFECTIVE. AND THERE IS -- THERE'S GENUINELY A SMALL RISK ASSOCIATED WITH IT. HOW ARE YOU GOING TO PERSUADE THE FDA? THAT'S GOING TO TAKE YOU A NUMBER OF MEETINGS IN THIS TIMEFRAME. WE'RE GOING TO BE SITTING THERE SORT OF MAKING SURE THAT THESE GO/NO-GO DECISIONS ARE ENABLING TO DO THE FILING.

CHAIRMAN KLEIN: I THINK AN IMPORTANT

POINT WAS MADE HERE THAT, DR. OLSON, AS YOU SAID, THE FDA IS GOING TO INSIST ON SAFETY. AND AS DR. TROUNSON SAID, AND AS THE APPLICANT SAID, IF THE FDA REQUIRES HUMAN PRIMATE AND THE RULES CHANGED TO PERMIT YOU TO DO NONHUMAN PRIMATES, THEY'RE GOING TO DO IT. SO THE SAFETY ISSUE WILL BE IMPOSED BY THE FDA. BUT THIS IS A DISEASE THAT DOESN'T HAVE MANY OPTIONS AND IT HAS TERRIBLE -- THIS IS AN INJURY ACTUALLY THAT HAS TERRIBLE IMPACTS ON THE FUTURE AND SHOULD A PATIENT BE ABLE TO BALANCE THESE RISKS IF THEY'RE TOTALLY INFORMED.

SO I THINK WE'VE HAD THE QUESTION DISCUSSED. IS THERE PUBLIC COMMENT ON THIS APPLICATION? SEEING NO PUBLIC COMMENT, I THINK IT'S APPROPRIATE, UNLESS THERE'S OTHER COMMENTS, TO CALL THE QUESTION.

MS. KING: ROBERT PRICE.

DR. PRICE: YES.

MS. KING: FLOYD BLOOM.

DR. BLOOM: YES.

MS. KING: LEEZA GIBBONS.

MS. GIBBONS: YES.

MS. KING: BOB KLEIN.

CHAIRMAN KLEIN: YES.

MS. KING: TED LOVE.

DR. LOVE: YES.
MS. KING: ED PENHOET.
DR. PENHOET: YES.
MS. KING: CLAIRE POMEROY.
DR. POMEROY: NO.
MS. KING: FRANCISCO PRIETO.
DR. PRIETO: YES.
MS. KING: ROBERT QUINT.
DR. QUINT: YES.
MS. KING: DUANE ROTH.
MR. ROTH: NO.
MS. KING: JOAN SAMUELSON.
MS. SAMUELSON: YES.
MS. KING: DAVID SERRANO-SEWELL.
MR. SERRANO-SEWELL: YES.
MS. KING: JEFF SHEEHY.
MR. SHEEHY: YES.
MS. KING: JON SHESTACK.
MR. SHESTACK: YES.
MS. KING: ART TORRES.
MR. TORRES: AYE.
CHAIRMAN KLEIN: ALL RIGHT. THAT VOTE, I TAKE IT, PREVAILED?
MR. HARRISON: YES. THE MOTION CARRIES.
CHAIRMAN KLEIN: THANK YOU. THE NEXT ITEM

IS 1422. WHOM ARE THE CONFLICTS -- WHO ARE THE CONFLICTS?

MR. HARRISON: LEVIN AND STEWARD.

CHAIRMAN KLEIN: DOES ANYONE WANT TO MAKE A MOTION TO MOVE THIS UP? I DON'T SEE ANY MOTION. MOVING ON TO 1459, DOES ANYONE WANT TO MAKE A MOTION TO MOVE THIS UP? I DO NOT SEE A MOTION.

LET ME SUGGEST THIS. WE LOST SEVERAL OF OUR MEMBERS AT THIS POINT AND IT'S 9:45. I THINK WE'VE GONE FAR ENOUGH THAT WE CAN COMPLETE THIS TOMORROW. APPRECIATE EVERYONE'S ATTENDANCE, AND I LOOK FORWARD TO ADDITIONAL LIVELY DISCUSSION.

BUT I WOULD LIKE TO SAY THE STAFF HAS PUT A HUGE AMOUNT OF EFFORT INTO THIS. AND EACH OF US COMES FROM A DIFFERENT BACKGROUND. EACH OF US BRINGS DIFFERENT EXPERIENCES WITH US TO THE TABLE. BUT IT IS WITH IMMENSE APPRECIATION AND RESPECT FOR THE EFFORT THE STAFF HAS PUT INTO THIS PROCESS. AND SOMETIMES THE POSITIONS WILL BE THE SAME AS INDIVIDUAL BOARD MEMBERS OR DIFFERENT, BUT I THINK WE SHOULD ALL GIVE A GREAT HAND OF APPLAUSE TO THE STAFF BECAUSE WE KNOW THEY PUT A HUGE OF AMOUNT EFFORT.

(APPLAUSE.)

CHAIRMAN KLEIN: SO LET ME ASK THIS

QUESTION. IT'S BEEN BROUGHT TO MY ATTENTION THAT THERE'S PUBLIC MEMBERS TO MAKE COMMENTS ON 1421, 1491, AND 1478. I WOULD SUGGEST IT WOULD BE MUCH BETTER TO MAKE THOSE TOMORROW; BUT IF IT'S IMPOSSIBLE FOR THOSE PEOPLE TO MAKE THOSE COMMENTS TOMORROW, I WOULD LIKE TO KNOW THAT. OKAY. THANK YOU VERY MUCH. THANK YOU FOR BRINGING THAT TO MY ATTENTION.

WE HAVE AN EARLY MORNING TOMORROW. WE'VE GOT A LOT TO MOVE THROUGH. AND I BELIEVE WE'RE RECONVENING AT 8:30. 8:30. AND THERE'S BREAKFAST FOR THE BOARD MEMBERS NEXT DOOR.

MS. PRYNE: AT 8 O'CLOCK NEXT DOOR.

CHAIRMAN KLEIN: BOARD MEMBERS ARE INVITED TO ANOTHER TWO OR THREE HOURS OF READING OF DOCUMENTS TONIGHT. WE ADJOURN.

(THE MEETING WAS THEN RECESSED AT 09:47 P.M. TO RECONVENE 8:30 A.M., OCTOBER 28, 2009.)

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 ITS REGULAR MEETING HELD AT THE LOCATION INDICATED BELOW

LUXE HOTEL
11461 SUNSET BOULEVARD
LOS ANGELES, CALIFORNIA
ON
OCTOBER 27, 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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